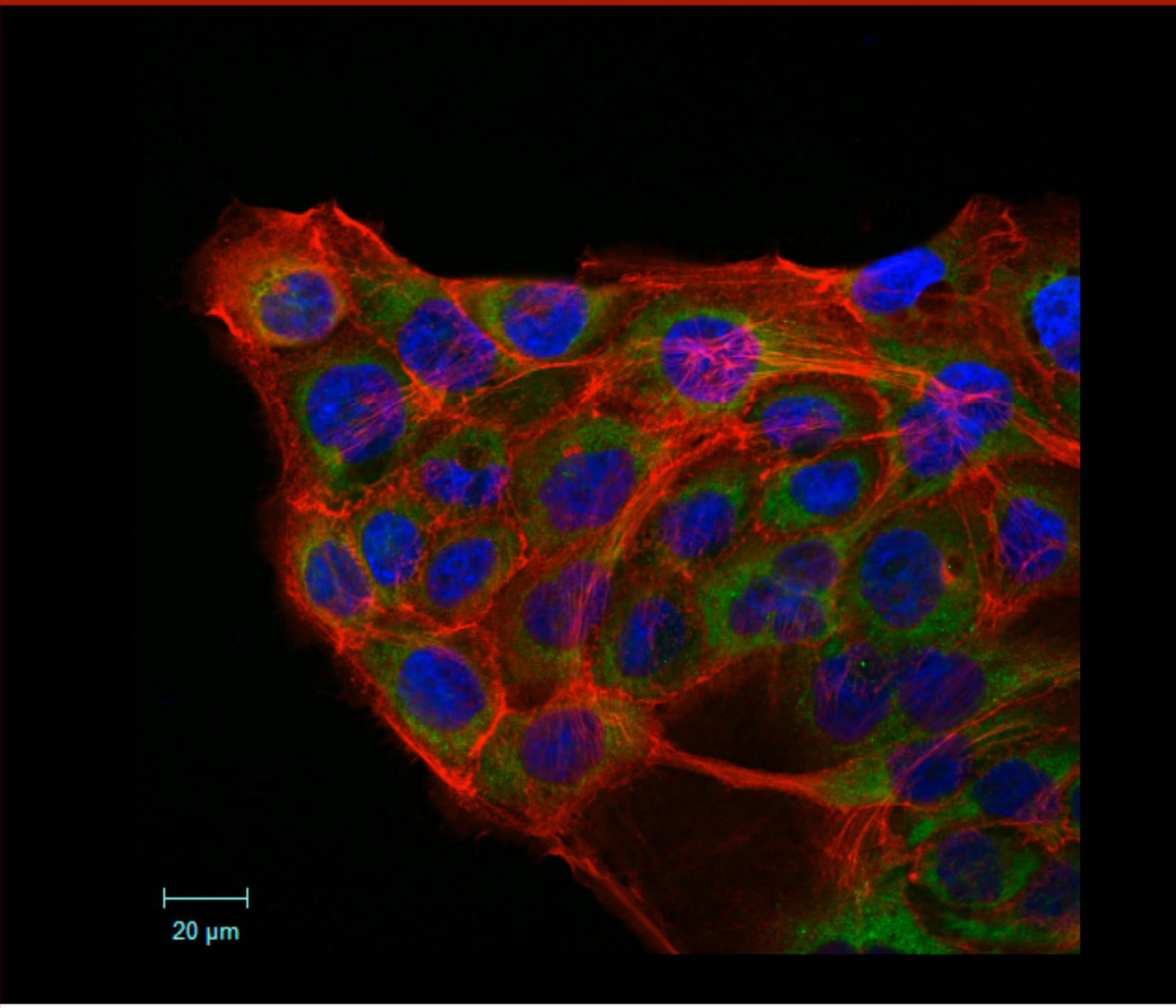
IRE

ISTITUTO NAZIONALE TUMORI

# REGINA ELENA

ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO




# Scientific Report 2018

*Confocal microscopy analysis of pancreatic adenocarcinoma primary cell culture fluorescently labelled with phalloidin (Red), to stain actin filaments, and anti-hMENA antibody (Green) to detect the actin regulatory protein hMENA. DAPI was used to counterstain nuclei. The image was acquired with Zeiss LSM 880 with Airyscan confocal laser scanning microscope equipped with a 63X 1.23 NA oil immersion objective.*

*Courtesy of Francesca Di Modugno*

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# CEO MESSAGE

## *Dr. Francesco Ripa di Meana*

**Dear Readers,**

The activities carried out in 2018 were centred at re-launching the Institute firstly in scientific research, in order to regain and strengthen its national and international competitive position and also through drafting up important collaboration agreements, reorganising the corporate enterprise and boosting activities and opportunities to compare and discuss results on an international scale. In regards to the health care assistance we provide to our fellow citizens, we focused primarily on rethinking patient care and expanding future medical activities more and more on precision medicine.

We achieved several significant milestones in 2018. The first achievement was having emerged from the regional financial administration we were under (a plan to restore the Institute's debt). The second, was having obtained an increase in research funding from the Ministry of Health and the third, was having received funding from the Lazio Region in order to hire professional staff and invest in technological resources. This year, we celebrated 10 years of robotic surgery, since it was first introduced in our Institute. It is important to highlight that we are the only Institute in all of Italy that adopts robotic surgery across all surgical specialties. We are also going ahead with building the first public Proton therapy unit in central Italy. It is a high precision instrument used to defeat several types of cancers. We also established the Molecular Tumor Board and the Phase 1 Clinical Center, which are among the first public centers in Italy. This led to new avenues in collaborating with pharmaceutical companies that require sound expertise.

The partnerships made with important and well known Institutes not only boosted our research activities, but reinforced our institute as an expert hub and assigned coordinators for regional and national projects. Our signed partnership protocol with the first University of Rome, La Sapienza, guarantees exchange training programs in higher education for young graduates and lays the foundation for establishing other agreements in the field of molecular research in sharing expertise and data.

At an international level, we encouraged to create collaborative partnerships with other Institutes to improve the quality and level of competitiveness of the scientific research produced, professional development as well as develop new clinical strategies for treating cancer patients. For instance, an example of this, is the agreement made with the St. Petersburg clinical center for Specialized Types of Medical Care (Oncologic). We also hosted various delegations from Asian countries with whom specific collaborative agreements are currently being made. Also this year, the IRE International Scientific Advisory Board (ISAB) meeting was held in order to assess our Institute's resources and research activities which provided us with valuable insight and advice on implementing the strategic plan. Another significant historical event that occurred is the ongoing expansion of the clinical-scientific and educational activities carried out in African countries by the San Gallicano Dermatological Institute.

Our clinical and research activities are strongly oriented towards precision medicine which has lead to forming a working group that focuses on gender medicine. Together with the Ministry of Health and implementing official decrees, it is committed to spreading the gender approach. This is an additional investment made towards future health care.
Together with diagnostic and clinical strategies, we also developed cutting-edge management models (risk management and quality, data management, information systems, databases and biobanks, etc…
Our motto "Putting the patient first" is not only a simple slogan we use but it is what we base our entire work ethic on.
The field of medicine continuously undergoes constant changes and therefore the organizational set-up for taking care of the patient must also make adjustments accordingly. We have therefore redesigned the organization (Corporate act) taking on more transversal and complementary structures, thus favoring the multidisciplinary approach that characterizes the Diagnostic Therapeutic Pathways (PDTA) and Disease Management teams that are ever on the increase for specific diseases.

We also developed and tested a new model for "cancer patient care pathways" that follow surgery, dermatological and rare cancers. Within the model, we included certificates/referrals that are prescribed by specialists and are available on demand for the user. From the time of diagnosis, it also allows rapid access to the rights of disabled patients with cancer. The procedure was implemented due to the experimental protocol signed by INPS (National Institute for Social Security) and approved by the Lazio Region, which will soon extend the model to all health care facilities.
The key word is innovation for scientific research and treatment institutes, as well as for fields of technology, digital, innovation and patient empowerment.
Based on this, let's build the future of IFO together!

# SCIENTIFIC DIRECTOR MESSAGE

## *Prof. Gennaro Ciliberto*

**Dear Readers,**

I am very pleased to introduce to you the 2018 Scientific Report of the IRCCS Istituto Nazionale Tumori "Regina Elena" of Rome.
The Institute is part of a larger Institute called the Istituti Fisioterapici Ospitalieri that embodies also the IRCCS Istituto Dermatologico San Gallicano, and is now in a very positive place after having gone through years of management instability.
After 10 long years of being governed under the regional financial re-entry plan, the Institute finally saw victory in the year 2018. Apart from reaching the latter milestone, 2018 also represents the year of opportunity, seeing the implementation of the new multi-year hiring plan as well as other important initiatives of the larger strategic plan which was conceived in 2017. It is in this regard that I would like to highlight that both myself and the ISG Scientific Director, Prof. Aldo Morrone, work in perfect synergy with the Director General, Dr Francesco Ripa di Meana, the Chief Medical Officer Dr. Branka Vujovic and the Administrative Director Dr. Laura Figorilli on common goals which include improving the efficiency of clinical care and the full integration of clinical and translational research for the shared benefits of patient centered care.
In regards to the specific scientific achievements of the Regina Elena National Cancer Institute, we were able to maintain the same high level of scientific productivity as the previous year which is reflected in the number of papers published in prestigious international journals. Furthermore, the Institute's performance in terms of attracting competitive grants has been superior to previous years with an approximate 25% success rate in grant applications.
I would also like to mention that the translational research groups have continued their activities as highlighted in other sections of this report. In particular, I would like to draw attention to the Melanoma Group who in collaboration with the Istituto San Gallicano conceived the Melanoma 4 project, the Rare Tumor Group which set up the Euracan database that tracks all new patients with rare cancers in adults under our care, the Brain Tumors Group which has started to elaborate a new research plan directed towards the study of gliomas using a radiomics approach.
In March 2018, the first international workshop on tumor evolution and heterogeneity of the cancer genome was held at the Istituto Regina Elena. The workshop was organized by Oreste Segatto and Rita Falcioni and saw the participation of prestigious scientists from the USA, Europe and Italy.
On 15th November 2018 another important event was the visit of the renewed International Scientific Advisory Board. This event is described in detail in a dedicated section of this report. It was an important opportunity to have our research assessed by a panel of world class and highly qualified scientists where we

received a series of important recommendations for the future direction of our Institute.

Finally, 2018 saw the start of our Molecular Tumor Board which initiated in September. Our MTB is among the first ones to be officially established in Italy. It is composed by a multidisciplinary team, as detailed in a dedicated section of this report. Within the spirit of implementing the concept of precision medicine in oncology, its main goal is to address complex cases of cancer patients who have exhausted standard therapies options and who are affected with malignancies with potentially actionable variants identified by deep molecular profiling, for which no approved anticancer drugs are available.

In summary, our Institute is constantly striving to improve its scientific performance through introducing innovative practices and establishing synergic integration between all disciplines.

Finally, I would like to thank everyone who has contributed to realizing this scientific report.

# MEDICAL DIRECTOR MESSAGE

*Dr. Branka Vujovic*

**Dear Readers,**

I have been the Corporate Health Director of the IRCCS IFO since 2017. In the first year of my administration, I was dedicated to getting to know IFO and understand the differences between the two "hearts" that make it up: the Regina Elena Institute and the San Gallicano Institute.
In addition, my attention was also focused on the following general objectives:

- support patient-centered care in every care unit;
- promote the multidisciplinary and multiprofessional approach;
- encourage the integration between research and clinical practice, also through the work of translational research groups,

The above objectives remain constant over time and across the two Institutes.

The Regina Elena National Cancer Institute, for a Corporate Health Director, is an opportunity to be continuously challenged in knowing how to combine both passion for research of care teams to patient care and to carry out activities concerning the clinical governance in this context. It is for this reason, in 2018, much attention was paid to constructing the IFO Triennial Strategic Plan and focusing on the role Regina Elena Institute plays within the Plan.

The main operational objectives pursued and implemented in 2018 were:

1. to increase existing Disease Management Teams and expand on the clinical conditions assessed, and patients cared for, treated and followed over time in a multidisciplinary manner;
2. to offer advocacy and provide more visibility to the professional groups or Clinical Centers dedicated to

the diagnosis, management, follow-up of patients with rare tumors and rare diseases;

3. to create opportunities for the visibility of the intellectual and professional resources of doctors, biologists, psychologists, nurses, technicians and other health care staff present in the Regina Elena Institute and IFO;
4. to actively participate in opportunities for discussion on research and clinical studies, through specific Commissions / Committees;
5. to be certified for Phase 1 experimental activities and the Clinical Trial Center;
6. to be certified in operating the Biobanks, in order to make patient care possible, and draw on research in the field of cancer genomics;
7. to support the development of all innovative activities directed towards the Institute's process efficiency, technostructures, and improvement in patient care.

Throughout 2018, the Corporate Health Office also pursued the objective of facilitating access to health care, which entailed activating the "Oncology Desk" the main point of contact for coordinating patients for diagnostic tests, introducing Disability Certificate services so that patients can obtain them directly within the Institute which are then sent to the National Social Security Institute (INPS) as well as working towards reducing the time required to pay legal benefits.

# QUALITY, ACCREDITATION, CLINICAL RISK MANAGEMENT (QuARC) UNIT

## *Head: Dr. Assunta De Luca*

### *Mission*

To improve integration between health professionals directly involved in care, assistance, research and the administrative component in order to better understand what are the improvement initiatives to ensure "quality" and "safe" care.
In particular, the Unit **QuARC**:

- defines the areas for the elaboration of Protocols, Procedures, Operating Instructions according to Evidence Based criteria;
- coordinates the study groups set up for the elaboration and dissemination of shared responsibility tools based on Quality Management System (QMS)
- adopts and implements the clinical risk management process for medical, nursing, technical health, rehabilitation, research and support (administrative) activities with the involvement of health and non-health professionals;
- To contribute to the verification and evaluation of the Quality System in accordance with the UNI EN ISO 9001 Certification and other Accreditations processes as OECI, JACIE etc;
- Propose organizational models aimed at preventing clinical risk.

### *Main activites 2018*

- Awarded UNI EN ISO 9001:2015 certification for all IFO (clinic, research and administrative units),
- Awarded National Italian Transplant Center certification for Ovarian tissue and fertility preservation Bank and for Skeletal Muscle Tissue Bank
- Supported Joint Accreditation Committee ISCT-Europe & EBMT (JACIE) accreditation for Ematology Unit
- Implemented all activities of "Annual Risk Management Plan - PARM" for 2018
- Educational and training program which consists of:
  1. Residential course (theoretical-practical) on quality system and risk management repeated in several editions, for the QuARC" local referents and health personnel
  2. On-the-job training in the individual departments/ services through the application of the tools quality proactives (FMEA, Cynical Audit, M&M review)
  3. Training on the Quality System instruments and dissemination of procedures that implement the recommendations of the Ministry of Health on "sentinel event" with repeated meetings with the "QuARC local referents" and the health care staff with explanation of the recommendation and its simulation.

### *Resources*

The QuARC Unit is made up of a medical hygienist, a nursing coordinator with proven experience in quality and clinical risk management, a nurse dedicated to the management of healthcare-acquired infections (HAIs) and an administrative expert in the management of the incident reporting information system (SIMES) and of the monitoring flows of adverse events and of all administrative support activities in the Unit.
The QuARC Unit spreads the culture of QUALITY and of a correct management of the CLINICAL RISK through The "IFO network for quality and safety of care" composed by "local referent" for each IFO's service (clinic, research and administrative).

# PHARMACOVIGILANCE UNIT

## *Head: Felice Musicco, Pharmacist*

### *Mission*

- Supporting and promoting reports of suspected drug adverse reactions (ADR); Activities in clinical wards to promote ADR reporting with doctors, nurses, technicians, etc.
- Monitoring safety of medicines: collect, assess, report, and analyze adverse events
- Registering and updating ADR reports in the National Network of Pharmacovigilance (Rete Nazionale di Farmacovigilanza RNF- AIFA) also in collaboration with QPPV of Pharmaceutical Industries and the Lazio GLASS pharmacovigilance regional group
- Review of research study protocols, pharmacovigilance section
- Reporting ADR in research studies
- Member of the Lazio Regional Panel for pharmacovigilance
- Registered PV person in EMA for IFO

### *Clinical Activities*

- Number of ADR reports registered in RNF: 56
- Drug safety information to doctors: highlight and internal transmission of alerts published by regulatory agencies (EMA, AIFA)
- Hospital reports, guidelines, procedures:
  - Updated procedures to report ADR to drugs published on the hospital website
  - Participation in OECI and other certification activities

### *Research Activities*

- Draft of Internal Procedures to report adverse drug reactions in clinical trials
- Preparation and review of the pharmacovigilance section in interventional and observational study protocols
- EudraVigilance Training Course in San Marino

### *Publications*

1. Il valore economico del beneficio clinico in oncologia: considerazioni economiche secondo la valutazione ESMO Ruggero Lasala, Fiorenzo Santoleri, Alessia Romagnoli, Felice Musicco - Giornale Italiano di Farmacia Clinica 32 (4), 160-168 - 2018

# EDUCATION AND TRAINING UNIT

## *Head: Dr. Tiziana Lavalle*

The IFO, as a Healthcare Company, has been identified by AGENAS (National Agency) as provider no. 1270 for Continuing Medical Education both for residential methodologies (RES) and, since June 2018, for field training methodologies (FSC). The I.F.O. has a Education Area "Raffaele Bastianelli", which houses 3 classrooms, respectively of 199, 90, 50 seats and the Training Service is made up of 1 manager and 4 collaborators, two with a health-care profile, two with an administrative profile.
The Budget made available to the Training Service was € 320,000, to be used for internal and external training events, internships and for the management of the activities supporting training events in the Education Area "Raffaele Bastianelli".
In 2018, the Company Training Plan (PFA) was approved with resolution no. 238 with a schedule of n. 158 training events, to which were added the events gradually created as business needs.
In 2018 has been concluded no. 99 ECM accredited events, of which 50 scheduled with a single edition, 11 scheduled with a total of 32 re-editions and n. 6 extemporaneously requested. All courses produced 792 hours of training attended by 1980 professionals.
The events took place at the "Raffaele Bastianelli" Education Area, at the Patient's Library computer room and other Meeting Rooms for small groups.
The Training Service of IFO managed, cooperating with the Scientific Direction, internship and fellowship for 84 students of eight Universities.

# ADMINISTRATIVE DIRECTOR

## *Head: Dr. Laura Figorilli*

### *Administration Office*

Nicoletta Avitabile
Santina Paola Cocuzza

The Administrative Officer manages and coordinates the administrative activities of the entire Institute, and considers the independence of each departmental unit (UOC). Furthermore, they have the responsibility of facilitating the strategic planning process along with setting up the conditions in order to verify efficiency, effectiveness and quality of the administration activities of the Institute.
The Administrative Officer works side by side the General Director in the administrative, financial and organizational management of the Institute, ensuring that all the necessary administrative interventions are implemented in order to carry out the activities of all the structures within the Institute. The Administrative Officer is also responsible for guaranteeing transparency and the regularity of all administrative activities. The Administration Officer provides their approval of the deliberative acts that are proposed by the Departmental Directors (UOC) and are adopted by the General Director
The Administration Office deals with all the technical/ administrative activities supporting health care services and both Scientific Directions concerning research matters.
The Administrative Officer:

- as a member of the Strategic Management, plays an active part in IFO's decision-making processes, such as establishing strategies for corporate development and innovation programmes, setting priorities and allocating resources to the various corporate functional areas;
- ensures the integration and harmony of administrative procedures of all the organisational structures of the institute, as well as leads the activities of the administrative organisational structures, promoting innovation and development;
- works closely with the Chief Medical Office toward developing new forms of integration between clinical and research areas;
- collaborates with the regional structures involved in the various business processes;
- cooperates with other health care structures within the territory for developing and producing a synergistic network for the healthcare system.

# OFFICE OF RESEARCH ADMINISTRATION (SAR)

## *Head: Dr. Cinzia Bomboni*

### *Staff*

Giovanni Cavallotti
Maria Assunta Fonsi
Giuseppina Gioffrè
Annalisa Marini
Samantha Mengarelli
Catia Minutiello

### *Mission*

The Research Administration Office (SAR) provides administrative support to the Scientific Directorates and researchers of the Regina Elena Institute and the San Gallicano Institute by carrying out the following activities:

- approve/modify/disapprove protocols of paperwork and storing all documents electronically;
- Prepare administrative procedures for creating and establishing research agreements, managing all expenses relating to funding from the Ministry of Health (Ricerca Corrente) and research funding from specific targeted projects (Ricerca Finalizzata) and related reporting;
- Create administrative procedures for drafting conventions regarding clinical trials and projects approved by the Ethics Committee and related reporting;
- Coordinate Conto Capitale Grant funding measures;
- Prepare administrative procedures for employing research collaborators and administrative support staff by through flexible contracts funded by research grants;
- Manage reimbursement of various types of expenditures for both permanent and non- permanent staff (missions, publications, staff development courses, etc.);

This office is under the supervision of the Administrative Director of the Institute where it carries out all assigned tasks as well as liaising with the Human Resources Unit, Economic Resources Unit, the Decision Making Acts Department, Occupational Medicine, in addition to the various Project Managers of specific targeted funded projects.

### *Activities*

During 2018 the SAR dealt with managing the administrative and economical aspects of public and privately research projects funded by the Regina Elena Institute (IRE).
The SAR handled the administrative and accounting procedures of all expenses concerning Ricerca Corrente 2018 funding (€3.372.599,57) for IRE and prepared the economic report for Ricerca Corrente 2017 funding (€3.534,201.08). This office also handled Ricerca Finalizzata funding for a total of € 4.339.433,85
In the same period, the SAR Office was appointed Coordinator of the Conto Capitale procedures and responsible for following up on all the procedures between the Services involved making sure all steps in process are done accurately. In particular, decrees set up in 2018 were prepared to concede the loans in the Conto Capitale 2016-2017, seeing the SAR assisting the Scientific Directorates with gathering the appropriate documentation to provide the Ministry of Health.
The SAR office also signed the provision of onerous agreements (within the scope of approved projects) andfree of charge licence agreements. During 2018, the SAR continued to manage projects from previous years, handled more than 170 projects and supported new projects in regards to budgets and new applications. For all the funded projects listed above, the SAR office followed through with all the administrative procedures concerning related expenditure.
In summary, during the 2018 the following activity were performed:

1. Reforming, analyzing and implementing a recruitment legislative framework;
2. Drafting Company Regulations on recruitment procedures for the fixed-term projects, managing projects pursuant to art. 15 septies, scholarships, self-employment, approved by legislative decree no. 972 of 23.11.2017;

3. Public calls for Co.Co.Co projects;
4. Extending contracts, renewing Co.Co.Co contracts funded by research projects;
5. Scholarships and scholarship renewals;
6. Occasional and intellectual work contracts
7. Withdrawal from Co.Co.Co contracts or scholarships
8. Taking care of all procedures relating to maternity leave and return from maternity leave;
9. Preparing and updating administrative paperwork according to different legislative regulations;
10. Developing, managing and updating databases relating to the various types of contracts for internal use (Scientific Management, Administrative Management, Personnel Office, Transparency) and external use (Ministry of Health).

Together with TTO, the SAR Office assists and supports researchers in the management of intellectual property, following all stages of the patenting process right through to the commercialization of them.
In 2018, 2 new national patent applications and 1 new PCT patent application were filed. A total of 13 patent families (IT, EPO and PCT) were managed.

During 2018, the SAR office activated more than 70 decrees relating to the acceptance of clinical trials.
After the Finance Office issues the invoices and monitors the receipts, the SAR Office prepares the financial statements for each study, where it acquired invoices and distributed them among the departments with regulations outlined in the decree (Administration, Pharmacy, Scientific Office, Other Departments/ Offices involved in the study, PI or UOC coordinator of the study) and followed the administrative procedures relating to handling expenses on the proceeds of the clinical trials.

# GOODS AND SERVICES ACQUISITION UNIT

## *Head: Mr. Giovanni Paolo D'Incecco Bayard de Volo, Lowyer*

The Goods and Services Acquisition Unit deals with suppliers and providers for the needs of the patient in hospital for what concernes medical device, medications, reagents, laboratory materials, laboratory equipment.

### *Staff*

Mrs Cristina Corsi
Mrs Zoe Tonda
Mrs Carol Scioscia
Mrs Giovanna Surace
Mrs Gabriella Ingrosso
Mrs Anita Fiumara
Mrs Cinzia La Padula
Mr Giovanni Ricci
Mr Fabrizio Gatto
Mrs Tiziana Chiari
Mr Massimiliano Romano
Mrs Angela De Simone
Mr Antonio De Paolis
Mr Domenico Fiorillo
Mr Gianluca Murru
Mrs Piera Brugnoli
Mrs Barbara Filipponi

The staff is organized in four different purchasing areas: medical device; medications, reagents and laboratory materials, bursar, and an independent purchase section dedicated to the research. This section deals with the purchasing for the "current and finalised" research. It is funded by public and private entities, and by the European Community. Around a thousand procurement procedures are executed every year.

# CONTROL AND VERIFICATION BOARD

## *President*

Prof. Paolo Marchetti

## *Members*

Prof. Angela Santoni
Dr. Roberto Scrivo
Prof. Maria Rosaria Torrisi

Decrees sanctioned by the President of the Lazio Region n. T00238 8.08.2013, n. T003568 20.11.2013 and approval from Health Minister (Prot. 8474 24.10.2013), active since December 2013 (IFO decree n. 959 6.12.2013) The Control and Verification Board determines the direction and objectives of the Institute's activities on an annual and multi-annual basis and verifies all activities carried out and the results achieved by each Department.

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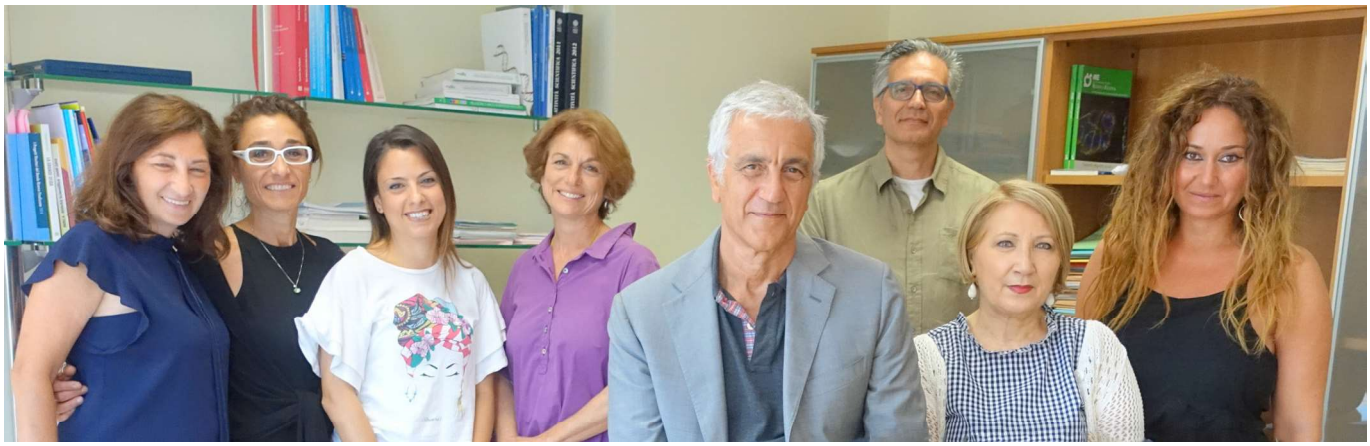
# SCIENTIFIC DIRECTORATE



There is an organizational structure specifically for research and development in oncology which culminates in the office of the Scientific Director
The Scientific Director to accomplish his goals is supported by the Scientific Directorate Offices:

**Secretariat:**
The secretariat office supports the scientific director in carrying out the function of coordination and promotion of research.

**Library:**
The Istitutional library accomplishes the following duties: provision of scientific documentation; biibliographic researches at the request of healthcare professionals; training services for the use of electronic resources also with personalized mini-courses for institutional users and for patients and families; management and updating of the bibliographic patrimony; collection for archiving of institutional publications; collaborates in the generation of the yearly report of research productivity (publications) to the Ministry of Health (Research Workflow)

**Grant Office (GO):**
The activities of the IRE GO are: communication, promotion, support and centralisation of project submission procedures. The GO manages and coordinates all project submission activities with the aim of promoting productivity and competitiveness of research. Every year on average the GO supports and coordinates more than 100 applications to competitive grants, Furthermore, the GO helps coordinationg the generation of the yearly report of research productivityto the Ministry of Health.

**Technology Transfer Office (TTO)**
The Technology Transfer Office (TTO) operates within the Scientific Directorates and cooperates with the IFO Patent Committee established by resolution no. 725 of 01.08.2016.
The TTO brings together the researchers' inventive proposals, promotes their protection and technology transfer. To this end, it assists and supports researchers in the management of intellectual property, from the start of the patenting process to external licensing or, alternatively, to commercial exploitation.

**Clinical Trial Monitoring**
Provides support during the activation, management, reporting and data processing of clinical tirals; manages IRE clinical database trials/SMART clinical trials platform; generates the yearly report of clinical research activity (number of active clinical trials, number of patients involved, ect.) to the Ministry of Health (Research Workflow).

**IRE Biobank - BBIRE**
BBIRE is an oncological biobank established with the main purpose of supporting medical-scientific research by providing high-quality biological samples, accurately annotated, necessary for carrying out research aimed at improving the characterization of different types of neoplasms and at the identification of new prognostic factors related to the development and metastatic dissemination of tumours. BBIRE participates in the National Network of Oncological Biobanks "RIBBO" and in the European infrastructure of Biobanks and Biomolecular Resources "BBMRI-IT" (Italian Node of the European Biobanking and Biomolecular Resources

Research Infrastructure). In the last years BBIRE has grown up to collect more than 10.000 tumor samples and more than 70.000 plasma samples from cancer patients, which are available, upon request to a steering committee, for research purposes.

### Clinical Trial Center - CTC

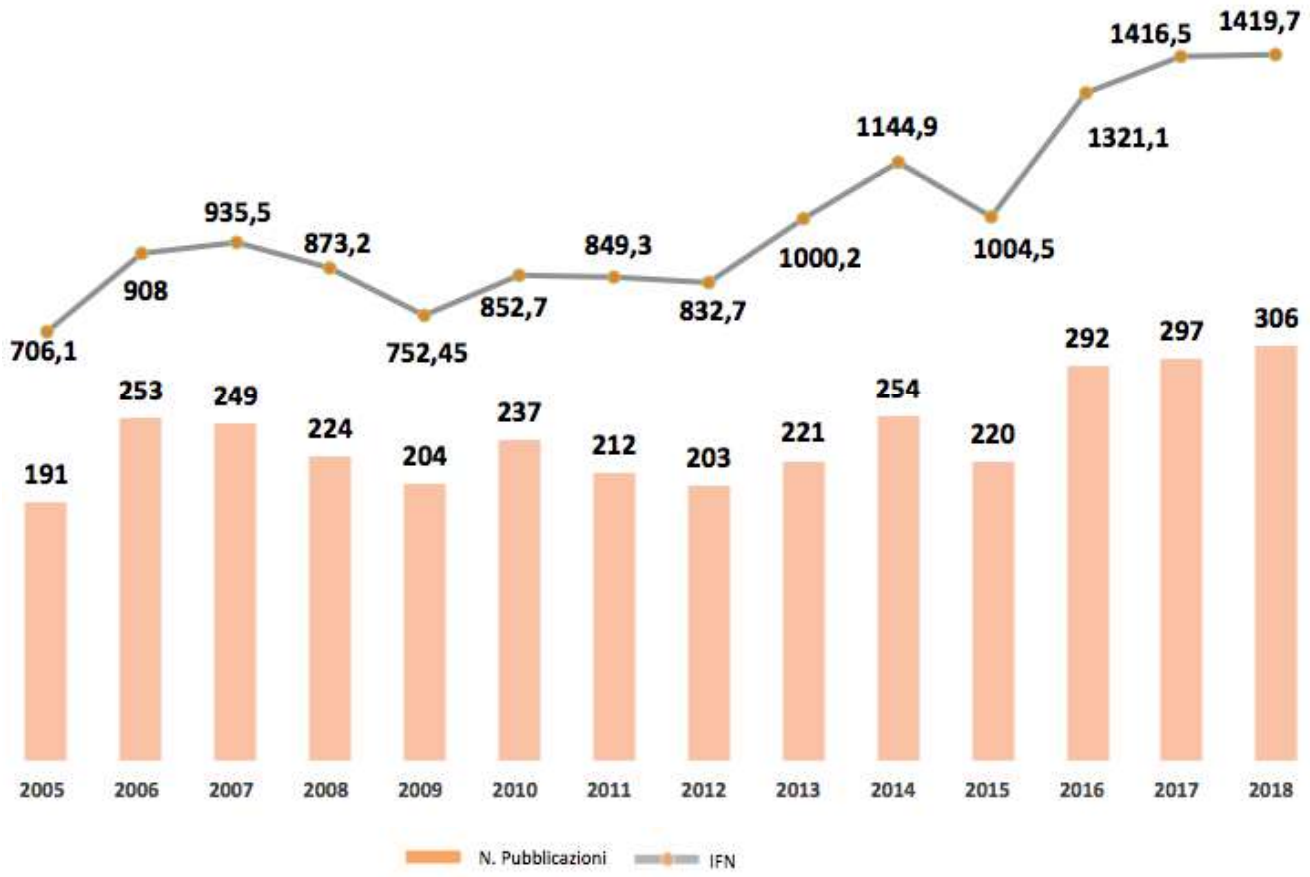
The Clinical Trial Center (CTC) is an organizational Unitshared between Istituto Nazionale Tumori Regina Elena and Istituto Dermatologico San Gallicano, that centralizes and unifies the coordination and monitoring of clinical trials, with the aim of providing management, methodological and biostatistical services to researchers, also promoting collaboration between them. Data Managers and Research Nurses supporting clinical trials are managed centrally by a CTC coordinator. Within the CTC is located the Secretariat of the local Ethical Committee. CTC provides a support, to the internal operating units, for the entire clinical trial process.

### Technical-Scientific Committee - CTS

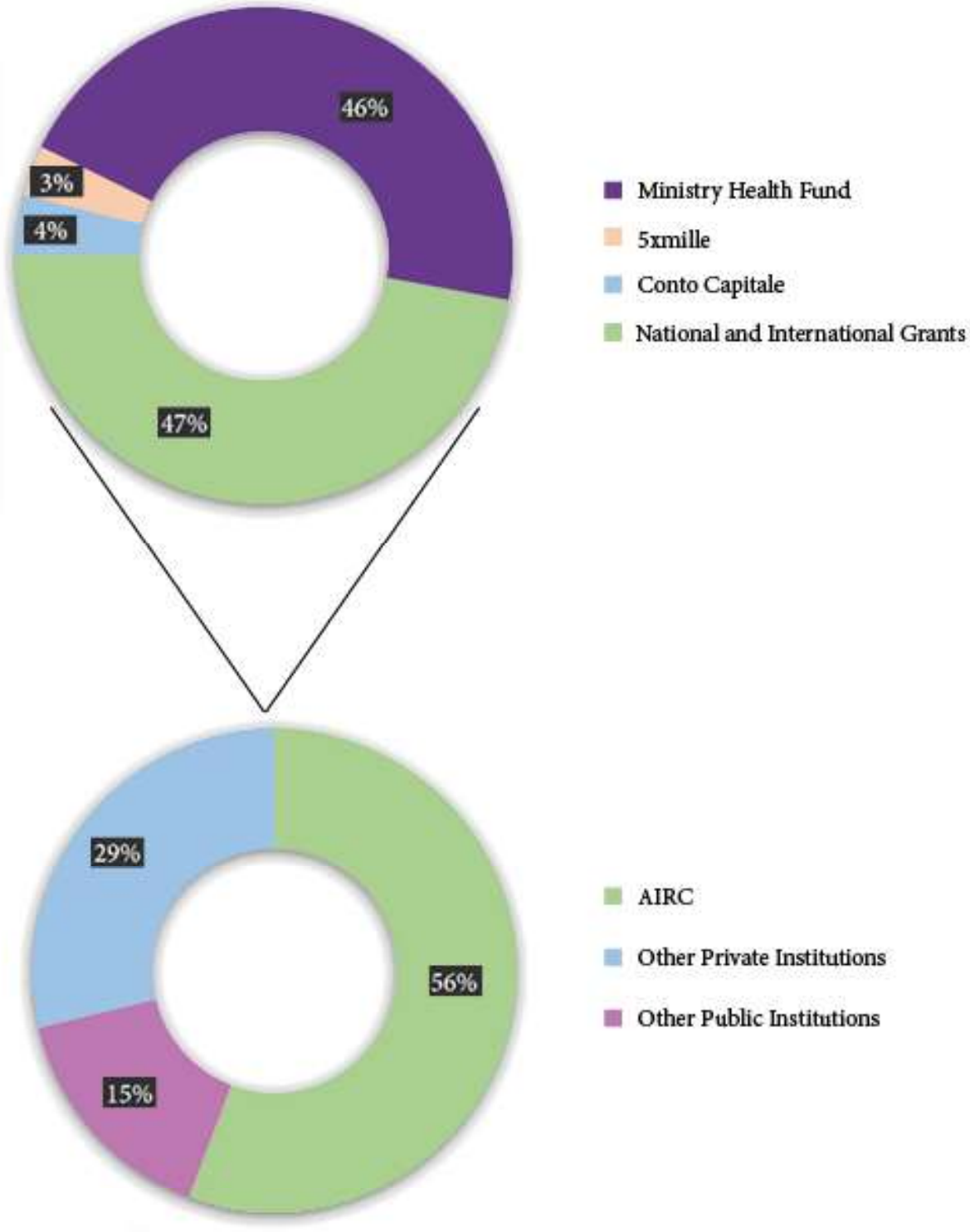
The CTS is an advisory and a supporting body for the clinical and research activities of the Institute and is chaired by the Scientific Director of IRE. According to Regional Law 2/2006 art. 9, is composed of ten other members appointed by the Board of Directors. The CTS is informed in advance of the scientific objectives by the Scientific Director and evaluates the annual report on scientific activity.

Experimental Research activities are carried out in the Department of Research, Advanced Diagnostics And Technological Innovation Department

# IRE Scientific Productivity years 2005-2018



Graph A - Distribution of the main National and International funding sources supporting IRE research




Graph B - Details on National and International grants source funding

# INTERNATIONAL SCIENTIFIC ADVISORY BOARD (ISAB)

During 2018, the IRCCS Regina Elena NATIONAL Cancer Institute decided to renew its International Scientific Advisory Board (ISAB). With decree No. 532 dated 10 July 2018, the following members were nominated by the Scientific and Technical Committee (CTS):

- Prof. Andrés Cervantes, Professor of Medicine at the University of Valencia, Head of the Department of Medical Oncology at the Hospital Clínico Universitario de Valencia - General Director of the Biomedical Research Institute INCLIVA;
- Prof. Henning Walczak, PhD Scientific Director of the Cancer Research UK-UCL Centre;
- Prof. Andrew V. Biankin, Regius Chair of Surgery/ Director of Translational Research Centre, University of Glasgow;
- Dr. Francesco M. Marincola, Chief Scientific Director Refuge Biotechnologies, Inc. Menlo Park, California;
- Prof. Anne Willis, Professor A E Willis OBE - Director, Medical Research Council Toxicology Unit, MRC Toxicology Unit, Leicester;
- Prof. Vincent Gregoire, MD, PhD, Hon FRCR (IE), Hon FRCR (UK) Département de Radiothérapie - Radiation Oncology Department - Centre Léon Bérard - Léon Bérard Cancer Center;
- Prof. Amanda Psyrri, Chief of Medical Oncology and Assistant Professor of Medicine, Institution Attikon University Hospital Department Medical Oncology Dept., Athens;
- Prof. Pierre-Alain Clavien, Chairman of Department of Surgery & Transplantation, University Hospital of Zurich, Switzerland

The first ISAB meeting was organized at IRE by the Scientific Directorate on November 15th 2018. Due to prior commitments only five ISAB members were able to attend: Andres Cervantes, Andrew Biankin, Francesco Marincola, Anne Willis, Amanda Psyrri and Pierre-Alain Clavien.

During the meeting, the ISAB members had the possibility to learn about translational research carried out at the institute through presenting key programs as well as via face-to-face meetings with several researchers. The meeting ended in a closed session among the ISAB members followed by an encounter with the Scientific Director and the Director General to present their first feedback. This first feedback session was then followed by a written report which was sent to the Scientific Director containing general comments and a series of recommendations made by the ISAB committee.

Below are the general comments and recommendations expressed by the ISAB board:

*Overall the panel considered that there was great potential at the IFO/IRE and the leadership should be congratulated on what has been achieved to date. The foundation for additional growth is strong, and the challenge now is to define a strategic path forward in a focused way that capitalises on strengths and creates critical mass and efficiency for optimal competitiveness. The following comments are the cumulative thoughts of the SAB after a day of interaction with IRE leadership and staff.*

*At the current time, it was not clear what was unique about the Institute and a unifying strategy is required to allow better translation of the scientific outputs into new clinical practise. This is understandable and expected, a challenge for many advanced institutes that grow rapidly. These challenges have been recognised by the leadership of IRE, leading to, amongst other efforts, to the convening of this SAB.*

*A short and long term strategy needs to be more clearly defined that would delineate IRE from other institutions. For example, it was agreed that most cancer treatments in the future will involve combination therapies. Therefore a strategy should include the rationale for the selection of combinations based around the cancer-, immune-biology and discovery biomarker research that is carried out by scientists at the IRE.*

Based on the inputs provided by ISAB members, the IRE scientific directorate has started to coordinate the elaboration of a strategic plan for research as one of the main objectives for year 2019.

# LIBRARY

## *Head: Dr. Gaetana Cognetti*

**Administrative Staff**
Domenico Verbicaro
**Professional staff**
Francesca Servoli, Graduated Specialized Librarian
Virginia Scarinci, fellow

### *Mission*

Aim of the Library is to guarantee easy access to updated scientific documentation, most on electronic support. Apart from acting as a library, it should also be considered a knowledge Centre which facilitates access to relevant documentation in order to favour the best clinical practices and the choices of patients. The Knowledge Centre aims to contribute health information literacy also promoting the exchange of information between different professional areas.

### *Location*

The Library is located near the main entrance of the Institute and offers a multimedia room with 15 computers. The Patient Library is located, since 2005, in a dedicated room providing quality information through professional staff and civil service volunteers using booklets for patients, scientific databases and trusted health portals.

### *Services*

- The Library offers its services to the medical staff. The Library supports research activities by offering scientific information, documentation and education.
- The Library supports the institutional clinical staff offering: consultation of the main biomedical databases; document delivery through interlibrary exchange system, NILDE (in 2018 total borrowing 289, total lending 145); organisation of training courses; the librarian staff offers also support to the bibliographic searches, systematic reviews and meta-analyses. The main activities of the library consist of managing: monographs and periodicals following international standards and updating of national union catalogues; reference desk also through the personalized service *Book a librarian*, tailored courses on demand by the users (31 meetings in 2018). In 2018, thanks also to the Bibliosan Network, the Library subscribed electronic resources: thousands of on line journals, databases as Embase, Scopus, Web of Science, Journal Citation Reports, BMJ BestPractice, Cochrane Library, Faculty 1000, Cinahl, etc.
- Inventory and accommodation of the library's paper heritage.

- The Patient Library offers information, using-booklets, databases and quality websites. Patients and their relatives can also use the multimedia room with Internet connection. There is also a Library for recreational reading. Since 2005 about 2000 patients and their relatives visited the Library. In 2018, 55 patients and family members asked for information (30 tailored search using Internet portals and websites and about 60 information booklets delivered).

## Research Activities

The Library is involved in various research and educational activity and participates in library networks. The Library collaborated with a project about health information literacy in old age population promoted by the Pescara AUSL. The results of the survey will be published in 2019. Library staff was also involved in the organization of scientific events, also reporting and presenting posters in various meeting in Italy and abroad. As far as information literacy is concerned, the library has organized: 4 CME courses on scientific documentation and narrative medicine, the participants were about 50, The Library has organized also courses concerning Bibliosan's resources and a course for nurses involved in early phase clinical trials. The library staff is involved in the teaching and tutorship of the most courses organized on site.

The Library coordinated the OECI Improvement Plan on patient involvement and empowerment, concerning humanization of the care, communication and information and produces and updates a census and a leaflet of the activities and services for patients offered by associations and institutional units inside the Institute. In 2018 Ethics Committee approved *INFO RP - An observational study of information prescription in Italy*. Patients will be directed to the consultation of information at the Patient Library, with prescription pads signed by the medical staff of the Endocrinology Unit.

The Library staff participates in the working group for the reporting of the Institute's scientific activity, required annually by the Italian Ministry of Health, and manages the institutional archive of publications.

All Library activities have been automated using of electronic shared systems. In particular, the Library participates in the following networks:

- **1. National Library Service (SBN)** - the Library's books are catalogued following the MeSH (Medical Subject Headings) and the National Library of Medicine (NLM) Classification;
- **2. Network Inter-Library Document Exchange (NILDE) -** document delivery service for exchanging scientific articles.
- **3. National Union Catalog of Periodicals (ACNP)** for the cataloguing and management on the web of the periodicals;
- **4. Library Network of Biomedical Research Institutes (Bibliosan)**;

## Publications


1. Cercato M.C. C, E., Fabi A, Bertazzi I, Scarinci V, Franceschini A, Cognetti F, Cenci C. Narrative Based Medicine: A Digital Diary during Chemotherapy Treatment to Personalize Patient Care (Pilot Study). *Tumori Journal*. 2018 104(4S): 194 (S40)a

2. Grassadonia A, Sperduti I, Vici P, Iezzi L, Brocco D, Gamucci T, Pizzuti L, Maugeri-Sacca M, Marchetti P, Cognetti G, De Tursi M, Natoli C, Barba M, Tinari N. Effect of Gender on the Outcome of Patients Receiving Immune Checkpoint Inhibitors for Advanced Cancer: A Systematic Review and Meta-Analysis of Phase III Randomized Clinical Trials. *J.Clin.Med*. 2018 Dec 12; 7(12): 10.3390/jcm7120542a IF:5.583.

3. Cognetti G. La chiave della salute sta in biblioteca. Biblioteche specializzate e Biblioteche di pubblica lettura al centro dell' informazione sanitaria per i professionisti ed i cittadini. Bibelot 24 (3), 2018

4. Cognetti, G. L'informazione sanitaria tra il dr Google e le risorse elettroniche di qualità. In: Ripensare la sanità ai tempi del digitale, a cura di G. Cosentino. Youcanprint, ISBN: 9788827848807, 2018

5. Cognetti G. La documentazione scientifica è la chiave per i professionisti della salute? In: Scuola di Ricerca. Corso di formazione specifica i n medicina generale .La medicina generale in ricerca "ci raccontiamo"VIII/2018 p. 34-38. Luglio 2018 http://www.omceo.bari.it/articoli/allegato/giornale-viii.-ediz.pdf

# JOUNAL OF EXPERIMENTAL & CLINICAL CANCER RESEARCH

## *Editor-in-Chief: Mauro Castelli, Phd*

**Deputy Editor**
Gabriella D'Orazi, MD, PhD
**Managing Editor**
Alice Castelli, PhD

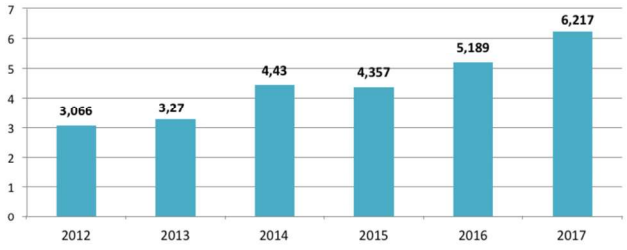
*Journal of Experimental & Clinical Cancer Research* has proceeded its editorial activity maintaining its partnership with the Publisher BioMed Central in London.
The journal publishes scientific studies on the experimental and clinical aspects of cancer research. Topics covered by the journal range from molecular oncology to tumor-microenvironment interaction and include new technologies (RNA-seq, oncogenomics, etc) for diagnostic and prognostic purpose.
2018 was a very successful year for Journal of Experimental & Clinical Cancer Research, the official scientific journal of the "Regina Elena" National Cancer Institute since 1986 obtaining an Impact Factor of 6.217, the highest record to date for the journal.
This result enabled Journal of Experimental & Clinical Cancer Research to remain secure in the 1st quartile of the 'Oncology' category with an improved ranking of 33rd/222, placing the journal in the 85th percentile for this category. This was a fantastic achievement for the journal.

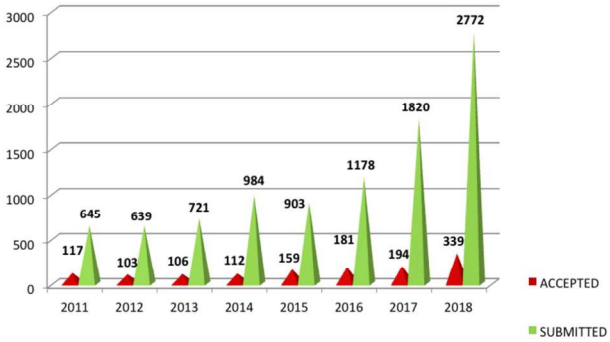
The main accomplishments achieved by *JECCR* in 2018 years are:

- Impact Factor: 6.217
- Ranking in the 1st quartile among International Oncology Journals
- Over 50% increasing of articles submitted
- Over 90% increasing of articles published
- JECCR publishes Original article, Reviews, Meeting Report and Commentary article
- Over 100.000 article accesses (online) each month

In conclusion the journal JECCR is a strategic source useful for the widespread of the scientific information in the community and it increases also the visibility and the prestige of the Regina Elena Cancer Institute, as the clinical, molecular and translational publications confirm.

*JECCR* online website:
http://jeccr.biomedcentral.com/



# PRESS OFFICE & PUBLIC RELATIONS

## *Chief Press Officer & Public Relation IFO*

**Lorella Salce**, website editing manager, corporate identity manager, social media manager &strategist

## *Staff*

**Simona Barbato**, press officer, website editor, social media editor, corporate identity referent
**Francesco Bianchini**, social media referent, videomaker
**Daniela Renna**, administrative collaborator, corporate identity referent
**Mauro Di Giovanni**, photographer
**Ivana Zardin**, photographer

## *Press office activities*

- communication strategy and plan
- Corporate identity and brand communication;
- Public Relation
- Media relations management: press releases, press conferences;
- Website: managing content, updating press section and news;
- Managing tv, radio and press interviews;
- New media communication (Facebook, Twitter, Youtube, Instagram);
- Digital press review


## *Annual activities report*

| | |
|---|---|
| **Press releases 2018** | **35** |
| **Agency launches 2018** | **200** |
| **Mass media presences 2018** | **1450 (newspaper, magazine, radio, tv)** |
| **News and internal communication items (mail everyone, closed-circuit tv) 2018** | **390** |
| **Facebook (8000 follower)** | **628 post; 2.2 million views** |
| **Youtube** | **444.000 views; 1.400.000 minutes watched** |
| **Twitter (1100 follower)** | **1074 tweet; 1140 mentions; 2205 retweets; 480.000 views** |
| **Instagram (700 follower)** | **273 post; 150.000 views** |
| **Linkedin (2100 follower)** | **134 post; 71.000 vews** |
| **Telegram** | **200 messages** |

## Here are some of the publiccommunication campaigns, web projects of 2018

- World Cancer Day campaign for promotion public awareness. *February 2018*
- 5x1000 campaign for the collection of the 5 per thousand tax option from taxpayers (a governmental initiative whereby for every thousand paid by a taxpayer). *April to July 2018*
- Press conference presenting Early Phase Studies Center, in the presence of Armando *Bartolazzi, Undersecretary of the Ministry of Health*, and Nicola Zingaretti President of the Lazio Region. *October 2018*
- Campaign for the European Researchers' Night : *celebrating ten years of Robotic Surgery* at Regina Elena Cancer Institute. *September 2018.*

# ETHICS COMMITTEE

**Chairman**
Prof. Francesco D'Agostino
*Expert in Bioethics*

**Vice Chairman**
Prof. Agata Amato Mangiameli
*Expert in Legal Matters*

**Members**
**Clinicians:** Dr. Enzo Maria Ruggeri, Prof. Vito Fenicia, Prof. Stefano Calvieri, Prof. Daniele Santini
**General Medicine:** Dr. Mario Falconi
**Pedriatician:** Dr. Raffaele Cozza
**Biostatistics:** Prof. Annarita Vestri
**Pharmacologist:** Prof. Lucia Negri
**Pharmacists:** Dr.ssa Antonia Marina la Malfa, Dr.ssa Silvia Murachelli, Dr.ssa Nicoletta Onori
**Genetist:** Prof. Giovanni Neri
**Volonteer Representative:** Elisabetta Iannelli, Lawyer
**Health Areas Representative:** Dr. Laura Iacorossi
**IRE Scientific Director:** Prof. Gennaro Ciliberto
**ISG Scientific Director:** Prof. Aldo Morrone Aldo
**IFO Chief Medical Officer:** Dr. Branka Vujovic
**Bietti Foud. Scientific Director:** Dr. Monica Varano
**Bietti Foud. Chief Medical Officer:** Dr. Giuseppe Di Chio
**Clinical Engineer:** Ing. Giuseppe Navanteri
**Nutrition Expert:** Prof. Giorgio Calabrese

The Central Ethics Commitee IRCCS Lazio expresses its opinion on trials to be managed in Regina Elena National Cancer Institute, San Gallicano Dermatological Institute and G.B. Bietti Foundation for ophthalmology.

During years 2018 the Central Ethics Commitee IRCCS Lazio examined and expressed its opinion on 119 studies including clinical trial protocols, observational studies and research projects, 173 substantial amendments.
Relatively to these items the ethics committee analyzed ethical and scientific aspects, the adequacy of the investigators and the structures involved and, above all, the methods and documents to be used to inform patients and obtain their informed consent.
The Ethics Committee meetings are held monthly and, if necessary and urgent, the opinion of their members on a particular case such as the use of drugs not commercially available is obtained by mail.

# ETHICS COMMITTEE SECRETARIAT

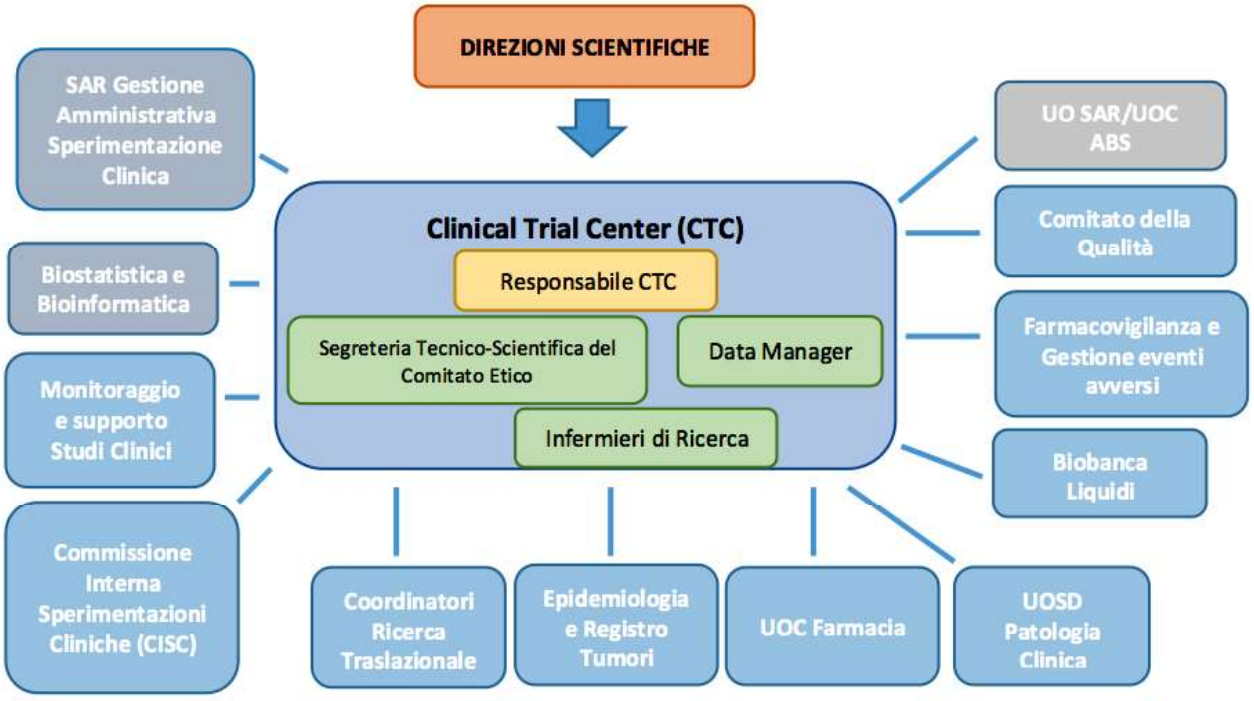
**Executive Secretary**
Anna D'Ambrosio

**Technical-Scientific Secretriat**
Diana Giannarelli, Maria Cecilia Ciacchella, Cecilia Fagioli, Barbara Matrascia, Federica Struglia.

# IFOs CLINICAL TRIAL CENTER

The CTC was established by Decree No. 308 dated 24 April 2018 and subsequently amended with Decree No. 602 dated 06 August 2018.The components of both the CTC and External Units is shown in Figure 8.The CTC performs the following functions:

- Coordinates and monitors the functional activities regarding the management of clinical trials within the IFO, acting as a qualified reference point;
- guarantees greater control of the clinical trials to the Scientific Directions of Regina Elena and San Gallicano Institutes and IFOs Medical Office;
- particular supports in the spontaneous non-profit research;
- interacts with the Departments involved in experimental research activities, coordinating the activities of the experiments aimed at:
  a) providing administrative, managerial, methodological and statistical services to researchers for the conception, design, planning, start-up phase, conduction, analysis and reporting of clinical studies so that these activities are carried out in compliance with the GoodClinicalPractice (GCP) and the protocols;
  b) supporting the management of authorization procedures as well as the conduction and financial reports of clinical studies;
  c) promoting, in profit and non-profit research, the professional development of all participating researchers in terms of compliance with GCPs and regulatory aspects;
  d) guaranteeing quality control of studies (experimental and observational studies) with profit and non-profit study promoters;
  e) supporting monitoring of information regarding the feasibility of studies in terms of potentially enrolled patients;
  f) increasing the synergistic collaboration between researchers involved in the studies;
  g) evaluating the experiments proposed by researchers at IFO, for which IFO takes on the role of Promoter, and monitors the progress of the approved studies;
  h) identifying areas of great strategic interest for the Institute and propose initiatives necessary for promoting clinical trial projects in these areas.



# BIOBANK - BBIRE

## *Head: Dr. Laura Conti*

| BBIRE | |
|---|---|
| **BBIRE-T** | **BBIRE-LB** |
| Edoardo Pescarmona<br>Responsabile UOC Anatomia Patologica | Laura Conti<br>Responsabile UOSD Patologia Clinica |
| Mirella Marino<br>Responsabile Assicurazione Qualità e Rischio Clinico | Giovanni Cigliana<br>Responsabile Assicurazione Qualità e Rischio Clinico |
| Simona di Martino - Biologo | Chiara Mandoj - Biologo |
| Valentina Laquintana - Biologo | Giulia Orlandi - Biologo |
| | Mustapha Haoui - Tecnico |

Biobanking is actually recognized as a basic enabling tool for cancer research, with the future of molecular and translational research relying heavily on the availability of high quality biospecimens linked to data on actual clinical outcomes. There are several benefits to having a consolidated approach to biobanking, including increased awareness of specimen availability, increased access for researchers from larger pools of samples, increased quality and consistency of samples from standardized collection procedures, and efficiencies. In 2014 the tumor Biobank of Regina Elena National Cancer Institute (BBIRE), an integral part of the scientific strategic plan of the Institute, was established as a joint initiative between the Clinical Pathology and Pathology Unit with the financial support of the Scientific Directorate. The main function of the biobank is to collect tissue (T) and body fluids (LB) samples in accordance with standardized criteria and cryoconserve them in order to provide biological material for approved cancer research projects. BBIRE includes a Steering Committee and an Operating Group. BBIRE is involved in a growing number of projects, and as a member of the European research network of Biobanks and Biomolecular Resources (BBMRI-ERIC) participates with European groups to large-scale multicenter projects. BBIRE collected more than >10,000 solid human tissue samples, and >40,000 fluid samples (such as blood, serum, plasma) as well as the associated clinical data of patients for follow-up.

# Tumor Tissue Biobank IRE

Sample collection 2017- 2019

| DEPARTMENT | PATHOLOGY | PATIENTS | SAMPLE PRESERVATION MODE | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | TUMOR TISSUE CRYOPRESERVATION | NOT TUMOR TISSUE CRYOPRESERVATION | TUMOR TISSUE OCT | NOT TUMOR TISSUE OCT | FFPE | NGS | TOTAL |
| ORTHOPEDIC SURGERY | Sarcoma | 115 | 1048 | 674 | 32 | 8 | 45 | 21 | 1828 |
| THORACIC SURGERY | Thymoma | 20 | 162 | 49 | 6 | 4 | 20 | | 241 |
| | Lung tumors | 140 | 752 | 677 | 64 | 38 | 125 | 70 | 1726 |
| | Mesothelioma | 2 | 8 | 0 | 1 | 0 | 1 | | 10 |
| | Lymphoma | 7 | 34 | 4 | 1 | 0 | 7 | | 46 |
| | Pleural effusion | 34 | 0 | 0 | 0 | 0 | 0 | | 0 |
| SURGERY A/PLASTIC SURGERY | Breast cancer | 54 | 294 | 213 | 22 | 14 | 51 | | 594 |
| GYNECOLOGICAL SURGERY | Uterine cancer | 75 | 569 | 184 | 26 | 3 | 66 | | 848 |
| | Ovarian cancer | 22 | 228 | 18 | 11 | 3 | 22 | | 282 |
| | Ovarian cancer + peritoneal washing | 39 | 465 | 93 | 19 | 3 | 34 | | 614 |
| | Peritoneal washing | 17 | 0 | 0 | 0 | 0 | 0 | | 0 |
| | Uterine carcinosarcoma | 6 | 77 | 17 | 7 | 0 | 6 | | 107 |
| UROLOGY SURGERY | Renal Cancer | 78 | 628 | 289 | 37 | 12 | 74 | | 1040 |
| | Bladder Cancer | 41 | 382 | 169 | 19 | 12 | 40 | | 622 |
| NEURO SURGERY | Brain cancer | 25 | 109 | 1 | 4 | 0 | 22 | 9 | 145 |
| HEPATOBILIARY SURGERY | Colon cancer | 50 | 255 | 191 | 21 | 15 | 47 | 12 | 531 |
| | Colon cancer/hepatic metastasis | 4 | 55 | 45 | 0 | 0 | 4 | | 104 |
| | Hepatic metastasis | 12 | 97 | 59 | 3 | 1 | 8 | | 168 |
| | Stomach cancer | 6 | 26 | 18 | 4 | 4 | 6 | | 58 |
| | Liver cancer | 7 | 35 | 30 | 11 | 0 | 7 | | 84 |
| | Pancreas cancer | 21 | 105 | 40 | 10 | 3 | 19 | | 177 |
| | Gist | 1 | 8 | 0 | 1 | 0 | 1 | | 10 |
| | Retroperitoneal sarcoma | 5 | 108 | 22 | 2 | 1 | 4 | | 137 |
| | Cholangiocarcinoma | 3 | 10 | 16 | 1 | 1 | 3 | | 31 |
| | Biliary tract cancer | 2 | 1 | 0 | 1 | 1 | 2 | | 3 |
| | Melanoma | 1 | 8 | 4 | 0 | 0 | 1 | 1 | 14 |
| OTOLARYNGOLOGY SURGERY | Head and neck cancer | 4 | 14 | 0 | 4 | 0 | 3 | | 21 |
| OTHERS | Metastasis (melanoma) | 15 | 78 | 0 | 6 | 0 | 15 | 15 | 114 |
| Total | | 825 | 5556 | 2813 | 313 | 123 | 633 | 128 | 9555 |

# Body Fluids Biobank IRE

Sample Collection (March 2015 - October 2019)

| DEPARTMENT | PATHOLOGY | PATIENTS | WITHDRAWALS | SAMPLE ALIQUOT (~500µL) | | | | 2mL* | 1mL | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Whole Blood | Plasma EDTA | Plasma Citrate | Serum | Plasma EDTA | PBMC | TOTAL |
| ORTHOPEDIC SURGERY | Sarcoma | 556 | 1497 | 2980 | 7888 | 998 | 6239 | 2669 | - | 20774 |
| THORACIC SURGERY | Thymoma | 26 | 26 | 52 | 195 | 13 | 102 | 20 | | 382 |
| | Lung cancer | 197 | 197 | 394 | 962 | - | 772 | 404 | - | 2532 |
| | Lymphoma | 4 | 4 | 8 | 26 | - | 16 | 6 | | 56 |
| MEDICAL ONCOLOGY 2 | Breast cancer | 69 | 71 | 141 | 327 | 201 | 483 | 15 | - | 1167 |
| GYNECOLOGICAL SURGERY/ BTO (Ovarian Tissue Biobank) | Uterine | | | | | | | | | |
| | Ovarian cancer/ | 239 | 245 | 488 | 343 | 735 | 1029 | 711 | - | 3306 |
| | Various | 70 | 70 | 140 | 468 | 207 | 330 | 119 | | 1264 |
| RADIOTHERAPY | Prostate/ Oropharynx/ Breast cancer | 163 | 514 | 1028 | 2802 | - | 2335 | 1198 | - | 7363 |
| MEDICAL ONCOLOGY 1 | Lung cancer (ACC LUNG) | 18 | 35 | 104 | - | - | - | 232 | 51 | 387 |
| NEURONCOLOGY/ NEURO SURGERY | Brain cancer | 66 | 83 | 166 | 281 | 239 | 356 | 203 | - | 1245 |
| | | 100 | 105 | 210 | 546 | - | 428 | 235 | | 1419 |
| ENDOCRINOLOGY | Medullary thyroid cancer | 18 | 18 | 36 | 4 | - | - | 34 | - | 74 |
| PLASTIC SURGERY/ MED. ONCOLOGY 1/2 | Melanoma | 48 | 83 | 164 | 366 | 6 | 370 | 260 | - | 1166 |
| GASTROENTEROLOGY | Hereditary colon cancer | 148 | 148 | 296 | 104 | - | - | 294 | - | 694 |
| MTB | Various | 21 | 28 | 56 | 40 | 9 | 74 | 107 | 5 | 291 |
| TRANSFUSION MED. | Healthy donor | 42 | 61 | 122 | 47 | 175 | 270 | 120 | - | 734 |
| TOTAL | | 1785 | 3185 | 6385 | 14399 | 2583 | 12804 | 6627 | 56 | 42854 |

# PARTECIPATION TO NETWORKS

# NETWORK

## *ALLEANZA CONTRO IL CANCRO - ACC*

IRE is one of the founder member of ACC, the largest Italian organization for cancer research, was established in 2002 by the Italian Ministry of Health as a network of six high standard institutes for comprehensive cancer patient care and research (IRCCS).
The primary aim of ACC is to promote the network among oncologic institutes pursuing mainly clinical and translational research in order to bring state of the art diagnostics and advanced therapeutics to patient care.
In addition to the aims of translational medicine, ACC also fosters research through international collaborative networks of excellence, such as:
Transcan > ACC is one of the funding agencies in this European network that coordinates translational research projects that are selected by means of high standard evaluation procedures. In 2016 a total of over 17 million euro was disbursed in research projects and the European Commission is currently evaluating funding for a further 5 million euro.
MD Anderson Sister Institution Network > ACC entered the Network to further expand the long-standing cooperation between the American Centre of Excellence and each of the high standard Institutes for both patient care and research (IRCSS). The agreement between the two institutions was signed during a mini symposium in Rome in 2016. The MD Anderson Cancer Center is the largest institute for clinical cancer research in the USA, constantly topping the rankings for innovation and quality of service. The MD Anderson Network brings together similar centres worldwide.

eatris

European infrastructure
for translational medicine

## A-IATRIS / EATRIS

A-IATRIS, Association Italian Advanced Translational Research Infrastructure, is a network of institutions of excellence on the national scene able to make specific and complementary contributions in the area of translational medicine. A-IATRIS represents the Italian node of EATRIS (European Advanced Translational Research Infrastructure in Medicine).
EATRIS is designed to bridge the gaps and deficits in the panorama of European translational medicine. Its objectives for EATRIS are:

- to support the process of translating research results into innovative strategies aimed at the prevention, diagnosis and treatment of diseases of particular health and economic importance for European member states;
- to build a beWer space in which the flow of information between basic research and clinical observations is bi-directional.

EORTC
European Organisation for Research
and Treatment of Cancer

*The future of cancer therapy*

## EORTC

European Organization for Research and Treatment of Cancer Is an independent, non-profit cancer research organisation, its mission is to coordinate and conduct international translational and clinical research to improve the standard of cancer treatment for patients.

## OECI

The "Organisation of European Cancer Institutes" is a nongovernmental, no-profit legal Entity established in 1979 to promote greater cooperation among European Cancer Centres and Institutes.

**AIMS**

- • Creating a critical mass of knowledge and skills that can identify and share new and improved models of care
- • Improving the quality of cancer care and translational research
- • Improving the quality of life for cancer patients
- • Provide a path of continuous improvement in order to homogenise the care of cancer patients according to shared
- European standards and quality levels.
- Facilitate the development of European multi-centre studies and the use of EU research funds OECI, on September 10,2015, has certified that IRE meets the quality standards for cancer treatment and research and has therefore obtained the qualification of Comprehensive Cancer Center, or oncology IRCCS with peculiar characteristics such as translational research, multidisciplinarity, continuous improvement of care, the production of guidelines and diagnostic-therapeutic pathways, continuous training and centrality.

## UICC

The Union for International Cancer Control's (UICC) rapidly increasing membership base of over 1000 organisations in more than 160 countries, represents the world's major cancer societies, ministries of health and patient groups and includes influential policy makers, researchers and experts in cancer prevention and control. UICC also boasts more than 50 strategic partners.

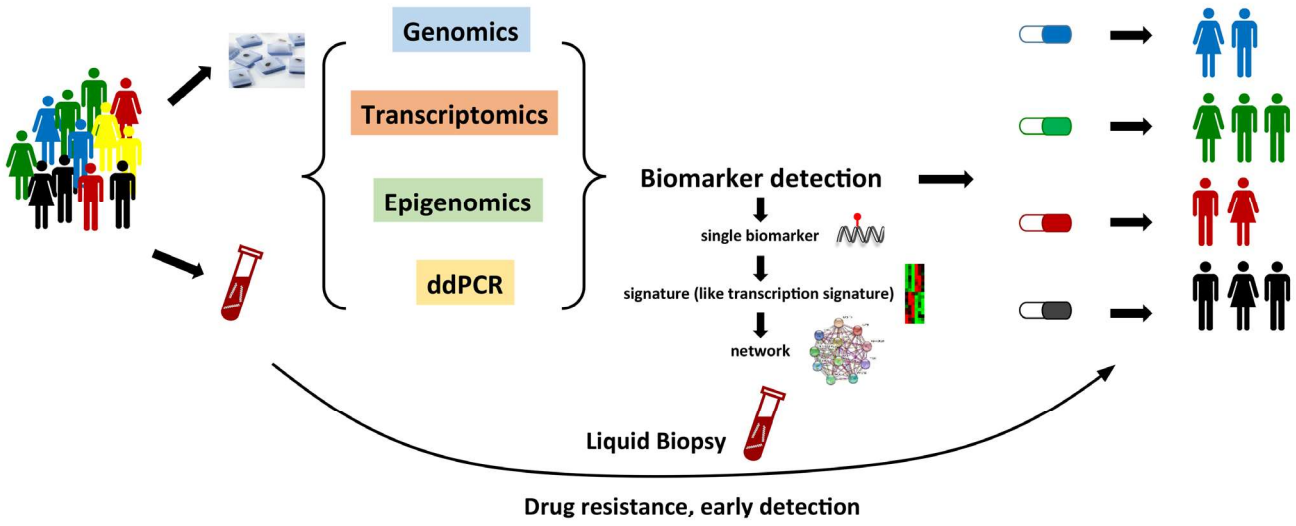
# SPECIAL GROUPS

# MOLECULAR TUMOR BOARD (MTB)

During the last few years, an increasing number of diagnostic methodologies based on innovative molecular techniques have been applied in oncology, revolutionizing the therapeutic approach to human malignancies. In order to appropriately use these new biotechnological tools, in September 2018, the Regina Elena National Cancer Institute has activated the Molecular Tumor Board (MTB), a multidisciplinary board made of health and research specialists (oncologists, biologists, biotechnologists , bioinformatics, etc ...) to interpret data coming from molecular analyses on tumor samples, with the aim of identifying the most suitable therapy for a specific patient in a specific moment. This is particularly important today since, from month to month, novel therapies become available, more and more effective, but often they are difficult to be assign outside the indications. Indeed, most of that drugs require a series of complex molecular assays to be performed before therapy assignment. This context is not available in all hospitals. The MTB was precisely born to give concrete answers to these needs, providing tools to manage these situations to doctors and patients. The MTB of Regina Elena National Cancer Institute has been active for a year, right now. During this period, the MTB has gradually become a reference for the most difficult clinical cases in our Institute, but not only. Indeed, cases concerning patients also followed in other Institues of Lazio have been reported to the attention of our MTB, that equally provided advices and, possibly, therapeutic recommendations. Particularly, the MTB members met themselves for 24 sessions, with an average of 15 days, examining a total of 39 clinical cases for which conventional treatments were no longer available but patient general conditions were still good (Performance Status 0-1). In 12 cases, through a detailed examination of clinical information and thanks to the application of specific biotechnological solutions such as next generation sequencing (NGS), both targeted (22-50 genes) or expanded (entire exome), digital PCR (dPCR) and advanced IHC and in situ hybridization, the MTB was able to identify specific point mutations potentially subject to molecular targeting, therefore recommending a non-standard target therapy. Of note, in 10 cases, point mutations and / or amplifications or fusions were investigated in tissue biopsies, identifying the presence of at least one aberration in 80.0% of the samples (8/10), 7 of which were associated to therapeutic targets. At the same time, in 13 cases, liquid biopsy was applied to blood samples to identify and follow the presence of specific point mutations over time, identifying a therapeutic target in 6/13 (46.2%) patients. In the majority of cases that, following the recommendation, were subjected to unconventional therapies (n = 9), a significant clinical response was observed, in some cases even very pronounced until complete remission. Importantly, we recorded two brilliant therapeutic responses obtained in subjects suffering from lung carcinoma that otherwise would not have had any other therapeutic option and would have rapidly undergone death. It is important to underline that in no case patients were charged from any costs, either with regard to the molecular analyses or with regard to drugs. In specific situations, the MTB has directly contacted the National and Regional Health Authorities to obtain special permits and financial support that allow the free administration of the chosen drug.

All this (still small) heritage of experience and knowledge has also been recently formalized in an online database, which represents a diary of the new opportunities offered by our molecular approaches. This database, which collects clinical and biological information and the history of MTB activity, will necessarily grow in the future, but it will certainly help to increase clinical and ethical standards, to better understand the rules of engagement of patients, to equip ourselves with even more powerful methodologies and, in a single word, to make MTB a widely applicable tool.

# GENOMICS TRANSLATIONAL WORKING GROUP




**Workflow of working group Genomics to detect biomarkers for precision medicine**

The working group (WG) Genomics is very heterogeneous and therefore inspiring in its composition including clinicians like surgeons, pathologists, clinical pathologists and oncologists but also biologists, bioinformaticians and biostatisticians.

## Mission

The group was created as a hub for the development and implementation of new technologies like Next Generation Sequencing, NanoString and digital PCR for research, but also especially for diagnostic purposes in order to foster innovations in the biomedical field. The major aim of this group is to enhance precision medicine which is becoming more and more important to increase the chances of successful treatment of oncologic patients. A comprehensive molecular study allows or aids in choosing the most promising drug for each individual patient.

## Research Activity

We are performing genomic, transcriptomic and epigenetic approaches to identify novel biomarkers that are able to improve the prediction of patients' prognosis and response to specific therapies. The genomic analysis includes the use of small to large panels of target genes up to whole exon sequencing in order to determine somatic or germline mutations (SNV), copy number variations (CNV) and small insertions/deletions. But the genomic stratification is only a part of the molecular analysis that is necessary to improve therapy recommendations and patient outcome. It becomes more and more evident that also non genomic factors are contributing to tumour initiation, promotion and progression. Therefore, we are also carrying out transcriptomic profiling to study long and small RNAs in patient tissue and serum but also in cell culture and mouse models (RNA-Seq, small RNA-Seq). But also dysregulated epigenetic modifications revealed to play an important role in tumours. Therefore, epigenomic approaches are routinely applied to investigate transcriptional signatures and pathways influenced by specific treatments, or cancer-relevant transcription factors, and to compare tumor to normal tissue (ChIP-Seq and ATAC-Seq, respectively).
The WG Genomics is also involved in several projects promoted by the *Alleanza Contro il Cancro* (Alliance Against Cancer, ACC) network, particularly in the context of the WG Lung, Breast, and Sarcoma. The institute was one of the very first to run the Lung Chip developed by ACC Genomics, aimed at assigning novel target therapies through expanded DNA profiling. In the WG ACC-Immunotherapy, that aspires to find novel biomarkers for the response to immunotherapy in non-small-cell lung cancer, the WG Genomics is one of the main centers for RNA sequencing and bioinformatics analysis.

## Clinical Activity

Our patients are both the study subject and the commissioners of better therapy. The NGS group aims at banning empiricism from cancer therapy and resorting to

innovative trial schemes based on molecular knowledge.
Within the activities of the cancer genomics working group, the contribute of the laboratory of molecular diagnostics (LMD), which operates in the department of Pathology, has gained increasing importance. Thanks to the availability of an S5 Thermo Fisher sequencer, the LMD, can provide diagnostic procedures that integrate conventional molecular diagnostics with targeted exome sequence analyses employing gene panels of different complexity. These activities support the diagnostic procedures required for assigning IRE patients to therapeutic protocols employing genomics-based anti-cancer drugs that are either approved by AIFA for routine clinical use or undergoing advanced experimentation in the clinical setting. This has led to a considerable increase in the number of NGS-based diagnostic tests with higher degree of quantitative complexity (number of genes to be analyzed) and qualitative (type of genomic alterations to be identified).
Therefore, in addition to the use of CE-IVD kits, in 2018 new and more complex gene panels were introduced into routine diagnostics allowing to quickly and accurately detect point mutations, small insertions / deletions, copy number variations (CNVs) and specific gene rearrangements. In this way it was possible to identify patients who could benefit from specific treatments already approved by the regulatory authorities, but also to 1) identify specific biological characteristics for diagnostic and prognostic purposes; 2) monitor the response to molecular target therapies and the onset of therapeutic resistance. 3) to identify the molecular alterations necessary for the enrollment of patients in clinical trials; 5) to carry out, for selected and particularly complex clinical cases, molecular analyses for personalized treatments not yet codified in guidelines (essentially in support of the activity of the Molecular Tumor Board IRE).
During the last year, CE-IVD and RUO NGS-panels have been used to diagnose 1140 patients (colorectal, lung, thyroid, gastric carcinomas, brain tumors, sarcoma and melanoma), 820 of whom displayed at least one somatic aberration. Of these, 740 were targetable or potentially targetable. In an effort to expand the clinical benefits of NGS, ongoing research projects include the design of dedicated NGS targeted panels to identify mutation patterns and signatures predictive of response to treatment in triple negative breast carcinoma, lung, colorectal and gastric cancers as well as glioblastoma, and to study somatic mutations affecting DNA repair genes in ovarian and breast tumors.
The Clinical Pathology Unit significantly supports activities for clinical trials, is involved in the development of an Institutional Biobank as a strategic link between clinical and research activities and is focused on the identification and validation of cancer-related molecular targets, the utilization of new technical approaches for tumor diagnosis and prognosis and monitoring in the context of innovative cancer therapies for the best bench-to-bedside clinical research application.
As part of the WG Genomics the unit is involved in genetic testing with NGS technology on the genes associated with the most frequent Hereditary Cancer syndromes (HCS) such as: Lynch syndrome (LS), Hereditary Breast and Ovary Cancer syndrome (HBOC), APC-associated polyposis and MUTYH-associated polyposis (AAP and MAP) and Multiple Endocrine Neoplasia syndrome type 1 and type 2 (MEN1 and MEN2). Included patients, more than 3700 so far, are those admitted to the outpatient's clinics of the hereditary colorectal cancer, hereditary breast and ovary cancer and endocrinology units of our Institution. Moreover, our unit receives DNA samples from other institutions all over the country.
Hereditary Cancer testing allows an in-depth cancer risk assessment for each patient, leading to improvements in health outcomes among carriers and members of their families.
Moreover, as to high-grade serous ovarian cancer (HGSOC), the presence of a deleterious BRCA mutation has been suggested to be a prognostic and predictive factor. Ovarian cancers arising in patients with germline BRCA mutations show increased and sustained susceptibility to platinum chemotherapy, with improved survival compared with sporadic ovarian cancers. Furthermore, studies with poly ADP ribose polymerase (PARP) inhibitors in BRCAmut recurrent ovarian cancer (ROC) patients have demonstrated clinical efficacy with improvements in progression-free survival (PFS), leading to their approval in the US and Europe.
In Non Small Cell Lung Carcinoma (NSCLC) liquid biopsy allows to identify patients whose tumors have specific EGFR mutations, thus making them eligible for EGFR-targeted therapies (e.g. erlotinib, afatinib). Liquid biopsy in these patients is also a valuable tool for the monitoring of disease progression and for the detection of mechanisms of resistance to EGFR-targeted therapies, e.g. EGFR T790M mutation. The early detection of T790M mutation is of great clinical value for switching to 3rd generation therapies (e.g. osimertinib - Tagrisso). The latter has been also recently approved by FDA as first-line treatment for EGFR+ NSCLC patients. Since March 2017 we have assigned an EGFR mutational status in 234 different blood samples from 139 patients, providing a minimally invasive tool to monitor and assign target therapy in NSCLC patients.

# NCR TRANSLATIONAL GROUP

Recent studies have revealed that about 90% of the eukaryotic genome is transcribed. Interestingly, only 1–2% of these transcripts encode for proteins, the majority are transcribed as non-coding RNAs (ncRNAs).

During the past few years ncRNAs, previously thought as transcriptional junk, have become a research goldmine. The functions of ncRNAs are likely diverse, and their underlying mechanisms are just beginning to be understood. For sure ncRNAs are important regulatory molecules of many cellular processes in development and diseases, among which cancer, and have been identified as the key gene expression regulators.

The NCR group is mainly focused on three classes of ncRNA: microRNAs (miRNAs) long-non-coding RNAs (lncRNAs) and circular RNAs (circRNAs).

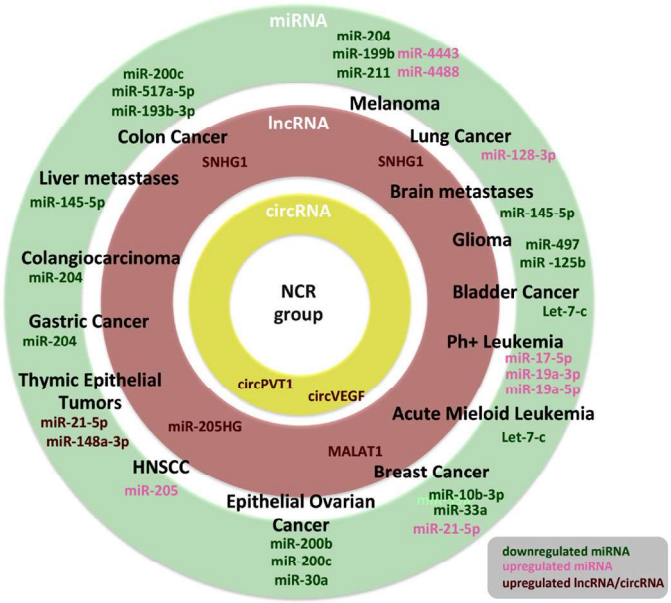
MiRNAs are small single-stranded molecules (20–24 nt) that derive from transcripts forming distinctive hairpin structures. The hairpin is processed into mature miRNA by two endonucleases, Drosha and Dicer, and forms the RNA induced silencing complex (RISC). The miRNAs will pair with complementary sequences on target mRNAs transcripts through the 3'UTR, leading to gene silencing of the target.

LncRNAs are non-protein coding transcripts >200 nt in length that have been shown to control every level of the multi-level regulated gene expression pathway. For example, they are implicated in post-transcriptional gene regulation through controlling protein synthesis, RNA maturation and transport, the amount of available functional miRNAs, and in transcriptional gene silencing through regulating the chromatin structure.

CircRNAs are a large class of endogenous RNAs, formed by exon skipping or back-splicing events as covalently closed loops, which are expressed abundantly in mammalian cells. CircRNAs can regulate transcription, RNA splicing and, as for lncRNAs, they can function as miRNA sponges.

The studies conducted by the NCR group are based on two principal approaches: a) one of more basic research approach that is intent to discovery the molecular mechanisms at the basis of miRNAs, lnRNAs and circRNAs deregulation and functions in cancer cells; b) the other one is based on translational research approaches aimed to identify, by genome-wide screening, miRNA, lncRNAs and circRNAs deregulated in tissue and liquid biopsies derived from cancer patients of our Institute, in way to discovery novel molecular biomarkers with clinical-prognostic impact and to develop innovative and more effective therapeutic approaches.

The research activity of NCR group, conducted in the last year, allowed to the identification of an intricate network between the three different classes of non-coding factors in several cancer types (Figure 1). The obtained results lead to a deeper understanding of the molecular pathways involved in tumorigenesis and represent the basis for the identification of novel powerful biomarkers.



# THE JOINT IRE-ISG MELANOMA TRANSLATIONAL GROUP

This Translational Group was initially conceived at the end of year 2017 together with the former Scientific Director of the San Gallicano Dermatological Institute Dr. Mauro Picardo and is continuing in collaboration with the present Scientific Director Dr. Aldo Morrone. Goal of the group is to establish a strategic alliance between our two Institutes in our fight of malignant melanoma, through sharing ideas, resources and expertise. Among the primary objectives of the group is the creation of a joint repository of tumor biopsies, re-biopsies and blood samples (liquid biopsies) collected longitudinally from melanoma

from initial diagnosis to disease relapse to therapy according to general principles outlined in the attached *diagram*. These samples will constitute an outstanding resource for *research* Translational studies directed to understand mechanisms at the basis of tumor progression, metastasis and *drug sensitivity or* resistance. In this context the groups also aims at the *desing and* application to joint research *projects and clinical* trials.

During the first year of activity the joint translational group has recruited over 20 patients into e serial, longitudinal sample collection program (see figure). In this real-life setting, the group aims at integrating radiomics (e.g. info extracted from medical imaging), post-genomics and liquid biopsy (circulating DNA and microRNAs) to anticipate relapse and disease progression. However, besides developing new biomarkers, the most important purpose of this group is to focus a multidisciplinary effort on melanoma patients and build a professional team comprising dermatologists, surgeons, clinical oncologists, dermo-pahologists, biotechnologists and immunologists working in close collaboration in a real-life setting. This will hopefully generate increased awareness of disease complexity and may help to explore therapeutic opportunities, funneling patients into enhanced diagnostic and therapeutic routines.

# RARE TUMORS TRANSLATIONAL GROUP

Tumors are for definition considered rare when incidence is less than 6 cases in 100.000 people per year, but altogether rare tumors account for approximately 25% of all cancers (approximately 18% solid rare cancers and 7% rare haematological diseases). Rare tumors are almost invariably associated with 5-year overall survival rates globally less than 50% as compared to 65% in common cancers. This overall worse prognosis is substantially linked to the limited medical expertise and the lack of evidence-based treatment guidelines that ultimately result from low frequency with scanty tissue banks and registries, few clinical trials, misdiagnosis (both clinical and pathological) and delayed diagnosis, all of which are serious obstacles to clinical decisions.

The estimates of incidence, prevalence and survival of rare cancers in Italy are based on the pool of the AIRTUM cancer registries (years 2000-2010) and it was estimated that about 360.000 people were diagnosed with new cancers in Italy in 2011, with an annual incidence rate of about 200 rare cancers per 100,000 corresponding to about 89,0000 new diagnoses annually.

With a yearly admittance of 1,000 new cases and 3,000 total patients being followed per year, IRCCS Regina Elena represents one recognized center for the diagnosis and treatment of rare solid tumors.

Over the past 10 years, IFO played an active role in the collaborative efforts of the national network on rare tumors (Rete Tumori Rari, RTR). Since 2016 IFO are involved in EURACAN (European network for Rare adult solid Cancer) and have become a European Referral Center for eight rare tumors (soft tissue, viscerae and bone sarcomas, rare neoplasm of the male genital organs, and of the urinary tract, neuroendocrine tumours, rare neoplasm if the digestive tract, rare neoplasm of endocrine organs, rare neoplasm of the thorax, rare neoplasm of the skin and eye melanoma, rare neoplasm of the brain and spinal cords). Main objectives of EURACAN are to improve the quality of care of all european patients affected with rare cancers enabling a major improvement in the access to centres of excellence for diagnosis and treatment and unifying the availability of optimal clinical practices in the EU by centralizing knowledge and experience, medical research, training, and resources. A European Collaborative Platform and a Clinical Patient Management System (CPMS) are actually in development in order to discuss and to share clinical cases of patients with rare tumors all over the european centres of the network.

Our Institute is actively involved in International collaboration and revision of specific guidelines of various type of rare tumors and is engaged in national and international clinical trials. **During the last year IFO, as EURACAN centre, was involved in ARCAGEN, a EORTC-SPECTA (Screening Cancer Patients for Efficient Clinical Trial Access) project to perform a molecular characterization of rare cancers. The collection of retrospective and prospective biological samples is ongoing.**

Clinical cases of rare tumors having access to our institute are discussed in meeting, scheduled on weekly or biweekly basis, by dedicated multidisciplinary disease management teams in order to assure an adequate clinical, radiological and pathological assessment leading to a correct diagnosis and an appropriate treatment inside or outside national or international experimental trials.

A dedicated group of data managers is actively involved in the prospective registration of all case of rare tumors accessing to our Institute on a database including all relevant clinical information and follow up updates. For some rare tumors (for example soft tissue and bone sarcomas) a regular process of institutional biobanking of blood and pathologic specimens is ongoing.

**In the next few months, a desk specifically addressed to patients with rare tumors and diseases will be activated in order to facilitate the access to diagnostic and therapeutic pathways.**

Increasing emphasis is moreover given to the collaboration with basic researchers to identify, as for more common cancers, molecular diagnostic, prognostic or predictive biomarkers and regular translational meetings, under the supervision of our Scientific Direction, are organized on bimonthly basis.Department of Clinical.

# GLIOMA TRANSLATIONAL GROUP

Despite standard multimodality treatment including surgery, radiotherapy and chemotherapy, the prognosis of malignant gliomas remains poor. The median survival in GBM patients is 15 months and the average 5-year survival rate is less than 9.8%, thus justifying the strong need for novel more effective therapies. With an increasing understanding of the heterogeneous molecular genetic/epigenetic background underlying the aggressive biological behavior of malignant gliomas, future therapeutic improvements for this devastating disease may stem from individualized profiling of GBM and the application of personalized medicine principles for targeted combination therapies. Successful biomaterial collection is a key requirement for the application of contemporary methodologies for the validation of candidate prognostic factors, the discovery of new biomarkers, a clinical implementation of precision medicine, and for therapeutic uses (eg, target therapies and immunotherapies). **For this aims, at the end of year 2017, the Regina Elena National Cancer Institute promoted the Glioma Translational Group** through multidisciplinary collaboration between clinicians and researchers**. The primary aim of this group is the creation of a joint repository of tumour tissue and blood samples** developing and maintaining a neuro-oncology biobank. Collaboration with a multidisciplinary team of clinicians, health care team members, as well as patients and their families, is essential in order to obtain informed consent, collect samples under strict standard operating procedures, and accurate clinical annotation. Collection of follow-up and clinical outcomes data is essential, especially for studies of biomarkers of survival or response to treatment.

In the glioma project the translational multidisciplinary group collaborate to collect **longitudinally** biospecimens including tumor tissue and **blood samples during all patients' disease trajectory, from diagnosis to progression. All patients also underwent to magnetic resonance examination for evaluation of morphological and non morphological features. Several studies are ongoing on glioma sequencing analysis with next generation sequencing, microenvironment evaluation and correlations between non-morphological radiological features and tumor molecular data. In the** era of personalized medicine, **translational approach** and the development of dedicated biobanks containing high-quality of biological and clinical data are critical to allow future researches and new treatment strategies in neuro-oncology.

# BREAST UNIT

## Coordinators: Roy De Vita MD

### Mission

To offer an integrated and quality program to guarantee the care of patients with a diagnosis of suspected or ascertained breast cancer in the various phases of diagnostic confirmation and therapy, in order to improve the continuity of care, consistent with the lines guide based on the available evidence and with the most current scientific research lines.
All patients will be offered the same entry possibilities into clinical trials that may be underway at the Institute for each individual case.
The program also aims to:

- improve waiting times for the therapeutic diagnostic process, by setting company standards;
- improve the information and communication aspects with the patient,
- optimize and monitor the quality levels of the care provided, through the identification of process and outcome indicators and the development of a data collection and analysis system.

Moreover the program intends to consolidate the relationships with voluntary associations through systematic participation, scientific dissemination initiatives, with the General Practitioners Association and with the Medical Association of Rome.
The program also implements the systematic data collection for patient monitoring using the EUSOMA software and according with EUSOMA requirements and standards in order to be able to compete at European level.

### Clinical Activities

The program is divided into the following phases:
A) Organization of activities: the assistance model
B) Patient access
C) Diagnostic phase: diagnostic therapeutic evaluation of the multidisciplinary team
D) Therapeutic phase
E) Follow-up
F) Advanced treatment of cancer

### Research Activities

Developing strategies for permanent professional training and information addressed to the citizens are part of the scientific/informative activities of the Breast Unit.

# HPV UNIT

## Coordinators: Luciano Mariani MD and Aldo Venuti MD

### Mission

Main mission is to formalize an organizational model of a "unified and coordinated space" in which originate jointly initiatives related to the topic of HPV. This organizational model is a tool to inform, train and network both patients and health workers involved in HPV-related pathologies, from gynecological area to the skin, comprising ENT, urological and proctologic diseases. Finally, HPV-Unit is organized to deliver HPV vaccines to women and men.

### Clinical Activities

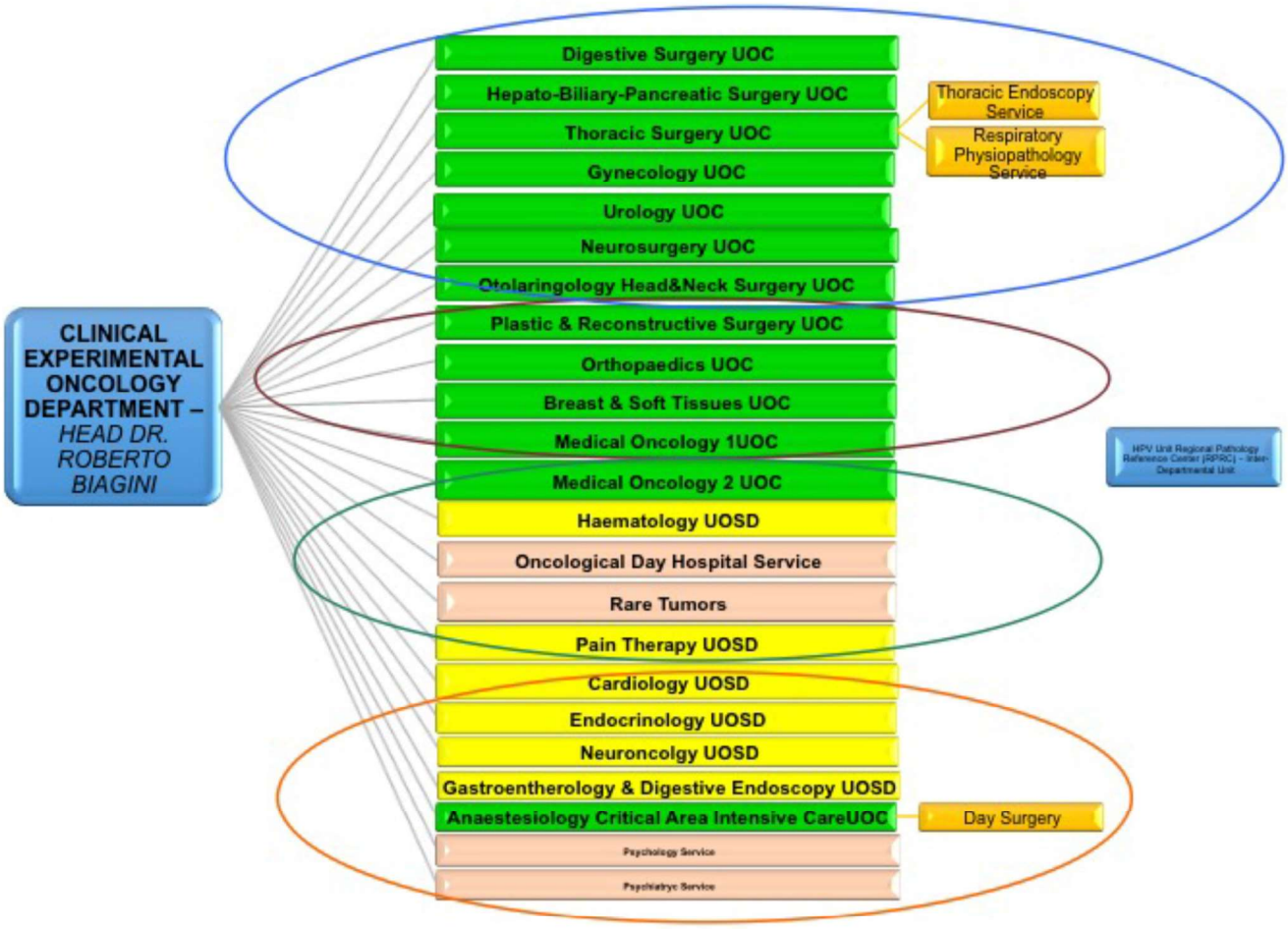
The primary activity was focused on coordinating diagnostic interventions by clinical interpretation of molecular data from assay tests, advice in evaluation of clinical cases by clinical teams, outpatients counseling and advising in preventive actions like individual screening or HPV vaccination. As a specific clinical activity of HPV-Unit, HPV vaccination to women as adjuvant therapy after conization was further improved indicating clinical effectiveness in disease relapse prevention up to 2years with beneficial effect as an adjuvant treatment additional to surgery. A large multicentric study will start in 2019/20 in which HPV-Unit/IRE will be involved as coordinating Center.

### Research Activities

Developing strategies for permanent professional training and information addressed to the citizens are part of the scientific/informative activities of HPV-UNIT. In particular, information about HPV-UNIT (the organizational model) to health workers was presented in many National and International Meetings. HPV-Unit was also involved in translational researches on: *New immunotherapies of HPV-associated cancers* A genetic vaccines is patent pending (Patent is expected in 2019-2020); *Molecular carcinogenesis.* Analysis of available data regarding modulation of TLRs and cytokines in HPV-associated cancer; *HPV molecular epidemiology.* For the first time, HPV-Unit data showed that latent infection by HPV16 is widespread in normal oropharyngeal tissues suggesting that the altered ability to eliminate latent infection could be risk factor for recurrent disease.

# DEPARTMENT OF CLINICAL AND EXPERIMENTAL ONCOLOGY

*Director: Dr. Roberto Biagini*


CLINICAL EXPERIMENTAL ONCOLOGY DEPARTMENT – HEAD DR. ROBERTO BIAGINI
Digestive Surgery UOC
Hepato-Biliary-Pancreatic Surgery UOC
Thoracic Surgery UOC
Gynecology UOC
Urology UOC
Neurosurgery UOC
Otolaringology Head&Neck Surgery UOC
Plastic & Reconstructive Surgery UOC
Orthopaedics UOC
Breast & Soft Tissues UOC
Medical Oncology 1UOC
Medical Oncology 2 UOC
Haematology UOSD
Oncological Day Hospital Service
Rare Tumors
Pain Therapy UOSD
Cardiology UOSD
Endocrinology UOSD
Neuroncolgy UOSD
Gastroentherology & Digestive Endoscopy UOSD
Anaestesiology Critical Area Intensive CareUOC
Psychology Service
Psychiatryc Service
Thoracic Endoscopy Service
Respiratory Physiopathology Service
Day Surgery

# DIGESTIVE SURGERY UNIT

## *Head: Alfredo Garofalo, MD*

## STAFF

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|---|
| **Fabio Carboni, MD** |
| **Orietta Federici, MD** |
| **Mario Valle, MD FACS** |
| **Settimio Zazza, MD** |
| **Manuel Giofrè, MD fellow** |
| **Vincenzo Farina, MD Trainees** |

## *Clinical Activity*

AMAD - Multidisciplinary Outpatient Clinic for the Digestive System, Activity Report 4/10/2016 - 5/12/2017

AMAD was activated the 1st October 2016.The activities are under the direct responsibility of Dr. Garofalo and are carried out by two Medical Managers an Oncologist Surgeon and a Medical Oncologist, who evaluate in a multidisciplinary way all patients affected by Neoplasms of the Digestive Apparatus, especially patients with Colo Rectal Carcinomas, providing initial visits and follow up visits, applying the paths described in the relevant PDTA and reporting to DMT, with the support of a Case Manager and making use of spaces specially created by all the other UOC, UOSD and Services.

In the period 4/10/2016 5/12/2017, AMAD activity can be summarized as follows:

Total visits: 491

First visits: 73

Follow up visits: 418

Of the 73 patients undergoing the First Visit:

10 were Ca metastases and were initiated to front line chemotherapy

6 were anus carcinomas, sent to chemotherapy radiotherapy

11 were sent to exclusive endoscopic treatment or follow up.

The remaining 46 patients were sent to the therapeutic path: PO and then admission for surgery; chemotherapy preoperative radiotherapy and then surgery for rectal cancers that can be recruited for multimodal treatment.

## Research Activity

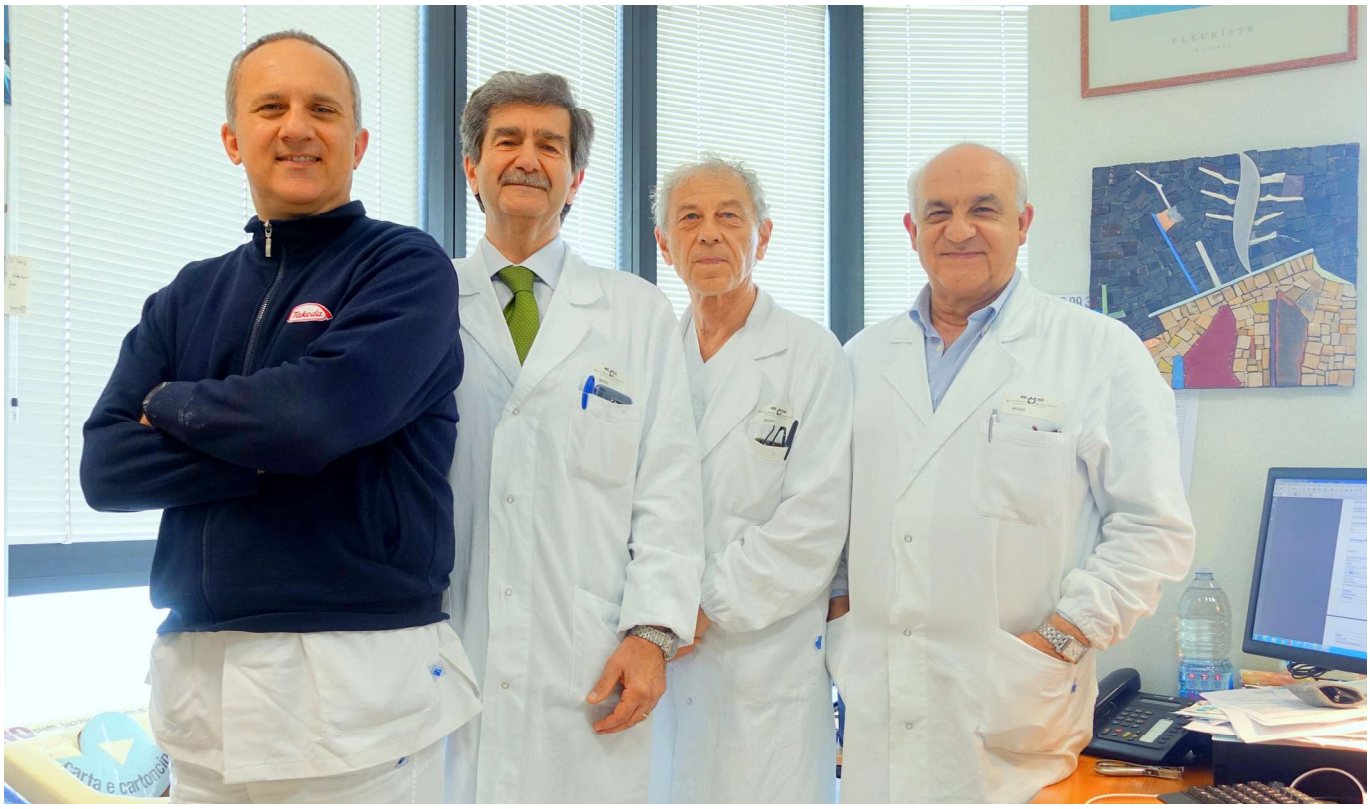
- *Gastric Carcinoma:* The Interdisciplinary Working Group has definitively codified the general integrated treatment strategy of gastric carcinoma. The Translational Research on this topic with the Group of Translational Oncogenomics directed by Dr. Giovani Blandino, gave the following results: Retrospective study with RNA Microarrays: gastric ca samples from patients operated in the Institute in the last four years have been compared to gastric ca samples from different structures in another region: the molecular typing of the two different series gives overlapping bitmaps. Four MiRNAs were identified that appear adjusted down or upregulated towards healthy tissue, and in particular the miRNA 204. A prospective study is still ongoing and patient enrolment is being continued.
- *Peritoneal Carcinosis:* The UOC has become, from experience and case studies, one of the two reference centres for pathology in Italy. A collaboration is underway with the Oncoteam SICO Peritoneal Carcinosis for the establishment of a National Register sponsored by the Italian Society of Oncological Surgery. A national survey on ovarian cancer carcinosis-derived is underway. In the Institute is ongoing: Pilot study of association between expression and heterogeneity of DNA damage markers and clinical outcomes in patients undergoing peritonectomy and hipec for peritoneal carcinosis from ovarian cancer. PI: Dr Mario Valle; Contractor: Dr Manuel Giofrè
- *Minimally Invasive Techniques in Surgical Oncology:* The experts are well aware of the work published by our group on laparoscopic displacement of peritoneal carcinosis and on hyper-thermal antiblastic perfusion of the abdomen in neoplastic axes intractable with the original technique and with mini-invasive access (Cancer Journal 2009, EJSO 2009). The group's experience in advanced minimally invasive surgery in over 15 years of activity also includes colon and rectum resection, wedge resectons of the stomach and small intestine, distal pancreasectomy, splenectomy for haematological diseases, adrenalectomy. PI: Dr. Mario Valle – Dr. Orietta Federici
- *Rectal Cancer:* Screening and Early Diagnosis of anus cancer by high-resolution cytology and anoscopy (HRA). Pilot study in collaboration between this UOC and the UOC of Infectious Dermatology of the San Gallicano Institute. PI: Dr Settimio Zazza; Dr Manuel Giofrè
- *Colorectal Tumors and Rare tumors of the Colon:* Patients are being recruited to test the new device ULTRAPLACAD (ULTRAsensitive PLAsmonic devices for early CAncer Diagnosis) within the framework of the European project (funds 15/07/R/33) headed by Dr Giacomini (Oncogenomics Laboratory). From the preliminary results, the possibility of identifying circulating neoplastic DNA, which could be of great use in the early diagnosis of primary tumors and relapses after treatment and in the indications for fron line chemotherapy, appears very promising. PI: Dr Fabio Carboni; Dr Settimio Zazza; Dr Ilaria Ciangola.
- *Retro Peritoneal Sarcoma:* This topic is discussed within sarcoma DMT activity. PI: Dr. Garofalo

## Publications

1. Carboni F, Federici O, Giofre M, Diodoro M, Valle M. Recurrence of Gallbladder Carcinoma 12 Years After Laparoscopic Cholecystectomy. Clin.Res.Hepatol.Gastroenterol. 2018 Aug 30. [Epub ahead of print]
2. Carboni F, Marandino F, Valle M. Late Isolated Subcutaneous Metastasis from Colon Cancer. ANZ J.Surg. 2018 Oct 22;
3. Carboni F, Valle M, Federici O, Covello R, Garofalo A. Giant Primary Retroperitoneal Dedifferentiated Liposarcoma. J.Gastrointest.Surg. 2018 Jun 29;
4. Pizzuti L, Sergi D, Mandoj C, Antoniani B, Sperati F, Chirico A, Di Lauro L, Valle M, Garofalo A, Vizza E, Corrado G, Tomao F, Rinaldi M, Carpano S, Maugeri-Sacca M, Conti L, Digiesi G, Marchetti P, De Maria R, Giordano A, Barba M, Carosi MA, Vici P. GLUT 1 Receptor Expression and Circulating Levels of Fasting Glucose in High Grade Serous Ovarian Cancer. J.Cell.Physiol. 2018 233(2): 1396a

# HEPATO BILIARY PANCREATIC SURGERY UNIT

## *Head: Gian Luca Grazi, MD, PhD*



## STAFF

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|---|
| **Marco D'Annibale, MD** |
| **Giovanna Grazioli, Chief Nurse** |
| **Andrea Oddi, MD** |
| **Pasquale Perri, MD** |

## *Mission*

To increase the knowledge for hepatobiliarypancreatic diseases surgically treatable. To treat, to propose innovation in the evaluation and in the cure and to study neoplastic diseases of the liver, pancreas and biliary tree. To evaluate the application of newly proposed surgical techniques, such as laparoscopy and robotics. To improve the postoperative approach of the patients with specific protocols of enhanced recovery after surgery
To offer surgical treatment for neoplastic colorectal diseases in a multidisciplinary setting. To define specific paths, from first suspected diagnosis to the appropriate treatment. To establish a stable network for referral and management of patients with hepatobiliary, pancreatic and colorectal tumors, in the view of the Regina Elena National Cancer Institute acting as a tertiary referring center for patients carrying such neoplasms.

## *Clinical Activity*

This is a General Surgery Unit with the main task of treating diseases of the liver, pancreas and o biliary tract. The vast majority of these surgical procedures are performed for malignant diseases, but also complex operations needed for benign diseases are carried out. Liver metastases from colorectal cancer are the condition for which the larger portion of the surgical procedures are performed. The second most frequent disease is hepatocellular carcinoma, which can arise in cirrhotic and non-cirrhotic patients. The remaining portion of liver resection are performed for cholangiocarcinomas, both in intrahepatic and in perihilar locations. The Unit is among the four of the Lazio Region Health System which constantly perform more than 50 surgical procedures for primary liver tumor each year.

There are a consistent number of procedures performed for pancreatic cancers, either for pancreas head or tail. Furthermore, the unit provides treatment for patients with colorectal neoplastic diseases. A multimodal approach for rectal cancers is usually offered to the patients.
A mini-invasive surgical program based on the laparoscopic and on the robotic techniques is fully active for hepatobiliary, pancreatic and colorectal procedures.
The average value of the DRG's produced by the Unit is 2.60.

## Research activity

This Unit cooperates with the Cancer Genome Atlas (TCGA), a collaboration between the National Cancer Institute (NCI) and National Human Genome Research Institute (NHGRI), that has generated comprehensive, multi-dimensional maps of the key genomic changes in 33 types of cancer and, in particular, in cholangiocarcinomas. The Cancer Genome Atlas (TCGA) is a comprehensive and coordinated effort to accelerate the understanding of the molecular basis of cancer through the application of genome analysis technologies, including large-scale genome sequencing.
The Units collaborates with the following national or international registries:

- **LiverGroup.org** a collaborative of international liver surgeons to study the outcomes of liver surgery
- **Euro-Cholangio-Net** The European Cholangiocarcinoma Network
- **I Go MILS** prospective national database of mini-invasive liver resections
- **IGOMIPS** Italian registry of mini-invasive pancreatic surgery
- **HeRCOLEStudy Group** Hepatocarcinoma Recurrence on the Liver Study Group

## Publications


1. Mancini R, Pattaro G, Diodoro MG, Sperduti I, Garufi C, Stigliano V, Perri P, Grazi GL, Cosimelli M. Tumor Regression Grade After Neoadjuvant Chemoradiation and Surgery for Low Rectal Cancer Evaluated by Multiple Correspondence Analysis: Ten Years as Minimum Follow-up. Clin Colorectal Cancer. 2018 Mar;17(1):e13-e19. doi: 10.1016/j.clcc.2017.06.004.

2. Nigri G, Petrucciani N, Pinna AD, Ravaioli M, Jovine E, Minni F, Grazi GL, Chirletti P, Balzano G, Ferla F, De Carlis L, Tisone G, Napoli N, Boggi U, Ramacciato G. Evolution of pancreatectomy with en bloc venous resection for pancreatic cancer in Italy. Retrospective cohort study on 425 cases in 10 pancreatic referral units. Int J Surg. 2018 Jul;55:103-109. doi:10.1016/j.ijsu.2018.05.025.

3. Schinzari V, Timperi E, Pecora G, Palmucci F, Gallerano D, Grimaldi A, Covino DA, Guglielmo N, Melandro F, Manzi E, Sagnotta A, Lancellotti F, Sacco L, Chirletti P, Grazi GL, Rossi M, Barnaba V. Wnt3a/β-Catenin Signaling Conditions Differentiation of Partially Exhausted T-effector Cells in Human Cancers. Cancer Immunol Res. 2018 Aug;6(8):941-952. doi: 10.1158/2326-6066.CIR-17-0712.

4. Ruzzenente A, Bagante F, Bertuzzo F, Aldrighetti L, Campagnaro T, Ercolani G, Conci S, Giuliante F, Dore A, Ferrero A, Torzilli G, Grazi GL, Ratti F, Cucchetti A, De Rose AM, Russolillo N, Cimino M, Perri P, Guglielmi A, Iacono C. Liver Resection for Neuroendocrine Tumor Liver Metastases Within Milan Criteria for Liver Transplantation. J Gastrointest Surg. 2019 Jan;23(1):93-100. doi:10.1007/s11605-018-3973-9.

5. Di Leo L, Vegliante R, Ciccarone F, Salvatori I, Scimeca M, Bonanno E, Sagnotta A, Grazi GL, Aquilano K, Ciriolo MR. Forcing ATGL expression in hepatocarcinoma cells imposes glycolytic rewiring through PPAR-α/p300-mediated acetylation of p53. Oncogene. 2019 Mar;38(11):1860-1875. doi:10.1038/s41388-018-0545-0.

6. Torregiani G, Claroni C, Covotta M, Naccarato A, Canfora M, Giannarelli D, Grazi GL, Tribuzi S, Forastiere E. Impact of a goal-directed fluid therapy on length of hospital stay and costs of hepatobiliarypancreatic surgery: a prospective observational study. J Comp Eff Res. 2018 Dec;7(12):1171-1179. doi: 10.2217/cer-2018-0041.

7. Papers produced by the Cancer Genome Atlas Research Network

8. Ellrott K, Bailey MH, Saksena G, Covington KR, Kandoth C, Stewart C, Hess J, Ma S, Chiotti KE, McLellan

M, Sofia HJ, Hutter C, Getz G, Wheeler D, Ding L; MC3 Working Group; Cancer Genome Atlas Research Scalable Open Science Approach for Mutation Calling of Tumor Exomes Using Multiple Genomic Pipelines. Cell Syst. 2018 Mar 28;6(3):271-281.e7. doi: 10.1016/j.cels.2018.03.002.

9. Schaub FX, Dhankani V, Berger AC, Trivedi M, Richardson AB, Shaw R, Zhao W, Zhang X, Ventura A, Liu Y, Ayer DE, Hurlin PJ, Cherniack AD, Eisenman RN, Bernard B, Grandori C; Cancer Genome Atlas Network. Pan-cancer Alterations of the MYC Oncogene and Its Proximal Network across the Cancer Genome Atlas. Cell Syst. 2018 Mar 28;6(3):282-300.e2. doi: 10.1016/j.cels.2018.03.003.

10. Way GP, Sanchez-Vega F, La K, Armenia J, Chatila WK, Luna A, Sander C, Cherniack AD, Mina M, Ciriello G, Schultz N; Cancer Genome Atlas Research Network, Sanchez Y, Greene CS. Machine Learning Detects Pan-cancer Ras Pathway Activation in The Cancer Genome Atlas. Cell Rep. 2018 Apr 3;23(1):172-180.e3. doi: 10.1016/j.celrep.2018.03.046.

11. Saltz J, Gupta R, Hou L, Kurc T, Singh P, Nguyen V, Samaras D, Shroyer KR, Zhao T, Batiste R, Van Arnam J; Cancer Genome Atlas Research Network, Shmulevich I, Rao AUK, Lazar AJ, Sharma A, Thorsson V. Spatial Organization and Molecular Correlation of Tumor-Infiltrating Lymphocytes Using Deep Learning on Pathology Images. Cell Rep. 2018 Apr 3;23(1):181-193.e7. doi: 10.1016/j.celrep.2018.03.086.

12. Campbell JD, Yau C, Bowlby R, Liu Y, Brennan K, Fan H, Taylor AM, Wang C, Walter V, Akbani R, Byers LA, Creighton CJ, Coarfa C, Shih J, Cherniack AD, Gevaert O, Prunello M, Shen H, Anur P, Chen J, Cheng H, Hayes DN, Bullman S, Pedamallu CS, Ojesina AI, Sadeghi S, Mungall KL, Robertson AG, Benz C, Schultz A, Kanchi RS, Gay CM, Hegde A, Diao L, Wang J, Ma W, Sumazin P, Chiu HS, Chen TW, Gunaratne P, Donehower L, Rader JS, Zuna R, Al-Ahmadie H, Lazar AJ, Flores ER, Tsai KY, Zhou JH, Rustgi AK, Drill E, Shen R, Wong CK; Cancer Genome Atlas Research Network, Stuart JM, Laird PW, Hoadley KA, Weinstein JN, Peto M, Pickering CR, Chen Z, Van Waes C. Genomic, Pathway Network, and Immunologic Features Distinguishing Squamous Carcinomas. Cell Rep. 2018 Apr 3;23(1):194-212.e6. doi: 10.1016/j.celrep.2018.03.063.

13. Ge Z, Leighton JS, Wang Y, Peng X, Chen Z, Chen H, Sun Y, Yao F, Li J, Zhang H, Liu J, Shriver CD, Hu H; Cancer Genome Atlas Research Network, Piwnica-Worms H, Ma L, Liang H. Integrated Genomic Analysis of the Ubiquitin Pathway across Cancer Types. Cell Rep. 2018 Apr 3;23(1):213-226.e3. doi:10.1016/j.celrep.2018.03.047.

14. Gao Q, Liang WW, Foltz SM, Mutharasu G, Jayasinghe RG, Cao S, Liao WW, Reynolds SM, Wyczalkowski MA, Yao L, Yu L, Sun SQ; Fusion Analysis Working Group; Cancer Genome Atlas Research Network, Chen K, Lazar AJ, Fields RC, Wendl MC, Van Tine BA, Vij R, Chen F, Nykter M, Shmulevich I, Ding L. Driver Fusions and Their Implications in the Development and Treatment of Human Cancers. Cell Rep. 2018 Apr 3;23(1):227-238.e3. doi: 10.1016/j.celrep.2018.03.050.

15. Knijnenburg TA, Wang L, Zimmermann MT, Chambwe N, Gao GF, Cherniack AD, Fan H, Shen H, Way GP, Greene CS, Liu Y, Akbani R, Feng B, Donehower LA, Miller C, Shen Y, Karimi M, Chen H, Kim P, Jia P, Shinbrot E, Zhang S, Liu J, Hu H, Bailey MH, Yau C, Wolf D, Zhao Z, Weinstein JN, Li L, Ding L, Mills GB, Laird PW, Wheeler DA, Shmulevich I; Cancer Genome Atlas Research Network, Monnat RJ Jr, Xiao Y, Wang C. Genomic and Molecular Landscape of DNA Damage Repair Deficiency across The Cancer Genome Atlas. Cell Rep. 2018 Apr 3;23(1):239-254.e6. doi:10.1016/j.celrep.2018.03.076.

16. Peng X, Chen Z, Farshidfar F, Xu X, Lorenzi PL, Wang Y, Cheng F, Tan L, Mojumdar K, Du D, Ge Z, Li J, Thomas GV, Birsoy K, Liu L, Zhang H, Zhao Z, Marchand C, Weinstein JN; Cancer Genome Atlas Research Network, Bathe OF, Liang H. Molecular Characterization and Clinical Relevance of Metabolic Expression Subtypes in Human Cancers. Cell Rep. 2018 Apr 3;23(1):255-269.e4. doi:10.1016/j.celrep.2018.03.077.

17. Jayasinghe RG, Cao S, Gao Q, Wendl MC, Vo NS, Reynolds SM, Zhao Y, Climente-González H, Chai S, Wang F, Varghese R, Huang M, Liang WW, Wyczalkowski MA, Sengupta S, Li Z, Payne SH, Fenyö D, Miner JH, Walter MJ; Cancer Genome Atlas Research Network, Vincent B, Eyras E, Chen K, Shmulevich I, Chen F, Ding L. Systematic Analysis of Splice-Site-Creating Mutations in Cancer. Cell Rep. 2018 Apr 3;23(1):270-281.e3. doi: 10.1016/j.celrep.2018.03.052.

18. Seiler M, Peng S, Agrawal AA, Palacino J, Teng T, Zhu P, Smith PG; Cancer Genome Atlas Research Network, Buonamici S, Yu L. Somatic Mutational Landscape of Splicing Factor Genes and Their Functional Consequences across 33 Cancer Types. Cell Rep. 2018 Apr 3;23(1):282-296.e4. doi: 10.1016/j.celrep.2018.01.088.

19. Chiu HS, Somvanshi S, Patel E, Chen TW, Singh VP, Zorman B, Patil SL, Pan Y, Chatterjee SS; Cancer Genome Atlas Research Network, Sood AK, Gunaratne PH, Sumazin P. Pan-Cancer Analysis of lncRNA Regulation Supports Their Targeting of Cancer Genes in Each Tumor Context. Cell Rep. 2018 Apr 3;23(1):297-312.e12. doi:10.1016/j.celrep.2018.03.064.

20. Ricketts CJ, De Cubas AA, Fan H, Smith CC, Lang M, Reznik E, Bowlby R, Gibb EA, Akbani R, Beroukhim R, Bottaro DP, Choueiri TK, Gibbs RA, Godwin AK, Haake S, Hakimi AA, Henske EP, Hsieh JJ, Ho TH, Kanchi RS, Krishnan B, Kwiatkowski DJ, Lui W, Merino MJ, Mills GB, Myers J, Nickerson ML, Reuter VE, Schmidt LS, Shelley CS, Shen H, Shuch B, Signoretti S, Srinivasan R, Tamboli P, Thomas G, Vincent BG, Vocke CD, Wheeler DA, Yang L, Kim WY, Robertson AG; Cancer Genome Atlas Research Network, Spellman PT, Rathmell WK, Linehan WM. The Cancer Genome Atlas Comprehensive Molecular Characterization of Renal Cell Carcinoma. Cell Rep. 2018 Apr 3;23(1):313-326.e5. doi: 10.1016/j.celrep.2018.03.075.

21. Taylor AM, Shih J, Ha G, Gao GF, Zhang X, Berger AC, Schumacher SE, Wang C, Hu H, Liu J, Lazar AJ; Cancer Genome Atlas Research Network, Cherniack AD, Beroukhim R, Meyerson M. Genomic and Functional Approaches to Understanding Cancer Aneuploidy. Cancer Cell. 2018 Apr 9;33(4):676-689.e3. doi: 10.1016/j.ccell.2018.03.007.

22. Berger AC, Korkut A, Kanchi RS, Hegde AM, Lenoir W, Liu W, Liu Y, Fan H, Shen H, Ravikumar V, Rao A, Schultz A, Li X, Sumazin P, Williams C, Mestdagh P, Gunaratne PH, Yau C, Bowlby R, Robertson AG, Tiezzi DG, Wang C, Cherniack AD, Godwin AK, Kuderer NM, Rader JS, Zuna RE, Sood AK, Lazar AJ, Ojesina AI, Adebamowo C, Adebamowo SN, Baggerly KA, Chen TW, Chiu HS, Lefever S, Liu L, MacKenzie K, Orsulic S, Roszik J, Shelley CS, Song Q, Vellano CP, Wentzensen N; Cancer Genome Atlas Research Network, Weinstein JN, Mills GB, Levine DA, Akbani R. A Comprehensive Pan-Cancer Molecular Study of Gynecologic and Breast Cancers. Cancer Cell. 2018 Apr 9;33(4):690-705.e9. doi: 10.1016/j.ccell.2018.03.014.

23. Wang Z, Yang B, Zhang M, Guo W, Wu Z, Wang Y, Jia L, Li S; Cancer Genome Atlas Research Network, Xie W, Yang D. lncRNA Epigenetic Landscape Analysis Identifies EPIC1 as an Oncogenic lncRNA that Interacts with MYC and Promotes Cell-Cycle Progression in Cancer. Cancer Cell. 2018 Apr 9;33(4):706-720.e9. doi:10.1016/j.ccell.2018.03.006.

24. Liu Y, Sethi NS, Hinoue T, Schneider BG, Cherniack AD, Sanchez-Vega F, Seoane JA, Farshidfar F, Bowlby R, Islam M, Kim J, Chatila W, Akbani R, Kanchi RS, Rabkin CS, Willis JE, Wang KK, McCall SJ, Mishra L, Ojesina AI, Bullman S, Pedamallu CS, Lazar AJ, Sakai R; Cancer Genome Atlas Research Network, Thorsson V, Bass AJ, Laird PW. Comparative Molecular Analysis of Gastrointestinal Adenocarcinomas. Cancer Cell. 2018 Apr 9;33(4):721-735.e8. doi:10.1016/j.ccell.2018.03.010.

25. Hoadley KA, Yau C, Hinoue T, Wolf DM, Lazar AJ, Drill E, Shen R, Taylor AM, Cherniack AD, Thorsson V, Akbani R, Bowlby R, Wong CK, Wiznerowicz M, Sanchez-Vega F, Robertson AG, Schneider BG, Lawrence MS, Noushmehr H, Malta TM; Cancer Genome Atlas Network, Stuart JM, Benz CC, Laird PW. Cell-of-Origin Patterns Dominate the Molecular Classification of 10,000 Tumors from 33 Types of Cancer. Cell. 2018 Apr 5;173(2):291-304.e6. doi: 10.1016/j.cell.2018.03.022.

26. Ding L, Bailey MH, Porta-Pardo E, Thorsson V, Colaprico A, Bertrand D, Gibbs DL, Weerasinghe A, Huang KL, Tokheim C, Cortés-Ciriano I, Jayasinghe R, Chen F, Yu L, Sun S, Olsen C, Kim J, Taylor AM, Cherniack AD, Akbani R, Suphavilai C, Nagarajan N, Stuart JM, Mills GB, Wyczalkowski MA, Vincent BG, Hutter CM, Zenklusen JC, Hoadley KA, Wendl MC, Shmulevich L, Lazar AJ, Wheeler DA, Getz G; Cancer Genome Atlas Research Network. Perspective on Oncogenic Processes at the End of the Beginning of Cancer Genomics. Cell. 2018 Apr 5;173(2):305-320.e10. doi: 10.1016/j.cell.2018.03.033.

27. Sanchez-Vega F, Mina M, Armenia J, Chatila WK, Luna A, La KC, Dimitriadoy S, Liu DL, Kantheti HS, Saghafinia S, Chakravarty D, Daian F, Gao Q, Bailey MH, Liang WW, Foltz SM, Shmulevich I, Ding L, Heins Z, Ochoa A, Gross B, Gao J, Zhang H, Kundra R, Kandoth C, Bahceci I, Dervishi L, Dogrusoz U, Zhou W, Shen H, Laird PW, Way GP, Greene CS, Liang H, Xiao Y, Wang C, Iavarone A, Berger AH, Bivona TG, Lazar AJ, Hammer GD, Giordano T, Kwong LN, McArthur G, Huang C, Tward AD, Frederick MJ, McCormick F, Meyerson M; Cancer Genome Atlas Research Network, Van Allen EM, Cherniack AD, Ciriello G, Sander C, Schultz N. Oncogenic Signaling Pathways in The Cancer Genome Atlas. Cell. 2018 Apr 5;173(2):321-337.e10. doi:10.1016/j.cell.2018.03.035.

28. Malta TM, Sokolov A, Gentles AJ, Burzykowski T, Poisson L, Weinstein JN, Kami ska B, Huelsken J, Omberg L, Gevaert O, Colaprico A, Czerwinska P, Mazurek S, Mishra L, Heyn H, Krasnitz A, Godwin AK, Lazar AJ; Cancer Genome Atlas Research Network, Stuart JM, Hoadley KA, Laird PW, Noushmehr H, Wiznerowicz M. Machine Learning Identifies Stemness Features Associated with Oncogenic Dedifferentiation. Cell. 2018 Apr 5;173(2):338-354.e15. doi:10.1016/j.cell.2018.03.034.

29. Huang KL, Mashl RJ, Wu Y, Ritter DI, Wang J, Oh C, Paczkowska M, Reynolds S, Wyczalkowski MA, Oak N, Scott AD, Krassowski M, Cherniack AD, Houlahan KE, Jayasinghe R, Wang LB, Zhou DC, Liu D, Cao S, Kim YW, Koire A, McMichael JF, Hucthagowder V, Kim TB, Hahn A, Wang C, McLellan MD, Al-Mulla F, Johnson KJ; Cancer Genome Atlas Research Network, Lichtarge O, Boutros PC, Raphael B, Lazar AJ, Zhang W, Wendl MC, Govindan R, Jain S, Wheeler D, Kulkarni S, Dipersio JF, Reimand J, Meric-Bernstam F, Chen K, Shmulevich I, Plon SE, Chen F, Ding L. Pathogenic Germline Variants in 10,389 Adult Cancers. Cell. 2018 Apr 5;173(2):355-370.e14. doi: 10.1016/j.cell.2018.03.039.

30. Bailey MH, Tokheim C, Porta-Pardo E, Sengupta S, Bertrand D, Weerasinghe A, Colaprico A, Wendl MC, Kim J, Reardon B, Ng PK, Jeong KJ, Cao S, Wang Z, Gao J, Gao Q, Wang F, Liu EM, Mularoni L, Rubio-Perez C, Nagarajan N, Cortés-Ciriano I, Zhou DC, Liang WW, Hess JM, Yellapantula VD, Tamborero D, Gonzalez-Perez A, Suphavilai C, Ko JY, Khurana E, Park PJ, Van Allen EM, Liang H; MC3 Working Group; Cancer Genome Atlas Research Network, Lawrence MS, Godzik A, Lopez-Bigas N, Stuart J, Wheeler D, Getz G, Chen K, Lazar AJ, Mills GB, Karchin R, Ding L. Comprehensive Characterization of Cancer Driver Genes and Mutations. Cell. 2018 Apr 5;173(2):371-385.e18. doi: 10.1016/j.cell.2018.02.060.

31. Chen H, Li C, Peng X, Zhou Z, Weinstein JN; Cancer Genome Atlas Research Network, Liang H. A Pan-Cancer Analysis of Enhancer Expression in Nearly 9000 Patient Samples. Cell. 2018 Apr 5;173(2):386-399.e12. doi:10.1016/j.cell.2018.03.027.

32. Liu J, Lichtenberg T, Hoadley KA, Poisson LM, Lazar AJ, Cherniack AD, Kovatich AJ, Benz CC, Levine DA, Lee AV, Omberg L, Wolf DM, Shriver CD, Thorsson V; Cancer Genome Atlas Research Network, Hu H. An Integrated TCGA Pan-Cancer Clinical Data Resource to Drive High-Quality Survival Outcome Analytics. Cell.2018 Apr 5;173(2):400-416.e11. doi: 10.1016/j.cell.2018.02.052.

33. Kahles A, Lehmann KV, Toussaint NC, Hüser M, Stark SG, Sachsenberg T, Stegle O, Kohlbacher O, Sander C; Cancer Genome Atlas Research Network, Rätsch G. Comprehensive Analysis of Alternative Splicing Across Tumors from 8,705 Patients. Cancer Cell. 2018 Aug 13;34(2):211-224.e6. doi: 10.1016/j.ccell.2018.07.001.

34. Korkut A, Zaidi S, Kanchi RS, Rao S, Gough NR, Schultz A, Li X, Lorenzi PL, Berger AC, Robertson G, Kwong LN, Datto M, Roszik J, Ling S, Ravikumar V, Manyam G, Rao A, Shelley S, Liu Y, Ju Z, Hansel D, de Velasco G, Pennathur A, Andersen JB, O'Rourke CJ, Ohshiro K, Jogunoori W, Nguyen BN, Li S, Osmanbeyoglu HU, Ajani JA, Mani SA, Houseman A, Wiznerowicz M, Chen J, Gu S, Ma W, Zhang J, Tong P, Cherniack AD, Deng C, Resar L; Cancer Genome Atlas Research Network, Weinstein JN, Mishra L, Akbani R. A Pan-Cancer Analysis Reveals High-Frequency Genetic Alterations in Mediators of Signaling by the TGF-β Superfamily. Cell Syst. 2018 Oct 24;7(4):422-437.e7. doi: 10.1016/j.cels.2018.08.010.

35. Wang Y, Xu X, Maglic D, Dill MT, Mojumdar K, Ng PK, Jeong KJ, Tsang YH, Moreno D, Bhavana VH, Peng X, Ge Z, Chen H, Li J, Chen Z, Zhang H, Han L, Du D, Creighton CJ, Mills GB; Cancer Genome Atlas Research Network, Camargo F, Liang H. Comprehensive Molecular Characterization of the Hippo Signaling Pathway in Cancer. Cell Rep. 2018 Oct 30;25(5):1304-1317.e5. doi:10.1016/j.celrep.2018.10.001.

# THORACIC SURGERY UNIT

*Head: Francesco Facciolo, MD*

## STAFF:

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|---|---|
| Sandro Carlini, MD | Antonio Ricciuti, Nurse |
| Edoardo Mercadante, MD | Alessio Calabretta, Nurse |
| Gabriele Alessandrini, MD | Emanuele Egidi, Nurse |
| Virna Cerasoli, MD | Vincenzo Lodico, Nurse |
| Felicita Corzani, MD | Paola Giordano, Nurse |
| Daniele Forcella, MD | Chiara Spadavecchia, Nurse |
| Enrico Melis, MD | Massimiliano De Vecchis, Nurse |
| Nicoletta De Bello, Nurse | Adriana Ciacci, Nurse |
| Claudia Ramacci, Case Manager | Raffaele Tomasone, Nurse |
| Valeria Simonetti, Nurse | Mirko Santoli, Healthcare Assistant |

## Mission

Surgical management of primary and secondary malignancies of the thorax (lung, mediastinum, pleura, chest wall, thoracic inlet, esophagus, trachea) with radical / palliative / diagnostic intent.

## Clinical Activity

Mainly focused on Locally Advanced Lung Cancer, Malignant Pleural Mesothelioma, Thymic Malignancies, Primary Tumors of the Chest Wall. Routinary employment of minimally-invasive techniques for major operations – Robot-Assisted Thoracoscopic Surgery (RATS); Video-Assisted Thoracoscopic Surgery (VATS) – and minimally-invasive diagnostic techniques – Fiber-Optic Bronchoscopy, EUS and EBUS. Implementation of protocols for early extubation after surgery, post-operative fast-track rehab, management of post-operative pain. Active cooperation with basic science departments for translational research.

## Research Activity

Collection and banking of tumoral and healthy tissue from lung cancers, thymomas, mesotheliomas for study of tumor's microenvironment and growth factors, cancer stem cells isolation and colture, identification of genomic signatures (miRNAs) and molecular prognostic factors; collection and banking of blood / serum / plasma samples from patients with malignancies of lung, thymus, pleura as circulating counterparts of tissutal samples for identification of peripheral diagnostic / prognostic markers. Active collaboration with ITMIG.

## Publications


1. Bailey MH, Tokheim C, Porta-Pardo E, Sengupta S, Bertrand D, Weerasinghe A, Colaprico A, Wendl MC, Kim J, Reardon B, Ng PK, Jeong KJ, Cao S, Wang Z, Gao J, Gao Q, Wang F, Liu EM, Mularoni L, Rubio-Perez C, Nagarajan N, Cortes-Ciriano I, Zhou DC, Liang WW, Hess JM, Yellapantula VD, Tamborero D, Gonzalez-Perez A, Suphavilai C, Ko JY, Khurana E, Park PJ, Van Allen EM, Liang H, MC3 Working Group, Cancer Genome Atlas Research Network, Lawrence MS, Godzik A, Lopez-Bigas N, Stuart J, Wheeler D, Getz G, Chen K, Lazar AJ, Mills GB, Karchin R, Ding L, Facciolo F(c.). Comprehensive Characterization of Cancer Driver Genes and Mutations. Cell. 2018 Apr 5; 173(2): 371a

2. Berger AC, Korkut A, Kanchi RS, Hegde AM, Lenoir W, Liu W, Liu Y, Fan H, Shen H, Ravikumar V, Rao A, Schultz A, Li X, Sumazin P, Williams C, Mestdagh P, Gunaratne PH, Yau C, Bowlby R, Robertson AG, Tiezzi DG, Wang C, Cherniack AD, Godwin AK, Kuderer NM, Rader JS, Zuna RE, Sood AK, Lazar AJ, Ojesina AI, Adebamowo C, Adebamowo SN, Baggerly KA, Chen TW, Chiu HS, Lefever S, Liu L, MacKenzie K, Orsulic S, Roszik J, Shelley CS, Song Q, Vellano CP, Wentzensen N, Cancer Genome Atlas Research Network, Weinstein JN, Mills GB, Levine DA, Akbani R. Facciolo F(c.) A Comprehensive Pan-Cancer Molecular Study of Gynecologic and Breast Cancers. Cancer.Cell. 2018 Apr 9; 33(4): 690a

3. Calzetta L, Matera MG, Facciolo F, Cazzola M, Rogliani P. Beclomethasone Dipropionate and Formoterol Fumarate Synergistically Interact in Hyperresponsive Medium Bronchi and Small Airways. Respir.Res. 2018 Apr 12; 19(1): 65a

4. Calzetta L, Rogliani P, Facciolo F, Rinaldi B, Cazzola M, Matera MG. N-Acetylcysteine Protects Human Bronchi by Modulating the Release of Neurokinin A in an Ex Vivo Model of COPD Exacerbation. Biomed.Pharmacother. 2018 Apr 7; 103: 1a

5. Campbell JD, Yau C, Bowlby R, Liu Y, Brennan K, Fan H, Taylor AM, Wang C, Walter V, Akbani R, Byers LA, Creighton CJ, Coarfa C, Shih J, Cherniack AD, Gevaert O, Prunello M, Shen H, Anur P, Chen J, Cheng H, Hayes DN, Bullman S, Pedamallu CS, Ojesina AI, Sadeghi S, Mungall KL, Robertson AG, Benz C, Schultz A, Kanchi RS, Gay CM, Hegde A, Diao L, Wang J, Ma W, Sumazin P, Chiu HS, Chen TW, Gunaratne P, Donehower L, Rader JS, Zuna R, Al-Ahmadie H, Lazar AJ, Flores ER, Tsai KY, Zhou JH, Rustgi AK, Drill E, Shen R, Wong CK, Cancer Genome Atlas Research Network, Stuart JM, Laird PW, Hoadley KA, Weinstein JN, Peto M, Pickering CR, Chen Z, Van Waes C. Facciolo F(c.) Genomic, Pathway Network, and Immunologic Features Distinguishing Squamous Carcinomas. Cell.Rep. 2018 Apr 3; 23(1): 194a

6. Chen H, Li C, Peng X, Zhou Z, Weinstein JN, Cancer Genome Atlas Research Network, Liang H. Facciolo F(c.) A Pan-Cancer Analysis of Enhancer Expression in nearly 9000 Patient Samples. Cell. 2018 Apr 5; 173(2): 386a

7. Chiappetta M,Facciolo F. Sternum Reconstruction using Titanium Plates Matched with "Sandwich" Gore-Tex Meshes. J.Vis.Surg. 2018 Mar 12; 4: 47a

8. Chiappetta M, Forcella D, Pierconti F, Facciolo F. Combined Treatment for Single Giant Pulmonary Metastasis from Osteosarcoma: From Inside to Outside. ANZ J.Surg. 2018 Nov; 88(11): E801a

9. Chiappetta M, Leuzzi G, Sperduti I, Bria E, Mucilli F, Lococo F, Spaggiari L, Ratto GB, Filosso PL, Facciolo F. Lymph-Node Ratio Predicts Survival among the Different Stages of Non-Small-Cell Lung Cancer: A Multicentre Analysis. Eur.J.Cardiothorac.Surg. 2018 Sep 6;

10. Chiappetta M, Marino M, Facciolo F. Unique Case of Atypical Type A Thymoma with Vertebral Metastasis and High 18-Fluorodeoxyglucose Avidity. ANZ J.Surg. 2018 Aug 17;

11. Chiu HS, Somvanshi S, Patel E, Chen TW, Singh VP, Zorman B, Patil SL, Pan Y, Chatterjee SS, Cancer Genome Atlas Research Network, Sood AK, Gunaratne PH, Sumazin P, Facciolo F(c.) Pan-Cancer Analysis of lncRNA Regulation Supports their Targeting of Cancer Genes in each Tumor Context. Cell.Rep. 2018 Apr 3; 23(1): 297a

12. di Martino S, Amoreo CA, Nuvoli B, Galati R, Strano S, Facciolo F, Alessandrini G, Pass HI, Ciliberto G, Blandino G, De Maria R, Cioce M. HSP90 Inhibition Alters the Chemotherapy-Driven Rearrangement of the Oncogenic Secretome. Oncogene. 2018 Mar; 37(10): 1369a

13. Di Modugno F, Spada S, Palermo B, Visca P, Iapicca P, Di Carlo A, Antoniani B, Sperduti I, Di Benedetto A, Terrenato I, Mottolese M, Gandolfi F, Facciolo F, Chen EI, Schwartz MA, Santoni A, Bissell MJ, Nistico P. HMENA Isoforms Impact NSCLC Patient Outcome through fibronectin/beta1 Integrin Axis. Oncogene. 2018 Oct; 37(42): 5605-5617a

14. Ding L, Bailey MH, Porta-Pardo E, Thorsson V, Colaprico A, Bertrand D, Gibbs DL, Weerasinghe A, Huang KL, Tokheim C, Cortes-Ciriano I, Jayasinghe R, Chen F, Yu L, Sun S, Olsen C, Kim J, Taylor AM, Cherniack AD, Akbani R, Suphavilai C, Nagarajan N, Stuart JM, Mills GB, Wyczalkowski MA, Vincent BG, Hutter CM, Zenklusen JC, Hoadley KA, Wendl MC, Shmulevich L, Lazar AJ, Wheeler DA, Getz G, Cancer Genome Atlas Research Network, Facciolo F(c.) Perspective on Oncogenic Processes at the End of the Beginning of Cancer Genomics. Cell. 2018 Apr 5; 173(2): 305a

15. Ellrott K, Bailey MH, Saksena G, Covington KR, Kandoth C, Stewart C, Hess J, Ma S, Chiotti KE, McLellan M, Sofia HJ, Hutter C, Getz G, Wheeler D, Ding L, MC3 Working Group, Cancer Genome Atlas Research Network. Facciolo F(c.) Scalable Open Science Approach for Mutation Calling of Tumor Exomes using Multiple Genomic Pipelines. Cell.Syst. 2018 Mar 28; 6(3): 271a

16. Gao Q, Liang WW, Foltz SM, Mutharasu G, Jayasinghe RG, Cao S, Liao WW, Reynolds SM, Wyczalkowski MA, Yao L, Yu L, Sun SQ, Fusion Analysis Working Group, Cancer Genome Atlas Research Network, Chen K, Lazar AJ, Fields RC, Wendl MC, Van Tine BA, Vij R, Chen F, Nykter M, Shmulevich I, Ding L. Facciolo F(c.) Driver Fusions and their Implications in the Development and Treatment of Human Cancers. Cell.Rep. 2018 Apr 3; 23(1): 227a

17. Ge Z, Leighton JS, Wang Y, Peng X, Chen Z, Chen H, Sun Y, Yao F, Li J, Zhang H, Liu J, Shriver CD, Hu H, Cancer Genome Atlas Research Network, Piwnica-Worms H, Ma L, Liang H, Facciolo F(c.). Integrated Genomic Analysis of the Ubiquitin Pathway Across Cancer Types. Cell.Rep. 2018 Apr 3; 23(1): 213a

18. Hoadley KA, Yau C, Hinoue T, Wolf DM, Lazar AJ, Drill E, Shen R, Taylor AM, Cherniack AD, Thorsson V, Akbani R, Bowlby R, Wong CK, Wiznerowicz M, Sanchez-Vega F, Robertson AG, Schneider BG, Lawrence MS, Noushmehr H, Malta TM, Cancer Genome Atlas Network, Stuart JM, Benz CC, Laird PW, Facciolo F(c.) Cell-of-Origin Patterns Dominate the Molecular Classification of 10,000 Tumors from 33 Types of Cancer. Cell. 2018 Apr 5; 173(2): 291a

19. Huang KL, Mashl RJ, Wu Y, Ritter DI, Wang J, Oh C, Paczkowska M, Reynolds S, Wyczalkowski MA, Oak N, Scott AD, Krassowski M, Cherniack AD, Houlahan KE, Jayasinghe R, Wang LB, Zhou DC, Liu D, Cao S, Kim YW, Koire A, McMichael JF, Hucthagowder V, Kim TB, Hahn A, Wang C, McLellan MD, Al-Mulla F, Johnson KJ, Cancer Genome Atlas Research Network, Lichtarge O, Boutros PC, Raphael B, Lazar AJ, Zhang W, Wendl MC, Govindan R, Jain S, Wheeler D, Kulkarni S, Dipersio JF, Reimand J, Meric-Bernstam F, Chen K, Shmulevich I, Plon SE, Chen F, Ding L, Facciolo F(c.) Pathogenic Germline Variants in 10,389 Adult Cancers. Cell. 2018 Apr 5; 173(2): 355a

20. Jayasinghe RG, Cao S, Gao Q, Wendl MC, Vo NS, Reynolds SM, Zhao Y, Climente-Gonzalez H, Chai S, Wang F, Varghese R, Huang M, Liang WW, Wyczalkowski MA, Sengupta S, Li Z, Payne SH, Fenyo D, Miner JH, Walter MJ, Cancer Genome Atlas Research Network, Vincent B, Eyras E, Chen K, Shmulevich I, Chen F, Ding L. Facciolo F(c.) Systematic Analysis of Splice-Site-Creating Mutations in Cancer. Cell.Rep. 2018 Apr 3; 23(1): 270a

21. Kahles A, Lehmann KV, Toussaint NC, Huser M, Stark SG, Sachsenberg T, Stegle O, Kohlbacher O, Sander C, Facciolo F(c.) Cancer Genome Atlas Research Network, Ratsch G. Comprehensive Analysis of Alternative Splicing Across Tumors from 8,705 Patients. Cancer.Cell. 2018 Aug 13; 34(2): 211a

22. Knijnenburg TA, Wang L, Zimmermann MT, Chambwe N, Gao GF, Cherniack AD, Fan H, Shen H, Way GP, Greene CS, Liu Y, Akbani R, Feng B, Donehower LA, Miller C, Shen Y, Karimi M, Chen H, Kim P, Jia P, Shinbrot E, Zhang S, Liu J, Hu H, Bailey MH, Yau C, Wolf D, Zhao Z, Weinstein JN, Li L, Ding L, Mills GB, Laird PW, Wheeler DA, Shmulevich I, Cancer Genome Atlas Research Network, Monnat RJ,Jr, Xiao Y, Wang C, Facciolo F(c.). Genomic and Molecular Landscape of DNA Damage Repair Deficiency Across the Cancer Genome Atlas. Cell.Rep. 2018 Apr 3; 23(1): 239a

23. Korkut A, Zaidi S, Kanchi RS, Rao S, Gough NR, Schultz A, Li X, Lorenzi PL, Berger AC, Robertson G, Kwong LN, Datto M, Roszik J, Ling S, Ravikumar V, Manyam G, Rao A, Shelley S, Liu Y, Ju Z, Hansel D, de Velasco G, Pennathur A, Andersen JB, O'Rourke CJ, Ohshiro K, Jogunoori W, Nguyen BN, Li S, Osmanbeyoglu HU, Ajani JA, Mani SA, Houseman A, Wiznerowicz M, Chen J, Gu S, Ma W, Zhang J, Tong P, Cherniack AD, Deng C, Resar L, Cancer Genome Atlas Research Network, Weinstein JN, Mishra L, Akbani R. Facciolo F(c.) A Pan-Cancer Analysis Reveals High-Frequency Genetic Alterations in Mediators of Signaling by the TGF-Beta Superfamily. Cell.Syst. 2018 Oct 24; 7(4): 422a

24. Liu J, Lichtenberg T, Hoadley KA, Poisson LM, Lazar AJ, Cherniack AD, Kovatich AJ, Benz CC, Levine DA, Lee AV, Omberg L, Wolf DM, Shriver CD, Thorsson V, Cancer Genome Atlas Research Network, Hu H, Facciolo F(c.) An Integrated TCGA Pan-Cancer Clinical Data Resource to Drive High-Quality Survival Outcome Analytics. Cell. 2018 Apr 5; 173(2): 400a

25. Liu Y, Sethi NS, Hinoue T, Schneider BG, Cherniack AD, Sanchez-Vega F, Seoane JA, Farshidfar F, Bowlby R, Islam M, Kim J, Chatila W, Akbani R, Kanchi RS, Rabkin CS, Willis JE, Wang KK, McCall SJ, Mishra L, Ojesina AI, Bullman S, Pedamallu CS, Lazar AJ, Sakai R, Cancer Genome Atlas Research Network, Thorsson V, Bass AJ, Laird PW, Facciolo F(c.). Comparative Molecular Analysis of Gastrointestinal Adenocarcinomas. Cancer.Cell. 2018 Apr 9; 33(4): 721a

26. Malta TM, Sokolov A, Gentles AJ, Burzykowski T, Poisson L, Weinstein JN, Kaminska B, Huelsken J, Omberg L, Gevaert O, Colaprico A, Czerwinska P, Mazurek S, Mishra L, Heyn H, Krasnitz A, Godwin AK, Lazar AJ, Cancer Genome Atlas Research Network, Stuart JM, Hoadley KA, Laird PW, Noushmehr H, Wiznerowicz M, Facciolo F(c.) Machine Learning Identifies Stemness Features Associated with Oncogenic Dedifferentiation. Cell. 2018 Apr 5; 173(2): 338a

27. Peng X, Chen Z, Farshidfar F, Xu X, Lorenzi PL, Wang Y, Cheng F, Tan L, Mojumdar K, Du D, Ge Z, Li J, Thomas GV, Birsoy K, Liu L, Zhang H, Zhao Z, Marchand C, Weinstein JN, Cancer Genome Atlas Research Network, Bathe OF, Liang H. Facciolo F(c.) Molecular Characterization and Clinical Relevance of Metabolic Expression Subtypes in Human Cancers. Cell.Rep. 2018 Apr 3; 23(1): 255a

28. Pilotto S, Sperduti I, Leuzzi G, Chiappetta M, Mucilli F, Ratto GB, Lococo F, Filosso PL, Spaggiari L, Novello S, Milella M, Santo A, Scarpa A, Infante M, Tortora G, Facciolo F, Bria E. Prognostic Model for Resected Squamous Cell Lung Cancer: External Multicenter Validation and Propensity Score Analysis Exploring the Impact of Adjuvant and Neoadjuvant Treatment. J.Thorac.Oncol. 2018 Apr; 13(4): 568a

29. Radovich M, Pickering CR, Felau I, Ha G, Zhang H, Jo H, Hoadley KA, Anur P, Zhang J, McLellan M, Bowlby R, Matthew T, Danilova L, Hegde AM, Kim J, Leiserson MDM, Sethi G, Lu C, Ryan M, Su X, Cherniack AD, Robertson G, Akbani R, Spellman P, Weinstein JN, Hayes DN, Raphael B, Lichtenberg T, Leraas K, Zenklusen JC, Cancer Genome Atlas Network, Fujimoto J, Scapulatempo-Neto C, Moreira AL, Hwang D, Huang J, Marino M, Korst R, Giaccone G, Gokmen-Polar Y, Badve S, Rajan A, Strobel P, Girard N, Tsao MS, Marx A, Tsao AS, Loehrer PJ. Facciolo F(c.) The Integrated Genomic Landscape of Thymic Epithelial Tumors. Cancer.Cell. 2018 Feb 12; 33(2): 244a

30. Ricciardi S, Cardillo G, Zirafa CC, Carleo F, Facciolo F, Fontanini G, Mutti L, Melfi F. Surgery for Malignant Pleural Mesothelioma: An International Guidelines Review. J.Thorac.Dis. 2018 Jan; 10(Suppl 2): S285a

31. Ricketts CJ, De Cubas AA, Fan H, Smith CC, Lang M, Reznik E, Bowlby R, Gibb EA, Akbani R, Beroukhim R, Bottaro DP, Choueiri TK, Gibbs RA, Godwin AK, Haake S, Hakimi AA, Henske EP, Hsieh JJ, Ho TH, Kanchi RS, Krishnan B, Kwiatkowski DJ, Lui W, Merino MJ, Mills GB, Myers J, Nickerson ML, Reuter VE, Schmidt LS, Shelley CS, Shen H, Shuch B, Signoretti S, Srinivasan R, Tamboli P, Thomas G, Vincent BG, Vocke CD, Wheeler DA, Yang L, Kim WY, Robertson AG, Cancer Genome Atlas Research Network, Spellman PT, Rathmell WK, Linehan WM. Facciolo F(c.) The Cancer Genome Atlas Comprehensive Molecular Characterization of Renal Cell Carcinoma. Cell.Rep. 2018 Apr 3; 23(1): 313a

32. Saltz J, Gupta R, Hou L, Kurc T, Singh P, Nguyen V, Samaras D, Shroyer KR, Zhao T, Batiste R, Van Arnam J, Cancer Genome Atlas Research Network, Shmulevich I, Rao AUK, Lazar AJ, Sharma A, Thorsson V. Facciolo F(c.) Spatial Organization and Molecular Correlation of Tumor-Infiltrating Lymphocytes using Deep Learning on Pathology Images. Cell.Rep. 2018 Apr 3; 23(1): 181a

33. Sanchez-Vega F, Mina M, Armenia J, Chatila WK, Luna A, La KC, Dimitriadoy S, Liu DL, Kantheti HS, Saghafinia S, Chakravarty D, Daian F, Gao Q, Bailey MH, Liang WW, Foltz SM, Shmulevich I, Ding L, Heins Z, Ochoa A, Gross B, Gao J, Zhang H, Kundra R, Kandoth C, Bahceci I, Dervishi L, Dogrusoz U, Zhou W, Shen H, Laird PW, Way GP, Greene CS, Liang H, Xiao Y, Wang C, Iavarone A, Berger AH, Bivona TG, Lazar AJ, Hammer GD, Giordano T, Kwong LN, McArthur G, Huang C, Tward AD, Frederick MJ, McCormick F, Meyerson M, Cancer Genome Atlas Research Network, Van Allen EM, Cherniack AD, Ciriello G, Sander C, Schultz N, Facciolo F(c.) Oncogenic Signaling Pathways in the Cancer Genome Atlas. Cell. 2018 Apr 5; 173(2): 321a

34. Schaub FX, Dhankani V, Berger AC, Trivedi M, Richardson AB, Shaw R, Zhao W, Zhang X, Ventura A, Liu Y, Ayer DE, Hurlin PJ, Cherniack AD, Eisenman RN, Bernard B, Grandori C, Cancer Genome Atlas Network. Facciolo F(c.) Pan-Cancer Alterations of the MYC Oncogene and its Proximal Network Across the Cancer Genome Atlas. Cell.Syst. 2018 Mar 28; 6(3): 282a

35. Seiler M, Peng S, Agrawal AA, Palacino J, Teng T, Zhu P, Smith PG, Cancer Genome Atlas Research Network, Buonamici S, Yu L. Facciolo F(c.) Somatic Mutational Landscape of Splicing Factor Genes and their Functional Consequences Across 33 Cancer Types. Cell.Rep. 2018 Apr 3; 23(1): 282a

36. Taylor AM, Shih J, Ha G, Gao GF, Zhang X, Berger AC, Schumacher SE, Wang C, Hu H, Liu J, Lazar AJ, Cancer Genome Atlas Research Network, Cherniack AD, Beroukhim R, Meyerson M, Facciolo F(c.) Genomic and Functional Approaches to Understanding Cancer Aneuploidy. Cancer.Cell. 2018 Apr 9; 33(4): 676a

37. Thorsson V, Gibbs DL, Brown SD, Wolf D, Bortone DS, Ou Yang TH, Porta-Pardo E, Gao GF, Plaisier CL, Eddy JA, Ziv E, Culhane AC, Paull EO, Sivakumar IKA, Gentles AJ, Malhotra R, Farshidfar F, Colaprico A, Parker JS, Mose LE, Vo NS, Liu J, Liu Y, Rader J, Dhankani V, Reynolds SM, Bowlby R, Califano A, Cherniack AD, Anastassiou D, Bedognetti D, Rao A, Chen K, Krasnitz A, Hu H, Malta TM, Noushmehr H, Pedamallu CS, Bullman S, Ojesina AI, Lamb A, Zhou W, Shen H, Choueiri TK, Weinstein JN, Guinney J, Saltz J, Holt RA, Rabkin CE, Cancer Genome Atlas Research Network, Lazar AJ, Serody JS, Demicco EG, Disis ML, Vincent BG, Shmulevich L, Marino M(c. The Immune Landscape of Cancer. Immunity. 2018 Apr 17; 48(4): 812a

38. Wang Y, Xu X, Maglic D, Dill MT, Mojumdar K, Ng PK, Jeong KJ, Tsang YH, Moreno D, Bhavana VH, Peng X, Ge Z, Chen H, Li J, Chen Z, Zhang H, Han L, Du D, Creighton CJ, Mills GB, Cancer Genome Atlas Research Network, Camargo F, Liang H. Facciolo F(c.) Comprehensive Molecular Characterization of the Hippo Signaling Pathway in Cancer. Cell.Rep. 2018 Oct 30; 25(5): 1304a

39. Wang Z, Yang B, Zhang M, Guo W, Wu Z, Wang Y, Jia L, Li S, Cancer Genome Atlas Research Network, Xie W, Yang D, Facciolo F(c.). LncRNA Epigenetic Landscape Analysis Identifies EPIC1 as an Oncogenic lncRNA that Interacts with MYC and Promotes Cell-Cycle Progression in Cancer. Cancer.Cell. 2018 Apr 9; 33(4): 706a

40. Way GP, Sanchez-Vega F, La K, Armenia J, Chatila WK, Luna A, Sander C, Cherniack AD, Mina M, Ciriello G, Schultz N, Cancer Genome Atlas Research Network, Sanchez Y, Greene CS, Facciolo F(c.). Machine Learning Detects Pan-Cancer Ras Pathway Activation in the Cancer Genome Atlas. Cell.Rep. 2018 Apr 3; 23(1): 172a

# GYNECOLOGIC ONCOLOGY AND ONCOFERTILTY CENTER UNIT

*Head: Enrico Vizza, MD, PHD*

## STAFF:

| MD |
|---|
| Ermelinda Baiocco |
| Benito Chiofalo |
| Giuseppe Cutillo |
| Emanuela Mancini |
| Luciano Mariani |
| Cristina Vincenzoni |
| Giuseppe Vocaturo |
| **Biologists** |
| Marcello Iacobelli |
| Anna Maria Lobascio |
| Livia Ronchetti |
| Lucia Cicchillitti |
| **Admin** |
| Arabella Bufalo |
| **Data Entry** |
| Ashanti Zampa |
| **Ward Nurses** |
| Fabiola Nazzicone (Head) |
| Tatiana Chierichetti |
| Fabiana Cipriani |
| Rosaria De Domenico |
| Fabiana Egidi |
| Valeria Fiumara |
| Alessandra Gullo |
| Rachele Morani |
| Francesca Parrini |
| Catalina Partenie |
| Sabrina Santini |
| **Ward Health Workers** |
| Andrea Iannarilli |
| Monika Szoldra |
| **Outpatient Clinic Nurses** |
| Eros Floridi (Head) |
| Aurora De Leo |
| Sonia Girasole |
| Emiliana Marinucci |
| Cristina Patone |
| Maria Piccolo |
| Enrica Ruffo |
| **Outpatient Clinic Health Workers** |
| Maria Di Luccio |
| Francesco Malci |

## *Mission*

To provide high-quality diagnostic and staging plan for women with suspect tumor of the female genital tract and for women with hormonal dependent cancers. To develop a patient tailored treatment program, including surgical treatment, adjuvants and neoadjuvants therapies and oncologic follow-up, based on a well-coordinated multidisciplinary team. Fertility preservation in young patients with oncologic diseases. To offer a state-of-the-art surgery, including ICG (indocyanine green) guided surgery and minimally invasive approaches (robotic and laparoscopic surgery).

## *Clinical Activity*

The Division has 18 in-patient beds, ten of which dedicated to the week-surgery activities, four to the day-surgery and four for the long-stay. We have available 2 full-day surgical rooms every week and one morning for day-surgery procedures. During 2018 more than 740 surgical operations were performed: 267 in day-surgery setting and 476 (64%) for suspect or histological confirmed tumor of the female reproductive tract. More than 90% of procedures were performed with a minimally invasive technique (laparoscopic or robotic). All surgical and medical treatments are planned in a

weekly multidisciplinary meeting that include surgeons, medical oncologists, radiotherapists, pathologists and radiologists. Particular attention is devoted to minimally invasive surgery (including single-site incision laparoscopic and robotic surgery) and fertility-preserving surgery in young patients with cervical, endometrial and ovarian cancer. Cryopreservation of ovarian tissue for women of reproductive age with several cancer types is available. The Division also includes an outpatient clinic dedicated to the diagnosis and staging of cancer, to the care of young patients with cancer for fertility preservation purposes and to the treatment of genital cancer precursor with a multidisciplinary HPV unit.

## Research Activity

The main fields of research include: 1) minimally invasive surgery (MIS) for the treatment of gynecological tumors, 2) inflammation lipid mediators in epithelial ovarian cancer, 3) bio-molecular characterization of endometrial cancer, 4) immunologic pathway of endometrial tumors, 5) ovarian tissue cryopreservation (bank of ovarian tissue). In the recent years all most innovative surgical tools in the field of MIS have been tested and adopted in our Division, including single-site incision laparoscopic and robotic surgery. Sentinel-node biopsy in endometrial and cervical cancer is commonly used in our division, regarding ovarian cancer preliminary results from a multicenter study have been published. A research on the pathway of lipid mediators in different stages and types of epithelial ovarian tumors is ongoing in collaboration with the University of Jena (Germany). A research aimed to understand immune escape mechanisms of endometrial adenocarcinomas is ongoing. Research of the bank of ovarian tissue is mainly focused on: 1) in vitro maturation of immature antral oocytes retrieved from the ovarian cortex, 2) validation of the procedures of freezing and thawing of the ovarian tissue, 3) extraction of genomic DNA from cancer patients for mutational analysis.

## Publications


1. Cianci S, Abatini C, Fagotti A, Chiofalo B, Tropea A, Biondi A, Scambia G, Pacelli F. Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for Peritoneal Malignancies using New Hybrid CO2 System: Preliminary Experience in Referral Center. Updates Surg. 2018 Aug 9;

2. Corrado G, Calagna G, Cutillo G, Insinga S, Mancini E, Baiocco E, Zampa A, Bufalo A, Perino A, Vizza E. The Patient and Observer Scar Assessment Scale to Evaluate the Cosmetic Outcomes of the Robotic Single-Site Hysterectomy in Endometrial Cancer. Int.J.Gynecol.Cancer. 2018 Jan; 28(1): 194a

3. Corrado G, Laquintana V, Loria R, Carosi M, de Salvo L, Sperduti I, Zampa A, Cicchillitti L, Piaggio G, Cutillo G, Falcioni R, Vizza E. Endometrial Cancer Prognosis Correlates with the Expression of L1CAM and miR34a Biomarkers. J.Exp.Clin.Cancer Res. 2018 Jul 6; 37(1): 139a

4. Corrado G, Vizza E, Cela V, Mereu L, Bogliolo S, Legge F, Ciccarone F, Mancini E, Gallotta V, Baiocco E, Monterossi G, Perri MT, Zampa A, Pasciuto T, Scambia G. Laparoscopic Versus Robotic Hysterectomy in Obese and Extremely Obese Patients with Endometrial Cancer: A Multi-Institutional Analysis. Eur.J.Surg.Oncol. 2018 Dec; 44(12): 1935-1941a

5. Corrado G, Vizza E, Legge F, Pedone Anchora L, Sperduti I, Fagotti A, Mancini E, Gallotta V, Zampa A, Chiofalo B, Scambia G. Comparison of Different Surgical Approaches for Stage IB1 Cervical Cancer Patients: A Multi-Institution Study and a Review of the Literature. Int.J.Gynecol.Cancer. 2018 Jun; 28(5): 1020a

6. De Robertis E, Caprino Miceli A, Colombo GL, Corcione A, Leykin Y, Scudeller L, Vizza E, Scollo P, Societa Italiana Ginecologia E Ostetricia, Societa Italiana Di Anestesia Analgesia Rianimazione E Terapia Intensiva. Effects of Deep Versus Moderate Neuromuscular Blockade in Laparoscopic Gynecologic Surgery on Postoperative Pain and Surgical Conditions: Protocol for a Randomized Controlled Trial. JMIR Res.Protoc. 2018 Jul 9; 7(7): e131a

7. Gamucci T, Pizzuti L, Natoli C, Mentuccia L, Sperduti I, Barba M, Sergi D, Iezzi L, Maugeri-Sacca M, Vaccaro A, Magnolfi E, Gelibter A, Barchiesi G, Magri V, D'Onofrio L, Cassano A, Rossi E, Botticelli A, Moscetti L, Omarini C, Fabbri MA, Scinto AF, Corsi D, Carbognin L, Mazzotta M, Bria E, Foglietta J, Samaritani R, Garufi C, Mariani L, Barni S, Mirabelli R, Sarmiento R, Graziano V, Santini D, Marchetti P, Tonini G, Di Lauro L, Sanguineti G, Paoletti G, Tomao S, De Maria R, Veltri E, Paris I, Giotta F, Latorre A, Giordano A, Ciliberto G, Vici P. A Multicenter REtrospective Observational Study of First-Line Treatment with PERtuzumab, Trastuzumab and Taxanes for Advanced HER2 Positive Breast Cancer Patients. RePer Study. Cancer.Biol.Ther. 2018 Nov 7; : 1a

8. Pizzuti L, Sergi D, Mandoj C, Antoniani B, Sperati F, Chirico A, Di Lauro L, Valle M, Garofalo A, Vizza E, Corrado G, Tomao F, Rinaldi M, Carpano S, Maugeri-Sacca M, Conti L, Digiesi G, Marchetti P, De Maria R, Giordano A, Barba M, Carosi MA, Vici P. GLUT 1 Receptor Expression and Circulating Levels of Fasting Glucose in High Grade Serous Ovarian Cancer. J.Cell.Physiol. 2018; 233(2): 1396a

9. Scambia G, Raffaelli R, Baggio S, Garzon S, Laganà AS, Sartori E, Vanzo F, Vizza E, Angioli R, Benedetto C, Cagnacci A, Candiani M, Carta G, Caserta D, Cherchi PL, Ciavattini A, Cicinelli E, Cobellis L, Cosmi E, D'Anna R, De Leo V, Di Paola R, Di Pinto A, Ercoli A, Facchinetti F, Ferrazzi E, Frusca T, Ghezzi F, Greco P, Liberati M, Loverro G, Nappi L, Palumbo M, Neri M, Perino A, Clemenza S, Piccione E, Peterlunger I, Rizzo N, Negri B, Simoncini T, Spinillo A, Venturini P L, Vergani P, Zullo F, Chiantera A, Colacurci N, Viora E, Franchi M. Needlestick Injuries among Obstetrics and Gynecology Trainees: A Study Design to Investigate an Underestimated Priority. Italian Journal of Gynaecology & Obstetrics. 2018; 30(3)

10. Sartori E, Franchi M, Capelli G, Cicinelli E, Colacurci N, De Vincenzo R, Landoni F, Maggino T, Masturzo B, Parazzini F, Scarfone G, Peccatori F, Romagnolo C, Scibilia G, Scollo P, Zola P, Garzon S, Raffaelli R, Busato E, Cetin I, Giovannini M, Zanni G C, Greggi S, Marconi A M, Rizzo N, Ruspa G, Meroni MG, Volpi EO, Simoncini T, Gadducci A, Ghezzi F, Laganà AS, Melis GB, Paoletti AM, Strobelt N, Spinillo A, Severi FM, Frusca T, Greco P, Nappi L, Ricci G, Vizza E, Papaccio M, Ratti M, Scambia G. Cancer in Pregnancy: Proposal of an Italian Multicenter Study. Gynecologic Oncology Group of the Italian Society of Gynæcology and Obstetrics (SIGO). Italian Journal of Gynæcology & Obstetrics. 2018; 30(3)

11. Sartori E, Ghezzi F, Cromi A, Miscioscia R, Laganà AS, Garzon S, Raffaelli R, Candiani M, Casarin J, Ciavattini A, Di Paola R, Greco P, Guaschino S, Marchesoni D, Milani R, Rizzo N,Venturini PL, Zullo F,Valente E,Vizza E, Scambia G, Franchi M. Learning Climate and Quality of Postgraduate Training in Gynecology and Obstetrics should be Assessed in Italian Training Courses. Italian Journal of Gynæcology & Obstetrics 2018; 30(3)

12. Uccella S, Falcone F, Greggi S, Fanfani F, De Iaco P, Corrado G, Ceccaroni M, Mandato VD, Bogliolo S, Casarin J, Monterossi G, Pinelli C, Mangili G, Cormio G, Roviglione G, Bergamini A, Pesci A, Frigerio L, Uccella S, Vizza E, Scambia G, Ghezzi F. Survival in Clinical Stage I Endometrial Cancer with Single Vs. Multiple Positive Pelvic Nodes: Results of a Multi-Institutional Italian Study. J.Gynecol.Oncol. 2018 Nov; 29(6): e100a

13. Uccella S, Malzoni M, Cromi A, Seracchioli R, Ciravolo G, Fanfani F, Shakir F, Gueli Alletti S, Legge F, Berretta R, Corrado G, Casarella L, Donarini P, Zanello M, Perrone E, Gisone B, Vizza E, Scambia G, Ghezzi F. Laparoscopic Vs Transvaginal Cuff Closure After Total Laparoscopic Hysterectomy: A Randomized Trial by the Italian Society of Gynecologic Endoscopy. Am.J.Obstet.Gynecol. 2018 May; 218(5): 500.e1a

14. Vizza E, Chiofalo B, Cutillo G, Mancini E, Baiocco E, Zampa A, Bufalo A, Corrado G. Robotic Single Site Radical Hysterectomy Plus Pelvic Lymphadenectomy in Gynecological Cancers. J.Gynecol.Oncol. 2018 Jan; 29(1): e2a

15. Vizza E, Corrado G, De Angeli M, Carosi M, Mancini E, Baiocco E, Chiofalo B, Patrizi L, Zampa A, Piaggio G, Cicchillitti L. Serum DNA Integrity Index as a Potential Molecular Biomarker in Endometrial Cancer. J.Exp.Clin. Cancer Res. 2018 Jan 30; 37(1): 16a

# UROLOGY UNIT

## *Head: Giuseppe Simone MD, PhD*

| STAFF |
|---|
| **Ruggiero Cantiani MD** |
| **Lamanna Luciano MD** |
| **Pompeo Vincenzo MD** |
| **Salvatore Guaglianone MD** |
| **Ferriero Maria Consiglia MD, PhD** |
| **Anceschi Umberto MD** |
| Contractors |
| **Tuderti Gabriele MD** |
| **Brassetti Aldo MD** |
| Researcher |
| **Manuela Costantini MD, PhD** |

## *Mission*

Providing the highest quality of medical and surgical care to uro-oncology patients. Developing and standardizing complex surgical procedures in uro-oncology; expanding indications of minimally invasive and robotic procedures; developing of clinical and translational research in the field of prostate cancer, kidney cancer and bladder cancer.

## *Clinical Activity*

The urological clinical activity mainly concerns minimally invasive surgery, especially robot- assisted and laparoscopic procedures. We have particularly expanded our expertise and gained experience in robotic radical cystectomy with totally intracorporeal reconstruction of orthotopic and etherotopic diversions, robot assisted radical nephrectomy with inferior vena cava tumor thrombectomy and in minimally invasive off clamp partial nephrectomy. All these complex surgical procedures are today a standard of care in our Institution.

## *Research Activities*

Clinical research on new minimally invasive surgical techniques, imaging advances in early cancer detection or imaging-guided surgery and oncologic outcomes after surgical treatments are our main research objectives. Translational research on molecular biomarkers, genetic and microenvironment tumor profiling, stem cells investigation, together with new *precision medicine* diagnostic and prognostic non invasive tools in urological malignancies as liquid biopsy are additional research activities that our Unit carries out in cooperation with dedicated departments of the Regina Elena National Cancer Institute and other prestigious national and international Institutions. The Urology Unit has been national site coordinator of observational studies and it is involved in multiple clinical trials on prostate cancer treatments, renal cancer and urothelial cancer.

## *Publications*

1. Anceschi U, Tuderti G, Lugnani F, Biava P, Malossini G, Luciani L, Cai T, Marsiliani D, Filianoti A, Mattevi D, Costantini M, Misuraca L, Simone G. Novel Diagnostic Biomarkers of Prostate Cancer: An Update. *Curr. Med. Chem.* 2018 Sep 13; [Epub ahead of print]

2. Appetecchia M, Lauretta R, Sperduti I, Gallucci M. Chromogranin A as a Biomarker for Prostate Cancer: Is it Actually Relevant for Clinical Practice? *Future Oncol.* 2018 Jun;14(13):1233-1235

3. Bertolo R, Autorino R, Simone G, Derweesh I, Garisto JD, Minervini A, Eun D, Perdona S, Porter J, Rha KH, Mottrie A, White WM, Schips L, Yang B, Jacobsohn K, Uzzo RG, Challacombe B, Ferro M, Sulek J, Capitanio U, Anele UA, Tuderti G, Costantini M, Ryan S, Bindayi A, Mari A, Carini M, Keehn A, Quarto G, Liao M, Chang K, Larcher A, De Naeyer G, De Cobelli O, Berardinelli F, Zhang C, Langenstroer P, Kutikov A, Chen D, De Luyk N, Sundaram CP, Montorsi F, Stein RJ, Haber GP, Hampton LJ, Dasgupta P, Gallucci M, Kaouk J, Porpiglia F. Outcomes of Robot-Assisted Partial Nephrectomy for Clinical T2 Renal Tumors: A Multicenter Analysis (ROSULA Collaborative Group). *Eur. Urol.* 2018 Aug; 74(2): 226a

4. Bertolo R, Simone G, Garisto J, Nakhoul G, Armanyous S, Agudelo J, Costantini M, Tuderti G, Gallucci M, Kaouk J. Off-Clamp Vs on-Clamp Robotic Partial Nephrectomy: Perioperative, Functional and Oncological Outcomes from a Propensity-Score Matching between Two High-Volume Centers. *Eur. J. Surg. Oncol.* 2018 Dec 9; [Epub ahead of print]

5. De Nunzio C, Brassetti A, Simone G, Lombardo R, Mastroianni R, Collura D, Muto G, Gallucci M, Tubaro A. Metabolic Syndrome Increases the Risk of Upgrading and Upstaging in Patients with Prostate Cancer on Biopsy: A Radical Prostatectomy Multicenter Cohort Study. *Prostate Cancer. Prostatic Dis.* 2018 Sep; 21(3): 438a

6. De Nunzio C, Pastore AL, Lombardo R, Simone G, Leonardo C, Mastroianni R, Collura D, Muto G, Gallucci M, Carbone A, Fuschi A, Dutto L, Witt JH, De Dominicis C, Tubaro A. The New Epstein Gleason Score Classification significantly Reduces Upgrading in Prostate Cancer Patients. *Eur. J. Surg. Oncol.* 2018 Jun;44(6):835-839

7. di Martino S, De Luca G, Grassi L, Federici G, Alfonsi R, Signore M, Addario A, De Salvo L, Francescangeli F, Sanchez M, Tirelli V, Muto G, Sperduti I, Sentinelli S, Costantini M, Pasquini L, Milella M, Haoui M, Simone G, Gallucci M, De Maria R, Bonci D. Renal Cancer: New Models and Approach for Personalizing Therapy. *J. Exp. Clin. Cancer Res.* 2018 Sep 5; 37(1): 217a

8. Filianoti A, Paganelli A, Bassi P, Simone G, Ranieri A. Leiomyoma of the Renal Capsule: Case Report and Literature Review. *Urologia.* 2018 Feb; 85(1): 34a

9. Moschini M, Soria F, Mathieu R, Xylinas E, D'Andrea D, Tan WS, Kelly JD, Simone G, Tuderti G, Meraney A, Krishna S, Konety B, Zamboni S, Baumeister P, Mattei A, Briganti A, Montorsi F, Galucci M, Rink M, Karakiewicz PI, Roupret M, Aziz A, Perry M, Rowe E, Koupparis A, Kassouf W, Scherr DS, Ploussard G, Boorjian SA, Sooriakumaran P, Shariat SF, European Association of Urology - Young Academic Urologists (EAU-YAU), Urothelial Carcinoma Working Group. Propensity-Score-Matched Comparison of Soft Tissue Surgical Margins Status between Open and Robotic-Assisted Radical Cystectomy. *Urol. Oncol.* 2018 Nov 13; [Epub ahead of print]

10. Oderda M, Marra G, Albisinni S, Altobelli E, Baco E, Beatrici V, Cantiani A, Carbone A, Ciccariello M, Descotes JL, Dubreuil-Chambardel M, Eldred-Evans D, Fasolis G, Ferriero M, Fiard G, Forte V, Giacobbe A, Kumar P, Lacetera V, Mozer P, Muto G, Papalia R, Pastore A, Peltier A, Piechaud T, Simone G, Roche JB, Roupret M, Rouviere O, Van Velthoven R, Gontero P. Accuracy of Elastic Fusion Biopsy in Daily Practice: Results of a Multicenter Study of 2115 Patients. *Int. J. Urol.* 2018 Dec; 25(12): 990a

11. Panebianco V, Barchetti G, Simone G, Del Monte M, Ciardi A, Grompone MD, Campa R, Indino EL, Barchetti F, Sciarra A, Leonardo C, Gallucci M, Catalano C. Negative Multiparametric Magnetic Resonance Imaging for Prostate Cancer: What's Next? *Eur. Urol.* 2018 Jul;74(1):48-54

12. Simone G, Anceschi U, Tuderti G, Misuraca L, Celia A, De Concilio B, Costantini M, Stigliano A, Minisola F, Ferriero M, Guaglianone S, Gallucci M. Robot-Assisted Partial Adrenalectomy for the Treatment of Conn's Syndrome: Surgical Technique, and Perioperative and Functional Outcomes. *Eur. Urol.* 2018 Aug 1; [Epub ahead of print]

13. Simone G, Misuraca L, Anceschi U, Minisola F, Ferriero M, Guaglianone S, Tuderti G, Gallucci M. Urethra and Ejaculation Preserving Robot-Assisted Simple Prostatectomy: Near-Infrared Fluorescence Imaging-Guided Madigan Technique. *Eur. Urol.* 2018 Dec 12; [Epub ahead of print]

14. Simone G, Misuraca L, Tuderti G, Minisola F, Ferriero M, Romeo G, Costantini M, Al-Rawashdah SF, Guaglianone S, Gallucci M. Purely Off-Clamp Robotic Partial Nephrectomy: Preliminary 3-Year Oncological and Functional Outcomes. *Int. J. Urol.* 2018 Jun;25(6):606-614

15. Simone G, Papalia R, Misuraca L, Tuderti G, Minisola F, Ferriero M, Vallati G, Guaglianone S, Gallucci M. Robotic Intracorporeal Padua Ileal Bladder: Surgical Technique, Perioperative, Oncologic and Functional Outcomes. *Eur. Urol.* 2018 Jun; 73(6): 934a

16. Simone G, Tuderti G, Anceschi U, Ferriero M, Costantini M, Minisola F, Vallati G, Pizzi G, Guaglianone S, Misuraca L, Gallucci M. "Ride the Green Light": Indocyanine Green-Marked Off-Clamp Robotic Partial Nephrectomy for Totally Endophytic Renal Masses. *Eur. Urol.* 2018 Sep 24; [Epub ahead of print]

17. Simone G, Tuderti G, Misuraca L, Anceschi U, Ferriero M, Minisola F, Guaglianone S, Gallucci M. Perioperative and Mid-Term Oncologic Outcomes of Robotic Assisted Radical Cystectomy with Totally Intracorporeal Neobladder: Results of a Propensity Score Matched Comparison with Open Cohort from a Single-Centre Series. *Eur. J. Surg. Oncol.* 2018 Sep; 44(9): 1432-1438a

18. Soria F, Moschini M, D'andrea D, Abufaraj M, Foerster B, Mathieu R, Gust KM, Gontero P, Simone G, Meraney A, Krishna S, Konety B, Roupret M, Perry M, Rowe E, Ploussard G, Boorjian SA, Wiklund P, Sooriakumaran P, Shariat SF. Comparative Effectiveness in Perioperative Outcomes of Robotic Versus Open Radical Cystectomy: Results from a Multicenter Contemporary Retrospective Cohort Study. *Eur. Urol. Focus.* 2018 Nov 16; [Epub ahead of print]

# NEUROSURGERY UNIT

## *Head: Riccardo Boccaletti, MD*

| STAFF |
|---|
| **Stefano Telera, MD** |
| **Fabio Cattani, MD** |
| **Piero Oppido, MD** |
| **Laura Raus, MD** |
| **Francesco Crispo, MD** |
| **Nurses** |
| **Cinzia Mori**<br>*Nurse Coordinator and Case Manager* |
| **Angelocola Anna** |
| **Balzano Silvana** |
| **De Martino Stefania** |
| **Lauro Gerarda** |
| **Rinaldi Sabrina** |
| **Fabiana Rosini** |
| **Valentina Joseph** |
| **Francesca Mastropietro** |
| **Administartive Assistant** |
| **Marzia Piccoli** |

## *Mission*

The activity of Neurosurgical Unit is mainly devoted to research, diagnosis and treatment of nervous system tumors, with a prevalent interest in malignant primary and secondary lesions. Our activity is deeply embedded in the multidisciplinary group of Neuro-Oncology, with the primary aim of defining more specific and active diagnostic and therapeutic strategies for the most relevant brain and spine tumors.

The research activity of the Unit of Neurosurgery is focused on several relevant topics, regarding translational and clinical studies on new bio-molecular characterization and therapeutic approaches in the integrated diagnosis and treatment of primitive and secondary tumors of the nervous system. As such, we take active part either to national and international cooperative groups or to relevant academic and sponsored clinical trials.

In the field of secondary CNS lesions, we cooperate with the Hematologic and Oncologic Units, offering important support into diagnostic and therapeutic processes of systemic and hematologic tumor diseases.

## *Clinical Activity*

In 2018 the Unit of Neurosurgery performed 160 surgical procedures, for intracranial pathologies (more than 110 cerebral tumors (gliomas, cerebral metastases, meningiomas, pituitary adenomas, intraventricular lesions), secondary CSF obstructive pathologies, spinal procedures (two thirds on metastatic spine lesions) and tumors of the peripheral nervous system. Ambulatory surgery for peripheral nerve compressive lesions, many of them, in patients affected by cancer diseases, included 23 procedures.

Following experience developed in the last decade, our activity has been devoted to increase the efficacy of new therapeutic strategies for primitive brain tumors: fluorescence guided microsurgical resection, neurophysiologic monitoring, intra-operative ecography, intratumoral antiblastic treatments, conformal radiotherapy, with eventual focal boost, adjuvant and/or concomitant chemotherapy, second surgery in specific cases.

Another relevant clinical issue is represented by the management of patients with brain metastases, due to the increasing frequency and complexity of the diagnostic and therapeutic approaches to this pathology and the prolonged survival afforded by new target therapies and combined chemotherapies.

In this field, the European Association of Neuro-Oncology (EANO) created a multidisciplinary Task Force to which a previous member of the Unit have took part, to draw evidence-based guidelines for patients with brain metastases from solid tumors, with the aim of defining a consensus review of evidence and recommendation for diagnosis by neuro-imaging and neuropathology, staging, prognostic factors and different

treatment options. The same goal is being pursued by the Italian Society of Neurosurgery (SINCH) which have recently create a Task Force (ST is a member of this group), to deliver the Italian version of such recommendation.
Specifically therapeutic options such surgery, stereotactic radiosurgery/stereotactic fractionated radiotherapy, whole brain radiotherapy, chemotherapy and targeted therapy (with particular attention to brain metastases from non-small cell lung cancer, melanoma, breast and renal cancer), and supportive care have been fully addressed.
In 2018 a large multicenter retrospective study, which involved Regina Elena Institute, San Giovanni and San Filippo Neri Hospitals in Rome, has been published, to review the current role of Steretactic Biopsy procedures to the diagnosis of neoplastic lesions in challenging area of the brain.
Furthermore, the endoscopic activity, both intraventricular and transphenoidal, has been maintained and developed.
As pituitary region tumors are concerned, a trans-nasal- trans-sphenoidal pure endoscopic approach is usually performed in cooperation with our collegues ENT surgeons.
In case of obstructive hydrocephalus or intraventricular tumors, an endoscopic transventricular approach with bioptic tumor sampling, opening and drainage of cystic components, as well as third ventriculostomy, represent the standard of care.
In the field of spinal tumors, different programs have been developed mainly considering the use of new technologies and surgical approaches.
Patients affected by metastatic spinal tumors have been treated with augmentation procedures (vertebroplasty and/or kyphoplasty), associated in many cases with open decompression procedures and percutaneous stabilization techniques. The recent introduction of silicon products as filling material beside standard PMMA, has been instrumental in performing complex cases with an increased margin of safety and efficacy.
For patients affected by intradural-extramedullary tumors the unilateral mini-invasive approach has become in the last decade, the standard of the care, minimizing surgical aggressiveness and reducing time of hospitalization. Neurophysiologic monitoring of the motor and sensory function have been also implemented and it is commonly employed during surgery of all intradural tumors.

## *Research Activity*

Research activity has been oriented either toward translational neuro-oncological projects as well as toward new, innovative, more effective surgical techniques.
In these years several cooperative studies with national and international institutions were pursued, activated or are in progress.
The aim of our multi-specialist translational group was to identify new molecular glioma biomarkers useful for better determine the diagnosis, prognosis and/or therapeutic response. To accomplish these goal we take advantage of an extensive database including retrospective as well prospective case series collected at IRE. Presently our database includes clinical and molecular information obtained from more than 800 patients affected with primary brain tumors (mainly malignant gliomas; more than 400 glioblastoma). An average of 60 patients are included every year.
On this basis we already analyzed the value of the expression of MGMT as a relevant predictor of therapeutic response and good prognosis in GBM patients.
Our research have underlined the importance of MGMT in the management of GBM patients; presently a large cooperative study with other Italian groups is in progress and the result are waited in the near future.
Utilizing the same data set, we are analyzing the information from patients affected by oligodendroglioma or astrocytoma, with the aim of defining the prognostic value of 1p/19q LOH (loss of heterozygosis) in this setting as well the potential predictive/prognostic factors in GBM long survivors.
Recently a cooperative study, under the auspices of Alliance Against Cancer (AIRC), has been focused on this setting of long survivors with the aim of deeply understand molecular characteristics as well as therapeutic strategies that explained their prolonged survival.
Another relevant issue is related to research and identification of circulating biomarkers for detection and prognosis of primary brain tumors. We already reported our recent study on serum microRNA signature in a cohort of malignant glioma patients, evaluating eleven circulating serum microRNAs, previously associated with brain tumors, as potential non-invasive diagnostic biomarkers for glioma patients. Preliminary data of this relevant study have already been published.
The role of microRNA have been also investigated

in brain metastases. In particular, it has been assessed whether aberrant expression of specific microRNAs could contribute to brain metastases. Comparison of primary lung tumors and their matched metastatic brain disseminations identified shared patterns of several microRNAs, including common down-regulation of miR-145-5p, which appeared to play a pivotal roles in malignancy progression and in metastasis.

In a very recent paper, it has been showed that the miR-128-3p, which is up-regulated in lung cancer tissues, has Drosha and Dicer, two key enzymes of miRNAs processing, as the main modulation targets leading to the widespread down-regulation of miRNA expression. We observed that the miRNAs downregulation induced by miR-128-3p may significantly contributed to the tumorigenic properties of lung cancer cells.

Such translational studies which are currently under development including the analysis of specimens of different types of solid tumor, appear very promising to try to elucidate the innermost mechanism of metastatic spread of neoplastic disease.

The potential contribute of cerebrospinal fluid flow cytometry analysis for early detection and characterization of tumor cells in the presence of leptomeningeal carcinomatosis, in the phases of the first diagnosis as well as during treatment, with the aim of monitoring the extent of residual disease is also under investigation. Our pilot study, recently published, documents the expression of prognostic markers as well as putative stem cell in breast cancer leptomeningeal metastasis, trough flow cytometric analyses of CSF samples.

Another relevant research activity is directed toward the evaluation of new surgical strategies in the treatment of brain tumors.

In particular, fluorescence-guided resection represents an interesting tool for identifying tumor tissue and increasing the extent of surgery, taking advantage of metabolic and structural changes induced by a natural precursor of heme biosynthetic pathway, 5 amino-levulinic acid (5-ALA).

Our experience regarding more than 100 patients affected by malignant cerebral tumors has been presented in several scientific meetings.

More than 90% of patients showed intraoperative red fluorescence of core tumor tissue. Mainly in recurrent GBM, when MRI documented heterogeneous lesions with enhancing area mixed with non enhanced gliotic scars, fluorescence -guided surgery allowed a better definition of active tumor, with net margins from perilesional "healthy" brain.

With regard to spinal tumors, vertebral pathological fractures represent one of the most challenging issues. Due to its minimal invasion and immediate pain relief balloon kyphoplasty has gained an increased popularity for the treatment of symptomatic tumor or osteoporotic vertebral fractures. However in cancer patients, kyphoplasty is more challenging due to frequent presence of cord compression and the incidence of overall complications is ten fold greater.

A randomized clinical study is continuing on spinal surgical augmentation (kyphoplasty and vertebroplasty) procedures in secondary neoplastic lesions, comparing the results obtained with conventional polimethylmethylacrylate (PMMA) and the new silicone material VK100 (the study was approved by our EC, activated and presently more than 55 patients have been accrued).

The result of a preliminary experience of 44 oncologic patients who underwent kyphoplasty with VK100 for vertebral compression fractures, in terms of safety of the procedure, pain reduction, functional capacity and quality of life has been published in 2018.

The emerging role and integration of minimally invasive surgery with Radiosurgery, the so called "separation surgery" has been investigated by the Neurosurgical and Radiotherapy Units with the purpose to present in 2019 a combined protocol of treatment.

## Publications


1. Callovini GM, Telera S, Sherkat S, Sperduti I, Callovini T, Carapella CM. How is Stereotactic Brain Biopsy Evolving? A Multicentric Analysis of a Series of 421 Cases Treated in Rome Over the Last Sixteen Years. *Clin. Neurol. Neurosurg.* 2018 174: 101-107a

2. Carapella CM, Gorgoglione N, Oppido PA. The Role of Surgical Resection in Patients with Brain Metastases. *Curr. Opin. Oncol.* 2018 Nov; 30(6): 390a

3. Carapella CM, Oppido PA. The Present Role of Surgery for Brain Metastases. *World Neurosurg.* 2018 Dec; 120: 423-425a

4. Frixa T, Sacconi A, Cioce M, Roscilli G, Ferrara FF, Aurisicchio L, Pulito C, Telera S, Carosi M, Muti P, Strano S, Donzelli S, Blandino G. MicroRNA-128-3p-Mediated Depletion of Drosha Promotes Lung Cancer Cell Migration. *Carcinogenesis.* 2018 Feb 9; 39(2): 293a

5. Policicchio D, Muggianu G, Dipellegrini G, Boccaletti R. Delayed Diagnosis of Post-Traumatic Aneurysm of Distal Anterior Cerebral Artery. *Surg. Neurol. Int.* 2018 Nov 1; 9: 222a

6. Telera S, Pompili A, Crispo F, Giovannetti M, Pace A, Villani V, Fabi A, Sperduti I, Raus L. Kyphoplasty with Purified Silicone VK100 (Elastoplasty) to Treat Spinal Lytic Lesions in Cancer Patients: A Retrospective Evaluation of 41 Cases. *Clin. Neurol. Neurosurg.* 2018 Aug; 171: 184a

# OTOLARYNGOLOGY HEAD AND NECK SURGERY UNIT

*Head: Giuseppe Spriano, MD*


## STAFF:

| | |
|---|---|
| Raul Pellini MD, | Cinzia Mori, Nurse Coordinator |
| Giovanni Cristalli, MD | Alba Ara Pina, Nurse |
| Valentina Manciocco, MD | Bruna Boldrini, Nurse |
| Barbara Pichi, MD | Serena Cucchiella, Nurse |
| Giuseppe Mercante, MD | Fernando Golino, Nurse |
| Paolo Marchesi, MD | Marina Macis, Nurse |
| Jacopo Zocchi, MD | Iolanda Mantuano, Nurse |
| Francesco Bianco, Audiometrist | Francesco Mautone, Nurse |
| Sonia Gambardella , Audiometrist | Debora Cacciato, Nurse Case Manager |
| Alessandra Masiello, Speech Therapist | |

## Mission

We are committed to maintaining our status as leader in the discovery, innovation and implementation of the best practices, research and clinical care in otolaryngology-head & neck surgery.
We contribute to improve the health of individuals and populations through innovation and excellence in otolaryngology-head & neck surgical practice and research. Our program has a strong multidisciplinary translational approach focused on different aspects of Head and Neck Oncology.

## Clinical Activities

Ear, nose and throat and maxillofacial oncological surgery. Treating of fairly common head and neck cancers to more complicated and difficult cases. Highly specialized surgical protocols and/or procedures are performed by the staff and every decision regarding clinical cases is submitted to the Head and Neck Disease Management Team, which includes specialists in surgery, radiation oncology, medical oncology, endocrinology, radiology, pathology, speech therapy, plastic and reconstructive surgery, dental and maxillofacial prosthetics, nutrition, and pain management. The group meets weekly and works together to meet their patients' diverse needs. The Unit of Otolaryngology Head and Neck Surgery provides a complete spectrum of head and neck services including Endocrine, Microvascular surgery and minimally invasive approaches including Robotics.

## Research Activities

8. Human papillomavirus involvement in Head and Neck cancer.
9. Trans Oral Robotic Surgery (TORS)
10. Feasibility and efficacy of electrochemotherapy in Head Neck Cancer
11. mRNA expression profiling in Head Neck Cancer

## Publications


1. De Virgilio A, Pellini R, Mercante G, Cristalli G, Manciocco V, Giannarelli D, Spriano G. Supracricoid Partial Laryngectomy for Radiorecurrent Laryngeal Cancer: A Systematic Review of the Literature and Meta-Analysis. *Eur. Arch. Otorhinolaryngol.* 2018 Jul; 275(7): 1671-1680a

2. Heffler E, Malvezzi L, Boita M, Brussino L, De Virgilio A, Ferrando M, Puggioni F, Racca F, Stomeo N, Spriano G, Canonica GW. Immunological Mechanisms Underlying Chronic Rhinosinusitis with Nasal Polyps. Expert Rev.Clin. Immunol. 2018 Sep; 14(9): 731.

3. Iocca O, Farcomeni A, Di Rocco A, Di Maio P, Golusinski P, Pardinas Lopez S, Savo A, Pellini R, Spriano G. Locally Advanced Squamous Cell Carcinoma of the Head and Neck: A Systematic Review and Bayesian Network Meta-Analysis of the Currently Available Treatment Options. *Oral Oncol.* 2018 May; 80: 40-51.

4. Lombardi D, Accorona R, Lambert A, Mercante G, Coropciuc R, Paderno A, Lancini D, Spriano G, Nicolai P, Vander Poorten V. Long-Term Outcomes and Prognosis in Submandibular Gland Malignant Tumors: A Multicenter Study. *Laryngoscope.* 2018 Dec; 128(12): 2745a

5. Lombardi D, Paderno A, Giordano D, Barbieri D, Taboni S, Piazza C, Cappelli C, Bertagna F, Barbieri V, Piana S, Bellafiore S, Spriano G, Mercante G, Nicolai P. Therapeutic Lateral Neck Dissection in Well-Differentiated Thyroid Cancer: Analysis on Factors Predicting Distribution of Positive Nodes and Prognosis. *Head Neck.* 2018 Feb; 40(2): 242a

6. Pichi B, Pellini R, DE Virgilio A, Spriano G. Electrochemotherapy: A Well-Accepted Palliative Treatment by Patients with Head and Neck Tumours. *Acta Otorhinolaryngol. Ital.* 2018 Jun; 38(3): 181a

7. Piludu F, Gangemi E, Marucci L, Guerrisi A, Pellini R, Covello R, Carlini P, Spriano G, Sanguineti G, Marzi S, Vidiri A. MRI Evaluation using DWI and T2WI of Residual Lymph Nodes in Patients Affected by Head and Neck Squamous Cell Carcinoma Treated with Chemo-Radiotherapy. *Curr. Med. Imaging Rev.* 2018 14(4): 599a

8. Rollo F, Dona' MG, Pellini R, Pichi B, Marandino F, Covello R, Benevolo M. Cytology and Direct Human Papillomavirus Testing on Fine Needle Aspirates from Cervical Lymph Node Metastases of Patients with Oropharyngeal Squamous Cell Carcinoma Or Occult Primary. *Cytopathology.* 2018 Oct; 29(5): 449-454a

9. Simon C, Caballero C, Gregoire V, Thurnher D, Koivunen P, Ceruse P, Spriano G, Nicolai P, Licitra L, Machiels JP, Hamoir M, Andry G, Mehanna H, Hunter KD, Dietz A, Rene Leemans C. Surgical Quality Assurance in Head and Neck Cancer Trials: An EORTC Head and Neck Cancer Group Position Paper Based on the EORTC 1420 'Best of' and 24954 'Larynx Preservation' Study. Eur.J.Cancer. 2018 Nov; 103: 69.

10. Spriano G, Mercante G, Pellini R, Ferreli F. Total Laryngectomy: A New Lateral Cervical Approach. *Clin. Otolaryngol.* 2018 Apr; 43(2): 784a

11. Wu R, Paolini F, Frank D, Kamdar D, Curzio G, Pichi B, Pellini R, Spriano G, Bonagura VR, Venuti A, Steinberg BM. Latent Human Papillomavirus Type 16 Infection is Widespread in Patients with Oropharyngeal Cancers. *Oral Oncol.* 2018 Mar; 78: 222a

# PLASTIC & RECONSTRUCTIVE SURGERY UNIT

*Head: Roy De Vita, MD*

## STAFF

| |
|---|
| **Alfredo Alteri, MD Assistants** |
| **Maurizio Costantni, MD Assistants** |
| **Stefano Feliciano, MD Assistants** |
| **Pierpaolo Gullo, MD Assistants** |
| **Massimo Panimolle, MD Assistants** |
| **Marcello Pozzi, MD Assistants** |
| **Antonio Varanese MD Assistants** |
| **Iolanda Mantuano, Nurse, Vice Head** |
| **Attilio Santolamazza, Nurse** |

## *Mission*

Plastic and Reconstructive Surgery is very important in the general management of oncologic patients of the Regina Elena National Cancer Institute and plays a seminal role in the therapeutic course of patients affected with breast cancer.

Our Unit is actively involved in the definition and use of innovative therapeutic protocols. In particular, the expertise obtained our Unit is cooperating with most representative national structures.

## Clinical Activity

- Breast reconstruction
- Biological Mesh in implant-based breast reconstruction surgery
- SoK Tissue Sarcoma - The Plastic Surgery Unit deals with all
- types of skin cancers (epitheliomas, melanomas, other skin cancers locations) that focus especially on craniofacial locations that require complex reconstructions and together with the Dermatology Unit are dedicated on preventing skin cancer diseases. In collaboration with the General and Orthopedic Surgery Unit, the activities are aimed against sarcomas of the limbs through the morphofunctional microsurgical reconstruction of the structures involved.
- Extravasation of anticancer drugs in Oncology: Prevention, treatment and outcomes The incidence of extravasation of anti neoplastic drugs reported in the literature, ranges from 3% to 6%. This percentage, however, is increasing for introducing new chemotherapeutic drugs such as Vinorelvina and Taxanes. While these drugs certainly represent an important therapeutic alternative in the treatment of solid tumors, particularly breast cancer, local toxicity levels are higher in these drugs than those that preceded them.

## Publications

1. De Vita R, Buccheri EM. Nipple Sparing Mastectomy and Direct to Implant Breast Reconstruction, Validation of the Safe Procedure through the use of Laser Assisted Indocyanine Green Fluorescent Angiography. Gland Surg. 2018 Jun; 7(3): 258a

2. De Vita R, Buccheri EM, Villanucci A, Pozzi M. Breast Reconstruction Actualized in Nipple-Sparing Mastectomy and Direct-to-Implant, Prepectoral Polyurethane Positioning: Early Experience and Preliminary Results. Clin. Breast Cancer. 2018 Dec 27;

3. Nava MB, Adams WP Jr, Botti G, Campanale A, Catanuto G, Clemens MW, Del Vecchio DA, De Vita R, Di Napoli A, Hall-Findlay E, Hammond D, Heden P, Mallucci P, Martin Del Yerro JL, Muti E, Rancati A, Randquist C, Salgarello M, Stan C, Rocco N. MBN 2016 Aesthetic Breast Meeting BIA-ALCL Consensus Conference Report. Plast. Reconstr. Surg. 2018 Jan; 141(1): 40a.

# ORTHOPAEDICS UNIT

*Head: Roberto Biagini, MD*

## STAFF

| MD |
|---|
| Leonardo Favale |
| Nicola Salducca |
| Carmine Zoccali |
| Jacopo Baldi |
| **Case Manager** |
| Wioletta Faltyn |
| **Data Manager** |
| Elisa Checcucci |

| Nurse |
|---|
| Giovanni Meogrossi |
| Rosario D'Angelo |
| Grazia Amato, Paolo Asquini |
| Fabio Conti |
| Antonella Cutini |
| Carolina Destito |
| Matteo Ferraro |
| Sabrina Ganzenua |
| Stefano Landi |
| Alessia Milotti |

## Mission

Aim of the division is to diagnose and care primary and secondary tumors of bone and soft tissue in pediatric and adult patients and to perform translational and clinical research in this field.
The unit performs every kind of orthopedic oncological operation for primitive and metastatic muscular-skeletal tumors in adults and pediatric patients.
During 2018, the unit has perfected computer assisted navigated techniques and reconstruction with titanium 3D-printing prostheses after bone tumor removal.

## Clinical Activity

Patients who need surgery for primary or secondary tumors of the bone and soft tissue are hosted in the ward (12 regular beds). The ward has a fully furnished (and painted) pediatric room with telematic-teaching service (available for long-term patients), videogames, books and comics. Five rooms out of seven are decorated with the intent of improving the patient's hospitalization experience.
Surgery in performed twice a week, every month, in one of the eight operating room of the operating block. Biopsies for bony or soft tissue lesions are performed, once a week, in a dedicated small operating room.
There are a total of three orthopedic clinics for outpatients: on Monday for benign and low-grade malignant tumors; on Wednesday for high grade sarcomas (multidisciplinary clinic in collaboration with Oncologist and Psychologist); on Friday for metastatic disease involving muskulskeletal system. On the first Friday of every month there is a dedicated outpatient clinic for exostoses and cartilaginous tumors (benign to low-grade malignant).
Once a week, on Wednesday, there is dedicated clinic for wound care and withdrawal of biopsy reports.
Twice a week takes place the Disease Management Team (DMT) meeting for the discussion of clinical cases. A Biobank collects biological samples from patients with musculoskeletal tumors, visceral sarcomas and muscular-skeletal metastasis.

## Research Activity

- Observational study: ISG-STS 10.01 Localized high-risk soft tissue sarcomas of the extremities and trunk wall in adults: an integrating approach comprising standard vs histotype-tailored neoadjuvant Chemotherapy.

- Phase III: open 5 -15 ISG/AIEOP EW1 Phase III trial on the efficacy of dose intensification in patients with non-metastatic Ewing Sarcoma.
- Phase III : open 2 -8 RECURR International Randomised controlled trial of Chemotherapy for the treatment of recurrent and primary refractory Ewing Sarcoma Phase II/III.
- **Sacral Chordoma** – IT – IRE Studio randomizzato e osservazionale sulla CHIRURGIA in confronto alla RADIOTERAPIA nella malattia primitiva localizzata ( SACRO ).
- **Naobiotix n. 301:** Studio multicentrico, randomizzato, in aperto, di fase II/III per confrontare l'efficacia di NBTXR3, impiantato con iniezione intratumorale e attivo mediante radioterapia, risposto alla sola radioterapia, in pazienti affetti da Sarcoma della parete dei tessuti molli degli arti e del tronco, localmente avanzato.
- **Studio asservazionale DAC** Studio clinico multicentrico osservazionale prospettico per la verifica dell'efficacia di un presidio medico chirurgico, DAC gel, per la prevenzione dell'infezione periprotesica a seguito di ricostruzione di ampie resezioni ossee con posizionamento di megaimpianto.
- **CTC/ctDNA** Studio del significato clinico di cellule ed acidi nucleici tumorali circolanti nei sarcomi dei tessuti molli e dell'osso. CTC/ctDNA nei sarcomi tessuti molli e dell'osso.

## Publications

1. Allegretti M, Casini B, Mandoj C, Benini S, Alberti L, Novello M, Melucci E, Conti L, Covello R, Pescarmona E, Milano GM, Annovazzi A, Anelli V, Ferraresi V, Biagini R, Giacomini P. Precision Diagnostics of Ewing's Sarcoma by Liquid Biopsy: Circulating EWS-FLI1 Fusion Transcripts. *Ther. Adv. Med. Oncol.* 2018 Jun 1; 10: 1758835918774337a

2. Baldi J, Attala D, Scotto di Uccio A, Laquintana V, Biagini R, Zoccali C. The Effectiveness of a Standard Drill Connected to a Core Biopsy Needle: How to Obtain Specimens in very Strong Bone Tumors. *Injury.* 2018 Aug; 49(8): 1612-1616a

3. Casali PG, Abecassis N, Bauer S, Biagini R, Bielack S, Bonvalot S, Boukovinas I, Bovee JVMG, Brodowicz T, Broto JM, Buonadonna A, De Alava E, Dei Tos AP, Del Muro XG, Dileo P, Eriksson M, Fedenko A, Ferraresi V, Ferrari A, Ferrari S, Frezza AM, Gasperoni S, Gelderblom H, Gil T, Grignani G, Gronchi A, Hannu A, Hassan B, Hohenberger P, Issels R, Joensuu H, Jones RL, Judson I, Jutte P, Kaal S, Kasper B, Kopeckova K, Krakorova DA, Le Cesne A, Lugowska I, Merimsky O, Montemurro M, Pantaleo MA, Piana R, Picci P, Piperno-Neumann S, Pousa AL, Reichardt P, Robinson MH, Rutkovski P, Safwat AA, Schoffski P, Sleijfer S, Stacchiotti S, Sundby Hall K, Unk M, Van Coevorden F, Van der Graaf W, Whelan J, Wardelmann E, Zaikova O, Blay JY, ESMO Guidelines Committee and EURACAN. Gastrointestinal Stromal Tumours: ESMO-EURACAN Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. *Ann. Oncol.* 2018 Oct 1; 29(Supplement_4): iv68-iv78a

4. Casali PG, Abecassis N, Bauer S, Biagini R, Bielack S, Bonvalot S, Boukovinas I, Bovee JVMG, Brodowicz T, Broto JM, Buonadonna A, De Alava E, Dei Tos AP, Del Muro XG, Dileo P, Eriksson M, Fedenko A, Ferraresi V, Ferrari A, Ferrari S, Frezza AM, Gasperoni S, Gelderblom H, Gil T, Grignani G, Gronchi A, Hannu A, Hassan B, Hohenberger P, Issels R, Joensuu H, Jones RL, Judson I, Jutte P, Kaal S, Kasper B, Kopeckova K, Krakorova DA, Le Cesne A, Lugowska I, Merimsky O, Montemurro M, Pantaleo MA, Piana R, Picci P, Piperno-Neumann S, Pousa AL, Reichardt P, Robinson MH, Rutkovski P, Safwat AA, Schoffski P, Sleijfer S, Stacchiotti S, Sundby Hall K, Unk M, Van Coevorden F, Van der Graaf W, Whelan J, Wardelmann E, Zaikova O, Blay JY, ESMO Guidelines Committee and EURACAN. Soft Tissue and Visceral Sarcomas: ESMO-EURACAN Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. *Ann. Oncol.* 2018 Oct 1; 29(Supplement_4): iv51-iv67a

5. Casali PG, Bielack S, Abecassis N, Aro HT, Bauer S, Biagini R, Bonvalot S, Boukovinas I, Bovee JVMG, Brennan B, Brodowicz T, Broto JM, Brugieres L, Buonadonna A, De Alava E, Dei Tos AP, Del Muro XG, Dileo P, Dhooge C, Eriksson M, Fagioli F, Fedenko A, Ferraresi V, Ferrari A, Ferrari S, Frezza AM, Gaspar N, Gasperoni S, Gelderblom H, Gil T, Grignani G, Gronchi A, Haas RL, Hassan B, Hecker-Nolting S, Hohenberger P, Issels R, Joensuu H, Jones RL, Judson I, Jutte P, Kaal S, Kager L, Kasper B, Kopeckova K, Krakorova DA, Ladenstein R, Le Cesne A, Lugowska I, Merimsky O, Montemurro M, Morland B, Pantaleo MA, Piana R, Picci P, Piperno-Neumann S, Pousa AL, Reichardt P, Robinson MH, Rutkowski P, Safwat AA, Schoffski P, Sleijfer S, Stacchiotti S, Strauss SJ, Sundby Hall K, Unk M, Van Coevorden F, van der Graaf WTA, Whelan J, Wardelmann E, Zaikova O, Blay JY, ESMO Guidelines Committee, PaedCan and ERN EURACAN. Bone Sarcomas: ESMO-PaedCan-EURACAN Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. *Ann. Oncol.* 2018 Oct 1; 29(Supplement_4): iv79a

6. Di Martile M, Desideri M, Tupone MG, Buglioni S, Antoniani B, Mastroiorio C, Falcioni R, Ferraresi V, Baldini N, Biagini R, Milella M, Trisciuoglio D, Del Bufalo D. Histone Deacetylase Inhibitor ITF2357 Leads to Apoptosis and Enhances Doxorubicin Cytotoxicity in Preclinical Models of Human Sarcoma. *Oncogenesis.* 2018 Feb 23; 7(2): 20a

7. Loria R, Laquintana V, Bon G, Trisciuoglio D, Frapolli R, Covello R, Amoreo CA, Ferraresi V, Zoccali C, Novello M, Del Bufalo D, Milella M, Biagini R, D'Incalci M, Falcioni R. HMGA1/E2F1 Axis and NFkB Pathways Regulate LPS Progression and Trabectedin Resistance. *Oncogene.* 2018 Nov; 37(45): 5926a

8. Paladini A, Lucatelli P, Cappelli F, Pizzi G, Anelli V, Amodeo EM, Beomonte Zobel D, Paladini L, Biagini R, Attala D, Zoccali C, Vallati GE. Osteoid Osteoma Treated with Radiofrequency Ablation in Non-Operating Room Anesthesia. A Different Way of Approaching Ablative Therapy on Osteoid Osteoma. *Eur. Rev. Med. Pharmacol. Sci.* 2018 Sep; 22(17): 5438a-5446

9. Zoccali C, Attala D, Rossi B, Zoccali G, Ferraresi V. Fibrous Dysplasia: An Unusual Case of a very Aggressive Form with Costo-Vertebral Joint Destruction and Invasion of the Contralateral D7 Vertebral Body. *Skeletal Radiol.* 2018 Nov;47(11):1571-1576

10. Zoccali, Carmine, Dario Attala, Alessandra Scotto, and Roberto Biagini. 2018. "Megaprosthesis for Metastasis of the Lower Limb." Chap. 14, In *Management of Bone Metastases*, 149-157: Springer.

11. Zoccali C, Baldi J, Attala D, Rossi B, Anelli V, Annovazzi A, Ferraresi V. Intralesional Vs. Extralesional Procedures for Low-Grade Central Chondrosarcoma: A Systematic Review of the Literature. *Arch. Orthop. Trauma Surg.* 2018 Jul; 138(7): 929a

12. Zoccali C, Baldi J, Catanea A, Calabrò F, Calabrò D. The Spine Deformities of the Adolescent: The Pediatrician's Approach. Quaderni ACP. 2018

# BREAST AND SOFT TISSUE SURGERY UNIT

## Head: Claudio Botti, MD

| STAFF |
|---|
| **Franco Graziano, MD** |
| **Loredana Piarulli, MD** |
| **Sonia Cappelli, MD** |
| **Fabio Pelle,MD** |
| **Giovanna Grazioli, Head Nurse** |
| **Elisabetta Canofari, nurse** |
| **Nadia D'Antoni, nurse** |
| **Maria Antonietta Di Ceglie, nurse** |
| **Fiorella Molinari, nurse** |
| **Maria Antonietta Picano, nurse** |
| **Viviana Ruspolini, nurse** |
| **Emanuela Vincenzi, nurse** |
| **Agostino Castaldo, nurse** |

## Mission

To take care of patients with tumors of the breast, melanomas and soft tissue sarcomas providing high-quality, patient oriented treatments according to the multidisciplinary evaluations (disease management team, DMT) aimed to improve survival and quality of life.

## Clinical Activity

The activity is divided into: muldisciplinary evaluation at the breast unit and other pathology oriented DMT, outpatient surgery, day surgery, hospitalization.
Type of surgery performed:
Conservative and radical surgery of breast tumors with particular reference to oncoplatic surgery (volume displacement techniques, volume replacement and innovative propeller flaps), immediate reconstrucive surgery in cases of mastectomy and preservation solutions of the skin and the nipple areola complex. Innovative prepectoral implant based breast reconstruction are currently explored in collaboration with the Division of Plastic and Reconstructive Surgery.
Complex demolitive surgery in locoregionally recurrent cases.
In selected cases intraoperative radiotherapy (IORT) is performed.
Locoregional treatment of primitive and recurrent melanoma (wide excision, sentinel lymph node biopsy, radical regional lymphadenectomy, hyperthermic-antiblastic perfusion in selected cases, electrochemotherapy).

## Research Activity

**Main research lines:**

- Identification of signature responsiveness to innovative drugs
- Identification of new imaging techniques in senology (CESM)
- Indocyanine green as an alternative method to other sentinel lymph node screening techniques,
- Innovative technical application of conservative volume--replacement oncoplasty by fascio-adipose propeller flaps set up by microsurgical anatomical dissection

**Collaborative studies ongoing:**

- Prospective validation of TAZ--score as a pathological complete response biomarker in patients with luminal B / HER2--positive breast cancer treated with trastuzumab--based neo-adjuvant therapy -- TRISKELE Trial
- Impact of expression of Hippo pathway components in patients with breast cancer treated or candidate for neoadjuvant chemotherapy
- E-cacy and Tolerability of Cario--Patient Neopardive Chemotherapy in Patients with Triple Negative Breast Cancer: Multicenter Observational Study. NeoCarbo study
- Predictidicve / Prognostic Biomarkers IdentificaMon in Triple--Negative Breast Cancer. NeoTAZ study

TAZ as a prognostic biomarker in patients with early breast cancer. PHOBOS Trial
Atorvastatin vs Observation in Patients with Initial Breast Cancer with High Ki--67 and Positivity for TAZ: randomized, non--comparative Phase II pre--surgical study

- Neo-Adjuvant Chemotherapy in Patients with Breast Cancer: Retrospective Evaluation of E-ectiveness and Tolerability
- Analysis of the predictive value of e-cacy of anti-neoplastic therapies based on the evaluation of molecular pathways associated with tumor stem cells: multi-setting and multitumor study. HIERARCHY Study
- Accuracy Diagnostics of Dual--Energy Digital Mammography (CESM) and Magnetic Resonance Imaging 3 Tesla Compared to Digital Mammography (FFDM) plus Ecography (US) in Detection and Characterization of Mammary Lesions: Results from an Open--Study Pilot, monocentric, prospective Molecular mechanism of quadruplex--targeted drugs: towards clinical candidate selection

## *Publications*

1. Mandoj C, Pizzuti L, Sergi D, Sperduti I, Mazzotta M, Di Lauro L, Amodio A, Carpano S, Di Benedetto A, Botti C, Ferranti F, Antenucci A, D'Alessandro MG, Marchetti P, Tomao S, Sanguineti G, Giordano A, Maugeri-Sacca M, Ciliberto G, Conti L, Vici P, Barba M. Observational Study of Coagulation Activation in Early Breast Cancer: Development of a Prognostic Model Based on Data from the Real World Setting. *J. Transl. Med.* 2018 May 16; 16(1): 129a

2. Pizzuti L, Sergi D, Sperduti I, Lauro LD, Mazzotta M, Botti C, Izzo F, Marchetti L, Tomao S, Marchetti P, Natoli C, Grassadonia A, Gamucci T, Mentuccia L, Magnolfi E, Vaccaro A, Cassano A, Rossi E, Botticelli A, Sini V, Sarobba MG, Fabbri MA, Moscetti L, Astone A, Michelotti A, De Angelis C, Bertolini I, Angelini F, Ciliberto G, Maugeri-Sacca M, Giordano A, Barba M, Vici P. Body Mass Index in HER2-Negative Metastatic Breast Cancer Treated with First-Line Paclitaxel and Bevacizumab. *Cancer. Biol. Ther.* 2018 Apr 3; 19(4): 328a

3. Vicini E, Invento A, Cuoghi M, Bafile A, Battaglia C, Biglia N, Busani M, Bussone R, Cianchetti E, Caruso F, Cucchi MC, Dessena M, Di Filippo F, Fabi A, Folli S, Friedman D, Macellari G, Mainente P, Murgo R, Neri A, Pollini GP, Palli D, Ricci F, Scalco G, Taffurelli M, Trunfio M, Galimberti V, Italian Society of Surgical Oncology (SICO) Breast Oncoteam. Neoadjuvant Systemic Treatment for Breast Cancer in Italy: The Italian Society of Surgical Oncology (SICO) Breast Oncoteam Survey. *Eur. J. Surg. Oncol.* 2018 Aug; 44(8): 1157a

# MEDICAL ONCOLOGY 1 UNIT

*Head: Francesco Cognetti, MD*

## STAFF

| | |
|---|---|
| Paolo Carlini, MD Assistant | Paola Malaguti, MD Senior Fellow |
| Michele Milella, MD Assistant | Domenica Pellegrini, MD Senior Fellows |
| Elvira Colella, MD Assistant | Chiara Spoto, MD Senior Fellows |
| Fabiana Cecere, MD Assistant | Vanja Vaccaro, MD Senior Fellow |
| Consuelo D'Ambrosio, MD Assistant | Sabrina Vari, MD Senior Fellows |
| Alessandra Fabi, MD Assistant | Giovanna Catania, Resident |
| Virginia Ferraresi, MD Assistant | Michela Palleschi, MD Senior Fellows |
| Gianluigi Ferretti, MD Assistant | Silvia Bastucci, Data Manager |
| Cecilia Nisticò, MD Assistant | Marianna Introna, Data Manager |
| Michelangelo Russillo, MD | Agnese Provenziani, Data Manager |
| Antonella Savarese, MD Assistant | Marianna Ferrara, Data Manager |
| Massimo Zeuli, MD Assistant | Sonia Borrelli, Data Manager |
| Simona Gasparro, MD Senior Fellow | Mariangela Lifrieri, Nurse Coordinator |

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|---|
| **Isabella Bertazzi, Nurse Coordinator** |
| **Pietro Calabretta, Nurse** |
| **Immacolata D'Orsi, Nurse** |
| **Giovanni Cortese, Nurse** |
| **Roberto Ferro, Nurse** |
| **Giampiero Giansanti, Nurse** |
| **Alessia Mariotti, Nurse** |
| **Gigliola Mammana, Nurse** |
| **Giuseppe Giambalvo, Nurse** |
| **Maria Di Santo, Nurse** |
| **Patrizia Minonne, Nurse** |
| **Wioletta Faltyn, Nurse** |
| **Maria Grazia Cioffi, Nurse** |
| **Arianna Cicerone, Nurse** |

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|---|
| **Lorena Scarton, Nurse** |
| **Gina Marcantonio, Nurse** |
| **Antonella Gagliardo, Nurse** |
| **Anna Franca Speranza, Nurse** |
| **Anna Maria Biscu, Nurse** |
| **Teresa Borruso, Nurse** |
| **Anna Maria Barberini, Nurse** |
| **Ornella Barlone, Nurse** |
| **Massimo Colantoni, Nuse** |
| **Alessandra Pasqua, Nurse** |
| **Alessia Barassi, Secretariat** |
| **Francesca Sabbatini, Secretariat** |
| **Massimo Andaloro, Administrative Collaborator** |

## Mission

The Division of Medical Oncology 1 has a long standing commitment in improving the diagnosis detection and treatment of solid cancers. The Division's clinical activity guarantees evidence-based treatments and clinical assistance for cancer patients requiring therapy disease monitoring and follow up. Moreover, the Division has been developing clinical research and new treatment strategies on solid tumors using both new immunotherapeutic agents such as checkpoint inhibitors or targeted agents for different tumors in addition to the classic antineoplastic drugs. The work's strategy is based on a multidisciplinary approach to the clinical aspects so assuring a personalized and integrated approach to the disease in the respect of the patient centrality and quality of life. The medical team is strongly oriented in creating collaborative pathways with national and international working groups and scientific societies and in participation to the strategic aims of the IRE.

## Clinical Activity

The Division of Medical Oncology 1 consists in 4 separate units: a) in-patient unit which includes 22 beds dedicated to highly complex diagnostic procedures, oncological treatments and management of severe toxicities; b) out-patient unit dedicated to the first visit of new patients and clinical follow up and oncologic genetic counseling; c) Day Hospital and Ambulatory Chemotherapy Services for administration of oral and intravenous antineoplastic drugs and supportive cares. d) Phase 1 Unit for early clinical trials.
Clinical activity is supported by weekly divisional meeting in order to share decisions on patients at first observation or critical clinical cases and ameliorate the internal procedures. Physicians of the Medical Oncology 1 are the most actively involved in all the interdisciplinary Disease Management Team (DMT). In each DMT, a group of physicians is dedicated to the treatment and follow up of patients according to national and international guidelines. Team members provide state of the art diagnosis and treatment of patients with solid cancers, and are able to follow the patient by continually updating the database that tracks the patient.

## Research Activity

The main research topics of the Division is the study of new drugs (targeted therapies, immunological checkpoint inhibitors, etc) their combinations and/or sequence and new strategies of integrated treatments in almost all solid tumors of the adult population. Some studies are also addressed to the treatment of pediatric bone sarcomas. The Division is committed to conducting national and international clinical trials in collaboration with industries or no-profit cooperative groups. During 2018, 82 clinical studies were ongoing in different tumors, with the enrolment of 552 patients. Field of interest of the Division is also the involvement

in projects that investigate and promote patient's quality of life (such as integrated medicine and narrative medicine) in collaboration with patient associations. The clinical research activity of the Division is sustained by five fully trained data manager with expertise in conducting clinical trials in good clinical practice. Special emphasis is moreover given to the collaboration with basic researchers to identify molecular prognostic or predictive biomarkers. This latter activity is shared with the internal laboratories department and with the research branch of other national cancer institutes. The medical division is also involved in the basic research that is carried out within its own laboratory, equipped with research personnel and instruments suitable for cell cultures and molecular diagnostics. The main field of activity is aimed at understanding the mechanisms of signal transduction and phosphorylation of tumor cells. This activity is supported with founds provided by national research organization (AIRC…). Most physicians of the Division are involved in scientific boards, guidelines editing groups and in national and international networks.

## Pubblications


1. Allegretti M, Casini B, Mandoj C, Benini S, Alberti L, Novello M, Melucci E, Conti L, Covello R, Pescarmona E, Milano GM, Annovazzi A, Anelli V, Ferraresi V, Biagini R, Giacomini P. Precision Diagnostics of Ewing's Sarcoma by Liquid Biopsy: Circulating EWS-FLI1 Fusion Transcripts. *Ther.Adv.Med.Oncol.* 2018 Jun 1; 10: 1758835918774337a

2. Allegretti M, Fabi A, Buglioni S, Martayan A, Conti L, Pescarmona E, Ciliberto G, Giacomini P. Tearing Down the Walls: FDA Approves Next Generation Sequencing (NGS) Assays for Actionable Cancer Genomic Aberrations. *J.Exp.Clin. Cancer Res.* 2018 Mar 5; 37(1): 47a

3. Annovazzi A, Rea S, Vici P, Fabi A, Sciuto R. Dual-Time 18F-FDG PET/CT for the Detection of Liver Metastases in Breast Cancer. *Nucl.Med.Commun.* 2018 Dec; 39(12): 1183-1189a

4. Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R, Kurata T, Chiappori A, Lee KH, de Wit M, Cho BC, Bourhaba M, Quantin X, Tokito T, Mekhail T, Planchard D, Kim YC, Karapetis CS, Hiret S, Ostoros G, Kubota K, Gray JE, Paz-Ares L, de Castro Carpeno J, Faivre-Finn C, Reck M, Vansteenkiste J, Spigel DR, Wadsworth C, Melillo G, Taboada M, Dennis PA, Ozguroglu M, PACIFIC Investigators. Milella M. (c.) Overall Survival with Durvalumab After Chemoradiotherapy in Stage III NSCLC. N.Engl.J.Med. 2018 Dec 13; 379(24): 2342.

5. Ascierto PA, Long GV, Robert C, Brady B, Dutriaux C, Di Giacomo AM, Mortier L, Hassel JC, Rutkowski P, McNeil C, Kalinka-Warzocha E, Savage KJ, Hernberg MM, Lebbe C, Charles J, Mihalcioiu C, Chiarion-Sileni V, Mauch C, Cognetti F, Ny L, Arance A, Svane IM, Schadendorf D, Gogas H, Saci A, Jiang J, Rizzo J, Atkinson V. Survival Outcomes in Patients with Previously Untreated BRAF Wild-Type Advanced Melanoma Treated with Nivolumab Therapy: Three-Year Follow-Up of a Randomized Phase 3 Trial. *JAMA Oncol.* 2018 Oct 25; [Epub ahead of print]

6. Barni S, Livraghi L, Morritti M, Vici P, Michelotti A, Cinieri S, Fontanella C, Porcu L, Del Mastro L, Puglisi F, ESEMPiO Study Group. Eribulin in the Treatment of Advanced Breast Cancer: Real-World Scenario from 39 Italian Centers - ESEMPiO Study. *Future Oncol.* 2018 Nov 9 [Epub ahead of print]

7. Bergamini A, Ferrandina G, Candiani M, Cormio G, Giorda G, Lauria R, Perrone AM, Scarfone G, Breda E, Savarese A, Frigerio L, Gadducci A, Mascilini F, Maneschi F, Cassani C, Marchetti C, Cecere SC, Biglia N, De Giorgi U, Raspagliesi F, Lorusso D, Mangili G. Laparoscopic Surgery in the Treatment of Stage I Adult Granulosa Cells Tumors of the Ovary: Results from the MITO-9 Study. *Eur.J.Surg.Oncol.* 2018 Jun;44(6):766-770

8. Bersanelli M, Giannarelli D, Castrignano P, Fornarini G, Panni S, Mazzoni F, Tiseo M, Rossetti S, Gambale E, Rossi E, Papa A, Cortellini A, Lolli C, Ratta R, Michiara M, Milella M, De Luca E, Soraru M, Mucciarini C, Atzori F, Banna GL, La Torre L, Vitale MG, Massari F, Rebuzzi SE, Facchini G, Schinzari G, Tomao S, Bui S, Vaccaro V, Procopio G, De Giorgi U, Santoni M, Ficorella C, Sabbatini R, Maestri A, Natoli C, De Tursi M, Di Maio M, Rapacchi E, Pireddu A, Sava T, Lipari H, Comito F, Verzoni E, Leonardi F, Buti S. INfluenza Vaccine Indication during Therapy with Immune Checkpoint Inhibitors: A Transversal Challenge. the INVIDIa Study. *Immunotherapy.* 2018 Oct; 10(14): 1229a

9. Brunetti O, Aprile G, Marchetti P, Vasile E, Casadei Gardini A, Scartozzi M, Barni S, Delfanti S, De Vita F, Di Costanzo F, Milella M, Cella CA, Berardi R, Cataldo I, Scarpa A, Basile D, Mazzuca F, Graziano G, Argentiero A, Santini D, Reni M, Cascinu S, Silvestris N. Systemic Chemotherapy for Advanced Rare Pancreatic Histotype Tumors: A Retrospective Multicenter Analysis. *Pancreas.* 2018 May 15; 47(6): 759-771a

10. Calabrese V, Menna P, Annibali O, Armento G, Carpino A, Cerchiara E, Greco C, Marchesi F, Spallarossa P, Toglia G, Reggiardo G, Minotti G. Fabi A. (c.) Early Diastolic Dysfunction After Cancer Chemotherapy: Primary Endpoint Results of a Multicenter Cardio-Oncology Study. *Chemotherapy.* 2018 63(2): 55a

11. Carnio S, Galetta D, Scotti V, Cortinovis DL, Antonuzzo A, Pisconti S, Rossi A, Martelli O, Cecere FL, Lunghi A, Del Conte A, Montagna ES, Topulli J, Pelizzoni D, Rapetti SG, Gianetta M, Pacchiana MV, Pegoraro V, Cataldo N, Bria E, Novello S. Chemotherapy-Induced Nausea and Vomiting (CINV) in Patients with Advanced Lung Cancer during the First-Line Treatment: Assessment by Physicians, Nurses, and Patients from an Italian Multicenter Survey. Support.Care Cancer. 2018 Jun; 26(6): 1841.

12. Casali PG, Abecassis N, Bauer S, Biagini R, Bielack S, Bonvalot S, Boukovinas I, Bovee JVMG, Brodowicz T, Broto JM, Buonadonna A, De Alava E, Dei Tos AP, Del Muro XG, Dileo P, Eriksson M, Fedenko A, Ferraresi V, Ferrari A, Ferrari S, Frezza AM, Gasperoni S, Gelderblom H, Gil T, Grignani G, Gronchi A, Hannu A, Hassan B, Hohenberger P, Issels R, Joensuu H, Jones RL, Judson I, Jutte P, Kaal S, Kasper B, Kopeckova K, Krakorova DA, Le Cesne A, Lugowska I, Merimsky O, Montemurro M, Pantaleo MA, Piana R, Picci P, Piperno-Neumann S, Pousa AL, Reichardt P, Robinson MH, Rutkovski P, Safwat AA, Schoffski P, Sleijfer S, Stacchiotti S, Sundby Hall K, Unk M, Van Coevorden F, Van der Graaf W, Whelan J, Wardelmann E, Zaikova O, Blay JY, ESMO Guidelines Committee and EURACAN. Gastrointestinal Stromal Tumours: ESMO-EURACAN Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. *Ann. Oncol.* 2018 Oct 1; 29(Supplement_4): iv68-iv78a

13. Casali PG, Abecassis N, Bauer S, Biagini R, Bielack S, Bonvalot S, Boukovinas I, Bovee JVMG, Brodowicz T, Broto JM, Buonadonna A, De Alava E, Dei Tos AP, Del Muro XG, Dileo P, Eriksson M, Fedenko A, Ferraresi V, Ferrari A, Ferrari S, Frezza AM, Gasperoni S, Gelderblom H, Gil T, Grignani G, Gronchi A, Hannu A, Hassan B, Hohenberger P, Issels R, Joensuu H, Jones RL, Judson I, Jutte P, Kaal S, Kasper B, Kopeckova K, Krakorova DA, Le Cesne A, Lugowska I, Merimsky O, Montemurro M, Pantaleo MA, Piana R, Picci P, Piperno-Neumann S, Pousa AL, Reichardt P, Robinson MH, Rutkovski P, Safwat AA, Schoffski P, Sleijfer S, Stacchiotti S, Sundby Hall K, Unk M, Van Coevorden F, Van der Graaf W, Whelan J, Wardelmann E, Zaikova O, Blay JY, ESMO Guidelines Committee and EURACAN. Soft Tissue and Visceral Sarcomas: ESMO-EURACAN Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. *Ann. Oncol.* 2018 Oct 1; 29(Supplement_4): iv51-iv67a

14. Casali PG, Bielack S, Abecassis N, Aro HT, Bauer S, Biagini R, Bonvalot S, Boukovinas I, Bovee JVMG, Brennan B, Brodowicz T, Broto JM, Brugieres L, Buonadonna A, De Alava E, Dei Tos AP, Del Muro XG, Dileo P, Dhooge C, Eriksson M, Fagioli F, Fedenko A, Ferraresi V, Ferrari A, Ferrari S, Frezza AM, Gaspar N, Gasperoni S, Gelderblom H, Gil T, Grignani G, Gronchi A, Haas RL, Hassan B, Hecker-Nolting S, Hohenberger P, Issels R, Joensuu H, Jones RL, Judson I, Jutte P, Kaal S, Kager L, Kasper B, Kopeckova K, Krakorova DA, Ladenstein R, Le Cesne A, Lugowska I, Merimsky O, Montemurro M, Morland B, Pantaleo MA, Piana R, Picci P, Piperno-Neumann S, Pousa AL, Reichardt P, Robinson MH, Rutkowski P, Safwat AA, Schoffski P, Sleijfer S, Stacchiotti S, Strauss SJ, Sundby Hall K, Unk M, Van Coevorden F, van der Graaf WTA, Whelan J, Wardelmann E, Zaikova O, Blay JY, ESMO Guidelines Committee, PaedCan and ERN EURACAN. Bone Sarcomas: ESMO-PaedCan-EURACAN Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. *Ann. Oncol.* 2018 Oct 1; 29(Supplement_4): iv79a

15. Catania G, Malaguti P, Gasparro S, Cognetti F, Vidiri A, Fabi A. Activity of Eribulin Mesylate in Brain Metastasis from Breast Cancer: A Stone in a Pond? *Oncology.* 2018 94(Suppl 1): 29a

16. Cazzaniga M, Verusio C, Ciccarese M, Fumagalli A, Sartori D, Ancona C, Airoldi M, Moretti G, Ficorella C, Arcangeli V, Diodati L, Zambelli A, Febbraro A, Generali D, Pistelli M, Garrone O, Musolino A, Vici P, Maur M, Mentuccia L, La Verde N, Bianchi G, Artale S, Blasi L, Piezzo M, Atzori F, Turletti A, Benedetto C, Cursano MC, Fabi A, Gebbia V, Schirone A, Palumbo R, Ferzi A, Frassoldati A, Scavelli C, Clivio L, Torri On Behalf Of The Eva Study Group, V. Everolimus (EVE) and Exemestane (EXE) in Patients with Advanced Breast Cancer Aged >/= 65 Years: New Lessons for Clinical Practice from the EVA Study. *Oncotarget.* 2018 Aug 7; 9(61): 31877a

17. Cazzaniga ME, Ciruelos E, Fabi A, Garcia-Saenz J, Lindman H, Mavroudis D, Schem C, Steger G, Timotheadou E, Zaman K, Torri V, MACBETH Group. Metastatic Or Locally Advanced Breast Cancer Patients: Towards an Expert Consensus on Nab-Paclitaxel Treatment in HER2-Negative Tumours-the MACBETH Project. *Cancer Chemother.Pharmacol.* 2018 Nov 20; [Epub ahead of print]

18. Cercato M.C. C, E., Fabi A, Bertazzi I, Scarinci V, Franceschini A, Cognetti F, Cenci C. Narrative Based Medicine: A Digital Diary during Chemotherapy Treatment to Personalize Patient Care (Pilot Study). *Tumori Journal.* 2018 104(4S): 194 (S40)a

19. Conciatori F, Bazzichetto C, Falcone I, Pilotto S, Bria E, Cognetti F, Milella M, Ciuffreda L. Role of mTOR Signaling in Tumor Microenvironment: An Overview. *Int.J.Mol.Sci.* 2018 Aug 19; 19(8): E2453a

20. Conciatori F, Ciuffreda L, Bazzichetto C, Falcone I, Pilotto S, Bria E, Cognetti F, Milella M. MTOR Cross-Talk in Cancer and Potential for Combination Therapy. *Cancers (Basel).* 2018 Jan 19; 10(1): E23

21. D'Aguanno S, Valentini E, Tupone MG, Desideri M, Di Martile M, Spagnuolo M, Buglioni S, Ercolani C, Falcone I, De Dominici M, Milella M, Rizzo MG, Calabretta B, Cota C, Anichini A, Trisciuoglio D, Del Bufalo D. Semaphorin 5A Drives Melanoma Progression: Role of Bcl-2, miR-204 and c-Myb. *J.Exp.Clin.Cancer Res.* 2018 Nov 19; 37(1): 278a

22. De Giorgi U, Carteni G, Giannarelli D, Basso U, Galli L, Cortesi E, Caserta C, Pignata S, Sabbatini R, Bearz A, Buti S, Lo Re G, Berruti A, Bracarda S, Cognetti F, Rastelli F, Fornarini G, Porta C, Turci D, Sternberg CN, Procopio G, Italian Nivolumab Renal Cell Cancer Early Access Program Group. Safety and Efficacy of Nivolumab for Metastatic Renal Cell Carcinoma: Real-World Results from an Expanded Access Programme. *BJU Int.* 2018 Jun 29 [Epub ahead of print]

23. De Placido S, Gallo C, De Laurentiis M, Bisagni G, Arpino G, Sarobba MG, Riccardi F, Russo A, Del Mastro L, Cogoni AA, Cognetti F, Gori S, Foglietta J, Frassoldati A, Amoroso D, Laudadio L, Moscetti L, Montemurro F, Verusio C, Bernardo A, Lorusso V, Gravina A, Moretti G, Lauria R, Lai A, Mocerino C, Rizzo S, Nuzzo F, Carlini P, Perrone F, GIM Investigators. Adjuvant Anastrozole Versus Exemestane Versus Letrozole, Upfront Or After 2 Years of Tamoxifen, in Endocrine-Sensitive Breast Cancer (FATA-GIM3): A Randomised, Phase 3 Trial. *Lancet Oncol.* 2018 Apr; 19(4): 474a

24. De Placido S, Giuliano M, Schettini F, Von Arx C, Buono G, Riccardi F, Cianniello D, Caputo R, Puglisi F, Bonotto M, Fabi A, Bilancia D, Ciccarese M, Lorusso V, Michelotti A, Bruzzese D, Veneziani BM, Locci M, De Laurentiis M, Arpino G. Human Epidermal Growth Factor Receptor 2 Dual Blockade with Trastuzumab and Pertuzumab in Real Life: Italian Clinical Practice Versus the CLEOPATRA Trial Results. *Breast.* 2018 Apr; 38: 86a

25. Del Curatolo A, Conciatori F, Cesta Incani U, Bazzichetto C, Falcone I, Corbo V, D'Agosto S, Eramo A, Sette G, Sperduti I, De Luca T, Marabese M, Shirasawa S, De Maria R, Scarpa A, Broggini M, Del Bufalo D, Cognetti F, Milella M, Ciuffreda L. Therapeutic Potential of Combined BRAF/MEK Blockade in BRAF-Wild Type Preclinical Tumor Models. *J.Exp.Clin.Cancer Res.* 2018 Jul 9; 37(1): 140a

26. Di Martile M, Desideri M, Tupone MG, Buglioni S, Antoniani B, Mastroiorio C, Falcioni R, Ferraresi V, Baldini N, Biagini R, Milella M, Trisciuoglio D, Del Bufalo D. Histone Deacetylase Inhibitor ITF2357 Leads to Apoptosis and Enhances Doxorubicin Cytotoxicity in Preclinical Models of Human Sarcoma. *Oncogenesis.* 2018 Feb 23; 7(2): 20a

27. di Martino S, De Luca G, Grassi L, Federici G, Alfonsi R, Signore M, Addario A, De Salvo L, Francescangeli F, Sanchez M, Tirelli V, Muto G, Sperduti I, Sentinelli S, Costantini M, Pasquini L, Milella M, Haoui M, Simone G, Gallucci M, De Maria R, Bonci D. Renal Cancer: New Models and Approach for Personalizing Therapy. *J.Exp.Clin.Cancer Res.* 2018 Sep 5; 37(1): 217a

28. Di Noia V, D'Argento E, Pilotto S, Ferrara MG, Milella M, Tortora G, Bria E. Exploiting MET Dysregulation in EGFR-Addicted Non-Small-Cell Lung Carcinoma: A further Step Toward Personalized Medicine. Transl.Lung Cancer.Res. 2018 Dec; 7(Suppl 4): S312.

29. Fabi A, Alesini D, Valle E, Moscetti L, Caputo R, Caruso M, Carbognin L, Ciccarese M, La Verde N, Arpino G, Cannita K, Paris I, Santini D, Montemurro F, Russillo M, Ferretti G, Filippelli G, Rossello R, Fabbri A, Zambelli A, Leonardi V, D'Ottavio AM, Nistico C, Stani S, Giampaglia M, Scandurra G, Catania G, Malaguti P, Giannarelli D, Cognetti F. T-DM1

and Brain Metastases: Clinical Outcome in HER2-Positive Metastatic Breast Cancer. *Breast.* 2018 Oct; 41: 137a

30. Ferrara R, Pilotto S, Caccese M, Grizzi G, Sperduti I, Giannarelli D, Milella M, Besse B, Tortora G, Bria E. Do Immune Checkpoint Inhibitors Need New Studies Methodology? *J. Thorac. Dis.* 2018 May; 10(Suppl 13): S1564a

31. Ferrari S, Bielack SS, Smeland S, Longhi A, Egerer G, Sundby Hall K, Donati D, Kevric M, Brosjo O, Comandone A, Werner M, Monge O, Palmerini E, Berdel WE, Bjerkehagen B, Paioli A, Lorenzen S, Eriksson M, Gambarotti M, Tunn PU, Jebsen NL, Cesari M, von Kalle T, Ferraresi V, Schwarz R, Bertulli R, Kasparek AK, Grignani G, Krasniqi F, Sorg B, Hecker-Nolting S, Picci P, Reichardt P. EURO-B.O.S.S.: A European Study on Chemotherapy in Bone-Sarcoma Patients Aged Over 40: Outcome in Primary High-Grade Osteosarcoma. *Tumori.* 2018 Jan-Feb; 104(1): 30a

32. Gandhi L, Rodriguez-Abreu D, Gadgeel S, Esteban E, Felip E, De Angelis F, Domine M, Clingan P, Hochmair MJ, Powell SF, Cheng SY, Bischoff HG, Peled N, Grossi F, Jennens RR, Reck M, Hui R, Garon EB, Boyer M, Rubio-Viqueira B, Novello S, Kurata T, Gray JE, Vida J, Wei Z, Yang J, Raftopoulos H, Pietanza MC, Garassino MC, KEYNOTE-189 Investigators. Cognetti F. (c.) Pembrolizumab Plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer. N.Engl.J.Med. 2018 May 31; 378(22): 2078.

33. Garassino MC, Cho BC, Kim JH, Mazieres J, Vansteenkiste J, Lena H, Corral Jaime J, Gray JE, Powderly J, Chouaid C, Bidoli P, Wheatley-Price P, Park K, Soo RA, Huang Y, Wadsworth C, Dennis PA, Rizvi NA, ATLANTIC Investigators, Milella M. collaborators. Durvalumab as Third-Line Or Later Treatment for Advanced Non-Small-Cell Lung Cancer (ATLANTIC): An Open-Label, Single-Arm, Phase 2 Study. *Lancet Oncol.* 2018 Apr; 19(4): 521a

34. Garassino MC, Gelibter AJ, Grossi F, Chiari R, Soto Parra H, Cascinu S, Cognetti F, Turci D, Blasi L, Bengala C, Mini E, Baldini E, Quadrini S, Ceresoli GL, Antonelli P, Vasile E, Pinto C, Fasola G, Galetta D, Macerelli M, Giannarelli D, Lo Russo G, de Marinis F. Italian Nivolumab Expanded Access Program in Nonsquamous Non-Small Cell Lung Cancer Patients: Results in Never-Smokers and EGFR-Mutant Patients. *J. Thorac. Oncol.* 2018 Aug; 13(8): 1146a

35. Gelderblom H, Cropet C, Chevreau C, Boyle R, Tattersall M, Stacchiotti S, Italiano A, Piperno-Neumann S, Le Cesne A, Ferraresi V, Penel N, Duffaud F, Cassier P, Toulmonde M, Casali P, Taieb S, Guillemaut S, Metzger S, Perol D, Blay JY. Nilotinib in Locally Advanced Pigmented Villonodular Synovitis: A Multicentre, Open-Label, Single-Arm, Phase 2 Trial. *Lancet Oncol.* 2018 May; 19(5): 639a

36. Gkountakos A, Pilotto S, Mafficini A, Vicentini C, Simbolo M, Milella M, Tortora G, Scarpa A, Bria E, Corbo V. Unmasking the Impact of Rictor in Cancer: Novel Insights of mTORC2 Complex. *Carcinogenesis.* 2018 Jun 28; [Epub ahead of print]

37. Iacorossi L, Gambalunga F, Fabi A, Giannarelli D, Marchetti A, Piredda M, De Marinis MG. Adherence to Oral Administration of Endocrine Treatment in Patients with Breast Cancer: A Qualitative Study. *Cancer Nurs.* 2018 Jan/Feb; 41(1): E57a

38. Iacorossi L, Gambalunga F, Molinaro S, De Domenico R, Giannarelli D, Fabi A. The Effectiveness of the Sport "Dragon Boat Racing" in Reducing the Risk of Lymphedema Incidence: An Observational Study. *Cancer Nurs.* 2018 Jun 22; [Epub ahead of print]

39. Imbimbo M, Ottaviano M, Vitali M, Fabbri A, Leuzzi G, Fiore M, Franceschini D, Pasello G, Perrino M, Schiavon M, Pruneri G, Dei Tos AP, Sangalli C, Garassino MC, Berardi R, Alessi A, Calareso G, Petrini I, Scorsetti M, Scotti V, Rosso L, Rea F, Pastorino U, Casali PG, Ramella S, Ricardi U, Abate-Daga L, Torri V, Trama A, Palmieri G, Marino M, Zucali PA, TYME network collaborators. Cecere FL (c.) Best Practices for the Management of Thymic Epithelial Tumors: A Position Paper by the Italian Collaborative Group for ThYmic MalignanciEs (TYME). Cancer Treat.Rev. 2018 Dec; 71: 76.

40. Kaufman HL, Russell JS, Hamid O, Bhatia S, Terheyden P, D'Angelo SP, Shih KC, Lebbe C, Milella M, Brownell I, Lewis KD, Lorch JH, von Heydebreck A, Hennessy M, Nghiem P. Updated Efficacy of Avelumab in Patients with Previously Treated Metastatic Merkel Cell Carcinoma After >/=1 Year of Follow-Up: JAVELIN Merkel 200, a Phase 2 Clinical Trial. *J. Immunother. Cancer.* 2018 Jan 19; 6(1): 7a

41. Lazzaro C, Barone C, Caprioni F, Cascinu S, Falcone A, Maiello E, Milella M, Pinto C, Reni M, Tortora G. An Italian Cost-Effectiveness Analysis of Paclitaxel Albumin (Nab-Paclitaxel) + Gemcitabine Vs Gemcitabine Alone for Metastatic Pancreatic Cancer Patients: The APICE Study. *Expert Rev.Pharmacoecon Outcomes Res.* 2018 18(4): 435-446a

42. Loria R, Laquintana V, Bon G, Trisciuoglio D, Frapolli R, Covello R, Amoreo CA, Ferraresi V, Zoccali C, Novello M, Del Bufalo D, Milella M, Biagini R, D'Incalci M, Falcioni R. HMGA1/E2F1 Axis and NFkB Pathways Regulate LPS Progression and Trabectedin Resistance. *Oncogene.* 2018 Nov; 37(45): 5926a

43. Maio M, Lewis K, Demidov L, Mandala M, Bondarenko I, Ascierto PA, Herbert C, Mackiewicz A, Rutkowski P, Guminski A, Goodman GR, Simmons B, Ye C, Yan Y, Schadendorf D, BRIM8 Investigators. Cognetti F. (c.) Adjuvant Vemurafenib in Resected, BRAF(V600) Mutation-Positive Melanoma (BRIM8): A Randomised, Double-Blind, Placebo-Controlled, Multicentre, Phase 3 Trial. Lancet Oncol. 2018 Apr; 19(4): 510.

44. Maschio M, Pauletto G, Zarabla A, Maialetti A, Ius T, Villani V, Fabi A, Koudriavtseva T, Giannarelli D. Perampanel in Patients with Brain Tumour-Related Epilepsy in Real-Life Clinical Practice: A Retrospective Analysis. *Int.J.Neurosci.* 2018 Dec 3; : 1a [Epub ahead of print]

45. Metro G, Passaro A, Lo Russo G, Bonanno L, Giusti R, Gregorc V, Capelletto E, Martelli O, Cecere FL, Giannarelli D, Luciani A, Bearz A, Tuzi A, Scotti V, Tonini G, Galetta D, Carta A, Soto Parra H, Rebonato A, Morabito A, Chiari R. Ceritinib Compassionate use for Patients with Crizotinib-Refractory, Anaplastic Lymphoma Kinase-Positive Advanced Non-Small-Cell Lung Cancer. *Future Oncol.* 2018 Feb; 14(4): 353a

46. Pace A, Mandoj C, Antenucci A, Villani V, Sperduti I, Casini B, Carosi M, Fabi A, Vidiri A, Koudriavtseva T, Conti L. A Predictive Value of Von Willebrand Factor for Early Response to Bevacizumab Therapy in Recurrent Glioma. *J.Neurooncol.* 2018 Jul; 138(3): 527a

47. Palermo B, Franzese O, Donna CD, Panetta M, Quintarelli C, Sperduti I, Gualtieri N, Foddai ML, Proietti E, Ferraresi V, Ciliberto G, Nistico P. Antigen-Specificity and DTIC before Peptide-Vaccination Differently Shape Immune-Checkpoint Expression Pattern, Anti-Tumor Functionality and TCR Repertoire in Melanoma Patients. *Oncoimmunology.* 2018 Sep 11; 7(12): e1465163a

48. Pasqualetti F, Pace A, Gonnelli A, Villani V, Cantarella M, Delishaj D, Vivaldi C, Molinari A, Montrone S, Pellerino A, Franchino F, Baldaccini D, Lombardi G, Lolli I, Catania F, Bazzoli E, Morganti R, Fabi A, Zagonel V, Bocci G, Fabrini MG, Ruda R, Soffietti R, Paiar F. Single-Agent Bevacizumab in Recurrent Glioblastoma After Second-Line Chemotherapy with Fotemustine: The Experience of the Italian Association of Neuro-Oncology. *Am.J.Clin.Oncol.* 2018 Dec; 41(12): 1272a

49. Pilotto S, Sperduti I, Leuzzi G, Chiappetta M, Mucilli F, Ratto GB, Lococo F, Filosso PL, Spaggiari L, Novello S, Milella M, Santo A, Scarpa A, Infante M, Tortora G, Facciolo F, Bria E. Prognostic Model for Resected Squamous Cell Lung Cancer: External Multicenter Validation and Propensity Score Analysis Exploring the Impact of Adjuvant and Neoadjuvant Treatment. *J.Thorac.Oncol.* 2018 Apr; 13(4): 568a

50. Piludu F, Gangemi E, Marucci L, Guerrisi A, Pellini R, Covello R, Carlini P, Spriano G, Sanguineti G, Marzi S, Vidiri A. MRI Evaluation using DWI and T2WI of Residual Lymph Nodes in Patients Affected by Head and Neck Squamous Cell Carcinoma Treated with Chemo-Radiotherapy. *Curr.Med.Imaging Rev.* 2018 14(4): 599a

51. Procopio G, Prisciandaro M, Iacovelli R, Cortesi E, Fornarini G, Facchini G, Carteni G, Sabbatini R, Del Bene G, Galli L, Caserta C, Multari AG, Bregni M, Massari F, Buti S, De Giorgi U, Zustovich F, Milella M, Calabro F, Mancini ML, Tortora G, Vernieri C, Santini D, Soraru M, Ricotta R, Masini C, Tucci M, Fedeli SL, Ortega C, Mecozzi A, Ratta R, Sternberg CN, Verzoni E. Safety and Efficacy of Cabozantinib in Metastatic Renal-Cell Carcinoma: Real-World Data from an Italian Managed Access Program. *Clin.Genitourin.Cancer.* 2018 Apr 19; 16(4): e945-e951a

52. Roila F, Fumi G, Ruggeri B, Antonuzzo A, Ripamonti C, Fatigoni S, Cavanna L, Gori S, Fabi A, Marzano N, Graiff C, De Sanctis V, Mirabile A, Serpentini S, Bocci C, Pino MS, Cilenti G, Verusio C, Ballatori E, NICSO (Network Italiano per le Cure di Supporto in Oncologia). Prevalence, Characteristics, and Treatment of Fatigue in Oncological Cancer Patients in Italy: A Cross-Sectional Study of the Italian Network for Supportive Care in Cancer (NICSO). *Support.Care Cancer.*

2018 Aug 6 [Epub ahead of print]

53. Russillo M, Ferretti G, Vidiri A, Gasparro S, Cognetti F, Pellegrini D, Fabi A. Impressive Long-Term Response with Pertuzumab and Trastuzumab in HER2-Positive Breast Cancer with Brain Metastasis. *In Vivo.* 2018 Jul-Aug; 32(4): 839a

54. Taralli S, Sollini M, Milella M, Perotti G, Filice A, Menga M, Versari A, Rufini V. (18)F-FDG and (68)Ga-Somatostatin Analogs PET/CT in Patients with Merkel Cell Carcinoma: A Comparison Study. *EJNMMI Res.* 2018 Jul 21; 8(1): 64a

55. Telera S, Pompili A, Crispo F, Giovannetti M, Pace A, Villani V, Fabi A, Sperduti I, Raus L. Kyphoplasty with Purified Silicone VK100 (Elastoplasty) to Treat Spinal Lytic Lesions in Cancer Patients: A Retrospective Evaluation of 41 Cases. *Clin. Neurol. Neurosurg.* 2018 Aug; 171: 184a

56. Vicini E, Invento A, Cuoghi M, Bafile A, Battaglia C, Biglia N, Busani M, Bussone R, Cianchetti E, Caruso F, Cucchi MC, Dessena M, Di Filippo F, Fabi A, Folli S, Friedman D, Macellari G, Mainente P, Murgo R, Neri A, Pollini GP, Palli D, Ricci F, Scalco G, Taffurelli M, Trunfio M, Galimberti V, Italian Society of Surgical Oncology (SICO) Breast Oncoteam. Neoadjuvant Systemic Treatment for Breast Cancer in Italy: The Italian Society of Surgical Oncology (SICO) Breast Oncoteam Survey. *Eur. J. Surg. Oncol.* 2018 Aug; 44(8): 1157a

57. Zoccali C, Attala D, Rossi B, Zoccali G, Ferraresi V. Fibrous Dysplasia: An Unusual Case of a very Aggressive Form with Costo-Vertebral Joint Destruction and Invasion of the Contralateral D7 Vertebral Body. *Skeletal Radiol.* 2018 Nov;47(11):1571-1576

58. Zoccali C, Baldi J, Attala D, Rossi B, Anelli V, Annovazzi A, Ferraresi V. Intralesional Vs. Extralesional Procedures for Low-Grade Central Chondrosarcoma: A Systematic Review of the Literature. *Arch. Orthop. Trauma Surg.* 2018 Jul; 138(7): 929a

# MEDICAL ONCOLOGY 2 UNIT

*Head: Luigi Di Lauro, MD*
*interim head from October 1st 2018: Patrizia Vici, MD*

## STAFF

| MD, Assistants |
|---|
| Antonella Amodio |
| Silvia Carpano |
| Francesca Conti |
| Marina Della Giulia |
| Fiorentino Izzo |
| Paolo Marolla |
| Giancarlo Paoletti |
| Massimo Rinaldi |
| Domenico Sergi |
| Riccardo Tonachella |
| Patrizia Vici |
| **MD, PhD** |
| Maddalena Barba |
| Marcello Maugeri-Saccà |
| **MD, Transient Staff** |
| Laura Pizzuti |
| Giacomo Barchiesi |
| Eriseld Krasniqi |
| Gioia Massimiani |
| **Chief Nurses** |
| Stefania Di Paolantonio |
| Valeria Colamartino |

| Nurses |
|---|
| Geolina Julita Amora |
| Arianna Bassotti |
| Paolo Bellucci |
| Federica Bertini |
| Viviana Boncristiano |
| Emanuela Di Certo |
| Francesca Gallina |
| Marisia Soares |
| Stefano Bucci |
| Ana Cristina Cadaru |
| Eleonora Peverini |
| Sabrina Pieretti |
| Sandra Cortese |
| **Data Manager** |
| Rosa Carbone |
| **Administrative Collaborator** |
| Ana Maria Edlisca |

## *Mission*

The Division of Medical Oncology 2 (OM2) aims at gaining insights in the management of solid tumors in adult cancer patients. Considerable attention is devoted to the design and conduct of several studies in collaboration with an increasingly growing pool of Nationl and International cancer centers. Our oncologists manage over 600 newly diagnosed cancer patients/year. Our personnel is "functionally" organized into subunits committed to a specific tumor for both the clinical and research activities. A multidisciplinary approach is systematically applied. Diagnostic and therapeutic decisions are constantly defined at an individual-patient level, which is refined over the course of weekly meetings called Disease Management Team (DMTs). Participation in these meetings is extremely interactive. A relevant percentage of patients whose cases are critically discussed over the DMTs course are

enrolled in clinical studies. Whenever economically sustainable and scientifically plausible, these studies include both clinical and pre-clinical/translational tasks. Feasibility is always carefully considered.

## Clinical Activity

The clinical activities of OM2 encompass an inpatient hospital service and outpatient clinics. Clinics: The outpatient clinics activities are driven by the site of cancer origin and specific clinical performance, i.e., 1st-time visit, routine controls and oncological screenings. The 1st-time visits take place in a dedicated clinic, for both patients managed in clinical practice and trials' participants. The waiting time for 1st-time visits or oncological screenings does not exceed 3 days. Hospitalization: All hospitalized patients are admitted to the OM2 Ward Service. The waiting time for admittance is of about 4 days. Day-Hospital: The waiting time for a patient 1st-time visit/admission does not exceed 4 days. The following performance are delivered to our patients, independently on the specific regimen: administration of chemotherapy/supporting therapies, advice from medical oncologists and collaborating specialists, diagnostic examinations, psychological support.

## Research Activity

In 2018, we further focused on efficacy and/or toxicity biomarkers which may inform decisions in patients with solid tumors. Concerning breast cancer (Bca), the OM2 coordinated the following multicentric Bca trials: 1. In the neoadjuvant setting, TRISKELE, NeoTaz, NeoCarbo, and TROIKA; 2. In the adjuvant setting, PHOBOS, and a study on the prognostic role of coagulation activation in early Bca (1); 3. In the advanced setting, PALBOSS (2), RePer (3), a study of pertuzumab in HER2+ met Bca, and a further study of HER2+ met Bca patients treated with trastuzumab-emtansine, and a study on body mass index in HER2- met Bca treated with 1st-line paclitaxel and bevacizumab (4).
We adhered with a non-coordinating role to the following trials: Neo-adjuvant chemotherapy in triple negative Bca (5), VasMUoss, MARIO, POSITIVE, BioItaLEE, VICTOR3, COMPLEEMENT-1, IMPASSION 131; PAINTER, NORMA, EVA, (6.a-c), ECHO, BRIDE, TiLT, GIM16-FEVEX, HERBA, Pro-HERBA,. We also adhered to a phase I dose escalation and cohort expansion trial of an a**nti**-PD-1 agent in advanced **solid tumors.** Our collaboration with the Nuclear Medicine Division resulted into one further manuscript (7).
Concerning solid tumors other than Bca, we adhered to several MITO trial in gynecological tumors, and focused on the HIPPO pathway within the HIERARCHY study, a spontaneous multicentric study coordinated by the OM2 (8-12). Our trial on DNA damage and HIPPO biomarkers in locally advanced/metastatic gastric cancer was awarded by the Ministry of Health. Research on cancer stem cells yielded 3 manuscripts (13-15). The OM2 work on ovarian cancer yielded one further publication (16). For the study of miR signature in relapsed, high-grade serous ovarian cancer, survival outcomes are in course of update. Additional activities have yielded further publications (17-21).

## Publications


1. Annovazzi A, Rea S, Vici P, Fabi A, Sciuto R. Dual-Time 18F-FDG PET/CT for the Detection of Liver Metastases in Breast Cancer. *Nucl. Med. Commun.* 2018 Dec; 39(12): 1183-1189a

2. Barnabei A, Strigari L, Persichetti A, Baldelli R, Rizza L, Annoscia C, Lauretta R, Cigliana G, Barba M, De Leo A, Appetecchia M, Torino F. Indirect Basal Metabolism Estimation in Tailoring Recombinant Human TSH Administration in Patients Affected by Differentiated Thyroid Cancer: A Hypothesis-Generating Study. *Front. Endocrinol. (Lausanne).* 2018 Feb 15; 9: 37a

3. Buglioni S, Melucci E, Sperati F, Pallocca M, Terrenato I, De Nicola F, Goeman F, Casini B, Amoreo CA, Gallo E, Diodoro MG, Pescarmona E, Vici P, Sergi D, Pizzuti L, Di Lauro L, Mazzotta M, Barba M, Fanciulli M, Vitale I, De Maria R, Ciliberto G, Maugeri-Saccà M. The Clinical Significance of PD-L1 in Advanced Gastric Cancer is Dependent on ARID1A Mutations and ATM Expression. *Oncoimmunology.* 2018 03/27; 7(8): e1457602a

4. Cazzaniga M, Verusio C, Ciccarese M, Fumagalli A, Sartori D, Ancona C, Airoldi M, Moretti G, Ficorella C, Arcangeli V,

Diodati L, Zambelli A, Febbraro A, Generali D, Pistelli M, Garrone O, Musolino A, Vici P, Maur M, Mentuccia L, La Verde N, Bianchi G, Artale S, Blasi L, Piezzo M, Atzori F, Turletti A, Benedetto C, Cursano MC, Fabi A, Gebbia V, Schirone A, Palumbo R, Ferzi A, Frassoldati A, Scavelli C, Clivio L, Torri On Behalf Of The Eva Study Group, V. Everolimus (EVE) and Exemestane (EXE) in Patients with Advanced Breast Cancer Aged >/= 65 Years: New Lessons for Clinical Practice from the EVA Study. *Oncotarget.* 2018 Aug 7; 9(61): 31877a

5. De Nicola F, Goeman F, Pallocca M, Sperati F, Pizzuti L, Melucci E, Casini B, Amoreo CA, Gallo E, Diodoro MG, Buglioni S, Mazzotta M, Vici P, Sergi D, Di Lauro L, Barba M, Pescarmona E, Ciliberto G, De Maria R, Fanciulli M, Maugeri-Sacca M. Deep Sequencing and Pathway-Focused Analysis Revealed Multigene Oncodriver Signatures Predicting Survival Outcomes in Advanced Colorectal Cancer. *Oncogenesis.* 2018 Jul 22; 7(7): 55a

6. Gamucci T, Pizzuti L, Natoli C, Mentuccia L, Sperduti I, Barba M, Sergi D, Iezzi L, Maugeri-Sacca M, Vaccaro A, Magnolfi E, Gelibter A, Barchiesi G, Magri V, D'Onofrio L, Cassano A, Rossi E, Botticelli A, Moscetti L, Omarini C, Fabbri MA, Scinto AF, Corsi D, Carbognin L, Mazzotta M, Bria E, Foglietta J, Samaritani R, Garufi C, Mariani L, Barni S, Mirabelli R, Sarmiento R, Graziano V, Santini D, Marchetti P, Tonini G, Di Lauro L, Sanguineti G, Paoletti G, Tomao S, De Maria R, Veltri E, Paris I, Giotta F, Latorre A, Giordano A, Ciliberto G, Vici P. A Multicenter REtrospective Observational Study of First-Line Treatment with PERtuzumab, Trastuzumab and Taxanes for Advanced HER2 Positive Breast Cancer Patients. RePer Study. *Cancer. Biol. Ther.* 2018 Nov 7 [Epub ahead of print]

7. Gamucci T, Pizzuti L, Sperduti I, Mentuccia L, Vaccaro A, Moscetti L, Marchetti P, Carbognin L, Michelotti A, Iezzi L, Cassano A, Grassadonia A, Astone A, Botticelli A, Magnolfi E, Di Lauro L, Sergi D, Fuso P, Tinari N, Barba M, Maugeri-Sacca M, Landucci E, Conti F, Sanguineti G, De Tursi M, Iafrate G, Giordano A, Ciliberto G, Natoli C, Vici P. Neoadjuvant Chemotherapy in Triple-Negative Breast Cancer: A Multicentric Retrospective Observational Study in Real-Life Setting. *J. Cell. Physiol.* 2018 Mar; 233(3): 2313a

8. Grassadonia A, Sperduti I, Vici P, Iezzi L, Brocco D, Gamucci T, Pizzuti L, Maugeri-Sacca M, Marchetti P, Cognetti G, De Tursi M, Natoli C, Barba M, Tinari N. Effect of Gender on the Outcome of Patients Receiving Immune Checkpoint Inhibitors for Advanced Cancer: A Systematic Review and Meta-Analysis of Phase III Randomized Clinical Trials. *J. Clin. Med.* 2018 Dec 12; 7(12): 10.3390/jcm7120542a

9. Hakoum MB, Kahale LA, Tsolakian IG, Matar CF, Yosuico VE, Terrenato I, Sperati F, Barba M, Schunemann H, Akl EA. Anticoagulation for the Initial Treatment of Venous Thromboembolism in People with Cancer. *Cochrane Database Syst. Rev.* 2018 Jan 24; 1: CD006649a

10. Mancini R, Noto A, Pisanu ME, De Vitis C, Maugeri-Sacca M, Ciliberto G. Metabolic Features of Cancer Stem Cells: The Emerging Role of Lipid Metabolism. *Oncogene.* 2018 37(18): 2367-2378a

11. Mandoj C, Pizzuti L, Sergi D, Sperduti I, Mazzotta M, Di Lauro L, Amodio A, Carpano S, Di Benedetto A, Botti C, Ferranti F, Antenucci A, D'Alessandro MG, Marchetti P, Tomao S, Sanguineti G, Giordano A, Maugeri-Sacca M, Ciliberto G, Conti L, Vici P, Barba M. Observational Study of Coagulation Activation in Early Breast Cancer: Development of a Prognostic Model Based on Data from the Real World Setting. *J. Transl. Med.* 2018 May 16; 16(1): 129a

12. Manic G, Signore M, Sistigu A, Russo G, Corradi F, Siteni S, Musella M, Vitale S, De Angelis ML, Pallocca M, Amoreo CA, Sperati F, Di Franco S, Barresi S, Policicchio E, De Luca G, De Nicola F, Mottolese M, Zeuner A, Fanciulli M, Stassi G, Maugeri-Sacca M, Baiocchi M, Tartaglia M, Vitale I, De Maria R. CHK1-Targeted Therapy to Deplete DNA Replication-Stressed, p53-Deficient, Hyperdiploid Colorectal Cancer Stem Cells. *Gut.* 2018 May;67(5):903-917

13. Matar CF, Kahale LA, Hakoum MB, Tsolakian IG, Etxeandia-Ikobaltzeta I, Yosuico VE, Terrenato I, Sperati F, Barba M, Schunemann H, Akl EA. Anticoagulation for Perioperative Thromboprophylaxis in People with Cancer. *Cochrane Database Syst. Rev.* 2018 Jul 11; 7: CD009447a

14. Maugeri-Sacca M, De Maria R. The Hippo Pathway in Normal Development and Cancer. *Pharmacol. Ther.* 2018 Jun; 186: 60a

15. Melucci E, Casini B, Ronchetti L, Pizzuti L, Sperati F, Pallocca M, De Nicola F, Goeman F, Gallo E, Amoreo CA, Sergi D, Terrenato I, Vici P, Di Lauro L, Diodoro MG, Pescarmona E, Barba M, Mazzotta M, Mottolese M, Fanciulli M,

Ciliberto G, De Maria R, Buglioni S, Maugeri-Sacca M. Expression of the Hippo Transducer TAZ in Association with WNT Pathway Mutations Impacts Survival Outcomes in Advanced Gastric Cancer Patients Treated with First-Line Chemotherapy. *J. Transl. Med.* 2018 Feb 5; 16(1): 22a

16. Pallocca M, Goeman F, De Nicola F, Melucci E, Sperati F, Terrenato I, Pizzuti L, Casini B, Gallo E, Amoreo CA, Vici P, Di Lauro L, Buglioni S, Diodoro MG, Pescarmona E, Mazzotta M, Barba M, Fanciulli M, De Maria R, Ciliberto G, Maugeri-Sacca M. Coexisting YAP Expression and TP53 Missense Mutations Delineates a Molecular Scenario Unexpectedly Associated with Better Survival Outcomes in Advanced Gastric Cancer. *J. Transl. Med.* 2018 Sep 4; 16(1): 247a

17. Pisanu ME, Maugeri-Sacca M, Fattore L, Bruschini S, De Vitis C, Tabbi E, Bellei B, Migliano E, Kovacs D, Camera E, Picardo M, Jakopin Z, Cippitelli C, Bartolazzi A, Raffa S, Torrisi MR, Fulciniti F, Ascierto PA, Ciliberto G, Mancini R. Inhibition of Stearoyl-CoA Desaturase 1 Reverts BRAF and MEK Inhibition-Induced Selection of Cancer Stem Cells in BRAF-Mutated Melanoma. *J. Exp. Clin. Cancer Res.* 2018 Dec 17; 37(1): 318a

18. Pizzuti L, Giordano A, Michelotti A, Mazzotta M, Natoli C, Gamucci T, De Angelis C, Landucci E, Diodati L, Iezzi L, Mentuccia L, Fabbri A, Barba M, Sanguineti G, Marchetti P, Tomao S, Mariani L, Paris I, Lorusso V, Vallarelli S, Cassano A, Airoldi F, Orlandi A, Moscetti L, Sergi D, Sarobba MG, Tonini G, Santini D, Sini V, Veltri E, Vaccaro A, Ferrari L, De Tursi M, Tinari N, Grassadonia A, Greco F, Botticelli A, La Verde N, Zamagni C, Rubino D, Cortesi E, Magri V, Pomati G, Scagnoli S, Capomolla E, Kayal R, Scinto AF, Corsi D, Cazzaniga M, Laudadio L, Forciniti S, Mancini M, Carbognin L, Seminara P, Barni S, Samaritani R, Roselli M, Portarena I, Russo A, Ficorella C, Cannita K, Carpano S, Pistelli M, Berardi R, De Maria R, Sperduti I, Ciliberto G, Vici P. Palbociclib Plus Endocrine Therapy in HER2 Negative, Hormonal Receptor-Positive, Advanced Breast Cancer: A Real-World Experience. J.Cell.Physiol. 2018 Dec 10 [Epub ahead of print]

19. Pizzuti L, Sergi D, Mandoj C, Antoniani B, Sperati F, Chirico A, Di Lauro L, Valle M, Garofalo A, Vizza E, Corrado G, Tomao F, Rinaldi M, Carpano S, Maugeri-Sacca M, Conti L, Digiesi G, Marchetti P, De Maria R, Giordano A, Barba M, Carosi MA, Vici P. GLUT 1 Receptor Expression and Circulating Levels of Fasting Glucose in High Grade Serous Ovarian Cancer. *J. Cell. Physiol.* 2018 233(2): 1396a

20. Pizzuti L, Sergi D, Sperduti I, Lauro LD, Mazzotta M, Botti C, Izzo F, Marchetti L, Tomao S, Marchetti P, Natoli C, Grassadonia A, Gamucci T, Mentuccia L, Magnolfi E, Vaccaro A, Cassano A, Rossi E, Botticelli A, Sini V, Sarobba MG, Fabbri MA, Moscetti L, Astone A, Michelotti A, De Angelis C, Bertolini I, Angelini F, Ciliberto G, Maugeri-Sacca M, Giordano A, Barba M, Vici P. Body Mass Index in HER2-Negative Metastatic Breast Cancer Treated with First-Line Paclitaxel and Bevacizumab. *Cancer. Biol. Ther.* 2018 Apr 3; 19(4): 328a

21. Terrenato I, Sperati F, Musicco F, Pozzi AF, di Turi A, Caterino M, de Lutio di Castelguidone E, Setola SV, Bellomi M, Neumaier CE, Conti L, Cigliana G, Merola R, Antenucci A, Orlandi G, Giordano A, Barba M, Canitano S. Iodixanol Versus Iopromide in Cancer Patients: Evidence from a Randomized Clinical Trial. *J. Cell. Physiol.* 2018 Mar; 233(3): 2572a

# HAEMATOLOGY AND STEM CELL TRANSPLANTATION UNIT

*Head: Andrea Mengarelli, MD*

## STAFF

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|---|---|
| Svitlana Gumenyuk MD, | Anna Attico Nurse, |
| Francesco Marchesi MD, | Giuseppina Cafarella Nurse, |
| Francesca Palombi MD, | Roberta Capobianco Nurse, |
| Francesco Pisani MD, | Eleonora D'Annibale Nurse, |
| Daniela Renzi MD, | Silvia Di Fraia Nurse, |
| Atelda Romano MD, | Katia Di Prospero Nurse, |
| Antonio Spadea MD | Serena Di Vincenzo Nurse, |
| Antonietta Pimpinella Nurse, | Gianluca Falzone Nurse, |
| Caterina Viggiani Nurse, | Alessandra Labella Nurse, |
| Ambra Albertini Nurse, | Giulia Lenzini Nurse, |

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| **Anna Petrucci Nurse,** |
| **Paola Presta Nurse,** |
| **Fabrizio Pochettino Nurse,** |
| **Romina Riccio Nurse,** |

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| **Daniela Todisco Nurse,** |
| **Raffaele Speranza Nurse,** |
| **Elena Papa Quality/Datamanager** |
| **Chiara Falcicchio Psychologist** |

## Mission

Hematology and Transplant Unit identifies its own reason for existence with the provision of care services and assistance of patients with hematologic malignancies, according to the policy and mission of Regina Elena National Cancer Institute of Rome. In this framework, through scientific research, the development of medical knowledge, and collaboration with other organizations at national and international level, Unit resolved to be a center of excellence for the diagnosis and treatment of such pathologies.

## Clinical Activity

Hematology and Transplant Unit is specialized in the evaluation, treatment and care of patients with lymphoma, leukemia, multiple myeloma, myelodysplastic syndrome and myeloproliferative disorder. Although chemotherapy remains an integral component of the treatment for most hematologic malignancies, the development of disease-specific or targeted therapeutics or biomarkers represents the research goal of our Unit investigators.
Treatments are delivered according to National and International clinical trials coordinated by cooperative groups (like GIMEMA, FIL, EORTC, IELSG) involved in the treatment of several onco-hematological diseases. For patients outside clinical trials, treatments are delivered according to Guide-Lines proposed by the most important Italian (SIE-SIES-GITMO) and International (ESMO-ELN-NCCN) hematologic clinical societies. Moreover, in order to better standardize the diagnostic and therapeutic algorithms for patients outside clinical trials, in 2019 five PDTA (Percorsi Diagnostici Terapeutici Assistenziali Aziendali) were updated by the Institute for the following malignancies: acute myeloid leukemia, chronic myeloid leukemia, follicular lymphoma, diffuse large B cell lymphoma and multiple myeloma.
Stem cell transplantation often is indicated for the treatment of hematologic malignancies. U.O.S.D. Ematologia e Trapianti is one of the 6 Institutions located in Rome who belongs to Rome Transplant Network (RTN), a Metropolitan Hematopoietic Stem Cell Transplant Program for adult patients established as a cooperative network. RTN is an innovative entity, which follows rules and standards established by The Joint Accreditation Committee ISCT-EBMT (JACIE) accreditation program. In june 2013, Policlinico "Tor Vergata" University Hospital, Regina Elena National Cancer Institute and Campus Biomedico University Hospital have been found to meet the standards of the JACIE for Autologous & Allogeneic Transplantation in Adult Patients, as lately certificated on 21.01.2014. The renewal of certification took place on February 2019.
In 2018 RTN registered 213 Transplants (61 allogeneic and 152 autologous), 56 of them performed in our Unit. The objectives of the RTN are: 1) to standardize transplants procedures; 2) to improve quality of transplant care; 3) to extend the potential of transplant activity over the metropolitan area; 4) to share expertise and professional education among healthcare providers; 5) to promote excellence of single transplant Centers; 6) to rationalize cost-management of public health.

## Research Activities

The effort of Hematology and Transplant Unit was aimed at carrying out clinical trials of primary relevance in different hematological malignancies working in cooperation with other hematological institutions. In particular, our Unit is a member of the following cooperative group:

- Gruppo Italiano Malattie EMatologiche dell'Adulto **(GIMEMA)**
- European Organisation for Research and Treatment of Cancer **(EORTC)**
- Fondazione Italiana Linfomi **(FIL)**
- International Extranodal Lymphoma Study Group **(IELSG)**
- Gruppo Romano Mielodisplasie **(GROM)**
- Gruppo Laziale Sindromi Mieloproliferative Croniche Ph1 neg.
- Sorveglianza Epidemiologica Infezioni Fungine in Emopatie Maligne **(SEIFEM)**
- • Dutch-Belgian Cooperative Trial Group for

Hematology Oncology **(HOVON)**

- Gruppo Italiano Trapianto Midollo Osseo **(GITMO).**
- *Diffuse Large B-Cell Lymphoma (DLBCL):* Up to 40% of DLBCL patients still experience treatment failure or disease relapse after conventional chemo-immunotherapy. To identify and validate a serum miRNA signature with prognostic value we planned a prospective non interventionist study in a cohort of newly diagnosed DLBCL patients uniformly treated with six courses of R-CHOP. Preliminary data suggest that high expression level of serum miR-22 in DLBCL at diagnosis is associated with a worse Progression-Free Survival and is independent of the currently used clinical prognostic index. This study has been published on *Journal of Experimental & Clinical Cancer Research* in 2018.
- *Non-Hodgkin Lymphoma:* Randomized trials comparing chemomobilization efficiency between lenograstim and biosimilar filgrastim are lacking. Our previous retrospective study suggested that lenograstim could be more effective than biosimilar filgrastim when used at the same conventional dosage (5 μg/kg) only in lymphoma patients undergoing peripheral blood stem cell mobilization. We planned a prospective randomized study comparing lenograstim 5 μg/kg with biosimilar filgrastim 10 μg/kg to verify the hypothesis of lenograstim superiority even at half the dosage. Preliminary results of this study have been published on *Transfusion* in 2018 after enrolling 60% of planned patients: lenograstim at conventional dosage has failed to demonstrate its superiority over biosimilar filgrastim at double dosage.
- *Autologous stem cell transplantation (ASCT):* the most widely used high-dose chemotherapy (HDC) before ASCT in lymphoma patients is BEAM regimen (carmustine, etoposide, cytarabine and melphalan), which is considered the gold standard both in United states and Europe. In Italy, the most frequently used alternative regimen is FEAM (fotemustine, etoposide, cytarabine and melphalan), in which carmustine is replaced by fotemustine, a third-generation chloroethyl-nitrosourea with a more favorable pulmonary toxicity profile, however not available in all European countries. We aimed to investigate in a retrospective study the comparison between FEAM and BEAM regimen in terms of efficacy and safety in lymphoma patients undergoing ASCT. 362 consecutive lymphoma patients transplanted in two centers of Rome (Sapienza University n=218, Regina Elena National Cancer Institute n=144) were analyzed: we did not observe differences between the groups in terms of 2 years PFS and OS but BEAM regimen seems to be better tolerated because of significantly lower rates of mucositis and infectious complications. This study was published on *Bone Marrow Transplantation* in 2018.
- The association between cytomegalovirus (CMV) and invasive fungal disease (IFD) after autologous stem cell transplant (ASCT) in Lymphoproliferative Malignancies was investigated by our Unit. We have reviewed our series of 347 ASCT in myeloma and lymphoma patients performed over a 14 years span with the aim of investigating the descriptive and analytical epidemiology of bacterial, CMV and IFD complications focusing on the association between CMV and IFD. This study was published on *International Journal of Molecular Sciences* in 2019.
- During the 2017, an original study of our Unit on the predictive value of Aspergillus PCR testing on bronchoalveolar lavage (BAL) fluid was published and object of commentary on *Leukemia and Lymphoma*. The results of the latter prompted us to propose to Sorveglianza Epidemiologica Infezioni Fungine in Emopatie Maligne (SEIFEM) Group a prospective multicentric study on evaluating the efficacy and safety of bronchoscopy with BAL as systematic diagnostic approach of lung infiltrates (LI) in hematologic patients. This study (SEIFEM BAL 2017), promoted and coordinated by our Unit, was conducted between January 2018 and September 2018 and 177 patients were enrolled and evaluable for analysis. We observed a significative better outcome of LI at day +30 and a significative better outcome in 120d-OS in those patients in which a BAL-driven antimicrobial treatment was possible. This study has been submitted for publication in 2019.
- In 2015 the Unit created a web-based intra-net system of data collection: *Progettoemat.it*. This software system features diversified disease-specific data-bases designed to meet the most important control requirements of the clinical endpoints such as survival, relapse , effectiveness of treatment protocols and more. This system provides for the transfer of clinical data of about a thousand of patients from paper to electronic format. In recent months the database has been continuously updated and modified according to the needs which arise during data entry. The work that has preceded the actual data entry aimed at

recovering all the records of patients who died, were lost or left the follow-up. A computer file was then created in which 1436 patients are included. The Unit chose to start with two diseases: Follicular Lymphoma (FL) and Diffuse Large Cell Lymphoma (DLBCL). To date 164 patients were included with FL and 286 patients with DLBCL. In September 2016 data-entry started about patients with multiple myeloma (so far 100 records were filed). The activity of the Secretariat and Data Manager also provides the database update of DMT and satisfaction questionnaires.

- The patients enrollment in the project *"Psychological Functioning and quality of life after autologous stem cell transplantation in patients with onco-hematological disease"* continued in 2018. The objective of this prospective longitudinal study is to assess the impact of graft on the quality of life and psychological functioning of adult patients undergoing ASCT, and to identify potential demographic, clinical, and psychological predictors of variables under study. The hypothesis is that patients with high scores of physical well-being , more education, lower levels of anxiety and depression, more resilient, more adaptive coping strategies, higher self-efficacy and increased social support before transplantation are those with better quality of life and psychological functioning immediately after transplantation and in a one year follow-up. In 2017 we enrolled 19 new patients, continued follow-up evaluation of all patients enrolled in the study (to date 75 patients), and administered a total of 230 questionnaires for measuring the quality of life, the perceived social support, the psychological distress, the resilience and self-efficacy before and after transplant procedure.
- As for clinical trials, during the 2018, 34 clinical research protocols proposed by Hematology and Transplant Unit and approved by Regina Elena I.F.O. Ethics Committee have been open to recruitment and 211 patients have been enrolled.

## Publications

SEIFEM 2017: from real life to an agreement on the use of granulocyte transfusions and colony-stimulating factors for prophylaxis and treatment of infectious complications in patients with hematologic malignant disorders.

Busca A, Cesaro S, Teofili L, Delia M, Cattaneo C, Criscuolo M, Marchesi F, Fracchiolla NS, Valentini CG, Farina F, Di Blasi R, Prezioso L, Spolzino A, Candoni A, Del Principe MI, Verga L, Nosari A, Aversa F, Pagano L; SEIFEM group (Sorveglianza Epidemiologica Infezioni Fungine in Ematologia). Expert Rev Hematol. 2018 Jan 3:1-14. doi: 10.1080/17474086.2018.1420472.

Predicting failure of hematopoietic stem cell mobilization before it starts: the predicted poor mobilizer (pPM) score.

1. Olivieri J, Attolico I, Nuccorini R, Pascale SP, Chiarucci M, Poiani M, Corradini P, Farina L, Gaidano G, Nassi L, Sica S, Piccirillo N, Pioltelli PE, Martino M, Moscato T, Pini M, Zallio F, Ciceri F, Marktel S, Mengarelli A, Musto P, Capria S, Merli F, Codeluppi K, Mele G, Lanza F, Specchia G, Pastore D, Milone G, Saraceni F, Di 1. Biagioli V, Piredda M, Annibali O, Tirindelli MC, Pignatelli A, Marchesi F, Mauroni MR, Soave S, Del Giudice E, Ponticelli E, Clari M, Cavallero S, Monni P, Ottani L, Sica S, Cioce M, Cappucciati L, Bonifazi F, Alvaro R, De Marinis MG, Gargiulo G. Development and Initial Validation of a Questionnaire to Assess Patients' Perception of Protective Isolation Following Haematopoietic Stem Cell Transplantation. *Eur. J. Cancer. Care. (Engl).* 2018 Oct 24; : e12955a

2. Bringhen S, Offidani M, Palmieri S, Pisani F, Rizzi R, Spada S, Evangelista A, Di Renzo N, Musto P, Marcatti M, Vallone R, Storti S, Bernardini A, Centurioni R, Aitini E, Palmas A, Annibali O, Angelucci E, Ferrando P, Baraldi A, Rocco S, Andriani A, Siniscalchi A, De Stefano V, Meneghini V, Palumbo A, Grammatico S, Boccadoro M, Larocca A. Early Mortality in Myeloma Patients Treated with First-Generation Novel Agents Thalidomide, Lenalidomide, Bortezomib at Diagnosis: A Pooled Analysis. *Crit. Rev. Oncol.* 2018 130: 27a

3. Broccoli A, Casadei B, Morigi A, Sottotetti F, Gotti M, Spina M, Volpetti S, Ferrero S, Spina F, Pisani F, Merli M, Visco C, Paolini R, Zilioli VR, Baldini L, Di Renzo N, Tosi P, Cascavilla N, Molica S, Ilariucci F, Rigolin GM, D'Alo F, Vanazzi A, Santambrogio E, Marasca R, Mastrullo L, Castellino C, Desabbata G, Scortechini I, Trentin L, Morello L, Argnani L, Zinzani PL. Italian Real Life Experience with Ibrutinib: Results of a Large Observational Study on 77 relapsed/refractory Mantle Cell Lymphoma. *Oncotarget.* 2018 May 4; 9(34): 23443a

4. Busca A, Cesaro S, Teofili L, Delia M, Cattaneo C, Criscuolo M, Marchesi F, Fracchiolla NS, Valentini CG, Farina F, Di Blasi R, Prezioso L, Spolzino A, Candoni A, Del Principe MI, Verga L, Nosari A, Aversa F, Pagano L, SEIFEM group (Sorveglianza Epidemiologica Infezioni Fungine in Ematologia). SEIFEM 2017: From Real Life to an Agreement on the use of Granulocyte Transfusions and Colony-Stimulating Factors for Prophylaxis and Treatment of Infectious Complications in Patients with Hematologic Malignant Disorders. *Expert Rev.Hematol.* 2018 Feb; 11(2): 155a

5. Calabrese V, Menna P, Annibali O, Armento G, Carpino A, Cerchiara E, Greco C, Marchesi F, Spallarossa P, Toglia G, Reggiardo G, Minotti G, Collaborators. Early Diastolic Dysfunction After Cancer Chemotherapy: Primary Endpoint Results of a Multicenter Cardio-Oncology Study. *Chemotherapy.* 2018 63(2): 55a

6. Cattaneo C, Di Blasi R, Skert C, Candoni A, Martino B, Di Renzo N, Delia M, Ballanti S, Marchesi F, Mancini V, Orciuolo E, Cesaro S, Prezioso L, Fanci R, Nadali G, Chierichini A, Facchini L, Picardi M, Malagola M, Orlando V, Trecarichi EM, Tumbarello M, Aversa F, Rossi G, Pagano L, SEIFEM Group. Bloodstream Infections in Haematological Cancer Patients Colonized by Multidrug-Resistant Bacteria. *Ann.Hematol.* 2018 Sep; 97(9): 1717-1726a

7. Connors JM, Jurczak W, Straus DJ, Ansell SM, Kim WS, Gallamini A, Younes A, Alekseev S, Illes A, Picardi M, Lech-Maranda E, Oki Y, Feldman T, Smolewski P, Savage KJ, Bartlett NL, Walewski J, Chen R, Ramchandren R, Zinzani PL, Cunningham D, Rosta A, Josephson NC, Song E, Sachs J, Liu R, Jolin HA, Huebner D, Radford J, ECHELON-1 Study Group. Mengarelli (c.) Brentuximab Vedotin with Chemotherapy for Stage III Or IV Hodgkin's Lymphoma. *N.Engl.J.Med.* 2018 Jan 25; 378(4): 331a

8. Cudillo L, Cerretti R, Picardi A, Mariotti B, De Angelis G, Cantonetti M, Postorino M, Ceresoli E, De Santis G, Nasso D, Pisani F, Scala E, Di Piazza F, Lanti A, William Arcese for the Rome Transplant Network. Allogeneic Hematopoietic Stem Cell Transplantation in Primary Cutaneous T Cell Lymphoma. *Ann.Hematol.* 2018 Jun; 97(6): 1041a

9. Di Veroli A, Buccisano F, Andriani A, Montanaro M, Latagliata R, Santoro C, Breccia M, Spirito F, Cedrone M, Anaclerico B, Leonetti Crescenzi S, Porrini R, De Muro M, Avvisati G, Tafuri A, Cimino G, Spadea A. Prognostic Factors for Thrombosis-Free Survival and overall Survival in Polycythemia Vera: A Retrospective Analysis of 623 PTS with Long Follow-Up. *Leuk.Res.* 2018 jun; 69: 18a

10. Di Veroli A, Campagna A, De Muro M, Maurillo L, Trawinska MM, LeonettiCrescenzi S, Petriccione L, Romano A, D'Addosio A, Cenfra A, Montanaro M, Felici S, Andriani A, Carmosino I, Niscola P, Montefusco E, Breccia M, Latagliata R. Deferasirox in the Treatment of Iron Overload during Myeloproliferative Neoplasms in Fibrotic Phase: Does Ferritin Decrement Matter? *Leuk.Res.* 2019 Jan; 76: 65a

11. Girmenia C, Annino L, Bertaina A, Mariotti B, Caselli D, Fanci R, Barberi W, Marchesi F, Carotti A, Ferrari A, Cerchiara E, Cupelli L, Arcioni F, Ribersani M, Proia A, Cartoni C, Girardi K, Venditti A, Cassetta MI, Fallani S, Novelli A. Voriconazole Treatment in Adults and Children with Hematological Diseases: Can it be used without Measurement of Plasma Concentration? *Med.Mycol.* 2018 56(3): 263a

12. Gurnari C, Latagliata R, Buccisano F, Piciocchi A, Fenu S, Mancini S, Fianchi L, Criscuolo M, Sarlo C, Romano A, Falconi G, Niscola P, Di Veroli A, Breccia M, Piccioni A, Aloe-Spiriti MA, Lo-Coco F, Voso MT, GROM-L (Gruppo Romano-Laziale MDS), GROM-L (Gruppo Romano-Laziale MDS). Erythropoietin Levels and Erythroid Differentiation Parameters in Patients with Lower-Risk Myelodysplastic Syndromes. *Leuk.Res.* 2018 Jul 10; 71: 89a

13. Iannitto E, Bellei M, Amorim S, Ferreri AJM, Marcheselli L, Cesaretti M, Haioun C, Mancuso S, Bouabdallah K, Gressin R, Tripodo C, Traverse-Glehen A, Baseggio L, Zupo S, Stelitano C, Castagnari B, Patti C, Alvarez I, Liberati AM, Merli M, Gini G, Cabras MG, Dupuis J, Tessoulin B, Perrot A, Re F, Palombi F, Gulino A, Zucca E, Federico M, Thieblemont C. Efficacy of Bendamustine and Rituximab in Splenic Marginal Zone Lymphoma: Results from the Phase II BRISMA/IELSG36 Study. *Br.J.Haematol.* 2018 Dec; 183(5): 755a

14. Marchesi F, Capria S, Giannarelli D, Trisolini SM, Ansuinelli M, Caputo MD, Serrao A, Gumenyuk S, Renzi D, Pupo L, Palombi F, Provenzano I, Di Rocco A, Pisani F, Romano A, Spadea A, Papa E, Canfora M, Cantonetti M, Mengarelli A. BEAMVs FEAM High-Dose Chemotherapy: Retrospective Study in Lymphoma Patients Undergoing Autologous Stem Cell Transplant. *Bone Marrow Transplant.* 2018 53(8): 1051-1054a

15. Marchesi F, Girmenia C, Goffredo BM, Salvatorelli E, Romano A, Mengarelli A, Minotti G, Menna P. Isavuconazole: Case Report and Pharmacokinetic Considerations. *Chemotherapy.* 2018 Nov 20; 63(5): 253a

16. Maschio M, Mengarelli A, Zarabla A, Giannarelli D, Maialetti A, Gumenyuk S, Renzi D, Palombi F, Pisani F, Romano A, Spadea A, Galie E, Marchesi F. Role of Pregabalin in Treatment of Polyneuropathy in Multiple Myeloma Patients: A Retrospective Study. Clin.Neuropharmacol. 2018 Dec 17[Epub ahead of print]

17. Marchesi F, Pimpinelli F, Ensoli F, Mengarelli A. Cytomegalovirus Infection in Hematologic Malignancy Settings Other than the Allogeneic Transplant. *Hematol. Oncol.* 2018 Apr; 36(2): 381a

18. Marchesi F, Regazzo G, Palombi F, Terrenato I, Sacconi A, Spagnuolo M, Donzelli S, Marino M, Ercolani C, Di Benedetto A, Blandino G, Ciliberto G, Mengarelli A, Rizzo MG. Serum miR-22 as Potential Non-Invasive Predictor of Poor Clinical Outcome in Newly Diagnosed, Uniformly Treated Patients with Diffuse Large B-Cell Lymphoma: An Explorative Pilot Study. *J. Exp. Clin. Cancer Res.* 2018 May 2; 37(1): 95a

19. Marchesi F, Vacca M, Giannarelli D, Ipsevich F, Pandolfi A, Gumenyuk S, Renzi D, Palombi F, Pisani F, Romano A, Spadea A, Papa E, Canfora M, Pierelli L, Mengarelli A. Lenograstim 5 microg/kg is Not Superior to Biosimilar Filgrastim 10 microg/kg in Lymphoma Patients Undergoing Peripheral Blood Stem Cell Mobilization After Chemotherapy: Preliminary Results from a Prospective Randomized Study. *Transfusion.* 2018 Feb 15;

20. Maschio M, Zarabla A, Maialetti A, Marchesi F, Giannarelli D, Gumenyuk S, Pisani F, Renzi D, Galie E, Mengarelli A. Prevention of Bortezomib-Related Peripheral Neuropathy with Docosahexaenoic Acid and Alpha-Lipoic Acid in Patients with Multiple Myeloma: Preliminary Data. *Integr. Cancer. Ther.* 2018 Dec; 17(4): 1115a

21. Menna P, Calabrese V, Armento G, Annibali O, Greco C, Salvatorelli E, Marchesi F, Reggiardo G, Minotti G. Pharmacology of Cardio-Oncology: Chronotropic and Lusitropic Effects of B-Type Natriuretic Peptide in Cancer Patients with Early Diastolic Dysfunction Induced by Anthracycline Or Nonanthracycline Chemotherapy. *J. Pharmacol. Exp. Ther.* 2018 Jul; 366(1): 158a

22. Menna P, Salvatorelli E, Armento G, Annibali O, Greco C, Marchesi F, Calabrese V, Reggiardo G, Minotti G. The Endogenous Lusitropic and Chronotropic Agent, B-Type Natriuretic Peptide, Limits Cardiac Troponin Release in Cancer Patients with an Early Impairment of Myocardial Relaxation Induced by Anthracyclines. *J. Pharmacol. Exp. Ther.* 2018 Dec; 367(3): 518a

23. Olivieri J, Attolico I, Nuccorini R, Pascale SP, Chiarucci M, Poiani M, Corradini P, Farina L, Gaidano G, Nassi L, Sica S, Piccirillo N, Pioltelli PE, Martino M, Moscato T, Pini M, Zallio F, Ciceri F, Marktel S, Mengarelli A, Musto P, Capria S, Merli F, Codeluppi K, Mele G, Lanza F, Specchia G, Pastore D, Milone G, Saraceni F, Di Nardo E, Perseghin P, Olivieri A. Predicting Failure of Hematopoietic Stem Cell Mobilization before it Starts: The Predicted Poor Mobilizer (pPM) Score. *Bone Marrow Transplant.* 2018 Apr; 53(4): 461a

24. Spagnuolo M, Regazzo G, De Dominici M, Sacconi A, Pelosi A, Korita E, Marchesi F, Pisani F, Magenta A, Lulli V, Cordone I, Mengarelli A, Strano S, Blandino G, Rizzo MG, Calabretta B. Transcriptional Activation of the miR-17-92 Cluster is Involved in the Growth-Promoting Effects of MYB in Human Ph-Positive Leukemia Cells. Haematologica. 2018 Aug 3 [Epub ahead of print]

25. Tendas A, Malandruccolo L, Venditti D, Costa A, Volta L, Annibali O, Marchesi F, Saltarelli D, de Fabritiis P, Arcese W, Bondanini F, Niscola P, Palumbo R. Gender, Age and Diagnosis Effect on Self-Perceived Pain in Hematological Patients: Retrospective Analysis of Two Case Series. *Ann. Palliat. Med.* 2018 May 9;

26. Tendas A, Marchesi F, Annibali O, Saltarelli D, Niscola P, Perrotti AP, Arcese W, Rome Transplant Network. Chemotherapy-Induced Nausea and Vomiting Prophylaxis in High-Dose Melphalan and Autologous Stem Cell Transplantation. *Clin. Lymphoma Myeloma Leuk.* 2018 Feb; 18(2): 161a

27. Tendas A, Marchesi F, Mengarelli A, Annibali O, Tomarchio V, Saltarelli D, Chierichini A, Di Venanzio M, Sollazzo F, Piedimonte M, Cupelli L, Bruno A, De Angelis G, Delbono L, Niscola P, Perrotti AP, de Fabritiis P, Arcese W, Rome Transplant Network. Prevention of Chemotherapy-Induced Nausea and Vomiting After High-Dose Melphalan and Stem Cell Transplantation: Review of the Evidence and Suggestions. Support.Care Cancer. 2018 Dec18 [Epub ahead of print]

28. Vidiri A, Minosse S, Piludu F, Pellini R, Cristalli G, Kayal R, Carlino G, Renzi D, Covello R, Marzi S. Cervical Lymphadenopathy: Can the Histogram Analysis of Apparent Diffusion Coefficient Help to Differentiate between Lymphoma and Squamous Cell Carcinoma in Patients with Unknown Clinical Primary Tumor? *Radiol.Med.* 2018 Sep 8 [Epub ahead of print]

# CARDIOLOGY UNIT

## *Head: Francesco Rulli, MD*

## STAFF

| |
|---|
| **Armando Carpino, MD** |
| **Maria Paola Cicini, MD** |
| **Fabio Maramao, MD** |
| **Nicola Antonio Morace, MD** |
| **Giuseppe Canio Toglia MD** |
| **Fabio De Luca, Nurse in Chief** |
| **Laura Cervellione, Nurse** |
| **Gianni Chiarabini, Nurse** |
| **Gianni Pompei, Nurse** |
| **Antonella Perenzin, Nurse** |

## *Mission*

The Cardiology Staff performs all non invasive cardiological diagnostic current required by the surgical facilities, medical oncology and dermatology Institutes. The patients are studies by consulting cardiological ECG, echo, stress ECG, 24 hours ECG and 24 hours monitoring blood pressure. Patients who belong to our Unit, with a path shared by colleagues practitioners, have a predetermined follow-up and facilitated in terms of access benefits with waiting times of 48 hours.

## *Clinical Activity*

The Cardiology Unit carries out assistance activities and clinical-instrumental advice to all cancer patients

Institute Regina Elena and S. Gallicano Institute.
The outpatient activity is dedicated to cancer patients who belong to the take in charge, to Day-hospital, Day-Surgery at the two Institutes and to all people in need of evaluation and ongoing monitoring of chemo-radiotherapy or remote treatment within the follow set up programmed by shared treatment protocols.

## Research Activity

The Cardiology operating Unit substantially has three aspects:

- Support to surgery in terms of preoperative cardiovascular function evaluation in the intraoperatorive emergency and in any patient's appreciation as a results of complications.
- The state of cardiological evaluation of the patient to be subjected to chemotherapy or radiotherapy, pre or post-surgery, given the already documented cardiotoxicity of some therapeutic lines and in particular of some specific groups of drugs. To this is added the periodic monitoring, clinical and instrumental, the treated patient, and in accordance with research protocols defined and shared with colleagues oncologists conforming with the guidelines defined by available.
- The UO Cardiology is part of the most solid and accreditated reality (domestic and international) associational cardiology and cardio-oncology, in the evaluation of cardiotoxic effects of some anticancer drugs, in research and in the development of myocardial damage markers in outcome and patient who underwent cardiac surgery for cancer.

## Publications

1. Calabrese V, Menna P, Annibali O, Armento G, Carpino A, Cerchiara E, Greco C, Marchesi F, Spallarossa P, Toglia G, Reggiardo G, Minotti G, Collaborators. Early Diastolic Dysfunction After Cancer Chemotherapy: Primary Endpoint Results of a Multicenter Cardio-Oncology Study. *Chemotherapy.* 2018 63(2): 55a Endocrinology Unit

# ENDOCRINOLOGY UNIT

*Head: Marialuisa Appetecchia, MD*

## STAFF

| Endocrinologists |
|---|
| Agnese Barnabei |
| Lauretta Rosa (professional contract January-June) |
| Chiefari Alfonsina (professional contract September-December) |
| Vottari Sebastiano (professional contract September-December) |
| **Area coordinator** |
| Sig. Eros Floridi |
| **Area nurses** |
| Aurora De Leo |
| Sonia Girasole |
| Emiliana Marinucci |
| Maria Piccolo |
| Enrica Ruffo |
| Giuliana Panico |
| **Area social health workers** |
| Malci Francesco |
| Maria Di Luccio |
| **Attending Endocrinologists** |
| Traineers from Endocrinology Specialization Schools of Universities La Sapienza - PTV- S. Andrea |

## Mission

The Oncological Endocrinology Unit operates in three areas: clinical, research and training. Its mission is to achieve excellence in the prevention, diagnosis and treatment of endocrine and neuroendocrine tumors and endocrine-metabolic sequelae in cancer patients, using diagnostic and therapeutic pathways (PDTA) and the use of DMT dedicated to the discussion of cancer patients thyroid (DMT Thyroid) and neuroendocrine tumors (DMT NET).
The research activities of the IFO Oncological Endocrinology Unit are focused on the evaluation and development of new tools useful in the diagnosis, treatment and monitoring of human endocrine and neuroendocrine tumors with particular attention to precision medicine.
In particular, the unit is involved in the clinical research of new prognostic markers (liquid biopsy) and new personalized drug delivery strategies (rhTSH), in the identification of correlations between hereditary syndromes such as Familial Polyposis and endocrine tumors, in the presence of mutations genetics (ATM gene) in those thyroid carcinomas associated with breast cancer. Other fields of interest include the study of the endocrine effects of cancer therapies, such as growth hormone deficiency (ghd) or hypopituitarism in brain neoplasms, hypogonadism and sexual dysfunction due to gonadal tumors or consequences of surgery, chemotherapy or radiotherapy and their impact on the quality of life of patients.
The Unit has collaborative relationships and participates in multicenter clinical trials with the main Italian Universities and Research Institutes, also within Scientific Societies (SIE, SIOMMS) and is the reference center for rare endocrine and neuroendocrine tumors (G4 and G6) of IFO IRCCS of Rome for the European ERN EURACAN Network for Rare Adult Solid Cancers.
The work setting is based on the constant attention to technical and professional quality and on the continuous improvement and updating of the techniques of service delivery and management, as well as on the preservation of the human aspect and on the quality of the relationship with patients and staff.

## Clinical Activities

### Thyroid carcinomas (Differentiated and Medullary)

Patients with thyroid nodules who are under our care appointed a diagnostic health-care path which provides diagnostic laboratory tests (thyroid hormones) and instrumental tools (i.e. echo-color doppler thyroid scan and FNAB) in order to diagnose the nature (benign/malignant) of the nodular lesion. In case of suspecting or overt malignancy, patients are sent to undergo surgery or other treatments as appropriate, depending on their individual evaluation.
Patients with a differentiated diagnosis of thyroid cancer are regularly included in the follow-up at the Endocrinology Unit where laboratory and instrumental tools are used to carry out routine checks.
For all patients with thyroid cancer the following services are available: routine medical checks (follow-up), physical examinations, evaluations through laboratory support in order to investigate the state of the disease. The optimal frequency of follow-up assessments are personalized, in accordance with the stage of the patient's illness.
The UOSD of Oncological Endocrinology follows to date approximately 2600 patients with Thyroid tumors (Differentiated and Medullary).

### Hereditary endocrine tumours syndromes

Hereditary tumor syndromes are increasingly recognized in the development of endocrine neoplasms. Depending on the tumor type, 10% to 40% of cases are associated with genetic disorders, including the classic multiple endocrine neoplasia syndromes (MEN1 and MEN2), hyperparathyroidism–jaw tumor syndrome, *SDH*-related familial paraganglioma-pheochromocytoma syndromes, von Hippel-Lindau syndrome, neurofibromatosis type 1, Carney complex, McCune-Albright syndrome, and familial nonmedullary thyroid cancer syndromes, as well as newer entities (MEN4, DICER1 syndrome, glucagon cell hyperplasia and neoplasia syndrome). Although some features commonly seen in familial disease (early onset, family history, multifocal neoplasia, multiorgan involvement) may alert one to the possibility of an underlying genetic predisposition, endocrine neoplasia syndromes tend to be phenotypically complex and heterogeneous and present variably with de novo mutations, making it difficult to recognize and classify on clinical grounds alone. In an era of precision medicine, pathologists play a central role in the diagnosis of familial cancer syndromes, by leading the way toward screening and molecular histopathology prediction models. In particular, the identification of "pathognomonic" morphologic and immunohistochemical "clues" is crucial to raise the possibility of an inherited genetic disorder and to guide further management, including gene testing, counseling, and targeted therapy. This review highlights the important genotype-phenotype correlations to consider in hereditary endocrine tumor syndromes and their associated clinical implications.
For these reasons an **outpatient clinic** dedicated to studying genetic counseling and prevention of hereditary

oncological diseases has been activated. It provides the following:
Multidisciplinary assessments or patients with suspected familial endocrine neoplasia having medical appointments with endocrinologists, geneticists, psychologists; along with the involvement of other specialists (oncologists, surgeons, gynecologists, gastroenterologists, molecular biologists, pathologists, radiologists) at different stages of diagnosis and therapy.They will also be undergoing molecular analyses for detecting small or large mutations in the genes responsible for: RET, MEN-1, VHL, SDHB, SDHD, SDHC. The patient with familial endocrine neoplasia is followed right from the first clinical suspicion of disease to molecular diagnosis, studying the family history to organizing follow-up examinations and indications for surgical treatment, and subsequent radio and chemotherapy treatments through to newer biological approaches, all with the support and help of a team of psychologists.

### Osteoporosis and bone metabolism disorders in cancer patients

In patients with oncological disease, most cases are long-term survivors who, as a result of therapeutic treatments, experience menopause at times early therefore, with frequent reoccurring problems related to bone metabolism, or due to demineralizing effects of some drugs (e.g.: steroids).
In these patients, treating metabolic bone disease becomes all the more necessary than in non-cancer patients, not only for the overall improvement of its compliance but also for the psychological implications.
It is also reported that some metabolic bone diseases tend to emulate clinically neoplastic diseases while others are true paraneoplastic disorders.
The Oncological Endocrinology Unit often sees cancer patients to set specific therapies for osteoporosis. Treating these patients need to be based on indicators other than those usually used in non-oncological patients with osteoporosis. All the more reason why an **outpatient clinic** dedicated has been activated.

### Thyroid cancer and Familial adenomatous polyposis (FAP)

Patients with FAP have a higher risk in developing cancer of the thyroid than the general population; therefore a follow-up visit that includes annual and ultrasound of the thyroid is needed. The Unit of Gastroenterology and Digestive Endoscopy is a Reference Center in the Lazio Region for FAP which, being rare disease, patients should be ensured to receive comprehensive clinical management, with dedicated paths, providing diagnostic evaluations and follow-ups of target organs, including the thyroid.
Diagnostic and therapeutic healthcare paths in patients with FAP APC POS / unknown mutations include undergoing endocrine tests due to the increased incidence of endocrine disease in these patients such as thyroid tumours
As a result, the Oncological Endocrinology Unit has activated a **dedicated clinical path** for these patients.
At moment, we are following approximately 81 patients affected with FAP and endocrine diseases.

### Neuroendocrine Tumors

Neuroendocrine tumors are very rare tumors that arise in the endocrine glands or endocrine cells dispersed in the body. The annual occurrence of these tumors is very low: 0.07 / 100,000 to gastrointestinal localization, 0.05 / 100,000 associated with Multiple Endocrine Neoplasia MEN-1 and / pancreatic 100,000. The sporadic forms have a higher incidence between 50-60 years, while the familiar forms are diagnosed earlier. Their incidence is still rising but nevertheless remain poorly known tumors, often characterized by a difficult diagnostic and therapeutic approach.The Oncological Endocrinology Unit follows to date approximately 270 patients with NETs and about 570 patients with pituitary tumors (Acromegaly 67).

**Other topics** we are interested in include:
Adrenal Tumors,
Fertility disorders in cancer patients,
Endocrine side-effects of anti-cancer therapies,
Pituitary Tumors and Adults Growth Hormone Deficiency (GHD).

Dedicated clinics for:

- secondary osteoporosis in cancer treatment (from 2011)
- patients with hereditary endocrinological syndromes (from 2011)
- thyroid cancer screening in patients with FAP (in collaboration with UOSD of Digestive Endoscopy IRE) (from 2009)
- endocrine-metabolic related disturbances and fluid and electrolyte in cancer patients

### Endocrinology Unit is a Regional referral center for adult GHD (from 2003) and an AIFA accredited center (2012) Lazio Region to:

metastatic and / or progressive thyroid tumors (medullary carcinoma)
osteoporosis in cancer patients,
metastatic and / or progressive pancreatic neuroendocrine

tumors
pituitary tumors (Cushing's disease).

## Research Activities

The research efforts of the Oncological Endocrinology Unit has long-standing commitment and care in improving the detection and treatment of endocrine and neuroendocrine cancers involve evaluating and developing novel clinical and laboratory tools useful in the diagnosis and monitoring of human endocrine and neuroendocrine cancers.
In particular, the Unit is involved with clinical research and new treatment strategies regarding thyroid and neuroendocrine tumours.
Other fields of interest include the endocrine effects of tumours or of related treatments, such as Growth Hormone Deficit (GHD) or hypopituitarism in brain neoplasms, hypogonadism and sexual dysfunctions due to gonadal tumours or consequences of surgery, chemotherapy or radiotherapy and their impact on the quality of life of the patients. Our group is mainly interested in identifying genetic risk factors involved in endocrine tumour susceptibility. Through a comprehensive analysis of tumour genomic features we have been able to propose diagnostic and prognostic markers to identify altered pathways that could be therapeutically targeted. We are also interested in defining markers associated with differences in anticancer drug response and toxicity. We are applying targeted and whole-exome next-generation sequencing to clinically well-characterized patients. The aim is to identify new therapeutic approaches to personalize cancer treatment. These efforts will collectively improve the diagnosis, prognosis and treatment of patients. Ongoing projects also include topics regarding:

- osteoporosis and bone metabolism disorders in cancer patients
- the endocrine-metabolic related disturbances and fluid and electrolyte in cancer patients.

## Publications


1. Appetecchia M, Lauretta R, Sperduti I, Gallucci M. Chromogranin A as a Biomarker for Prostate Cancer: Is it Actually Relevant for Clinical Practice? *Future Oncol.* 2018 Jun; 14(13):1233-1235

2. Barnabei A, Strigari L, Persichetti A, Baldelli R, Rizza L, Annoscia C, Lauretta R, Cigliana G, Barba M, De Leo A, Appetecchia M, Torino F. Indirect Basal Metabolism Estimation in Tailoring Recombinant Human TSH Administration in Patients Affected by Differentiated Thyroid Cancer: A Hypothesis-Generating Study. *Front. Endocrinol. (Lausanne).* 2018 Feb 15; 9: 37a

3. Lauretta R, Sansone M, Romanelli F, Appetecchia M. Gender in Endocrinological Diseases: Biological and Clinical Differences. *Ital J Gender-Specific Med.* 2017 3(3): 109a

4. Lauretta R, Sansone M, Sansone A, Romanelli F, Appetecchia M. Gender in Endocrine Diseases: Role of Sex Gonadal Hormones. *Int. J. Endocrinol.* 2018 Oct 21; 2018: 4847376a

5. Persichetti A, Bizzarri G, Guglielmi R, Barnabei A, Bianchini A, Coccaro C, Appetecchia M, Papini E. Ultrasound-Guided Laser Ablation for Local Control of Neck Recurrences of Medullary Thyroid Cancer. A Feasibility Study. *Int. J. Hyperthermia.* 2018 Sep 11; 1a

6. Sansone A, Fegatelli DA, Pozza C, Fattorini G, Lauretta R, Minnetti M, Romanelli F, Lucatelli P, Corona M, Bezzi M, Lombardo F, Lenzi A, Gianfrilli D. Effects of Percutaneous Varicocele Repair on Testicular Volume: Results from a 12-Month Follow-Up. *Asian J. Androl.* 2018 Dec 25; [Epub ahead of print]

7. Sponziello M, Benvenuti S, Gentile A, Pecce V, Rosignolo F, Virzi AR, Milan M, Comoglio PM, Londin E, Fortina P, Barnabei A, Appetecchia M, Marandino F, Russo D, Filetti S, Durante C, Verrienti A. Whole Exome Sequencing Identifies a Germline MET Mutation in Two Siblings with Hereditary Wild-Type RET Medullary Thyroid Cancer. *Hum. Mutat.* 2018 Mar; 39(3): 371a

8. Trimboli P, Lauretta R, Barnabei A, Valabrega S, Romanelli F, Giovanella L, Appetecchia M. Procalcitonin as a Postoperative Marker in the Follow-Up of Patients Affected by Medullary Thyroid Carcinoma. *Int. J. Biol. Markers.* 2018 May; 33(2): 156a

# NEURONCOLOGY UNIT

## *Head: Andrea Pace, MD*

## STAFF

| | |
|---|---|
| Edvina Galiè, MD | Maria Andreina Rotondi, Social worker |
| Marta Maschio, MD | Lara Guariglia, Psychologist |
| Tatiana Koudriavtseva, MD | Sonia Ieraci, Psychologist |
| Veronica Villani, MD | Cristiano Parisi, Physioterapist |
| Daniela Alò, Nurse | Stefano Di Felice, Physioterapist |
| Roberta Rafaelli, Nurse | Margaux Lamaro, Physioterapist |
| Giuliana Graziano, Technician | Silvia Focarelli, Data Manager |
| Gianluca Petreri, Technician | Antonio Tanzilli, Neuro-psychologist |
| Alessia Zizzari, Physioterapist | Andrea Maialetti, Neuro-psychologist |
| Andrea Minnetti, Physiotherapist | Research collaborations with graduate and undergraduate students |
| Luciano Urbani, Physiotherapist | |
| Dario Benincasa, Neurologist | Marzia Piccoli |

## Mission

Clinical and research activity of Neuroncology Unit is dedicated to the diagnosis, therapeutical approaches and supportive and palliative care of primary brain tumors. Moreover, the Unit is involved in clinical and research activity related to Central and Peripheral Nervous System neurological complications of cancer and neurotoxicity of anticancer treatments.

## Clinical Activity

The clinical activities of Neuroncology Unit include:

- Neurology clinic
- Neuro-oncology clinic
- Brain tumors related epilepsy
- Neuropathic Pain Clinic
- Neuropsychology and cognitive rehabilitation
- Neuro-oncologic Day Service for chemotherapy and supportive treatment of brain tumor patients
- Neurophysiology lab (Electromyography, Electroencephalography, Evoked Potentials)
- Rehabilitation service specialized in cancer rehabilitation for in- and out-patients
- Palliative and supportive home care for brain tumor patients

## Research Activity

The research activity of Neurology Unit is focused on several topics. These include:

- *Clinical neuro-oncology* - The role of chemotherapy in recurrent malignant brain tumor has been evaluated in phase II trials exploring the activity and toxicity of several anticancer agents: temozolomide, fotemustine, bevacizumab, carboplatin, ortataxel, regorafenib. Recent trials have been launched including: weekly carboplatin AUC2 in recurrent malignant glioma; cloropromazine associated to temozolomide in newly diagnosed GBM.
- Next generation sequencing in glioma patients for identification of potential target therapy:NGS panels assessment allowing the simultaneous analysis of both DNA and RNA in order to identify either the presence of point variants and fusion genes or variations in the number of gene copies with a panel of 50 genes that are recognized to have a key role in tumour development, with the aim to identify potential therapeutic target
- *Clinical Benefit of antiangiogenic treatment* - The aim of this study was to evaluate the clinical benefit of bevacizumab therapy alone or in combination in the treatment of recurrent glioma. Preliminary results have been presented in national and international scientific meetings. The final paper is in press.
- *Cognitive impairment assessment and rehabilitation* - The role of cognitive rehabilitation programs has been investigated in different setting of care (in patients, outpatients, home care setting). Preliminary data showed beneficial effects of a computer-based cognitive rehabilitation programme and positive impact on Quality of Life in neuro-oncological patients. Preliminary results have been presented in national and international scientific meetings.
- *Home-care for brain tumor patients* - The efficacy of a program of comprehensive palliative care for brain tumour patients supported by the Lazio Regional Health System was evaluated analyzing place of death, caregiver satisfaction, re-hospitalization rate and the impact on Health System costs. The results of this project have been presented in national and international scientific meeting.
- *Palliative neuro oncology and telemedicine* -
- We developed a health WEB site portal applied to Neuro-Oncology supportive and palliative care issues (www.portaleneuroncologia.it). Neuroncology Unit of IRE is involved in an international project aimed to define guidelines and treatment recommendations on supportive and palliative care in brain tumor patients. The guidelines produced by the palliative care task force have been recently published on Lancet Oncology.
- *Peripheral neurotoxicity of anticancer drugs* - We are involved in an international study:The Chemotherapy-Induced Peripheral Neuropathy Outcome Measures Standardization (CIPerinoms) including 20 European and US oncology and neurology centres specifically designed to compare the validity and reliability of different methods proposed for the assessment of chemotherapy-induced peripheral neuropathy in a formal way. The results have been published on Annals of Oncology, European Journal of Cancer and Journal of Peripheral Nervous System. A randomized, single institution, placebo controlled study exploring the role of antioxidant neuroprotection with vitamin E in cisplatin ototoxicity has been concluded. The final results have been published recently on Head and Neck Journal.

- *Rehabilitation in Oncology* - Neuroncology Unit research activity includes the clinical research and methodological assessment of rehabilitation strategies in oncology. In a recent study we retrospectively analyzed the Rehabilitation pathways in brain tumor patients in the first twelve months of disease. A retrospective analysis of services utilization in 719 patients. The final results have been published on Supportive Care in Cancer.
- *Role of comorbidities in the elderly glioblastoma - A prospective study:* This study evaluated the impact of comorbidities on outcomes in elderly GBM patients. Comorbid conditions were indentified with the modified version of the Cumulative Illness Rating Scale (CIRS). The results showed that comorbidities play an important prognostic role in elderly with GBM. Preliminary results have been presented in national and international scientific meetings. The final results have been submitted for publication.
- *The prognostic value of pyrosequencing-detected MGMT-promoter hypermethylation in newly diagnosed patients with glioblastoma* – We collected tumour samples of GBM patients who underwent surgery or biopsy and were/are followed at the Neuro-oncology Unit of National Cancer Institute Regina Elena. Preliminary data showed that patients with a cut-off <35% of methylation had a shorter PFS but not significant difference we observed in terms of overall survival. A multicentric study, with the participation of Italian neuroncology centers, on the methylation status of glioblastoma determined with pyrosequencing is ongoing.
- *Headache as a presenting symptom of glioma: a cross-sectional study.* Five hundred and twenty-seven patients were interviewed; 66 (12.5%) of them had headache as a presenting symptom of brain tumour. In our sample, headache resembled a tension-type headache in 31 patients (6% of all glioma cases) and the classic benign thunderclap headache (BTH) was found in 28 cases (5% of all glioma cases). The paper has been submitted for publication.
- *Tumor related Epilepsy* - The Center of Tumor-related Epilepsy is Coordinator of Italian League Against Epilepsy (LICE) Study Group on "Brain tumor-related Epilepsy". This group includes 35 Italian epilepsy centers.

## Ongoing Clinical Trials (2018)

- Primary headache in malignant glioma patients. Multicentric observational study. Ongoing
- Development of an EORTC QoL cancer survivorship questionnaire. Multicentric international EORTC study. Closed
- Perampanel in patients with brain tumour-related epilepsy in real-life clinical practice. Effect of perampamel in add-on on seizures control, cognition and quality of life in patients with brain tumor related epilepsy. Observational pilot study.
- Effect of perampanel in combination with ketone bodies on the proliferation rate of human glioma cell lines and stem cell-like glioblastoma-derived cells"
- Retrospective collaborative cohort study on the efficacy of antiepileptic drugs in patients with glioblastoma and tumor related epileps. In collaboration with University of Bergen, Norway
- Rational drug repositioning for an efficient and safe combined therapeutic approach to glioblastoma multiforme.
- Rehabilitation for Brain Tumor patients affected by epilepsy (Associazione Blaze) Ongoing
- Medical decision capacity in Brain Tumor patients. Assessment and neurocognitive correlations.
- Coagulation/complement activation and cerebral hypoperfusion in relapsing-remitting multiple sclerosis. MoH project. In collaboration with Università di Roma La Sapienza

## Publications

1. Di Stefano AL, Berzero G, Ducray F, Eoli M, Pichiecchio A, Farina LM, Cuccarini V, Brunelli MC, Diamanti L, Condette Auliac S, Salmaggi A, Silvani A, Giometto B, Pace A, Vidiri A, Bourdain F, Bastianello S, Ceroni M, Marchioni E. "Stroke-Like" Events After Brain Radiotherapy: A Large Series with Long-Term Follow-Up. Eur.J.Neurol. 2018 Nov 24; [Epub ahead of print]

2. Galgani A, Palleria C, Iannone LF, De Sarro G, Giorgi FS, Maschio M, Russo E. Pharmacokinetic Interactions of Clinical Interest between Direct Oral Anticoagulants and Antiepileptic Drugs. Front.Neurol. 2018 Dec 7; 9: 1067a

3. Lai S, Molfino A, Mecarelli O, Pulitano P, Morabito S, Pistolesi V, Romanello R, Zarabla A, Galani A, Frassetti N, Aceto P, Lai C, Study Group on Geriatric Nephrology of the Italian Society of Nephrology. Neurological and Psychological Changes in Hemodialysis Patients before and After the Treatment. Ther.Apher.Dial. 2018 Oct; 22(5): 530a

4. Lombardi G, De Salvo GL, Brandes AA, Eoli M, Ruda R, Faedi M, Lolli I, Pace A, Daniele B, Pasqualetti F, Rizzato S, Bellu L, Pambuku A, Farina M, Magni G, Indraccolo S, Gardiman MP, Soffietti R, Zagonel V. Regorafenib Compared with Lomustine in Patients with Relapsed Glioblastoma (REGOMA): A Multicentre, Open-Label, Randomised, Controlled, Phase 2 Trial. Lancet Oncol. 2018 Dec 3 [Epub ahead of print]

5. Maschio M, Pauletto G, Zarabla A, Maialetti A, Ius T, Villani V, Fabi A, Koudriavtseva T, Giannarelli D. Perampanel in Patients with Brain Tumour-Related Epilepsy in Real-Life Clinical Practice: A Retrospective Analysis. Int.J.Neurosci. 2018 Dec 3; : 1-10 [Epub ahead of print]

6. Maschio M, Zarabla A, Maialetti A, Marchesi F, Giannarelli D, Gumenyuk S, Pisani F, Renzi D, Galie E, Mengarelli A. Prevention of Bortezomib-Related Peripheral Neuropathy with Docosahexaenoic Acid and Alpha-Lipoic Acid in Patients with Multiple Myeloma: Preliminary Data. Integr.Cancer.Ther. 2018 Dec; 17(4): 1115a

7. Maschio M, Zarabla A, Maialetti A, Sperati F, Dinapoli L, Dispenza S, Petreri G, Cantelmi T. Lacosamide on Background Eeg Activity in Brain Tumor-Related Epilepsy Patients: A Case Series Study. Brain Behav. 2018 Nov; 8(11): e01067a

8. Pace A, Mandoj C, Antenucci A, Villani V, Sperduti I, Casini B, Carosi M, Fabi A, Vidiri A, Koudriavtseva T, Conti L. A Predictive Value of Von Willebrand Factor for Early Response to Bevacizumab Therapy in Recurrent Glioma. J.Neurooncol. 2018 Jul; 138(3): 527a.

9. Pace A, Villani V. Palliative and Supportive Care of Patients with Intracranial Glioma. Prog.Neurol.Surg. 2018 31: 229-237

10. Pace A, Villani V. 2018. "Palliative Care and Palliative Rehabilitation: Approaches to the End-of-Life." In Neurorehabilitation in Neuro-Oncology, edited by M. Bartolo, R. Soffietti and M. Klein. 1st ed.: Springer International Publishing.

11. Pace A, Walbert T. Simultaneous Care in Neuro-Oncology. Neuro Oncol. 2018 Feb 19; 20(3): 302a

12. Pasqualetti F, Pace A, Gonnelli A, Villani V, Cantarella M, Delishaj D, Vivaldi C, Molinari A, Montrone S, Pellerino A, Franchino F, Baldaccini D, Lombardi G, Lolli I, Catania F, Bazzoli E, Morganti R, Fabi A, Zagonel V, Bocci G, Fabrini MG, Ruda R, Soffietti R, Paiar F. Single-Agent Bevacizumab in Recurrent Glioblastoma After Second-Line Chemotherapy with Fotemustine: The Experience of the Italian Association of Neuro-Oncology. Am.J.Clin.Oncol. 2018 Dec; 41(12): 1272a

13. Plantone D, Koudriavtseva T. Current and Future use of Chloroquine and Hydroxychloroquine in Infectious, Immune, Neoplastic, and Neurological Diseases: A Mini-Review. Clin.Drug Investig. 2018 Aug; 38(8): 653-671a

14. Russo M, Villani V, Taga A, Genovese A, Terrenato I, Manzoni GC, Servadei F, Torelli P, Pace A. Headache as a Presenting Symptom of Glioma: A Cross-Sectional Study. Cephalalgia. 2018 Apr; 38(4): 730a

15. Telera S, Pompili A, Crispo F, Giovannetti M, Pace A, Villani V, Fabi A, Sperduti I, Raus L. Kyphoplasty with Purified Silicone VK100 (Elastoplasty) to Treat Spinal Lytic Lesions in Cancer Patients: A Retrospective Evaluation of 41 Cases. Clin.Neurol.Neurosurg. 2018 Aug; 171: 184a.

16. van Leeuwen M, Husson O, Alberti P, Arraras JI, Chinot OL, Costantini A, Darlington AS, Dirven L, Eichler M, Hammerlid EB, Holzner B, Johnson CD, Kontogianni M, Kaer TK, Morag O, Nolte S, Nordin A, Pace A, Pinto M, Polz K, Ramage J, Reijneveld JC, Serpentini S, Tomaszewski KA, Vassiliou V, Verdonck-de Leeuw IM, Vistad I, Young TE, Aaronson NK, van de Poll-Franse LV, EORTC QLG. Understanding the Quality of Life (QOL) Issues in Survivors of Cancer: Towards the Development of an EORTC QOL Cancer Survivorship Questionnaire. Health.Qual.Life.Outcomes. 2018 Jun 4; 16(1): 114a

# GASTROENTEROLOGY AND DIGESTIVE ENDOSCOPY UNIT

## *Head: Vittoria Stigliano , MD*

## STAFF

| |
|---|
| **Paola CAPRA, Lead Nurse** |
| **Laura ARGENTO, Nurse** |
| **Daniela CANNONE, Nurse** |
| **Alessandra CINTI, Nurse** |
| **Susanna PAMPINELLA, Nurse** |
| **Marina SANTAMARIA, Nurse** |
| **Cinzia TORESI, Health Worker** |
| **Mario DI STEFANO, Health Worker** |

| |
|---|
| **Daniela ASSISI, MD** |
| **Rocco LAPENTA, MD** |
| **Cinzia QUONDAMCARLO, MD** |
| **Lupe SANCHEZ METE, MD** |
| **Elena MANNISI, MD** |
| **2 PhD students of "La Sapienza" University of Rome** |

### *Mission*

Gastroenterology and Digestive Endoscopy Unit plays a critical role in the oncological prevention, the diagnosis and treatment of gastrointestinal cancer.
We can boast an extensive experience and expertise in the field of Colorectal cancer screening in high (i.e. Hereditary Colorectal Cancer Syndromes affected individuals) and average risk population (i.e. Breast cancer patients).
The Unit is equipped with new advanced endoscopic technologies that allow a thorough evaluation of

gastrointestinal tract improving precancerous lesion/ early cancer detection and treatment.
Another important area of interest and development is Nutritional support in cancer patients. Patients with cancer, particularly gastrointestinal and head and neck cancer, are at high risk for malnutrition that negatively impact on oncological treatment outcome. The Unit offers an outpatients/inpatients nutrition clinic for cancer patients, and provide endoscopic approach to achieve enteral access if necessary.

## Clinical Activity

### Diagnostic-Operative Endoscopy

In addition to the standard diagnostic and therapeutic procedures, the Unit provides a number of specialised procedures:

- diagnosis and treatment of precancerous and cancerous lesions of the upper and lower gastrointestinal tract, through the use of high definition endoscopes, digital chromoendoscopy and in the near future the Confocal laser endomicroscopy technology which allows *in vivo* histological examination
- diagnosis and staging of gastrointestinal submucosal lesions, rectal, pancreatic, mediastinic and lung tumours through the use of endoscopic ultrasound (EUS,EUS-FNA,EBUS-TBNA)
- diagnosis and treatment of precancerous and cancerous lesions of the small bowel through the use of capsule endoscopy and, in selected cases, of therapeutic enteroscopy
- diagnosis and palliative treatment of gastrointestinal, pancreatic and biliary tree cancer
- emergency endoscopy for acute gastrointestinal bleeding
- Percutaneous Endoscopic Gastrostomy (PEG) for long term enteral nutrition

### Reference Centres and Counselling for Outpatients and Inpatients

- Since 2005, the Unit has been recognized Reference Centre of Lazio Region for Familial Adenomatous Polyposis (FAP) and since September 2017 Reference Centre of Lazio Region for Lynch syndrome and Peutz Jeghers syndrome. The Hereditary Colorectal cancer syndromes Clinics of the Unit guarantees an adequate management of these rare diseases.
- Since 2009 the Unit has been recognized Reference Centre of Lazio Region for celiac disease
- Nutritional counselling is offered to patients at risk of malnutrition at diagnosis, during and after therapies and adequate nutritional support is set up.
- A counselling is offered for all the gastroenterological and hepato-bilio-pancreatic diseases

## Research Activity

The major research interest of our Unit is in the field of colorectal cancer, in particular of familial and hereditary colorectal cancer.
Further fields of interest are EUS and biliary stent
During 2018 we pursued the following Research Projects

- "Toxins produced by intestinal bacteria and predisposing genetic variations: a dangerous link for colorectal cancer development?" (Ricerca Finalizzata PE-2011-02347510) in cooperation with Istituto Superiore di Sanità. Principal Investigator: Dr Vittoria Stigliano
- RC Project: Identification of new susceptibility genes for Hereditary colorectal cancer Principal Investigator: Dr Lupe Sanchez Mete
- Funded Project: Randomised, double-blind, placebo-controlled study of the, efficacy, safety and tolerability of EPA-FFA gastro-resistant capsules, in patients with Familial Adenomatous Polyposis (FAP); funded by SLA Pharma. Principal Investigator: Dr Vittoria Stigliano

## Publications

1. Mancini R, Pattaro G, Diodoro MG, Sperduti I, Garufi C, Stigliano V, Perri P, Grazi GL, Cosimelli M. Tumor Regression Grade After Neoadjuvant Chemoradiation and Surgery for Low Rectal Cancer Evaluated by Multiple Correspondence Analysis: Ten Years as Minimum Follow-up. Clin Colorectal Cancer. 2018 Mar;17(1): e13-e19. doi: 10.1016/j.clcc.2017.06.004. Epub 2017 Aug 9.

2. Sanchez-Mete L, Stigliano V. Tumori. 2019 Feb;105(1):12-21. doi: 10.1177/0300891618792461. Epub 2018 Aug 17. Update on small bowel surveillance in hereditary colorectal cancer syndromes.

# ANESTHESIA, INTENSIVE CARE AND PAIN THERAPY UNIT

*Head: Ester Forastiere, MD*

## STAFF

| | |
|---|---|
| Maria Sofra | Francesca Romana Giordano |
| Piera Di Angelo | Giulia Torregiani |
| Francesca Principi | Emanuela Venti |
| Paolo Moricca | Lorella Pelagalli |
| Luana Fabrizi, | Felice Centulio |
| Luca Colantonio | Antonio Calamaro |
| Maria Elena Marcelli | Giampiero Pontrandolfi |
| Cecilia Coccia | Francesco Rendina |
| Federico Pierconti | Carmela Stigliano |
| Alessandra Costantino | Lamberto Laurenzi |
| Ilaria Monteferrante | Claudia Claroni |
| Claudia Frigieri | Gabriele Tola |

## Title

All of the above are level I MD's with Master degree in Anesthesiology, Intensive Care and Pain Therapy

## Mission

Perioperative evaluation of surgical patients. Management of intraoperative anesthesiology. Perioperative assistance to patients undergoing surgery. Intensive care of medical and surgical oncologic patients. Non operating room anesthesia (NORA). Pain management of oncologic patients.

## Clinical Activity

**Perioperative Medicine**: management of perioperative patients for the following surgeries: thoracic surgery, urology, gynecology, plastic and reconstructive surgery, breast surgery, dermatology, neurosurgery, major orthopedic surgery, ORL surgery, digestive surgery, hepatobiliopancreatic surgery. Anesthesiologists participate in the Disease management teams of the various surgical teams.
**Intensive care** of surgical, oncologic and hematological patients.
**NORA:** sedation of patients in invasive procedures: interventional radiology, bronchoscopy, gastrocolonoscopy, CPRE, EBUS.
**Pain therapy clinic**: positioning of vascular accesses, PICC and PORT, treatment of oncologic pain with invasive and non invasive procedures.

## Research Activities

Translational clinical research protocols, approved by the Ethics Committee with a retrospective, prospective, observational, randomized prospective structure.
Collaboration with multi center studies, with National Cancer Institute of Milan, and the Cattolica Sacro Cuore Rome.
Scientific events on subjects closely associated with Anesthesiology:

- Hot Topics in Thoracic Anesthesia, December 2019, 5th edition.
- La Terapia Intensiva nel XXI secolo: Focus sull'ospite, 20 June 2019
- Current studies
- Decurarization After Thoracic Anesthesia – Reversal neuromuscolar block double blind prospective randomized multicenter study in thoracic surgery.
- DIANA Study multicenter, international, prospective, observational cohort in critically ill patients receiving empirical antibiotic therapy for suspected or confirmed infections at the Intensive Care Unit (ICU).
- Active surveillance of postoperative pulmonary infectious complication in thoracic surgery and antimicrobial prophylaxis stewardship.
- Intraoperative esophageal pressure monitoring in videolaparoscopic surgery.

## Pubblications


1. Chiappetta M, Forcella D, Pierconti F, Facciolo F. Combined Treatment for Single Giant Pulmonary Metastasis from Osteosarcoma: From Inside to Outside. *ANZ J. Surg.* 2018 Nov; 88(11): E801a

2. Claroni C, Covotta M, Torregiani G, Forastiere E. In Response. *Anesth. Analg.* 2018 Apr; 126(4): 1426a

3. Pasero D, Sangalli F, Baiocchi M, Blangetti I, Cattaneo S, Paternoster G, Moltrasio M, Auci E, Murrino P, Forfori F, Forastiere E, De Cristofaro MG, Deste G, Feltracco P, Petrini F, Tritapepe L, Girardis M. Experienced use of Dexmedetomidine in the Intensive Care Unit: A Report of a Structured Consensus. *Turk. J. Anaesthesiol. Reanim.* 2018 Jun; 46(3): 176a

4. Telera S, Pompili A, Crispo F, Giovannetti M, Pace A, Villani V, Fabi A, Sperduti I, Raus L. Kyphoplasty with Purified Silicone VK100 (Elastoplasty) to Treat Spinal Lytic Lesions in Cancer Patients: A Retrospective Evaluation of 41 Cases. *Clin. Neurol. Neurosurg.* 2018 Aug; 171: 184a

5. Torregiani G, Claroni C, Covotta M, Naccarato A, Canfora M, Giannarelli D, Grazi GL, Tribuzi S, Forastiere E. Impact of a Goal-Directed Fluid Therapy on Length of Hospital Stay and Costs of Hepatobiliarypancreatic Surgery: A Prospective Observational Study. *J. Comp. Eff. Res.* 2018 Nov 19;

# PSYCHOLOGY UNIT

## *Head: Patrizia Pugliese, Psychologist*

## STAFF

| |
|---|
| **Maria Perrone, Psychologist** |
| **Gabriella Maggi, Psychologist** |
| **Maria Franca Condoleo, Psychologist** |
| **Giovanna D'antonio, Psychologist** |
| **Anita Caruso, Psychologist** |
| **Paola Torti, Psychologist** |
| **Chiara Falcicchio, Psychologist** |
| **Alessandro Bonucci, Psychologist** |

## *Mission*

Unit of Psychology is focused on prevention, treatment and rehabilitation of psychological suffering and on quality of life in clinical and research activity.

## *Clinical Activities*

The main clinical approach for achieving these objectives is the integration of psychological care within the medical care in DMT and in the departments of oncology and dermatology, aimed to decrease both the psychological suffering and direct and indirect costs. The psychologists use individual, group, couple and family psychotherapies, phone support. The clinical activity includes also the mediation of the psychologist in the doctor-patient relationship and in the therapeutic pathway. Other activities are the integration of psychologists with the other professionals involved in the setting of care (nurses and volunteers) and the creation of a network of Lazio psychologists, working in various hospitals and local structures, for a correct sending patients.

The productivity of the service is in line with the

budget negotiation 2018. In accordance with project of humanization, the Psychology Unit has achieved levels of satisfaction in 96% of patients.

## Research Activities

### Quality of life study

The study "Facilitatori e/o barriere all'accesso al supporto psicologico in pazienti oncologici: uno studio multicentrico" aims to identify the clinical, demographic, psychosocial factors and the pathway of patients sending associated with adherence to psychological support in cancer patients. The study coordinator is IRE, in collaboration with the psycho-oncology structures of the Lazio region.

The study "I costi sociali del cancro: valutazione di impatto sociale ed economico sui malati e sui caregiver" assess the social and economic impact of the disease on patients and their families with the objective of promoting actions aimed at improving this aspect. The study is ongoing.

### Translational study

The studies "Epigenetic control of breast cancer progression: animal and clinical studies" (Ministero della Salute) and "Stile di vita come fattore di rischio nella progressione del tumore al seno: indagine sui biomarcatori neuroendocrini e molecolari dello stress" (Fondazione Umberto Veronesi) in collaboration with IRE Medical Oncology and ISS were aimed to elucidate the molecular mechanisms involved in the effects of stress on breast cancer progression both in animal models and in high risk breast cancer patients.

Since July 2012 to date the clinical study enrolled 80 women (mean age = 50.5). At a median follow up of 20 months 40 women were evaluable for the first analysis.

The results showed that after six months of chemotherapy, patients showed increased levels of depression as well as cortisol and serum chemokine MIP-1b LFA-IV-, which has not only a tumor-promoting role but also is directly related with a poor prognosis. As concern psychological tests no difference emerged after six months after chemotherapy. However, the average score detected using the Beck depression inventory (BDI) indicated mild depression. Interestingly, we found increased levels of BDNF associated to decreased anxiety and depression levels at 12 months' follow-up. Overall, data indicate that psychological factors can affect physiological responses in breast cancer patients. This is especially relevant since stressful events and negative affective states can amplify the consequences of the pathology precipitating disease progression and promoting recurrence. Further analyses are in progress in order to detect disease recurrence and increase the strength of the data.

## Publications

1. Caruso A, Vigna C, Gremigni P. The Cancer Worry Scale Revised for Breast Cancer Genetic Counseling. *Cancer Nurs.* 2018 Jul/Aug; 41(4): 311a

# PHASE 1 INVESTIGATION UNIT

During 2018, the IFO Research Institutes addressed the preparatory path for the self-certification of the Phase 1 Clinical Center "Early Phase" pursuant the requirements of AIFA Determination of 19 June 2015 number 809/2015 and the subsequent inspection visit.
The activities carried out included the logistical-technological structuring of an hospital ward, the recruitment and training of professionals, the documents and agreements setting with other Clinical Support Units. These activities began in January and ended, with the inspection visit by the GCP Inspection Office, in September.
The Clinical Center is equipped with:

- DH beds no. 5 and hospitalization h24 n. 2
- Technologies for monitoring and surveillance of patients as a sub-intensive therapy
- Dedicated staff
- A network of support Clinical Units and Professionals for each type of study prepared according to the AIFA Resolution n. 809/2015
- AIFA conformity certification for phase 1 studies
- "Temperature controlled" transport systems
- Operating procedures for activities related to the investigations paths and relations with other internal or external structures of the IFO.

After the AIFA inspection visit, the Clinical Center evaluated n. 7 Phase 1 studies in dermatology and oncology. One study has been launched and concluded. Two further studies have been opened. The first involves the administration of anti-PD-1 monoclonal antibodies in patients with advanced solid tumors, the second open study involves the administration of an association of drugs (an anti-ligand 1 antibody and an interleukin) with increasing dose in patients with solid tumors (bladder, prostate, colon, kidney, lung).

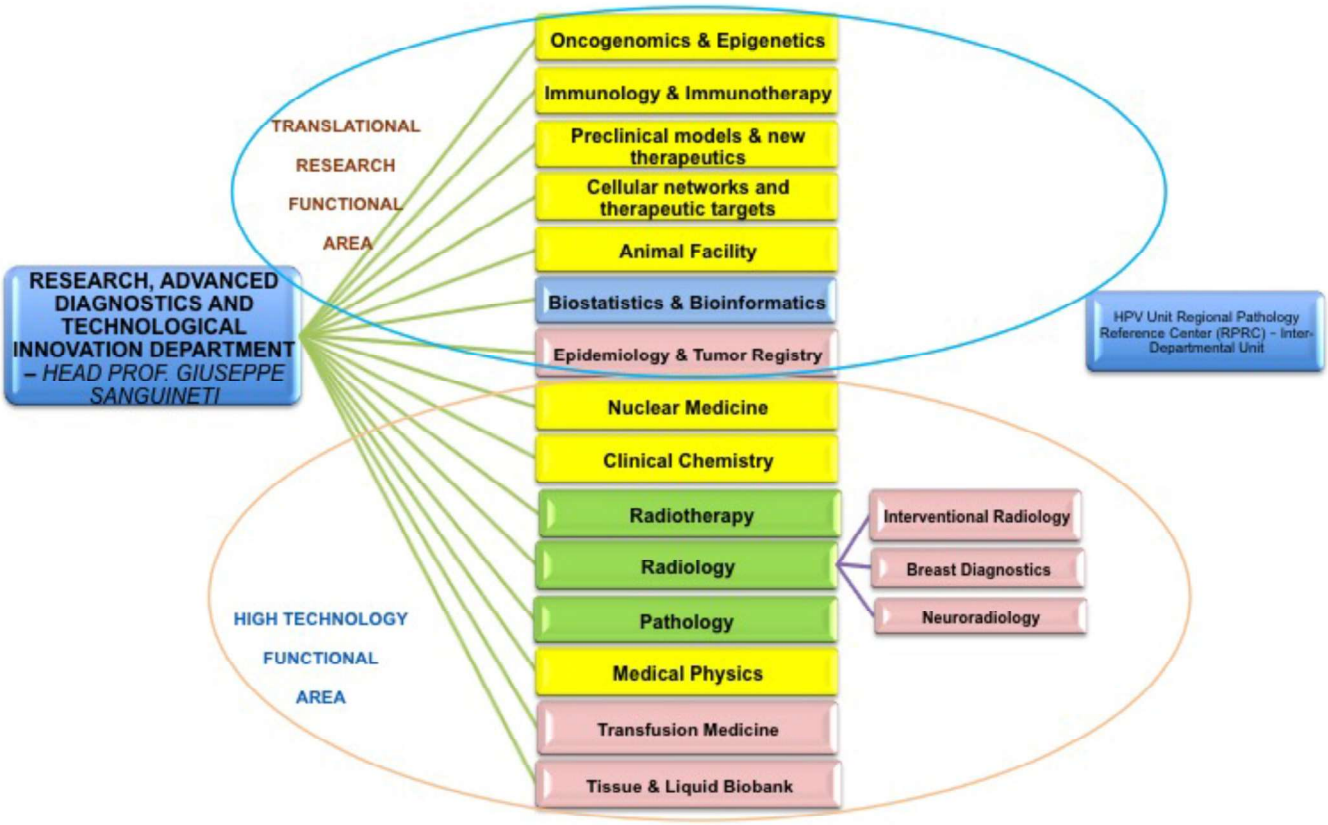
The staff of the Phase 1 Clinical Center, in 2018, carried out training in the following areas:

- BLSD, ALS
- Good Clinical Practices
- Advanced simulation in emergency / urgency by addressing 5 clinical pictures: cardiorespiratory arrest, anaphylactic shock, stroke, myocardial infarction, massive bleeding
- Simulation of assisted intra-hospital transport
- Administration, monitoring and management of complications of chemotherapy and immunotherapyand has participated in numerous oncology conferences.

Preparation activities for self-certification have been scheduled for 2019 of laboratories of Pathological Anatomy, Cutaneous Histopathology, Clinical Pathology and Microbiology and the establishment and preparation of the CTQT (Clinical Trial Quality Team) for non-profit studies with promoter IFO.

# DEPARTMENT OF RESEARCH ADVANCE DIAGNOSTICS AND TECHNOLOGICAL INNOVATION

*Director: Prof. Giuseppe Sanguinetti*


RESEARCH, ADVANCED DIAGNOSTICS AND TECHNOLOGICAL INNOVATION DEPARTMENT – HEAD PROF. GIUSEPPE SANGUINETI
TRANSLATIONAL RESEARCH FUNCTIONAL AREA
HIGH TECHNOLOGY FUNCTIONAL AREA
Oncogenomics & Epigenetics
Immunology & Immunotherapy
Preclinical models & new therapeutics
Cellular networks and therapeutic targets
Animal Facility
Biostatistics & Bioinformatics
Epidemiology & Tumor Registry
Nuclear Medicine
Clinical Chemistry
Radiotherapy
Radiology
Pathology
Medical Physics
Transfusion Medicine
Tissue & Liquid Biobank
Interventional Radiology
Breast Diagnostics
Neuroradiology
HPV Unit Regional Pathology Reference Center (RPRC) - Inter-Departmental Unit

# ONCOGENOMICS AND EPIGENETICS UNIT

*Head: Giovanni Blandino, MD, PhD*

## STAFF:

| |
|---|
| Giulia Fontemaggi (Senior Post-Doc) |
| Silvia Di Agostino (Senior Post-Doc) |
| Federica Ganci (Post-Doc) |
| Sara Donzelli (Post-Doc) |
| Federica Lo Sardo (Post-Doc) |
| Frauke Goeman (Post-Doc) |
| Valeria Canu (PhD student) |
| Andrea Sacconi (Bioinformatic) |
| Fabio Valenti (PhD) |
| Marco Varmi (Technician) |
| Roberto Bernardi (Administrative collaborator) |
| Sabrina Strano (MD) |
| Claudio Pulito (Post-Doc) |
| Etleva Korita (PhD) |
| Anna Maria Biroccio (PhD) |
| Erica Salvati (Senior Post-Doc) |
| Pasquale Zizza (Post-Doc) |
| Angela Rizzo (Post-Doc) |
| Sara Iachettini (Post-Doc) |
| Eleonora Petti (Post-Doc) |
| Roberto Dinami (Post-Doc) |

| |
|---|
| Carmen D'Angelo (Technician) |
| Vittoria Sabia (Master Student) |
| Angela Dello Stritto (Master Student) |
| Carmen Maresca (Technician) |
| Patrizio Giacomini (MD) |
| Matteo Allegretti (Post-Doc) |
| Katia Messana (Post-Doc) |
| Elisa Tremante |
| (Post-Doc) |
| Elena Giordani (Technician) |
| Rocco Fraioli (Technician) |
| Paolo Romania (Post-doc) |
| Oreste Segatto (MD) |
| Sergio Anastasi (Senior Post-Doc) |
| Dante Lamberti (Post-Doc) |
| Giulia Cristinziano (PhD student) |
| Maria Giulia Rizzo (PhD) |
| Giulia Regazzo (PhD student) |
| Manuela Spagnuolo (Post-doc) |
| Francesca Lospinoso Severini (Master Student) |
| Ana Belen Diaz Mendez (PhD student) |

## Mission

Developing more precise diagnostic approaches to predict cancer progression and prognosis is the key to precision medicine. The mission of the Oncogenomic and Epigenetic Unit mirrors at specific genomic and epigenetic alterations in both solid and hematopoietic malignancies that hold the potential to represent novel cancer biomarkers or druggable targets. This is pursued through genome wide approaches applied to cell systems, animal models, tissues and biological fluids (ctDNA and non-coding RNAs) of cancer patients.

## Clinical Activity

The Oncogenomic and Epigenetic Unit actively contributes to the clinical research activity of Regina Elena National Cancer Institute through:

- The generation of molecularly and clinically annotated databases of specific types of tumors. This also includes the collection and the storage of DNA, RNA and proteins from both tissues and biological fluids from cancer patients.
- The establishment of datasets of raw data from genome wide analysis (coding and con-coding RNA profiles, RNA-Seq and DNA mutational analysis) of matched cancer lesions.
- The establishment of early passage culture from melanoma, breast, lung, ovary, endometrial, head and neck cancer lesions.

## Research Activity

The research objectives of the Oncogenomic and Epigenetic Unit are pursed through the integrated experimental work of the following groups:

- Blandino's group is actively pursuing the identification of molecular biomarkers (non-coding RNAs) whose association with the TP53 status may predict recurrence of head and neck cancers.
- Biroccio's group is actively investigating the extra-telomeric role of TRF2 in oncogenesis with the aim to identify novel therapeutic targets for antitumoral therapies in colon cancer.
- Giacomini's group is actively developing and optimizing nanoparticles built around a ferritin nanocage core unit optimized for the in vivo delivery of several chemotherapeutics. A novel humanized antibody to ERBB2 that overcomes resistance to Trastuzumab and Pertuzumab is under intense preclinical and regulatory analyses.
- Rizzo's group is actively investigating the role of extracellular circulating miRNAs in hematopoietic malignancies as promising biomarkers for disease classification and outcome prediction.
- Segatto's group is challenging the generation of cell systems and animal models of intrahepatic cholangiocarcinoma carrying FGFR2 alterations to envisage novel therapeutic approaches with HSP90 inhibitors.

## Publications


1. Allegretti M, Casini B, Mandoj C, Benini S, Alberti L, Novello M, Melucci E, Conti L, Covello R, Pescarmona E, Milano GM, Annovazzi A, Anelli V, Ferraresi V, Biagini R, Giacomini P. Precision Diagnostics of Ewing's Sarcoma by Liquid Biopsy: Circulating EWS-FLI1 Fusion Transcripts. *Ther. Adv. Med. Oncol.* 2018 Jun 1; 10: 1758835918774337a

2 Allegretti M, Fabi A, Buglioni S, Martayan A, Conti L, Pescarmona E, Ciliberto G, Giacomini P. Tearing Down the Walls: FDA Approves Next Generation Sequencing (NGS) Assays for Actionable Cancer Genomic Aberrations. *J. Exp. Clin. Cancer Res.* 2018 Mar 5; 37(1): 47a

3 Amato J, Platella C, Iachettini S, Zizza P, Musumeci D, Cosconati S, Pagano A, Novellino E, Biroccio A, Randazzo A, Pagano B, Montesarchio D. Tailoring a Lead-Like Compound Targeting Multiple G-Quadruplex Structures. Eur. J. Med. Chem. 2018 Nov 27 [Epub ahead of print]

4 Belloni L, Di Cocco S, Guerrieri F, Nunn ADG, Piconese S, Salerno D, Testoni B, Pulito C, Mori F, Pallocca M, Sacconi A, Vivoli E, Marra F, Strano S, Blandino G, Levrero M, Pediconi N. Targeting a Phospho-STAT3-miRNAs Pathway Improves Vesicular Hepatic Steatosis in an in Vitro and in Vivo Model. *Sci. Rep.* 2018 Sep 11; 8(1): 13638a

5 Blandino G, Di Agostino S. New Therapeutic Strategies to Treat Human Cancers Expressing Mutant p53 Proteins. *J. Exp. Clin. Cancer Res.* 2018 Feb 15; 37(1): 30a

6. Buglioni S, Melucci E, Sperati F, Pallocca M, Terrenato I, De Nicola F, Goeman F, Casini B, Amoreo CA, Gallo E, Diodoro MG, Pescarmona E, Vici P, Sergi D, Pizzuti L, Di Lauro L, Mazzotta M, Barba M, Fanciulli M, Vitale I, De Maria R, Ciliberto G, Maugeri-Saccà M. The Clinical Significance of PD-L1 in Advanced Gastric Cancer is Dependent on ARID1A Mutations and ATM Expression. *Oncoimmunology.* 2018 03/27; 7(8): e1457602a.

7. D'Aguanno S, Valentini E, Tupone MG, Desideri M, Di Martile M, Spagnuolo M, Buglioni S, Ercolani C, Falcone I, De Dominici M, Milella M, Rizzo MG, Calabretta B, Cota C, Anichini A, Trisciuoglio D, Del Bufalo D. Semaphorin 5A Drives Melanoma Progression: Role of Bcl-2, miR-204 and c-Myb. *J. Exp. Clin. Cancer Res.* 2018 Nov 19; 37(1): 278a

8. De Nicola F, Goeman F, Pallocca M, Sperati F, Pizzuti L, Melucci E, Casini B, Amoreo CA, Gallo E, Diodoro MG, Buglioni S, Mazzotta M, Vici P, Sergi D, Di Lauro L, Barba M, Pescarmona E, Ciliberto G, De Maria R, Fanciulli M, Maugeri-Sacca M. Deep Sequencing and Pathway-Focused Analysis Revealed Multigene Oncodriver Signatures Predicting Survival Outcomes in Advanced Colorectal Cancer. *Oncogenesis.* 2018 Jul 22; 7(7): 55a

9. Di Agostino S, Valenti F, Sacconi A, Fontemaggi G, Pallocca M, Pulito C, Ganci F, Muti P, Strano S, Blandino G. Long Non-Coding MIR205HG Depletes Hsa-miR-590-3p Leading to Unrestrained Proliferation in Head and Neck Squamous Cell Carcinoma. *Theranostics.* 2018 Feb 12; 8(7): 1850a

10. di Martino S, Amoreo CA, Nuvoli B, Galati R, Strano S, Facciolo F, Alessandrini G, Pass HI, Ciliberto G, Blandino G, De Maria R, Cioce M. HSP90 Inhibition Alters the Chemotherapy-Driven Rearrangement of the Oncogenic Secretome. *Oncogene.* 2018 Mar; 37(10): 1369a

11. Di Modugno F, Caprara V, Chellini L, Tocci P, Spadaro F, Ferrandina G, Sacconi A, Blandino G, Nistico P, Bagnato A, Rosano L. HMENA is a Key Regulator in Endothelin-1/beta-arrestin1-Induced Invadopodial Function and Metastatic Process. *Proc. Natl. Acad. Sci. U.S.A.* 2018 Mar 20; 115(12): 3132a

12. Donzelli S, Milano E, Pruszko M, Sacconi A, Masciarelli S, Iosue I, Melucci E, Gallo E, Terrenato I, Mottolese M, Zylicz M, Zylicz A, Fazi F, Blandino G, Fontemaggi G. Expression of ID4 Protein in Breast Cancer Cells Induces Reprogramming of Tumour-Associated Macrophages. *Breast Cancer Res.* 2018 Jun 19; 20(1): 59a

13. Falvo E, Malagrino F, Arcovito A, Fazi F, Colotti G, Tremante E, Di Micco P, Braca A, Opri R, Giuffre A, Fracasso G, Ceci P. The Presence of Glutamate Residues on the PAS Sequence of the Stimuli-Sensitive Nano-Ferritin Improves in Vivo Biodistribution and Mitoxantrone Encapsulation Homogeneity. *J. Control. Release.* 2018 Apr 10; 275: 177a

14. Ferraiuolo M, Pulito C, Finch-Edmondson M, Korita E, Maidecchi A, Donzelli S, Muti P, Serra M, Sudol M, Strano S, Blandino G. Agave Negatively Regulates YAP and TAZ Transcriptionally and Post-Translationally in Osteosarcoma Cell Lines. *Cancer Lett.* 2018 Oct 1; 433: 18a

15. Finotti A, Allegretti M, Gasparello J, Giacomini P, Spandidos DA, Spoto G, Gambari R. Liquid Biopsy and PCR-Free Ultrasensitive Detection Systems in Oncology (Review). *Int. J. Oncol.* 2018 Oct; 53(4): 1395a

16. Folgiero V, Sorino C, Pallocca M, De Nicola F, Goeman F, Bertaina V, Strocchio L, Romania P, Pitisci A, Iezzi S, Catena V, Bruno T, Strimpakos G, Passananti C, Mattei E, Blandino G, Locatelli F, Fanciulli M. Che-1 is Targeted by c-Myc to Sustain Proliferation in Pre-B-Cell Acute Lymphoblastic Leukemia. *EMBO Rep.* 2018 Mar; 19(3): e44871

17. Frixa T, Sacconi A, Cioce M, Roscilli G, Ferrara FF, Aurisicchio L, Pulito C, Telera S, Carosi M, Muti P, Strano S, Donzelli S, Blandino G. MicroRNA-128-3p-Mediated Depletion of Drosha Promotes Lung Cancer Cell Migration. *Carcinogenesis.* 2018 Feb 9; 39(2): 293a.

18. Gasparello J, Allegretti M, Tremante E, Fabbri E, Amoreo CA, Romania P, Melucci E, Messana K, Borgatti M, Giacomini P, Gambari R, Finotti A. Liquid Biopsy in Mice Bearing Colorectal Carcinoma Xenografts: Gateways Regulating the Levels of Circulating Tumor DNA (ctDNA) and miRNA (ctmiRNA). *J. Exp. Clin. Cancer Res.* 2018 Jun 26; 37(1): 124a

19. Hopkins BL, Nadler M, Skoko JJ, Bertomeu T, Pelosi A, Shafaei PM, Levine K, Schempf A, Pennarun B, Yang B, Datta D, Bucur O, Ndebele K, Oesterreich S, Yang D, Giulia Rizzo M, Khosravi-Far R, Neumann CA. A Peroxidase Peroxiredoxin 1-Specific Redox Regulation of the Novel FOXO3 microRNA Target Let-7. *Antioxid. Redox Signal.* 2018 Jan 1; 28(1): 62a

20. Iachettini S, Trisciuoglio D, Rotili D, Lucidi A, Salvati E, Zizza P, Di Leo L, Del Bufalo D, Ciriolo MR, Leonetti C, Steegborn C, Mai A, Rizzo A, Biroccio A. Pharmacological Activation of SIRT6 Triggers Lethal Autophagy in Human Cancer Cells. *Cell.Death Dis.* 2018 Sep 24; 9(10): 996a

21. Lamberti D, Cristinziano G, Porru M, Leonetti C, Egan JB, Shi CX, Buglioni S, Amoreo CA, Castellani L, Borad MJ, Alema S, Anastasi S, Segatto O. HSP90 Inhibition Drives Degradation of FGFR2 Fusion Proteins: Implications for Treatment of Cholangiocarcinoma. Hepatology. 2018 Aug 1 [Epub ahead of print]

22. Lo Sardo F, Strano S, Blandino G.YAP and TAZ in Lung Cancer: Oncogenic Role and Clinical Targeting. *Cancers (Basel).* 2018 May 6; 10(5): 10.3390/cancers10050137a

23. Marchesi F, Regazzo G, Palombi F, Terrenato I, Sacconi A, Spagnuolo M, Donzelli S, Marino M, Ercolani C, Di Benedetto A, Blandino G, Ciliberto G, Mengarelli A, Rizzo MG. Serum miR-22 as Potential Non-Invasive Predictor of Poor Clinical Outcome in Newly Diagnosed, Uniformly Treated Patients with Diffuse Large B-Cell Lymphoma: An Explorative Pilot Study. *J.Exp.Clin.Cancer Res.* 2018 May 2; 37(1): 95a

24. Masciarelli S, Capuano E, Ottone T, Divona M, De Panfilis S, Banella C, Noguera NI, Picardi A, Fontemaggi G, Blandino G, Lo-Coco F, Fazi F. Retinoic Acid and Arsenic Trioxide Sensitize Acute Promyelocytic Leukemia Cells to ER Stress. *Leukemia.* 2018 Feb; 32(2): 285a

25. Migliore C, Morando E, Ghiso E, Anastasi S, Leoni VP, Apicella M, Cora' D, Sapino A, Pietrantonio F, De Braud F, Columbano A, Segatto O, Giordano S. MiR-205 Mediates Adaptive Resistance to MET Inhibition Via ERRFI1 Targeting and Raised EGFR Signaling. *EMBO Mol.Med.* 2018 Sep; 10(9): 10.15252/emmm.201708746a

26. Muti P, Donzelli S, Sacconi A, Hossain A, Ganci F, Frixa T, Sieri S, Krogh V, Berrino F, Biagioni F, Strano S, Beyene J, Yarden Y, Blandino G. MiRNA-513a-5p Inhibits Progesterone Receptor Expression and Constitutes a Risk Factor for Breast Cancer: The hOrmone and Diet in the ETiology of Breast Cancer Prospective Study. *Carcinogenesis.* 2018 Feb 9; 39(2): 98a

27. Porru M, Pompili L, Caruso C, Biroccio A, Leonetti C. Targeting KRAS in Metastatic Colorectal Cancer: Current Strategies and Emerging Opportunities. *J.Exp.Clin.Cancer Res.* 2018 Mar 13; 37(1): 57a

28. Pruszko M, Milano E, Zylicz A, Zylicz M, Blandino G, Fontemaggi G. Zebrafish as Experimental Model to Establish the Contribution of Mutant p53 and ID4 to Breast Cancer Angiogenesis in Vivo. *J.Thorac.Dis.* 2018 Mar; 10(3): E231a

29. Radovich M, Pickering CR, Felau I, Ha G, Zhang H, Jo H, Hoadley KA, Anur P, Zhang J, McLellan M, Bowlby R, Matthew T, Danilova L, Hegde AM, Kim J, Leiserson MDM, Sethi G, Lu C, Ryan M, Su X, Cherniack AD, Robertson G, Akbani R, Spellman P, Weinstein JN, Hayes DN, Raphael B, Lichtenberg T, Leraas K, Zenklusen JC, Cancer Genome Atlas Network, Fujimoto J, Scapulatempo-Neto C, Moreira AL, Hwang D, Huang J, Marino M, Korst R, Giaccone G, Gokmen-Polar Y, Badve S, Rajan A, Strobel P, Girard N, Tsao MS, Marx A, Tsao AS, Loehrer PJ. Blandino G (c.) The Integrated Genomic Landscape of Thymic Epithelial Tumors. *Cancer.Cell.* 2018 Feb 12; 33(2): 244a

30. Sestito, R., Blandino, G., Bagnato,A. A Novel p53-Mediated miR-30a/ZEB2 Regulatory Network in the Control of Breast Cancer Progression. *Non-Coding RNA Investigation.* 2018 2(0)a

31. Spagnuolo M, Regazzo G, De Dominici M, Sacconi A, Pelosi A, Korita E, Marchesi F, Pisani F, Magenta A, Lulli V, Cordone I, Mengarelli A, Strano S, Blandino G, Rizzo MG, Calabretta B. Transcriptional Activation of the miR-17-92 Cluster is Involved in the Growth-Promoting Effects of MYB in Human Ph-Positive Leukemia Cells. Haematologica. 2018 Aug 3 [Epub ahead of print]

32. Tang GH, Satkunam M, Pond GR, Steinberg GR, Blandino G, Schunemann HJ, Muti P. Association of Metformin with Breast Cancer Incidence and Mortality in Patients with Type II Diabetes: A GRADE-Assessed Systematic Review and Meta-Analysis. *Cancer Epidemiol.Biomarkers Prev.* 2018 Jun; 27(6): 627a

# IMMUNOLOGY AND IMMUNOTHERAPY UNIT

## *Head: Paola Nistico', MD*

## STAFF

| |
|---|
| **Francesca Di Modugno, PhD** |
| **Stefania Miccadei, PhD** |
| **Anna Maria Mileo, PhD** |
| **Aldo Venuti, MD** |
| **Silvia Baldari, Post-doc** |
| **Luca Cardone, Post-doc** |
| **Anna Di Carlo, Post-doc** |
| **Roberta Melchionna, Post-doc** |
| **Belinda Palermo, Post-doc** |
| **Francesca Paolini, Post-doc** |
| **Antonella Sistigu, Post-doc** |
| **Gabriele Toietta, Post-doc** |
| **Paola Trono, Post-doc** |
| **Annalisa Tocci, PhD Student** |
| **Giulia Campo, Fellow** |
| **Carla Mottini, Fellow** |
| **Giuliana Falasca, Technician** |
| **Mariangela Panetta, Technician** |
| **Maria Vincenza Sarcone, Administrative collaborator** |
| **Melo Alanne Rayssa Da Silva, Student** |
| **Dario Vinicio Guglietta, Student** |
| **Edoardo Mortato, Student** |

## *Mission*

This Unit is focused on understanding the immune response against tumor by studying the biological processes and signaling pathways involved in the complex interaction between tumor cells, extracellular matrix (ECM), cancer associated fibroblasts (CAFs) and immune cells. Our aim is to provide the rational for designing novel treatment to be used in combination with immunotherapy, able to overcome therapy resistance. In cooperation with the HPV Unit we participate in programs of cancer prevention on HPV vaccination for males and we are defining new formulations of DNA vaccines against HPV oncoproteins. The mission is: to develop and standardize methodologies of immunomonitoring; establish preclinical models of patient-derived organotypic cultures of tumors; identify surrogate biological markers of clinical response, focusing on immune checkpoint inhibitor treatment; to identify novel targets related to the tumor microenvironment, suitable for developing CAR T cells able to infiltrate solid tumors. Close cooperation with the clinical departments is a cornerstone of our Unit to support patient immunoprofiling to define combined immunotherapeutic clinical trials.

## *Research activity*

Tumorigenesis and tumor progression relies on the dialectics between tumor cells, the ECM and its remodeling enzymes, neighboring cells and soluble cues. This Unit has been focused on the role of the

actin cytoskeleton as a platform of signaling affecting carcinogenesis, cell invasion and immunosuppressive processes. We have identified a novel role of hMENA as crucial player in the cross-talk between tumor cells and CAFs, by regulating the GAS6-AXL pathway. Starting from our previous results that early node-negative NSCLC patients show a prolonged disease-free survival (DFS) when expressing high tumor hMENA11a/low stromal fibronectin (FN1), we have explored the role of hMENA splicing in the recruitment of specific immune cells. We found that tertiary Lymphoid Structures (TLS), sites of transient lymphoid neo-genesis and determinants of antitumor immunity, are associated with a favorable clinical outcome in NSCLC patients and that the expression of hMENA$^{11a}$, in the presence of low stromal FN1, associated with an intratumoral localization of TLS. Differently the absence of hMENA$^{11a}$ along with the expression of hMENA/hMENAΔv6 and high stromal FN1 associate with a peritumoral localization of TLS, indicating a crucial role of hMENA splicing in regulating a tumor immune microenvironment favoring or hampering TLS inclusion in the tumor core. We have identified that one of the mechanism identified is to ascribe at the role that hMENA11a exerts in positively regulating the expression of LTβR, involved in TLS neogenesis.

The Unit has established a platform of immune monitoring to identify biomarkers of response to immune-checkpoint blockade and has identified a novel CD8 T cell population we are in depth studying in NSCLC patients. To identify new combined immuno-chemotherapies we are characterizing the mechanisms by which Type-I-IFNs induce cancer stem cells during immunogenic chemotherapy and we are studying the immunogenicity of cancer stem cells. We have also explored the role of polyphenols in increasing the cell sensitivity to chemotherapy, to identify whether polyphenols may minimize toxicity and side effects of chemotherapy. In oropharyngeal cancer, we noted that latent infection of HPV16 is a risk factor for recurrent disease. Novel vaccines against HPV-associated pathologies were developed and patented with a proved dual activity as preventive and therapeutic vaccines, at least in animal models.

## Publications


1. Barros MR,Jr, de Melo CML, Barros MLCMGR, de Cassia Pereira de Lima,R., de Freitas AC, Venuti A. Activities of Stromal and Immune Cells in HPV-Related Cancers. *J.Exp.Clin.Cancer Res.* 2018 Jul 5; 37(1): 137a

2. Barros MR,Jr, de Oliveira THA, de Melo CML, Venuti A, de Freitas AC. Viral Modulation of TLRs and Cytokines and the Related Immunotherapies for HPV-Associated Cancers. *J.Immunol.Res.* 2018 May 2; 2018: 2912671a

3. Castiello L, Sestili P, Schiavoni G, Dattilo R, Monque DM, Ciaffoni F, Iezzi M, Lamolinara A, Sistigu A, Moschella F, Pacca AM, Macchia D, Ferrantini M, Zeuner A, Biffoni M, Proietti E, Belardelli F, Arico E. Disruption of IFN-I Signaling Promotes HER2/Neu Tumor Progression and Breast Cancer Stem Cells. *Cancer.Immunol.Res.* 2018 Jun; 6(6): 658a

4. Cordeiro MN, De Lima RCP, Paolini F, Melo ARDS, Campos APF, Venuti A, De Freitas AC. Current Research into Novel Therapeutic Vaccines Against Cervical Cancer. *Expert Rev.Anticancer Ther.* 2018 Apr; 18(4): 365a

5. Di Modugno F, Caprara V, Chellini L, Tocci P, Spadaro F, Ferrandina G, Sacconi A, Blandino G, Nistico P, Bagnato A, Rosano L. HMENA is a Key Regulator in Endothelin-1/beta-arrestin1-Induced Invadopodial Function and Metastatic Process. *Proc.Natl.Acad.Sci.U.S.A.* 2018 Mar 20; 115(12): 3132a

6. Di Modugno F, Spada S, Palermo B, Visca P, Iapicca P, Di Carlo A, Antoniani B, Sperduti I, Di Benedetto A, Terrenato I, Mottolese M, Gandolfi F, Facciolo F, Chen EI, Schwartz MA, Santoni A, Bissell MJ, Nistico P. HMENA Isoforms Impact NSCLC Patient Outcome through fibronectin/beta1 Integrin Axis. *Oncogene.* 2018 Oct; 37(42): 5605-5617a

7. Di Rocco G, Baldari S, Gentile A, Capogrossi M, Toietta G. Protein Disulfide Isomerase as a Prosurvival Factor in Cell Therapy for Muscular and Vascular Diseases. *Stem Cell.Res.Ther.* 2018 Oct; 9(1): 250a

8. Dianzani C, Paolini F, Conforti C, Silvestre M, Flagiello F, Venuti A. Human Papillomavirus in Skin Tags: A Case Series. *Dermatol.Pract.Concept.* 2018 Oct 31; 8(4): 295a

9. Franconi, R., E. Illiano, F. Paolini, S. Massa, A. Venuti, and O. C. Demurtas. 2018. "Rapid and Low-Cost Tools Derived from Plants to Face Emerging/Re-Emerging Infectious Diseases and Bioterrorism Agents." In *Defence Against Bioterrorism*: Springer.

10. Galluzzi L, Vitale I, Aaronson SA, Abrams JM, Adam D, Agostinis P, Alnemri ES, Altucci L, Amelio I, Andrews DW, Annicchiarico-Petruzzelli M, Antonov AV, Arama E, Baehrecke EH, Barlev NA, Bazan NG, Bernassola F, Bertrand MJM, Bianchi K, Blagosklonny MV, Blomgren K, Borner C, Boya P, Brenner C, Campanella M, Candi E, Carmona-Gutierrez D, Cecconi F, Chan FK, Chandel NS, Cheng EH, Chipuk JE, Cidlowski JA, Ciechanover A, Cohen GM, Conrad M, Cubillos-Ruiz JR, Czabotar PE, D'Angiolella V, Dawson TM, Dawson VL, De Laurenzi V, De Maria R, Debatin KM, DeBerardinis RJ, Deshmukh M, Di Daniele N, Di Virgilio F, Dixit VM, Dixon SJ, Duckett CS, Dynlacht BD, El-Deiry WS, Elrod JW, Fimia GM, Fulda S, Garcia-Saez AJ, Garg AD, Garrido C, Gavathiotis E, Golstein P, Gottlieb E, Green DR, Greene LA, Gronemeyer H, Gross A, Hajnoczky G, Hardwick JM, Harris IS, Hengartner MO, Hetz C, Ichijo H, Jaattela M, Joseph B, Jost PJ, Juin PP, Kaiser WJ, Karin M, Kaufmann T, Kepp O, Kimchi A, Kitsis RN, Klionsky DJ, Knight RA, Kumar S, Lee SW, Lemasters JJ, Levine B, Linkermann A, Lipton SA, Lockshin RA, Lopez-Otin C, Lowe SW, Luedde T, Lugli E, MacFarlane M, Madeo F, Malewicz M, Malorni W, Manic G, Marine JC, Martin SJ, Martinou JC, Medema JP, Mehlen P, Meier P, Melino S, Miao EA, Molkentin JD, Moll UM, Munoz-Pinedo C, Nagata S, Nunez G, Oberst A, Oren M, Overholtzer M, Pagano M, Panaretakis T, Pasparakis M, Penninger JM, Pereira DM, Pervaiz S, Peter ME, Piacentini M, Pinton P, Prehn JHM, Puthalakath H, Rabinovich GA, Rehm M, Rizzuto R, Rodrigues CMP, Rubinsztein DC, Rudel T, Ryan KM, Sayan E, Scorrano L, Shao F, Shi Y, Silke J, Simon HU, Sistigu A, Stockwell BR, Strasser A, Szabadkai G, Tait SWG, Tang D, Tavernarakis N, Thorburn A, Tsujimoto Y, Turk B, Vanden Berghe T, Vandenabeele P, Vander Heiden MG, Villunger A, Virgin HW, Vousden KH, Vucic D, Wagner EF, Walczak H, Wallach D, Wang Y, Wells JA, Wood W, Yuan J, Zakeri Z, Zhivotovsky B, Zitvogel L, Melino G, Kroemer G. Molecular Mechanisms of Cell Death: Recommendations of the Nomenclature Committee on Cell Death 2018. *Cell Death Differ.* 2018 Mar; 25(3): 486a

11. Manic G, Signore M, Sistigu A, Russo G, Corradi F, Siteni S, Musella M, Vitale S, De Angelis ML, Pallocca M, Amoreo CA, Sperati F, Di Franco S, Barresi S, Policicchio E, De Luca G, De Nicola F, Mottolese M, Zeuner A, Fanciulli M, Stassi G, Maugeri-Sacca M, Baiocchi M, Tartaglia M, Vitale I, De Maria R. CHK1-Targeted Therapy to Deplete DNA Replication-Stressed, p53-Deficient, Hyperdiploid Colorectal Cancer Stem Cells. *Gut.* 2018 May;

12. Manic G, Sistigu A, Corradi F, Musella M, De Maria R, Vitale I. Replication Stress Response in Cancer Stem Cells as a Target for Chemotherapy. *Semin. Cancer Biol.* 2018 Dec; 53: 31-41a

13. Palermo B, Franzese O, Donna CD, Panetta M, Quintarelli C, Sperduti I, Gualtieri N, Foddai ML, Proietti E, Ferraresi V, Ciliberto G, Nisticò P. Antigen-Specificity and DTIC before Peptide-Vaccination Differently Shape Immune-Checkpoint Expression Pattern, Anti-Tumor Functionality and TCR Repertoire in Melanoma Patients. *Oncoimmunology.* 2018 Sep 11;7(12):e1465163

14. Wu R, Paolini F, Frank D, Kamdar D, Curzio G, Pichi B, Pellini R, Spriano G, Bonagura VR, Venuti A, Steinberg BM. Latent Human Papillomavirus Type 16 Infection is Widespread in Patients with Oropharyngeal

# PRECLINICAL MODELS AND NEW THERAPEUTIC AGENTS UNIT

*Head: Anna Bagnato, PhD*

## STAFF

| |
|---|
| Valeriana Di Castro, PhD, Staff Scientist |
| Donatella Del Bufalo, PhD, Staff Scientist |
| Rossella Galati, PhD, Staff Scientist |
| Laura Rosanò, PhD, Project leader |
| Daniela Trisciuoglio, PhD, Project leader |
| Roberta Cianfrocca, PhD |
| Rosanna Sestito, PhD |
| Piera Tocci, PhD |
| Lidia Chellini, PhD |
| Simona D'Aguanno, PhD |
| Marta Di Martile, PhD |
| Luigi Fattore, PhD |
| Elisabetta Valentini, PhD , FIRC Fellow |

| |
|---|
| Maria Grazia Tupone, PhD, FIRC Fellow |
| Antonio Candiloro, Head Staff Technician |
| Aldo Lupo, Staff Technician |
| Valentina Caprara, Technician |
| Marianna Desideri, Technician |
| Barbara Nuvoli, Technician |
| Andrea Cerri, Technician |
| Maria Vincenza Sarcone, Administrative collaborator |
| Adele Petricca, Administrative collaborator |
| Simona Carcasole, Student |
| Francesca Blandino, Student |
| Marco Rosichini, Student |
| Daniele Rizzo, Student |

## Mission

The aim of this Unit is to develop latest advances in cancer modeling, including patient-derived xenografts, and organoid/tumoroid technology (ovarian, lung, colon cancer, melanoma, mesothelioma) to better validate therapeutic targets and predict patient responses. In these models we investigate the critical pathways (i.e. endothelin-1, estrogen, or bcl2/bcl-xL signaling) that become intertwined to cause cancer, providing insight into pathway networks that might be targeted therapeutically. In particular, organoids/tumoroids are 3D structures constituted by multiple organ-specific cell types that self-organize and can function as miniature organs that mimic in vivo pathophysiology, with wide applications for cancer modeling, drug screening, drug optimization, and personalized medicine. The heterogeneity within specific types of cancer, and the unique biological features and therapeutic vulnerabilities of specific subtypes of cancer can be exploited in these models to provide more tailored treatment to patients. Finally, preclinical models can provide an understanding of the escape pathways to cancer therapy, thereby helping to define strategies to overcome drug resistance.

## Research activity

This Unit will explore novel preclinical models with different approaches to understanding the host interactions and networks driving the malignant and resistant phenotype, and how this information can reveal a clearer understanding of cancer biology, and how it can be exploited to identify new actionable nodes for novel approaches for cancer detection and treatment to yield more durable treatment responses by using rational combinations.

The research activity of the Unit concerns:

**(PI A. Bagnato)**

We discovered key nodes driven by endothelin-1 (ET-1)/β-arrestin-1 (β-arr1) pathway with new potential targets for cancer therapy. In particular, we demonstrated that ET-1/β-arr1 pathway orchestrates an unpredicted crosstalk between mutant TP53 (mutp53) and other key players of malignancy, YAP/TAZ. These two oncogenic intertwined pathways concur to the malignant phenotype of high-grade serous ovarian cancers (HG-SOC), sustaining cancer cell survival, invasion and drug resistance. In this scenario, we provided examples of how targeting ET-1R/β-arr1 activities may disclose unexplored opportunities for therapy in mutp53 cancers, as HG-SOC. To design and identify drug combinations for the treatment of mutp53 expressing tumors, we analyze dual ET-1R antagonists, approved for non-oncological indication, that can efficiently hamper mutp53/YAP cross-talk, reducing tumor size and metastatic progression, indicating the drug repositioning of ET-1R antagonists can improve the current treatments for HG-SOC. This work, based on patient-derived preclinical models, is expected to provide the scientific rationale for the design of more effective therapeutic strategies.

(PI L. Rosanò)

The cellular plasticity is critical during tumor dissemination. ET-1R/-β-arr1 pathway regulates cytoskeletal dynamics and the formation of invasive protrusions, named invadopodia. The β-arr1-driven interactome, including IQGAP, triggered by ET-1 leads to enhanced invadopodial activity, and metastatic spread of ovarian cancer. By defining these first steps of metastatic dissemination, we provide the ways for focusing efforts on the aspects of metastasis that will improve patient outcomes.

**(PI D. Del Bufalo)**

Our group has a long-standing interest in the non-canonical activities of bcl-2, and its impact on tumor progression, in particular in preclinical melanoma models. In the last year, we unveiled an interplay among bcl-2, miR-204, c-Myb and Semaphorin 5A (Sema5A) in melanoma progression, Thus, bcl-2 increased the stability of Sema5A through c-Myb, to favour cell migration and invasion and the formation of vasculogenic structures. In parallel, we demonstrated, in zebrafish models, that the bcl-xL/interleukin-8 (IL-8) axis was important for promoting melanoma angiogenesis and aggressiveness by an autocrine effect of IL-8 on its CXCR2 receptor, Of clinical relevance, bcl-xL expression significantly correlated with the expression of IL-8 and other markers of melanoma progression. More importantly, a high level of co-expression of bcl-xL and IL-8 was associated with poor prognosis in melanoma patients. An in-depth understanding of such molecular mechanisms may provide the basis for therapeutic targeting of bcl2/bcl-xL-expressing melanoma.

**(PI Galati)**

This study aims to assess novel potential biomarker for the early diagnosis of malignant mesothelioma (MM). Alterations in MM microenvironment via exposure to

asbestos can influence the estradiol (E2) biosynthesis, resulting in altered levels of hormonally active estrogens that influence MM development and growth. To exploit the role of E2 as a potential predictive biomarker, people with a history of asbestos exposure have been subjected to analysis of serum E2 levels for the early diagnosis of MM. To exploit the mechanisms activated by E2 in MM pathogenesis, we evaluated HIF1α, one of the molecular targets induced by E2. An improvement of the effect of radiotherapy and chemotherapy in preclinical models of MM was observed after reduction of HIF1α expression. The understanding of E2 and its axis in MM will allow to discover new therapeutic targets and will guide to evaluate the aromatase inhibitor exemetane, or similar compounds, in new combinatorial regimens for MM treatment.

## Publications


1. Bagnato A,Rosano L. Endothelin-1 Receptor Drives Invadopodia: Exploiting how Beta-Arrestin-1 Guides the Way. *Small GTPases.* 2018 Sep 3; 9(5): 394a
2. Benedetti S, Catalani S, Palma F, Canonico B, Luchetti F, Galati R, Papa S, Battistelli S. Acyclovir Induces Cell Cycle Perturbation and Apoptosis in Jurkat Leukemia Cells, and Enhances Chemotherapeutic Drug Cytotoxicity. *Life Sci.* 2018 Dec 15; 215: 80a
3. Chellini L, Caprara V, Spadaro F, Sestito R, Bagnato A, Rosano L. Regulation of Extracellular Matrix Degradation and Metastatic Spread by IQGAP1 through Endothelin-1 Receptor Signaling in Ovarian Cancer. *Matrix Biol.* 2018 Oct 24; a.
4. Chellini L, Monteleone V, Lombari M, Caldarola S, Loreni F. The Oncoprotein Myc Controls the Phosphorylation of S6 Kinase and AKT through Protein Phosphatase 2A. *J. Cell. Biochem.* 2018 Dec; 119(12): 9878-9887a
5. D'Aguanno S, Valentini E, Tupone MG, Desideri M, Di Martile M, Spagnuolo M, Buglioni S, Ercolani C, Falcone I, De Dominici M, Milella M, Rizzo MG, Calabretta B, Cota C, Anichini A, Trisciuoglio D, Del Bufalo D. Semaphorin 5A Drives Melanoma Progression: Role of Bcl-2, miR-204 and c-Myb. *J. Exp. Clin. Cancer Res.* 2018 Nov 19; 37(1): 278a
6. Del Curatolo A, Conciatori F, Cesta Incani U, Bazzichetto C, Falcone I, Corbo V, D'Agosto S, Eramo A, Sette G, Sperduti I, De Luca T, Marabese M, Shirasawa S, De Maria R, Scarpa A, Broggini M, Del Bufalo D, Cognetti F, Milella M, Ciuffreda L. Therapeutic Potential of Combined BRAF/MEK Blockade in BRAF-Wild Type Preclinical Tumor Models. *J. Exp. Clin. Cancer Res.* 2018 Jul 9; 37(1): 140a
7. Di Martile M, Desideri M, Tupone MG, Buglioni S, Antoniani B, Mastroiorio C, Falcioni R, Ferraresi V, Baldini N, Biagini R, Milella M, Trisciuoglio D, Del Bufalo D. Histone Deacetylase Inhibitor ITF2357 Leads to Apoptosis and Enhances Doxorubicin Cytotoxicity in Preclinical Models of Human Sarcoma. *Oncogenesis.* 2018 Feb 23; 7(2): 20a
8. di Martino S, Amoreo CA, Nuvoli B, Galati R, Strano S, Facciolo F, Alessandrini G, Pass HI, Ciliberto G, Blandino G, De Maria R, Cioce M. HSP90 Inhibition Alters the Chemotherapy-Driven Rearrangement of the Oncogenic Secretome. *Oncogene.* 2018 Mar; 37(10): 1369a
9. Di Modugno F, Caprara V, Chellini L, Tocci P, Spadaro F, Ferrandina G, Sacconi A, Blandino G, Nistico P, Bagnato A, Rosano L. HMENA is a Key Regulator in Endothelin-1/beta-arrestin1-Induced Invadopodial Function and Metastatic Process. *Proc. Natl. Acad. Sci. U.S.A.* 2018 Mar 20; 115(12): 3132a
10. Ferrara M, Sessa G, Fiore M, Bernard F, Asteriti IA, Cundari E, Colotti G, Ferla S, Desideri M, Buglioni S, Trisciuoglio D, Del Bufalo D, Brancale A, Degrassi F. Small Molecules Targeted to the Microtubule-Hec1 Interaction Inhibit Cancer Cell Growth through Microtubule Stabilization. *Oncogene.* 2018 37(2): 231a
11. Gabellini C, Gomez-Abenza E, Ibanez-Molero S, Tupone MG, Perez-Oliva AB, de Oliveira S, Del Bufalo D, Mulero V. Interleukin 8 Mediates Bcl-xL-Induced Enhancement of Human Melanoma Cell Dissemination and Angiogenesis in a Zebrafish Xenograft Model. *Int. J. Cancer.* 2018 142(3): 584-596a

12. Iachettini S, Trisciuoglio D, Rotili D, Lucidi A, Salvati E, Zizza P, Di Leo L, Del Bufalo D, Ciriolo MR, Leonetti C, Steegborn C, Mai A, Rizzo A, Biroccio A. Pharmacological Activation of SIRT6 Triggers Lethal Autophagy in Human Cancer Cells. *Cell.Death Dis.* 2018 Sep 24; 9(10): 996a

13. Loria R, Laquintana V, Bon G, Trisciuoglio D, Frapolli R, Covello R, Amoreo CA, Ferraresi V, Zoccali C, Novello M, Del Bufalo D, Milella M, Biagini R, D'Incalci M, Falcioni R. HMGA1/E2F1 Axis and NFkB Pathways Regulate LPS Progression and Trabectedin Resistance. *Oncogene.* 2018 Nov; 37(45): 5926a

14. Monaco G, La Rovere R, Karamanou S, Welkenhuyzen K, Ivanova H, Vandermarliere E, Di Martile M, Del Bufalo D, De Smedt H, Parys JB, Economou A, Bultynck G. A Double Point Mutation at Residues Ile14 and Val15 of Bcl-2 Uncovers a Role for the BH4 Domain in both Protein Stability and Function. *Febs j.* 2018 285(1): 127a

15. Nuvoli B, Camera E, Mastrofrancesco A, Briganti S, Galati R. Modulation of Reactive Oxygen Species Via ERK and STAT3 Dependent Signalling are Involved in the Response of Mesothelioma Cells to Exemestane. *Free Radic.Biol.Med.* 2018 Feb 1; 115: 266a

16. Pisanu ME, Maugeri-Sacca M, Fattore L, Bruschini S, De Vitis C, Tabbi E, Bellei B, Migliano E, Kovacs D, Camera E, Picardo M, Jakopin Z, Cippitelli C, Bartolazzi A, Raffa S, Torrisi MR, Fulciniti F, Ascierto PA, Ciliberto G, Mancini R. Inhibition of Stearoyl-CoA Desaturase 1 Reverts BRAF and MEK Inhibition-Induced Selection of Cancer Stem Cells in BRAF-Mutated Melanoma. *J.Exp.Clin.Cancer Res.* 2018 Dec 17; 37(1): 318a

17. Sestito, R., Blandino, G., Bagnato, A. A Novel p53-Mediated miR-30a/ZEB2 Regulatory Network in the Control of Breast Cancer Progression. *Non-Coding RNA Investigation.* 2018 Jul 6; 2

18. Trisciuoglio D, Di Martile M, Del Bufalo D. Emerging Role of Histone Acetyltransferase in Stem Cells and Cancer. *Stem Cells Int.* 2018 Dec 16; 2018: 8908751a

# CELLULAR NETWORKS AND MOLECULAR THERAPEUTIC TARGETS UNIT

*Head: Silvia Soddu, MD, PhD*

## STAFF

| |
|---|
| Rita Falcioni, PhD, staff scientist |
| Marco Giorgio Paggi, MD, staff scientist |
| Alessandra Verdina, PhD, staff scientist |
| Gabriella D'Orazi, MD, PhD, project leader |
| Cinzia Rinaldo, PhD, project leader |
| Giulia Bon, PhD, project leader |
| Giuliana Di Rocco, PhD, project leader |
| Maria Pia Gentileschi, technician |
| Claudia Abbruzzese, PhD, post-doc |
| Claudia Contadini, PhD, post-doc |

| |
|---|
| Giulia Federici, PhD, post-doc |
| Alessia Garufi, PhD, post-doc |
| Rossella Loria, PhD, post-doc |
| Silvia Matteoni, PhD, post-doc |
| Laura Monteonofrio, PhD, post-doc |
| Davide Valente, PhD, FIRC fellow |
| Micol Di Segni, PhD student |
| Ilaria Virdia, PhD student |
| Michele Persico, MD student |
| Daniela Bona, PhD, administrative collaborator |

## Mission

Cellular networks and new therapeutic targets are key areas for innovation in the field of cancer therapy. The potential targeted pathways for personalized cancer therapies consist in oncogenic signals and the events generated by biochemical and/or genetic alterations that characterize cancer cells. Our mission is to develop and sustain sound expertise in these areas by strategically linking them to understanding the hierarchy of therapeutic targets and the molecular mechanisms underpinning the pharmacological action of innovative therapies. This Unit has a dual function. On one hand, it aids researchers and clinicians to plan preclinical and clinical research activities, as well as to conduct, stimulate and support research programs integrated into innovative investigator-driven clinical trials. On the other hand, it assists other researchers who aim to discover and plan to develop novel biomarkers and new therapeutic agents.

## Clinical Activity

The Unit Cellular Networks and Molecular Therapeutic Targets contributes to the clinical research activity of the Regina Elena National Cancer Institute on the following projects:

Biobank of sarcoma's tissues and cells. In collaboration with the Orthopedics Unit, Dr. Falcioni contributes to developing a biobank of sarcoma's tissues and cells. Biochemical and molecular characterization of the cultured cells are performed in addition to the standard storing procedures.

Working Groups of "Alleanza Contro il Cancro". Dr Falcioni and Dr. Paggi are the Institutional Representatives for IRE of the Sarcoma and Glioblastoma Working Groups, respectively.

Repurposing of chlorpromazine in the treatment of glioblastoma: In collaboration with the Neuroncology Unit, Dr. Paggi contributes to a Phase II clinical trial. Chlorpromazine (CPZ) is an antipsychotic drug employed since more than six decades. Recent reports, as well as our own studies, ascribe to CPZ the ability to strongly hinder glioblastoma cell growth in preclinical settings. The clinical trial involves the combination of CPZ with the standard treatment with temozolomide in the first line protocol.

Classification of ATM variants of unknown significance (VUS) by functional test. Due to its complex genomic organization, the large number of polymorphisms, and the presence of mutations without hot-spots, gene sequencing is not sufficient to classify rare variants with unknown significance. We are employing a functional test based on p53 mitotic centrosomal localization (p53-MCL) in peripheral blood mononuclear cells to improve our ability to identify pathogenic variants of the ATM gene.

## Research Activity

The research objectives of the Unit "Cellular Networks and Molecular Therapeutic Targets" are pursed through the integrated experimental work of the following groups:

Falcioni's group actively contributes to the identification of new re-arrangement in sarcoma. Furthermore, her group is investigating the molecular mechanisms responsible for the resistance to therapy with T-DM1 in Breast Cancer and Dabrafenib in BRAF-mutant melanoma to identify novel therapeutic targets in both tumors.

Paggi's group actively contributes to drug repurposing in the treatment of glioblastoma multiforme. According to the present regulations from drug authorities, therapeutic approaches with novel drugs must travel a long and expensive journey in order to reach the bedside. Therefore, intelligent and rational drug repurposing or repositioning are possible strategies to develop new therapies implicating lower risks, shorter timelines to bedside and lower costs. To this end, we employ cell biology and proteomic approaches to analyze pharmacodynamic characteristics of old drugs amenable of repositioning in the therapy of glioblastoma multiforme.

D'Orazi's group is actively investigating the relative contribution of the apoptotic and autophagic pathways in response to several anticancer drugs and phytochemical compounds; particular attention is dedicated to the HIPK2-p53 pathway

Soddu's group is actively pursuing the molecular characterization of mitosis and cytokinesis functions of proteins, such as p53, HIPK2, and histone H2B, usually involved in the DNA damage response. Particular attention has been dedicated to 1) the contribution of centrosomal p53 in the recently discovered *mitotic surveillance pathway*; 2) the recruitment by Aurora-B kinase of HIPK2 and extrachromosomal histone H2B at the intercellular bridge connecting sibling cells.

## Publications


1. Corrado G, Laquintana V, Loria R, Carosi M, de Salvo L, Sperduti I, Zampa A, Cicchillitti L, Piaggio G, Cutillo G, Falcioni R, Vizza E. Endometrial Cancer Prognosis Correlates with the Expression of L1CAM and miR34a Biomarkers. *J.Exp.Clin.Cancer Res.* 2018 Jul 6; 37(1): 139a

2. Di Martile M, Desideri M, Tupone MG, Buglioni S, Antoniani B, Mastroiorio C, Falcioni R, Ferraresi V, Baldini N, Biagini R, Milella M, Trisciuoglio D, Del Bufalo D. Histone Deacetylase Inhibitor ITF2357 Leads to Apoptosis and Enhances Doxorubicin Cytotoxicity in Preclinical Models of Human Sarcoma. *Oncogenesis.* 2018 Feb 23; 7(2): 20a

3. Di Rocco G, Baldari S, Gentile A, Capogrossi M, Toietta G. Protein Disulfide Isomerase as a Prosurvival Factor in Cell Therapy for Muscular and Vascular Diseases. *Stem Cell.Res.Ther.* 2018 Oct; 9(1): 250a

4. Di Rocco G, Baldari S, Pani G, Toietta G. Stem Cells Under the Influence of Alcohol: Effects of Ethanol Consumption on stem/progenitor Cells. *Cell Mol.Life Sci.* 2018 Oct 10 [Epub ahead of print]

5. Granato M, Gilardini Montani MS, Angiolillo C, D'Orazi G, Faggioni A, Cirone M. Cytotoxic Drugs Activate KSHV Lytic Cycle in Latently Infected PEL Cells by Inducing a Moderate ROS Increase Controlled by HSF1, NRF2 and p62/SQSTM1. *Viruses.* 2018 Dec 24; 11(1): pii: E8a

6. La Torre M, Merigliano C, Burla R, Mottini C, Zanetti G, Del Giudice S, Carcuro M, Virdia I, Bucciarelli E, Manni I, Vinciguerra GR, Piaggio G, Riminucci M, Cumano A, Bartolazzi A, Verni F, Soddu S, Gatti M, Saggio I. Mice with Reduced Expression of the Telomere-Associated Protein Ft1 Develop p53-Sensitive Progeroid Traits. *Aging Cell.* 2018 Apr 10; 17(4): e12730a

7. Loria R, Laquintana V, Bon G, Trisciuoglio D, Frapolli R, Covello R, Amoreo CA, Ferraresi V, Zoccali C, Novello M, Del Bufalo D, Milella M, Biagini R, D'Incalci M, Falcioni R. HMGA1/E2F1 Axis and NFkB Pathways Regulate LPS Progression and Trabectedin Resistance. *Oncogene.* 2018 Nov; 37(45): 5926a

8. Monteonofrio L, Valente D, Ferrara M, Camerini S, Miscione R, Crescenzi M, Rinaldo C, Soddu S. HIPK2 and Extrachromosomal Histone H2B are Separately Recruited by Aurora-B for Cytokinesis. *Oncogene.* 2018 Jun; 37(26): 3562a

9. Petroni M, Sardina F, Infante P, Bartolazzi A, Locatelli E, Fabretti F, Di Giulio S, Capalbo C, Cardinali B, Coppa A, Tessitore A, Colicchia V, Sahun Roncero M, Belardinilli F, Di Marcotullio L, Soddu S, Comes Franchini M, Petricci E, Gulino A, Giannini G. MRE11 Inhibition Highlights a Replication Stress-Dependent Vulnerability of MYCN-Driven Tumors. *Cell.Death Dis.* 2018 Aug 30; 9(9): 895a

10. Rotte A, D'Orazi G, Bhandaru M. Nobel Committee Honors Tumor Immunologists. *J.Exp.Clin.Cancer Res.* 2018 Oct 30; 37(1): 262a

11. Scaglione A, Monteonofrio L, Parisi G, Cecchetti C, Siepi F, Rinaldo C, Giorgi A, Verzili D, Zamparelli C, Savino C, Soddu S, Vallone B, Montemiglio LC. Effects of Y361-Auto-Phosphorylation on Structural Plasticity of the HIPK2 Kinase Domain. *Protein Sci.* 2018 Mar; 27(3): 725a

# SAFU UNIT

## *Head: Maurizio Fanciulli, PhD*


## STAFF

| |
|---|
| Federico De Marco (MD PhD, Staff Scientist) |
| Carlo Leonetti (PhD, Staff Scientist) |
| Giulia Piaggio (PhD, Staff Scientist) |
| Giancarlo Cortese (Staff Technician) |
| Tiziana Bruno (Staff Technician) |
| Enrico Spugnini (Veterinary) |
| Aymone Gurtner (Project Leader) |
| Francesca De Nicola (Senior Scientist) |
| Simona Iezzi (Senior Scientist) |
| Isabella Manni (Senior Scientist) |
| Silvia Baldari (Post-Doc) |

| |
|---|
| Valeria Catena (Post-Doc) |
| Matteo Pallocca (Post-Doc) |
| Davide Angeli (Post-Doc) |
| Stefano Scalera (Post-Doc) |
| Manuela Porru (Post-Doc) |
| Cristina Sorino (Post-Doc) |
| Luca Pompili (PhD Student) |
| Susanna Falcucci (Graduate Student) |
| Bruno Amadio (Technician) |
| Adele Petricca (Administrative collaborator) |

## Mission

The mission of the SAFU UOSD focuses on the establishment of innovative mouse models of human cancer including implantation of tumor specimens into immunocompromised mice at the heterotopic and orthotopic sites and genetically engineered mouse models. All mouse models are devoted to study cancer initiation, immune system roles, tumor angiogenesis, environmental carcinogenesis, invasion as well as response to novel anticancer strategy. Currently, several models are being designed to allow in vivo imaging of tumor development from earlier stages and to follow tumor response to therapeutics. Besides to the research activities, this UOSD has the responsibility for day-to-day management of the Institute animal house. In agreement, this structure coordinates the activity of Animal Welfare Body (D.Lgs. n.26/2014), evaluating scientific projects in which are involved animal experimentations.

## Research activity:

Developing drugs that target KRAS, the most frequently mutated oncogene in cancer, has not been successful despite much concerted efforts dedicated towards it in the last thirty years. Considering the key role this driver oncogene plays, the pharmacological drugging of KRAS remains a key challenge for cancer research. In this context , Dr. Leonetti showed that the targeting of G-quadruplex (G4) structures present in the G4 motifs of the human KRAS promoter, by a the G4 ligand EMICORON could be a promising strategy, as this compound exhibited a marked antitumoral activity against patient-derived xenografts (PDXs) both alone and also by increasing the therapeutic efficacy of the FOLFIRI standard chemotherapeutic regimen.

R-loops are nucleic acid structures that form when an RNA strand invades double-stranded DNA. This produces a Watson- Crick RNA-DNA hybrid and displaces the non-hybridized strand as single-stranded DNA. R-loops participate in a number of physiological processes, but they also represent a source of DNA damage and genomic instability. The appropriate processing of R-loops is essential to avoid a number of human neurodegenerative disorders or cancer. During this year Dr. Fanciulli's Group investigated the role of the protein Che-1 in R-loops formation and processing. In multiple myeloma cells, Che-1 was found associated with R-loops and its depletion by siRNA induced a strong increase of these structures. Notably, a Drip-seq analysis showed that most of R-loops induced by Che-1 depletion localize to active chromatin sites. At the same time, in collaboration with Dr. Locatelli at the "Bambino Gesù" Hospital, Dr. Fanciulli's group demonstrated that Che-1 is overexpressed in pediatric B-cell precursor acute lymphoblastic leukemia (BCP-ALL) during disease onset and at relapse, and that its depletion inhibits the proliferation of BCP-ALL cells. Furthermore, we report that c-Myc regulates Che-1 expression by direct binding to its promoter and describe a strict correlation between Che-1 expression and c-Myc expression. RNA-seq analyses upon Che-1 or c-Myc depletion reveal a strong overlap of the respective controlled pathways. Genome-wide ChIP-seq experiments suggest that Che-1 acts as a downstream effector of c-Myc.

Dr. De Marco during the year 2018 has been focusing on the role of proteome oxidative damage, generated by the UV-B; UV-A, and the shortwave visible components of the solar radiation, in keratinocytes, melanocytes and dermal fibroblasts. Experimental data from in vitro experiments and ex vivo assays indicate that proteome oxidative adducts have a distinct role in impairing the genomic and the proteomic repairing machinery, suppressing apoptosis and deregulating the cell/matrix interaction. Thus damaged or inappropriately repaired DNA persists longer, carcinogenic alterations are generated at an increased pace and potentially carcinogenic clones can establish and grow. The transformant clones eventually generated, are then endowed in a deeply dysregulated microenvironment as cell/matrix signalling, inflammation and immune reaction, are also critically subverted, unleashing transformant clones to expand and progress to a full neoplastic phenotype. Thus UV radiation, in addition to be a cancer initiating agent has also a specific cancer promoting activity.

Dr. Gurtner studies aim at identify mutp53-dependent miRNAs and their target genes as useful prognostic and/or predictive biomarkers of response to therapy in patients with CRC. Since for many genes putatively regulated by mutp53 identified in these studies there are drugs approved by the FDA or undergoing clinical trials, these results open the way to identify "vulnerabilities" of mutp53 with studies on organoids derived from patients. In this context, Dr. Gurtner actively collaborates with the laboratory of Dr. Nicola Valeri at Sutton, one of the leading experts on patient-derived organoids (PDOs).

Dr. Piaggio studied the role of the immunological systemic macroenvironment before and during tumour development using bioluminescent genetically

modified mouse models of breast and pancreatic cancer. Moreover, her research deals with cancer patients sera characterization of new non-invasive diagnostic and/or prognostic biomarkers being especially interested in the study of the involvement of NETosis biomarkers. In this regard, she actively have collaborated with the Gynaecology Unit directed by Dr. Enrico Vizza for the analysis of specific NET biomarkers in the serum of patients with endometrial cancer.

## Publications


1. Aurisicchio L, Pallocca M, Ciliberto G, Palombo F. The Perfect Personalized Cancer Therapy: Cancer Vaccines Against Neoantigens. *J. Exp. Clin. Cancer Res.* 2018 Apr 20; 37(1): 86a

2. Belloni L, Di Cocco S, Guerrieri F, Nunn ADG, Piconese S, Salerno D, Testoni B, Pulito C, Mori F, Pallocca M, Sacconi A, Vivoli E, Marra F, Strano S, Blandino G, Levrero M, Pediconi N. Targeting a Phospho-STAT3-miRNAs Pathway Improves Vesicular Hepatic Steatosis in an in Vitro and in Vivo Model. *Sci. Rep.* 2018 Sep 11; 8(1): 13638a

3. Buglioni S, Melucci E, Sperati F, Pallocca M, Terrenato I, De Nicola F, Goeman F, Casini B, Amoreo CA, Gallo E, Diodoro MG, Pescarmona E, Vici P, Sergi D, Pizzuti L, Di Lauro L, Mazzotta M, Barba M, Fanciulli M, Vitale I, De Maria R, Ciliberto G, Maugeri-Saccà M. The Clinical Significance of PD-L1 in Advanced Gastric Cancer is Dependent on ARID1A Mutations and ATM Expression. *Oncoimmunology.* 2018 03/27; 7(8): e1457602a

4. Caforio M, Sorino C, Iacovelli S, Fanciulli M, Locatelli F, Folgiero V. Recent Advances in Searching c-Myc Transcriptional Cofactors during Tumorigenesis. *J. Exp. Clin. Cancer Res.* 2018 Sep 27; 37(1): 239a

5. Carafa V, Nebbioso A, Cuomo F, Rotili D, Cobellis G, Bontempo P, Baldi A, Spugnini EP, Citro G, Chambery A, Russo R, Ruvo M, Ciana P, Maravigna L, Shaik J, Radaelli E, De Antonellis P, Tarantino D, Pirolli A, Ragno R, Zollo M, Stunnenberg HG, Mai A, Altucci L. RIP1-HAT1-SirT Complex Identification and Targeting in Treatment and Prevention of Cancer. *Clin. Cancer Res.* 2018 Jun 15; 24(12): 2886-2900a

6. Corrado G, Laquintana V, Loria R, Carosi M, de Salvo L, Sperduti I, Zampa A, Cicchillitti L, Piaggio G, Cutillo G, Falcioni R, Vizza E. Endometrial Cancer Prognosis Correlates with the Expression of L1CAM and miR34a Biomarkers. *J. Exp. Clin. Cancer Res.* 2018 Jul 6; 37(1): 139a

7. De Nicola F, Goeman F, Pallocca M, Sperati F, Pizzuti L, Melucci E, Casini B, Amoreo CA, Gallo E, Diodoro MG, Buglioni S, Mazzotta M, Vici P, Sergi D, Di Lauro L, Barba M, Pescarmona E, Ciliberto G, De Maria R, Fanciulli M, Maugeri-Sacca M. Deep Sequencing and Pathway-Focused Analysis Revealed Multigene Oncodriver Signatures Predicting Survival Outcomes in Advanced Colorectal Cancer. *Oncogenesis.* 2018 Jul 22; 7(7): 55a

8. Di Domenico EG, Cavallo I, Bordignon V, Prignano G, Sperduti I, Gurtner A, Trento E, Toma L, Pimpinelli F, Capitanio B, Ensoli F. Inflammatory Cytokines and Biofilm Production Sustain Staphylococcus Aureus Outgrowth and Persistence: A Pivotal Interplay in the Pathogenesis of Atopic Dermatitis. *Sci. Rep.* 2018 Jun 28; 8(1): 9573a

9. Di Martino MT, Zazzeroni F, Donadelli M, Chiodoni C, Caraglia M, Scotlandi K, Meschini S, Leonetti C. Reprogramming Tumor-Immune Cell Interface in Solid and Hematological Malignancies to Enhance Response to Therapy. *J. Exp. Clin. Cancer Res.* 2018 Mar 5; 37(1): 48a

10. Folgiero V, Sorino C, Locatelli F, Fanciulli M. A New Baby in the c-Myc-Directed Transcriptional Machinery: Che-1/AATF. *Cell. Cycle.* 2018 17(11): 1286-1290a.

11. Folgiero V, Sorino C, Pallocca M, De Nicola F, Goeman F, Bertaina V, Strocchio L, Romania P, Pitisci A, Iezzi S, Catena V, Bruno T, Strimpakos G, Passananti C, Mattei E, Blandino G, Locatelli F, Fanciulli M. Che-1 is Targeted by c-Myc to Sustain Proliferation in Pre-B-Cell Acute Lymphoblastic Leukemia. *EMBO Rep.* 2018 Mar; 19(3): e44871 [pii]a

12. Giarra S, Zappavigna S, Campani V, Abate M, Cossu AM, Leonetti C, Porru M, Mayol L, Caraglia M, De Rosa G.

Chitosan-Based Polyelectrolyte Complexes for Doxorubicin and Zoledronic Acid Combined Therapy to Overcome Multidrug Resistance. *Pharmaceutics.* 2018 Oct 9; 10(4): 10.3390/pharmaceutics10040180a

13. Iachettini S, Trisciuoglio D, Rotili D, Lucidi A, Salvati E, Zizza P, Di Leo L, Del Bufalo D, Ciriolo MR, Leonetti C, Steegborn C, Mai A, Rizzo A, Biroccio A. Pharmacological Activation of SIRT6 Triggers Lethal Autophagy in Human Cancer Cells. *Cell.Death Dis.* 2018 Sep 24; 9(10): 996a

14. Iacobini C, Blasetti Fantauzzi C, Bedini R, Pecci R, Bartolazzi A, Amadio B, Pesce C, Pugliese G, Menini S. Galectin-3 is Essential for Proper Bone Cell Differentiation and Activity, Bone Remodeling and Biomechanical Competence in Mice. *Metabolism.* 2018 Jun; 83: 149a

15. La Torre M, Merigliano C, Burla R, Mottini C, Zanetti G, Del Giudice S, Carcuro M, Virdia I, Bucciarelli E, Manni I, Vinciguerra GR, Piaggio G, Riminucci M, Cumano A, Bartolazzi A, Verni F, Soddu S, Gatti M, Saggio I. Mice with Reduced Expression of the Telomere-Associated Protein Ft1 Develop p53-Sensitive Progeroid Traits. *Aging Cell.* 2018 Apr 10; 17(4): e12730a

16. Manic G, Signore M, Sistigu A, Russo G, Corradi F, Siteni S, Musella M, Vitale S, De Angelis ML, Pallocca M, Amoreo CA, Sperati F, Di Franco S, Barresi S, Policicchio E, De Luca G, De Nicola F, Mottolese M, Zeuner A, Fanciulli M, Stassi G, Maugeri-Sacca M, Baiocchi M, Tartaglia M, Vitale I, De Maria R. CHK1-Targeted Therapy to Deplete DNA Replication-Stressed, p53-Deficient, Hyperdiploid Colorectal Cancer Stem Cells. *Gut.* 2018 67(5):903-917

17. Mattioli E, Andrenacci D, Garofalo C, Prencipe S, Scotlandi K, Remondini D, Gentilini D, Di Blasio AM, Valente S, Scarano E, Cicchilitti L, Piaggio G, Mai A, Lattanzi G. Altered Modulation of Lamin A/C-HDAC2 Interaction and p21 Expression during Oxidative Stress Response in HGPS. *Aging Cell.* 2018 Oct; 17(5): e12824a

18. Melucci E, Casini B, Ronchetti L, Pizzuti L, Sperati F, Pallocca M, De Nicola F, Goeman F, Gallo E, Amoreo CA, Sergi D, Terrenato I, Vici P, Di Lauro L, Diodoro MG, Pescarmona E, Barba M, Mazzotta M, Mottolese M, Fanciulli M, Ciliberto G, De Maria R, Buglioni S, Maugeri-Sacca M. Expression of the Hippo Transducer TAZ in Association with WNT Pathway Mutations Impacts Survival Outcomes in Advanced Gastric Cancer Patients Treated with First-Line Chemotherapy. *J.Transl.Med.* 2018 Feb 5; 16(1): 22a

19. Menini S, Iacobini C, de Latouliere L, Manni I, Ionta V, Blasetti Fantauzzi C, Pesce C, Cappello P, Novelli F, Piaggio G, Pugliese G. The Advanced Glycation End-Product N() -Carboxymethyllysine Promotes Progression of Pancreatic Cancer: Implications for Diabetes-Associated Risk and its Prevention. *J.Pathol.* 2018 Jun;245(2):197-208

20. Pallocca M, Goeman F, De Nicola F, Melucci E, Sperati F, Terrenato I, Pizzuti L, Casini B, Gallo E, Amoreo CA, Vici P, Di Lauro L, Buglioni S, Diodoro MG, Pescarmona E, Mazzotta M, Barba M, Fanciulli M, De Maria R, Ciliberto G, Maugeri-Sacca M. Coexisting YAP Expression and TP53 Missense Mutations Delineates a Molecular Scenario Unexpectedly Associated with Better Survival Outcomes in Advanced Gastric Cancer. *J.Transl.Med.* 2018 Sep 4; 16(1): 247a

21. Porru M, Pompili L, Caruso C, Biroccio A, Leonetti C. Targeting KRAS in Metastatic Colorectal Cancer: Current Strategies and Emerging Opportunities. *J.Exp.Clin.Cancer Res.* 2018 Mar 13; 37(1): 57a

22. Porru M, Pompili L, Caruso C, Leonetti C. Xenograft as in Vivo Experimental Model. *Methods Mol.Biol.* 2018 1692: 97a

23. Rosati J, Ferrari D, Altieri F, Tardivo S, Ricciolini C, Fusilli C, Zalfa C, Profico DC, Pinos F, Bernardini L, Torres B, Manni I, Piaggio G, Binda E, Copetti M, Lamorte G, Mazza T, Carella M, Gelati M, Valente EM, Simeone A, Vescovi AL. Establishment of Stable iPS-Derived Human Neural Stem Cell Lines Suitable for Cell Therapies. *Cell.Death Dis.* 2018 Sep 17; 9(10): 937a.

24. Scioli MG, Artuso S, D'Angelo C, Porru M, D'Amico F, Bielli A, Gentile P, Cervelli V, Leonetti C, Orlandi A. Adipose-Derived Stem Cell-Mediated Paclitaxel Delivery Inhibits Breast Cancer Growth. *PLoS One.* 2018 Sep 7; 13(9): e0203426a

25. Sette G, Salvati V, Giordani I, Pilozzi E, Quacquarini D, Duranti E, De Nicola F, Pallocca M, Fanciulli M, Falchi M, Pallini R, De Maria R, Eramo A. Conditionally Reprogrammed Cells (CRC) Methodology does Not Allow the in Vitro Expansion of Patient-Derived Primary and Metastatic Lung Cancer Cells. *Int. J. Cancer.* 2018 143(1):88-99

26. Spadaccio C, Nappi F, De Marco F, Sedati P, Taffon C, Nenna A, Crescenzi A, Chello M, Trombetta M, Gambardella I, Rainer A. Implantation of a Poly-L-Lactide GCSF-Functionalized Scaffold in a Model of Chronic Myocardial Infarction. *J. Cardiovasc. Transl. Res.* 2017 Feb; 10(1): 47a

27. Spugnini EP, Logozzi M, Di Raimo R, Mizzoni D, Fais S. A Role of Tumor-Released Exosomes in Paracrine Dissemination and Metastasis. *Int. J. Mol. Sci.* 2018 Dec 10; 19(12): E3968a

28. Vizza E, Corrado G, De Angeli M, Carosi M, Mancini E, Baiocco E, Chiofalo B, Patrizi L, Zampa A, Piaggio G, Cicchillitti L. Serum DNA Integrity Index as a Potential Molecular Biomarker in Endometrial Cancer. *J. Exp. Clin. Cancer Res.* 2018 Jan 30; 37(1): 16a

29. Welcker D, Jain M, Khurshid S, Jokic M, Hohne M, Schmitt A, Frommolt P, Niessen CM, Spiro J, Persigehl T, Wittersheim M, Buttner R, Fanciulli M, Schermer B, Reinhardt HC, Benzing T, Hopker K. AATF Suppresses Apoptosis, Promotes Proliferation and is Critical for Kras-Driven Lung Cancer. *Oncogene.* 2018 Mar; 37(11): 1503a

# BIOSTATISTICS AND BIOINFORMATICS UNIT

## *Head: Diana Giannarelli, Biostatistician*

| STAFF |
|---|
| **Francesca Sperati, Biostatistician** |
| **Isabella Sperduti, Biostatistician** |
| **Irene Terrenato, Biostatistician** |
| **Marco Canfora, IT Informatic Specialist** |

### *Mission*

The Biostatistical and Bioinformatic Unit gives statistical advice for the protocol design related to observational and experimental studies. It is a support for the researchers in study design choice, randomization procedures identification, sample size calculation and Case Report Form definition.
This Unit performs the statistical analysis of clinical and laboratory data and develops new technique of data analysis, as required from the always increasing complexity of available information. It performs also systematic reviews and meta-analysis on clinically relevant aspects.
On the informatic side the Unit develops and implements databases related to clinical trial and research projects as well as particular pathologies. The Unit develops Web based platform in client/server environment.

### *Research Activities*

The Unit implements the most advanced statistical and methodological techniques to analyze data arrays. Along with the basic ways of analyzing data multivariate approaches are followed using available softwares as SPSS, Medcalc, Comprehensive Meta-analysis, PASS, NCSS and specific routines developed in R environment. Data coming from our single center and multicenter studies

are formally checked together with investigators and strategies are constantly discussed. Our support starts with the study design and sample size determination using the most appropriate and innovative clinical trial design, and goes on focusing on protocol development and randomization scheme. During the study we support the investigators with interim analysis and database management. When writing the paper we perform the analysis and discuss the interpretation of results. Our activity includes systematic reviews and meta-analysis as well as the most recent techniques of analysis as propensity score and network meta-analysis. The informatic section develops with Visual Studio 2012. NET4 software web based platforms to manage clinical data related to patients enrolled in research projects. It is involved also in the design and implementation of web site with the software Joomla. In collaboration we study the possibility of reducing high-dimensional data to develop models for interpreting prognostic and predictive role of factors.

## Publications


1. Annaloro C, Airaghi L, Giannarelli D, Mometto G, Orsatti A, Saporiti G, Grifoni FI, Baldini M, Tagliaferri E, Vincenti D, Maira D, Onida F, Cortelezzi A. Prospective Evaluation of Metabolic Syndrome and its Features in a Single-Center Series of Hematopoietic Stem Cell Transplantation Recipients. *Ann. Hematol.* 2018 97(12): 2471-2478a

2. Antonini G, De Berardinis E, Del Giudice F, Busetto GM, Lauretti S, Fragas R, Chung BI, Conti SL, Giannarelli D, Sperduti I, Gross MS, Perito PE. Inflatable Penile Prosthesis Placement, Scratch Technique and Postoperative Vacuum Therapy as a Combined Approach to Definitive Treatment of Peyronie's Disease. *J. Urol.* 2018 200(3): 642-647a

3. Appetecchia M, Lauretta R, Sperduti I, Gallucci M. Chromogranin A as a Biomarker for Prostate Cancer: Is it Actually Relevant for Clinical Practice? *Future Oncol.* 2018 Jun;

4. Basile S, Pinelli S, Benedetti Panici P, Angioli R, Plotti F, Giannarelli D, Fossati R, Rosati CM, Salerno MG. Association between Helicobacter Pylori Infection and Vulvar Lichen Sclerosus: A Clinical Comparative Study. *Eur. J. Dermatol.* 2018 Jan 16;

5. Bersanelli M, Buti S, De Giorgi U, Di Maio M, Giannarelli D, Banna GL. Influenza Vaccination in Advanced Cancer Patients Undergoing Immunotherapy with Anti-PD-1/PD-L1 Immune Checkpoint Inhibitors: What Data do we have for the Clinical Recommendation? *Recenti Prog. Med.* 2018 Nov; 109(11): 540a

6. Bersanelli M, Giannarelli D, Castrignano P, Fornarini G, Panni S, Mazzoni F, Tiseo M, Rossetti S, Gambale E, Rossi E, Papa A, Cortellini A, Lolli C, Ratta R, Michiara M, Milella M, De Luca E, Soraru M, Mucciarini C, Atzori F, Banna GL, La Torre L, Vitale MG, Massari F, Rebuzzi SE, Facchini G, Schinzari G, Tomao S, Bui S, Vaccaro V, Procopio G, De Giorgi U, Santoni M, Ficorella C, Sabbatini R, Maestri A, Natoli C, De Tursi M, Di Maio M, Rapacchi E, Pireddu A, Sava T, Lipari H, Comito F, Verzoni E, Leonardi F, Buti S. INfluenza Vaccine Indication during Therapy with Immune Checkpoint Inhibitors: A Transversal Challenge. the INVIDIa Study. *Immunotherapy.* 2018 Oct; 10(14): 1229a

7. Bracarda S, Galli L, Maruzzo M, Lo Re G, Buti S, Favaretto A, Di Costanzo F, Sacco C, Merlano M, Mucciarini C, Zafarana E, Romito S, Maestri A, Giorgio CG, Ionta MT, Turci D, De Giorgi U, Procopio G, Cortesi E, Giannarelli D, Porta C. Negative Prognostic Factors and Resulting Clinical Outcome in Patients with Metastatic Renal Cell Carcinoma Included in the Italian Nivolumab-Expanded Access Program. *Future Oncol.* 2018 Jun; 14(14): 1347a

8. Buglioni S, Melucci E, Sperati F, Pallocca M, Terrenato I, De Nicola F, Goeman F, Casini B, Amoreo CA, Gallo E, Diodoro MG, Pescarmona E, Vici P, Sergi D, Pizzuti L, Di Lauro L, Mazzotta M, Barba M, Fanciulli M, Vitale I, De Maria R, Ciliberto G, Maugeri-Saccà M. The Clinical Significance of PD-L1 in Advanced Gastric Cancer is Dependent on ARID1A Mutations and ATM Expression. *Oncoimmunology.* 2018 03/27; 7(8): e1457602a .

9. Calabro L, Morra A, Giannarelli D, Amato G, D'Incecco A, Covre A, Lewis A, Rebelatto MC, Danielli R, Altomonte M, Di Giacomo AM, Maio M. Tremelimumab Combined with Durvalumab in Patients with Mesothelioma (NIBIT-MESO-1): An Open-Label, Non-Randomised, Phase 2 Study. *Lancet Respir. Med.* 2018 Jun; 6(6): 451a

10. Callovini GM, Telera S, Sherkat S, Sperduti I, Callovini T, Carapella CM. How is Stereotactic Brain Biopsy Evolving? A Multicentric Analysis of a Series of 421 Cases Treated in Rome Over the Last Sixteen Years. *Clin. Neurol. Neurosurg.* 2018 174: 101-107a

11. Capone M, Giannarelli D, Mallardo D, Madonna G, Festino L, Grimaldi AM, Vanella V, Simeone E, Paone M, Palmieri G, Cavalcanti E, Caraco C, Ascierto PA. Baseline Neutrophil-to-Lymphocyte Ratio (NLR) and Derived NLR could Predict overall Survival in Patients with Advanced Melanoma Treated with Nivolumab. *J. Immunother. Cancer.* 2018 Jul 16; 6(1): 74a

12. Carbone A, Sperduti I, DE Simone P, Piemonte P, Ferrari A, Buccini P, Silipo V, Iorio A, Frascione P, Eibenschutz L. Daylight Photodynamic Therapy: Experience in the Treatment of Actinic Keratosis in San Gallicano Institute of Rome and a Review of Literature. *G. Ital. Dermatol. Venereol.* 2018 Jan 24;

13. Corrado G, Laquintana V, Loria R, Carosi M, de Salvo L, Sperduti I, Zampa A, Cicchillitti L, Piaggio G, Cutillo G, Falcioni R, Vizza E. Endometrial Cancer Prognosis Correlates with the Expression of L1CAM and miR34a Biomarkers. *J. Exp. Clin. Cancer Res.* 2018 Jul 6; 37(1): 139a

14. Corrado G, Vizza E, Legge F, Pedone Anchora L, Sperduti I, Fagotti A, Mancini E, Gallotta V, Zampa A, Chiofalo B, Scambia G. Comparison of Different Surgical Approaches for Stage IB1 Cervical Cancer Patients: A Multi-Institution Study and a Review of the Literature. *Int. J. Gynecol. Cancer.* 2018 Jun; 28(5): 1020a

15. Danielli R, Cisternino F, Giannarelli D, Calabro L, Camerini R, Savelli V, Bova G, Dragonetti R, Di Giacomo AM, Altomonte M, Maio M. Long-Term Follow Up of Metastatic Melanoma Patients Treated with Thymosin Alpha-1: Investigating Immune Checkpoints Synergy. *Expert Opin. Biol. Ther.* 2018 Jul; 18(sup1): 77a

16. De Nicola F, Goeman F, Pallocca M, Sperati F, Pizzuti L, Melucci E, Casini B, Amoreo CA, Gallo E, Diodoro MG, Buglioni S, Mazzotta M, Vici P, Sergi D, Di Lauro L, Barba M, Pescarmona E, Ciliberto G, De Maria R, Fanciulli M, Maugeri-Sacca M. Deep Sequencing and Pathway-Focused Analysis Revealed Multigene Oncodriver Signatures Predicting Survival Outcomes in Advanced Colorectal Cancer. *Oncogenesis.* 2018 Jul 22; 7(7): 55a

17. De Virgilio A, Pellini R, Mercante G, Cristalli G, Manciocco V, Giannarelli D, Spriano G. Supracricoid Partial Laryngectomy for Radiorecurrent Laryngeal Cancer: A Systematic Review of the Literature and Meta-Analysis. *Eur. Arch. Otorhinolaryngol.* 2018 Jul; 275(7): 1671-1680a

18. Del Bene G, Calabro F, Giannarelli D, Plimack ER, Harshman LC, Yu EY, Crabb SJ, Pal SK, Alva AS, Powles T, De Giorgi U, Agarwal N, Bamias A, Ladoire S, Necchi A, Vaishampayan UN, Niegisch G, Bellmunt J, Baniel J, Galsky MD, Sternberg CN. Neoadjuvant Vs. Adjuvant Chemotherapy in Muscle Invasive Bladder Cancer (MIBC): Analysis from the RISC Database. *Front. Oncol.* 2018 Nov 19; 8: 463a

19. Del Curatolo A, Conciatori F, Cesta Incani U, Bazzichetto C, Falcone I, Corbo V, D'Agosto S, Eramo A, Sette G, Sperduti I, De Luca T, Marabese M, Shirasawa S, De Maria R, Scarpa A, Broggini M, Del Bufalo D, Cognetti F, Milella M, Ciuffreda L. Therapeutic Potential of Combined BRAF/MEK Blockade in BRAF-Wild Type Preclinical Tumor Models. *J. Exp. Clin. Cancer Res.* 2018 Jul 9; 37(1): 140a

20. di Martino S, De Luca G, Grassi L, Federici G, Alfonsi R, Signore M, Addario A, De Salvo L, Francescangeli F, Sanchez M, Tirelli V, Muto G, Sperduti I, Sentinelli S, Costantini M, Pasquini L, Milella M, Haoui M, Simone G, Gallucci M, De Maria R, Bonci D. Renal Cancer: New Models and Approach for Personalizing Therapy. *J. Exp. Clin. Cancer Res.* 2018 Sep 5; 37(1): 217a

21. Di Modugno F, Spada S, Palermo B, Visca P, Iapicca P, Di Carlo A, Antoniani B, Sperduti I, Di Benedetto A, Terrenato I, Mottolese M, Gandolfi F, Facciolo F, Chen EI, Schwartz MA, Santoni A, Bissell MJ, Nistico P. HMENA Isoforms Impact NSCLC Patient Outcome through fibronectin/beta1 Integrin Axis. *Oncogene.* 2018 Oct; 37(42): 5605-5617a

22. Donzelli S, Milano E, Pruszko M, Sacconi A, Masciarelli S, Iosue I, Melucci E, Gallo E, Terrenato I, Mottolese M, Zylicz M, Zylicz A, Fazi F, Blandino G, Fontemaggi G. Expression of ID4 Protein in Breast Cancer Cells Induces Reprogramming of Tumour-Associated Macrophages. *Breast Cancer Res.* 2018 Jun 19; 20(1): 59a

23. Fabi A, Alesini D, Valle E, Moscetti L, Caputo R, Caruso M, Carbognin L, Ciccarese M, La Verde N, Arpino G, Cannita K, Paris I, Santini D, Montemurro F, Russillo M, Ferretti G, Filippelli G, Rossello R, Fabbri A, Zambelli A, Leonardi V, D'Ottavio AM, Nistico C, Stani S, Giampaglia M, Scandurra G, Catania G, Malaguti P, Giannarelli D, Cognetti F. T-DM1 and Brain Metastases: Clinical Outcome in HER2-Positive Metastatic Breast Cancer. *Breast*. 2018 Oct; 41: 137a

24. Ferrara R, Pilotto S, Caccese M, Grizzi G, Sperduti I, Giannarelli D, Milella M, Besse B, Tortora G, Bria E. Do Immune Checkpoint Inhibitors Need New Studies Methodology? *J. Thorac. Dis.* 2018 May; 10(Suppl 13): S1564a

25. Gamucci T, Pizzuti L, Natoli C, Mentuccia L, Sperduti I, Barba M, Sergi D, Iezzi L, Maugeri-Sacca M, Vaccaro A, Magnolfi E, Gelibter A, Barchiesi G, Magri V, D'Onofrio L, Cassano A, Rossi E, Botticelli A, Moscetti L, Omarini C, Fabbri MA, Scinto AF, Corsi D, Carbognin L, Mazzotta M, Bria E, Foglietta J, Samaritani R, Garufi C, Mariani L, Barni S, Mirabelli R, Sarmiento R, Graziano V, Santini D, Marchetti P, Tonini G, Di Lauro L, Sanguineti G, Paoletti G, Tomao S, De Maria R, Veltri E, Paris I, Giotta F, Latorre A, Giordano A, Ciliberto G, Vici P. A Multicenter REtrospective Observational Study of First-Line Treatment with PERtuzumab, Trastuzumab and Taxanes for Advanced HER2 Positive Breast Cancer Patients. RePer Study. *Cancer. Biol. Ther.* 2018 Nov 7; : 1a

26. Gamucci T, Pizzuti L, Sperduti I, Mentuccia L, Vaccaro A, Moscetti L, Marchetti P, Carbognin L, Michelotti A, Iezzi L, Cassano A, Grassadonia A, Astone A, Botticelli A, Magnolfi E, Di Lauro L, Sergi D, Fuso P, Tinari N, Barba M, Maugeri-Sacca M, Landucci E, Conti F, Sanguineti G, De Tursi M, Iafrate G, Giordano A, Ciliberto G, Natoli C, Vici P. Neoadjuvant Chemotherapy in Triple-Negative Breast Cancer: A Multicentric Retrospective Observational Study in Real-Life Setting. *J. Cell. Physiol.* 2018 Mar; 233(3): 2313a

27. Garassino MC, Crino L, Catino A, Ardizzoni A, Cortesi E, Cappuzzo F, Bordi P, Calabro L, Barbieri F, Santo A, Altavilla G, Ambrosio F, Mini E, Vasile E, Morgillo F, Scoppola A, Bengala C, Follador A, Tedde N, Giannarelli D, Lo Russo G, Vitiello F. Nivolumab in Never-Smokers with Advanced Squamous Non-Small Cell Lung Cancer: Results from the Italian Cohort of an Expanded Access Program. *Tumour Biol.* 2018 Nov; 40(11): 1010428318815047a

28. Garassino MC, Gelibter AJ, Grossi F, Chiari R, Soto Parra H, Cascinu S, Cognetti F, Turci D, Blasi L, Bengala C, Mini E, Baldini E, Quadrini S, Ceresoli GL, Antonelli P, Vasile E, Pinto C, Fasola G, Galetta D, Macerelli M, Giannarelli D, Lo Russo G, de Marinis F. Italian Nivolumab Expanded Access Program in Nonsquamous Non-Small Cell Lung Cancer Patients: Results in Never-Smokers and EGFR-Mutant Patients. *J. Thorac. Oncol.* 2018 Aug; 13(8): 1146a

29. Gobbini E, Pilotto S, Pasello G, Polo V, Di Maio M, Arizio F, Galetta D, Petrillo P, Chiari R, Matocci R, Di Costanzo A, Di Stefano TS, Aglietta M, Cagnazzo C, Sperduti I, Bria E, Novello S. Effect of Contract Research Organization Bureaucracy in Clinical Trial Management: A Model from Lung Cancer. *Clin. Lung Cancer.* 2018 Mar; 19(2): 191a

30. Grassadonia A, Sperduti I, Vici P, Iezzi L, Brocco D, Gamucci T, Pizzuti L, Maugeri-Sacca M, Marchetti P, Cognetti G, De Tursi M, Natoli C, Barba M, Tinari N. Effect of Gender on the Outcome of Patients Receiving Immune Checkpoint Inhibitors for Advanced Cancer: A Systematic Review and Meta-Analysis of Phase III Randomized Clinical Trials. *J. Clin. Med.* 2018 Dec 12; 7(12): 10.3390/jcm7120542a

31. Grossi F, Crino L, Logroscino A, Canova S, Delmonte A, Melotti B, Proto C, Gelibter A, Cappuzzo F, Turci D, Gamucci T, Antonelli P, Marchetti P, Santoro A, Giusti S, Di Costanzo F, Giustini L, Del Conte A, Livi L, Giannarelli D, de Marinis F. Use of Nivolumab in Elderly Patients with Advanced Squamous Non-Small-Cell Lung Cancer: Results from the Italian Cohort of an Expanded Access Programme. *Eur. J. Cancer.* 2018 Sep; 100: 126a

32. Hakoum MB, Kahale LA, Tsolakian IG, Matar CF, Yosuico VE, Terrenato I, Sperati F, Barba M, Schunemann H, Akl EA. Anticoagulation for the Initial Treatment of Venous Thromboembolism in People with Cancer. *Cochrane Database Syst. Rev.* 2018 Jan 24; 1: CD006649a

33. Iacorossi L, Gambalunga F, Fabi A, Giannarelli D, Marchetti A, Piredda M, De Marinis MG. Adherence to Oral Administration of Endocrine Treatment in Patients with Breast Cancer: A Qualitative Study. *Cancer Nurs.* 2018 Jan/Feb; 41(1): E57a

34. Iacorossi L, Gambalunga F, Molinaro S, De Domenico R, Giannarelli D, Fabi A. The Effectiveness of the Sport "Dragon Boat Racing" in Reducing the Risk of Lymphedema Incidence: An Observational Study. *Cancer Nurs.* 2018 Jun 22;

35. Iacovelli R, De Giorgi U, Galli L, Zucali P, Nole F, Sabbatini R, Fraccon AP, Basso U, Mosca A, Atzori F, Santini D, Facchini G, Fornarini G, Pasini F, Masini C, Massari F, Buti S, Sava T, Sacco C, Ricotta R, Sperduti I, Tortora G, Porta C. Is it Possible to Improve Prognostic Classification in Patients Affected by Metastatic Renal Cell Carcinoma with an Intermediate Or Poor Prognosis? *Clin. Genitourin. Cancer.* 2018 Oct; 16(5): 355-359.e1.

36. Kahale LA, Hakoum MB, Tsolakian IG, Matar CF, Terrenato I, Sperati F, Barba M, Yosuico VE, Schunemann H, Akl EA. Anticoagulation for the Long-Term Treatment of Venous Thromboembolism in People with Cancer. *Cochrane Database Syst. Rev.* 2018 Jun 19; 6: CD006650a

37. Kahale LA, Tsolakian IG, Hakoum MB, Matar CF, Barba M, Yosuico VE, Terrenato I, Sperati F, Schunemann H, Akl EA. Anticoagulation for People with Cancer and Central Venous Catheters. *Cochrane Database Syst. Rev.* 2018 Jun 1; 6: CD006468a

38. Ludovini V, Ricciuti B, Tofanetti FR, Mencaroni C, Giannarelli D, Sidoni A, Reda MS, Siggillino A, Baglivo S, Crino L, Bellezza G, Chiari R, Metro G. KRAS Mutation and DNA Repair and Synthesis Genes in Non-Small-Cell Lung Cancer. *Mol. Clin. Oncol.* 2018 Dec; 9(6): 689a

39. Madonna G, Ballesteros-Merino C, Feng Z, Bifulco C, Capone M, Giannarelli D, Mallardo D, Simeone E, Grimaldi AM, Caraco C, Botti G, Fox BA, Ascierto PA. PD-L1 Expression with Immune-Infiltrate Evaluation and Outcome Prediction in Melanoma Patients Treated with Ipilimumab. *Oncoimmunology.* 2018 Sep 5; 7(12): e1405206a.

40. Magnani C, Calvieri A, Giannarelli D, Espino M, Casale G. Peripherally Inserted Central Catheter, Midline, and "Short" Midline in Palliative Care: Patient-Reported Outcome Measures to Assess Impact on Quality of Care. *J. Vasc. Access.* 2018 Dec 3; : 1129729818814732a

41. Magnani C, Giannarelli D, Calvieri A, Dardeli A, Eusepi G, Restuccia MR, Mastroianni C, Casale G. Breakthrough Cancer Pain Tailored Treatment: Which Factors Influence the Medication Choice? an Observational, Prospective and Cross-Sectional Study in Patients with Terminal Cancer. *Postgrad. Med. J.* 2018 Oct; 94(1116): 566a

42. Mancini R, Pattaro G, Diodoro MG, Sperduti I, Garufi C, Stigliano V, Perri P, Grazi GL, Cosimelli M. Tumor Regression Grade After Neoadjuvant Chemoradiation and Surgery for Low Rectal Cancer Evaluated by Multiple Correspondence Analysis: Ten Years as Minimum Follow-Up. *Clin. Colorectal Cancer.* 2018 Mar; 17(1): e13a

43. Mandoj C, Pizzuti L, Sergi D, Sperduti I, Mazzotta M, Di Lauro L, Amodio A, Carpano S, Di Benedetto A, Botti C, Ferranti F, Antenucci A, D'Alessandro MG, Marchetti P, Tomao S, Sanguineti G, Giordano A, Maugeri-Sacca M, Ciliberto G, Conti L, Vici P, Barba M. Observational Study of Coagulation Activation in Early Breast Cancer: Development of a Prognostic Model Based on Data from the Real World Setting. *J. Transl. Med.* 2018 May 16; 16(1): 129a

44. Manic G, Signore M, Sistigu A, Russo G, Corradi F, Siteni S, Musella M, Vitale S, De Angelis ML, Pallocca M, Amoreo CA, Sperati F, Di Franco S, Barresi S, Policicchio E, De Luca G, De Nicola F, Mottolese M, Zeuner A, Fanciulli M, Stassi G, Maugeri-Sacca M, Baiocchi M, Tartaglia M, Vitale I, De Maria R. CHK1-Targeted Therapy to Deplete DNA Replication-Stressed, p53-Deficient, Hyperdiploid Colorectal Cancer Stem Cells. *Gut.* 2018 May;

45. Marchesi F, Capria S, Giannarelli D, Trisolini SM, Ansuinelli M, Caputo MD, Serrao A, Gumenyuk S, Renzi D, Pupo L, Palombi F, Provenzano I, Di Rocco A, Pisani F, Romano A, Spadea A, Papa E, Canfora M, Cantonetti M, Mengarelli A. BEAMVs FEAM High-Dose Chemotherapy: Retrospective Study in Lymphoma Patients Undergoing Autologous Stem Cell Transplant. *Bone Marrow Transplant.* 2018 53(8): 1051-1054a

46. Marchesi F, Regazzo G, Palombi F, Terrenato I, Sacconi A, Spagnuolo M, Donzelli S, Marino M, Ercolani C, Di Benedetto A, Blandino G, Ciliberto G, Mengarelli A, Rizzo MG. Serum miR-22 as Potential Non-Invasive Predictor of Poor Clinical Outcome in Newly Diagnosed, Uniformly Treated Patients with Diffuse Large B-Cell Lymphoma: An Explorative Pilot Study. *J. Exp. Clin. Cancer Res.* 2018 May 2; 37(1): 95a

47. Marchesi F, Vacca M, Giannarelli D, Ipsevich F, Pandolfi A, Gumenyuk S, Renzi D, Palombi F, Pisani F, Romano A, Spadea A, Papa E, Canfora M, Pierelli L, Mengarelli A. Lenograstim 5 microg/kg is Not Superior to Biosimilar Filgrastim 10 microg/kg in Lymphoma Patients Undergoing Peripheral Blood Stem Cell Mobilization After Chemotherapy:

Preliminary Results from a Prospective Randomized Study. *Transfusion.* 2018 Feb 15;

48. Marzi S, Farneti A, Vidiri A, Di Giuliano F, Marucci L, Spasiano F, Terrenato I, Sanguineti G. Radiation-Induced Parotid Changes in Oropharyngeal Cancer Patients: The Role of Early Functional Imaging and Patient-/treatment-Related Factors. *Radiat. Oncol.* 2018 Oct 1; 13(1): 189a

49. Maschio M, Pauletto G, Zarabla A, Maialetti A, Ius T, Villani V, Fabi A, Koudriavtseva T, Giannarelli D. Perampanel in Patients with Brain Tumour-Related Epilepsy in Real-Life Clinical Practice: A Retrospective Analysis. *Int. J. Neurosci.* 2018 Dec 3; : 1a

50. Maschio M, Zarabla A, Maialetti A, Marchesi F, Giannarelli D, Gumenyuk S, Pisani F, Renzi D, Galie E, Mengarelli A. Prevention of Bortezomib-Related Peripheral Neuropathy with Docosahexaenoic Acid and Alpha-Lipoic Acid in Patients with Multiple Myeloma: Preliminary Data. *Integr. Cancer. Ther.* 2018 Dec; 17(4): 1115a

51. Maschio M, Zarabla A, Maialetti A, Sperati F, Dinapoli L, Dispenza S, Petreri G, Cantelmi T. Lacosamide on Background Eeg Activity in Brain Tumor-Related Epilepsy Patients: A Case Series Study. *Brain Behav.* 2018 Nov; 8(11): e01067a

52. Matar CF, Kahale LA, Hakoum MB, Tsolakian IG, Etxeandia-Ikobaltzeta I, Yosuico VE, Terrenato I, Sperati F, Barba M, Schunemann H, Akl EA. Anticoagulation for Perioperative Thromboprophylaxis in People with Cancer. *Cochrane Database Syst. Rev.* 2018 Jul 11; 7: CD009447a

53. Melucci E, Casini B, Ronchetti L, Pizzuti L, Sperati F, Pallocca M, De Nicola F, Goeman F, Gallo E, Amoreo CA, Sergi D, Terrenato I, Vici P, Di Lauro L, Diodoro MG, Pescarmona E, Barba M, Mazzotta M, Mottolese M, Fanciulli M, Ciliberto G, De Maria R, Buglioni S, Maugeri-Sacca M. Expression of the Hippo Transducer TAZ in Association with WNT Pathway Mutations Impacts Survival Outcomes in Advanced Gastric Cancer Patients Treated with First-Line Chemotherapy. *J. Transl. Med.* 2018 Feb 5; 16(1): 22a

54. Metro G, Giannarelli D, Sidoni A, Chiari R, Bellezza G. Anaplastic Lymphoma Kinase Immunohistochemistry Scores do Not Predict Sensitivity to Crizotinib in Fluorescence in Situ Hybridization-Positive Non-Small Cell Lung Cancer Patients. *Int. J. Biol. Markers.* 2018 33(4): 549-550a

55. Metro G, Passaro A, Lo Russo G, Bonanno L, Giusti R, Gregorc V, Capelletto E, Martelli O, Cecere FL, Giannarelli D, Luciani A, Bearz A, Tuzi A, Scotti V, Tonini G, Galetta D, Carta A, Soto Parra H, Rebonato A, Morabito A, Chiari R. Ceritinib Compassionate use for Patients with Crizotinib-Refractory, Anaplastic Lymphoma Kinase-Positive Advanced Non-Small-Cell Lung Cancer. *Future Oncol.* 2018 Feb; 14(4): 353a

56. Molica S, Giannarelli D, Mirabelli R, Levato L, Kay NE, Shanafelt TD. Chronic Lymphocytic Leukemia International Prognostic Index: A Systematic Review and Meta-Analysis. *Blood.* 2018 Jan 18; 131(3): 365a

57. Molica S, Giannarelli D, Mirabelli R, Levato L, Shanafelt TD. Chronic Lymphocytic Leukemia International Prognostic Index (CLL-IPI) in Patients Receiving Chemoimmuno Or Targeted Therapy: A Systematic Review and Meta-Analysis. *Ann. Hematol.* 2018 Oct; 97(10): 2005a

58. Molica S, Giannarelli D, Mirabelli R, Levato L, Shanafelt TD. The Magnitude of Improvement in Progression-Free Survival with Targeted Therapy in relapsed/refractory Chronic Lymphocytic Leukemia Based on Prognostic Risk Category: A Systematic Review and Meta-Analysis. *Leuk. Lymphoma.* 2018 Dec 5; : 1a

59. Pace A, Mandoj C, Antenucci A, Villani V, Sperduti I, Casini B, Carosi M, Fabi A, Vidiri A, Koudriavtseva T, Conti L. A Predictive Value of Von Willebrand Factor for Early Response to Bevacizumab Therapy in Recurrent Glioma. *J. Neurooncol.* 2018 Jul; 138(3): 527a

60. Palermo B, Franzese O, Donna CD, Panetta M, Quintarelli C, Sperduti I, Gualtieri N, Foddai ML, Proietti E, Ferraresi V, Ciliberto G, Nistico P. Antigen-Specificity and DTIC before Peptide-Vaccination Differently Shape Immune-Checkpoint Expression Pattern, Anti-Tumor Functionality and TCR Repertoire in Melanoma Patients. *Oncoimmunology.* 2018 Sep 11; 7(12): e1465163a

61. Pallocca M, Goeman F, De Nicola F, Melucci E, Sperati F, Terrenato I, Pizzuti L, Casini B, Gallo E, Amoreo CA, Vici P, Di

Lauro L, Buglioni S, Diodoro MG, Pescarmona E, Mazzotta M, Barba M, Fanciulli M, De Maria R, Ciliberto G, Maugeri-Sacca M. Coexisting YAP Expression and TP53 Missense Mutations Delineates a Molecular Scenario Unexpectedly Associated with Better Survival Outcomes in Advanced Gastric Cancer. *J. Transl. Med.* 2018 Sep 4; 16(1): 247a

62. Pilotto S, Sperduti I, Leuzzi G, Chiappetta M, Mucilli F, Ratto GB, Lococo F, Filosso PL, Spaggiari L, Novello S, Milella M, Santo A, Scarpa A, Infante M, Tortora G, Facciolo F, Bria E. Prognostic Model for Resected Squamous Cell Lung Cancer: External Multicenter Validation and Propensity Score Analysis Exploring the Impact of Adjuvant and Neoadjuvant Treatment. *J. Thorac. Oncol.* 2018 Apr; 13(4): 568a

63. Pinelli S, Artini PG, Basile S, Obino MER, Sergiampietri C, Giannarelli D, Simi G, Cela V. Estrogen Treatment in Infertile Women with Premature Ovarian Insufficiency in Transitional Phase: A Retrospective Analysis. *J. Assist. Reprod. Genet.* 2018 Mar;

64. Pizzuti L, Sergi D, Mandoj C, Antoniani B, Sperati F, Chirico A, Di Lauro L, Valle M, Garofalo A, Vizza E, Corrado G, Tomao F, Rinaldi M, Carpano S, Maugeri-Sacca M, Conti L, Digiesi G, Marchetti P, De Maria R, Giordano A, Barba M, Carosi MA, Vici P. GLUT 1 Receptor Expression and Circulating Levels of Fasting Glucose in High Grade Serous Ovarian Cancer. *J. Cell. Physiol.* 2018 233(2): 1396a

65. Pizzuti L, Sergi D, Sperduti I, Lauro LD, Mazzotta M, Botti C, Izzo F, Marchetti L, Tomao S, Marchetti P, Natoli C, Grassadonia A, Gamucci T, Mentuccia L, Magnolfi E, Vaccaro A, Cassano A, Rossi E, Botticelli A, Sini V, Sarobba MG, Fabbri MA, Moscetti L, Astone A, Michelotti A, De Angelis C, Bertolini I, Angelini F, Ciliberto G, Maugeri-Sacca M, Giordano A, Barba M, Vici P. Body Mass Index in HER2-Negative Metastatic Breast Cancer Treated with First-Line Paclitaxel and Bevacizumab. *Cancer. Biol. Ther.* 2018 Apr 3; 19(4): 328a

66. Reda G, Fattizzo B, Cassin R, Mattiello V, Tonella T, Giannarelli D, Massari F, Cortelezzi A. Predictors of Atrial Fibrillation in Ibrutinib-Treated CLL Patients: A Prospective Study. *J. Hematol. Oncol.* 2018 Jun 11; 11(1): 79a

67. Reda G, Riva M, Fattizzo B, Cassin R, Giannarelli D, Pennisi M, Freyrie A, Cairoli R, Molteni A, Cortelezzi A. Bone Marrow Fibrosis and Early Hematological Response as Predictors of Poor Outcome in Azacitidine Treated High Risk-Patients with Myelodysplastic Syndromes Or Acute Myeloid Leukemia. *Semin. Hematol.* 2018 Oct; 55(4): 202a

68. Russo M, Villani V, Taga A, Genovese A, Terrenato I, Manzoni GC, Servadei F, Torelli P, Pace A. Headache as a Presenting Symptom of Glioma: A Cross-Sectional Study. *Cephalalgia.* 2018 Apr; 38(4): 730a

69. Telera S, Pompili A, Crispo F, Giovannetti M, Pace A, Villani V, Fabi A, Sperduti I, Raus L. Kyphoplasty with Purified Silicone VK100 (Elastoplasty) to Treat Spinal Lytic Lesions in Cancer Patients: A Retrospective Evaluation of 41 Cases. *Clin. Neurol. Neurosurg.* 2018 Aug; 171: 184a

70. Terrenato I, Sperati F, Musicco F, Pozzi AF, di Turi A, Caterino M, de Lutio di Castelguidone E, Setola SV, Bellomi M, Neumaier CE, Conti L, Cigliana G, Merola R, Antenucci A, Orlandi G, Giordano A, Barba M, Canitano S. Iodixanol Versus Iopromide in Cancer Patients: Evidence from a Randomized Clinical Trial. *J. Cell. Physiol.* 2018 Mar; 233(3): 2572a

71. Torregiani G, Claroni C, Covotta M, Naccarato A, Canfora M, Giannarelli D, Grazi GL, Tribuzi S, Forastiere E. Impact of a Goal-Directed Fluid Therapy on Length of Hospital Stay and Costs of Hepatobiliarypancreatic Surgery: A Prospective Observational Study. *J. Comp. Eff. Res.* 2018 Nov 19;

72. Trestini I, Carbognin L, Sperduti I, Bonaiuto C, Auriemma A, Melisi D, Salvatore L, Bria E, Tortora G. Prognostic Impact of Early Nutritional Support in Patients Affected by Locally Advanced and Metastatic Pancreatic Ductal Adenocarcinoma Undergoing Chemotherapy. *Eur. J. Clin. Nutr.* 2018 May; 72(5): 772a

73. Vennarecci G, Ferraro D, Tudisco A, Sandri GBL, Guglielmo N, Berardi G, Sperduti I, Ettorre GM. The ALPPS Procedure: Hepatocellular Carcinoma as a Main Indication. an Italian Single-Center Experience. *Updates Surg.* 2018 Sep 25;

# CLINICAL PATHOLOGY UNIT

*Head: Laura Conti, MD, PhD*


## STAFF

| |
|---|
| Antenucci A., BS |
| Cigliana G., BS |
| Cochi S, BS |
| Cordone I., MD, PhD |
| D'Alessandro M.G., BS |
| Digiesi G., MD |
| Mandoj C., BS |
| Martayan A., BS |
| Masi S., BS, PhD |
| Merola R., BS |
| Orlandi G., BS |
| Rosito I., BS |
| Vercillo G., MD |

| Technicians |
|---|
| Fontinovo R., Coordinator |
| Ascani R. |
| Attanasio M. |
| Autullo L. |
| De Bellis F. |
| Del Carlo C. |
| Giommi S. |
| Lattanzio C. |
| Pasquale A. |
| Pisani S. |
| Spinosa P. |
| Preziosi E., Administrative Collaborator |

Dr. Conti is Professor of the School of Medicine at "La Sapienza" University of Rome and of the post graduate Specialization Course in Clinical Pathology and teaching at second level Master in Pediatric Hematology .
She is a member of the Scientific Societies SISET, ELAS and Regional Delegate of the SIBIOC. She has participated as invited speaker to numerous national and international meetings and has been the principal investigator and/or coordinator of studies granted by scientific organizations, author of numerous papers published in international journals and co-editor of 5 volumes of Medicine.

## Mission

Clinical Pathology performs laboratory biological tests using the most modern techniques of investigation, that contribute to the clinical management of oncologic patients submitted to conventional and experimental therapies.

The Unit significantly supports activities for clinical trials and is involved in the development of an Institutional Biobank as a strategic link between clinical and research activities. The research program is focused on the identification and validation of cancer-related molecular targets, the utilization of new technical approaches for tumor diagnosis, prognosis and monitoring in the context of innovative cancer therapies, for the best bench-to-bedside clinical research application.
The Clinical Pathology has already been certified with a UNI EN ISO 9001:2008 and is now transitioning to ISO 9001:2015.

## Clinical Activities

In 2018, about 1,000,000 examinations were carried out return of 4.000.000 Euro.

### Onco-haematology

Innovative activities include the Primary Central Nervous System Lymphoma diagnosis by flow cytometry (FC) through disaggregation of a single brain stereotactic core biopsy for a better classification and management of brain lesions; leptomeningeal metastasis diagnosis and monitoring by cerebrospinal fluid FC and Minimal Residual Disease assessment in Multiple Myeloma by an original FC strategy of analysis based on intra-cytoplasmic immunoglobulin (cy-Ig) light chains ratio evaluated on patient-specific plasma cells immune profile. More recently the FC studies include an innovative antibodies combination for MM MRD assessment in patients undergoing anti-CD38 (daratumumab) treatment.

### Molecular Diagnostics

Liquid biopsy
In Non Small Cell Lung Carcinoma (NSCLC) patients liquid biopsy allows to identify patients whose tumors have specific EGFR mutations, thus making them eligible for EGFR-targeted therapies (e.g. erlotinib). Liquid biopsy in these patients is also a valuable tool for the monitoring of disease progression and for the detection of mechanisms of resistance to EGFR-targeted therapies, e.g. EGFR T790M mutation. The early detection of T790M mutation is of great clinical value for switching to 3rd generation therapies (e.g. osimertinib - Tagrisso). The latter has been also recently approved by FDA as first-line treatment for EGFR+ NSCLC patients.

### Hereditary Cancer syndromes (HCS)

Genetic testing with NGS technology on the genes associated with the most frequent HCS such as: Lynch syndrome (LS), Hereditary Breast and Ovary Cancer syndrome (HBOC), APC-associated polyposis and MUTYH-associated polyposis (AAP and MAP) and Multiple Endocrine Neoplasia syndrome type 1 and type 2 (MEN1 and MEN2). Moreover, in selected cases, a pan-hereditary cancer panel (HCS - Sophia Genetics) with 27 cancer-associated genes will be used. As to Hereditary Colorectal Cancer (HCC), a custom gene panel has been developed including POLE, POLD1, NTHL1, MSH3, BMPR1A, GREM1 and SMAD4 genes and been will be used for patients with diagnosis suspicion of HCC and no mutations in the genes included in the above-mentioned HCS panel.

### Pheochromocytoma and Paraganglioma

Pheochromocytoma and paraganglioma are rare tumors that arise from neural crest tissue: pheochromocytoma forms in the adrenal medulla whereas paragangliomas form outside the adrenal gland. Certain inherited disorders increase the risk of both tumors: MEN2, von Hippel-Lindau (VHL), Neurofibromatosis type 1 (NF1) and Hereditary Paraganglioma Syndrome. According to the diagnosis suspicion of either of the above-mentioned syndromes genetics testing of the specific disease-related genes will be performed.

### Cytogenetics

The broad applications in oncohaematology are: identification of specific chromosome abnormalities, monitoring disease progression and the success of therapy and bone marrow transplantation (PDTA Leucemia Acuta, PDTA Mieloma Multiplo, PDTA Leucemia Mieloide Cronica).
Besides, we search for actionable genetic abnormalities to improve the prognosis of sarcoma patients (PDTA Sarcomi).

## Research Activities

**Diagnostic harmonization initiative on Multiple Myeloma for Gruppo Laziale Mieloma Multiplo.**
PI Cordone I
The project aims to reach a consensus among regional laboratories specialized on onco-haematology diagnosis regarding the flow cytometry antibodies panel, data analysis and clinical report for Multiple Myeloma diagnosis and monitoring.
The network is also focusing on the positive selection of the plasma cell population by immune-magnetic beads separation, for a better assessment of the cytogenetic profile in plasma cell disorders.

**Role of Che-1 in transgenic mouse model of Multiple Myeloma**
PI Cigliana G
In collaboration with the SAFU laboratory, we investigated the role of Che-1, a Rna binding protein witch is involved in the control of transcription and cellular proliferation by regulating the state of the chromatin and by increasing its accessibility in Multiple Myeloma (MM). In particular we performed Serum Protein Electrophoresis (SPEP) to detect the levels of immunoglobulins in serum of the Vk*Myc transgenic mouse model, which, through activating c-Myc oncogene in maturing B cells, recapitulates the pathogenesis and clinical manifestations of human MM, including progression from MGUS to plasma cell expansions (Chesi et al.; Cancer Cell 2008). At this purpose CD138+ neoplastic cells were isolated from the bone marrow (BM) of these mice and manipulated for knockdown of Che1 by siRna and transplanted into 5 recipient wild-type mice for each group. The delay in disease progression in Che-1 depleted MM cells, it was been recognize by analyzing the levels of immunoglobulins in murine serum, as a distinct band (M-spike).

**Cost/Effectiveness evaluation of three different strategies in preventing transient hypocalcaemia after total thyroidectomy**
PI Digiesi G
A multicenter prospective randomized study out at the Department of Otolaryngology Head and Neck Surgery at the Department of Otolaryngology of the Reggio Emilia Hospital, was carried from December 2016 until June 2018. Primary endpoint of the study was to identify the best among three different strategies in terms of cost/effectiveness to manage transient post-surgical hypocalcaemia, in order to safely discharge the patient, limiting the time of hospitalization. Secondary endpoints were to evaluate:the efficacy of 3-hours post-operative plasmatic iPTH as early indicator of post-surgical hypocalcemia the efficacy of serum calcium and ionized calcium as early indicators of post-surgical hypocalcemia 24 and 48 hours after total thyroidectomy.

**Upper extremity venous thrombosis in cancer patients with peripherally inserted central inserted catheters**
PI Conti L
Symptomatic PICC related deep venous Thrombosis (DVT) are frequent in cancer patients receiving chemotherapy. In collaboration with the Vascular Access Management Team we conducted a retrospective cohort study in cancer patients who underwent PICC placement for the administration of chemotherapy to evaluate the incidence of upper extremity venous thrombosis (UEVT) and establish the most predictive risk factors for the development of PICC-related thrombosis in cancer patients during chemotherapic treatment, for the future design of an integrated care pathway (ICT) that could be used to prevent thrombotic events. All patients were followed for a minimum of 6 months after PICC insertion, unless they died during this period. Factors previously associated with catheter-related thrombosis, including side of catheter placement, tip location, tumor type, inherited and acquired thrombophilia and environmental factors have been evaluated.

**Pilot study: validation of the use of PIVKA-II serum test in monitoring progression of Hepatocellular Carcinoma (HCC) in liver transplant candidate patients. Stratification of patients with increased risk of HCC recurrence after liver transplantation. Prospective study**
PI Digiesi G
PIVKA-II test is able to predict the most aggressive HCC forms. The aim of the study is to show if this test will improve the early comprehension of the HCC forms that show a higher recurrence risk in patients selected

for liver transplant. The project is in progress, at present, we enrolled seven patients. Four patients with diagnosis of HCC and cirrhosis, and three patients with diagnosis of cirrhosis with HCC.

**Implementing a Biobank of Biological Fluid at IRE supported by Scientific Advisory Board**

PI Conti L

A "Biobank" refers to a standardized collection of human biological materials, including tissues, blood and blood products, DNA and medical data collected and stored with appropriate informed consent.

Biobanking is actually recognized as a basic enabling tool for cancer research, with the future of molecular and translational research relying heavily on the availability of high quality biospecimens linked to data on actual clinical outcomes. There are several benefits to having a consolidated approach to biobanking, including increased awareness of specimen availability, increased access for researchers from larger pools of samples, increased quality and consistency of samples from standardized collection procedures, and increased efficiencies.

The Anatomy Pathology Division and the Clinical Pathology Unit of the Regina Elena National Cancer Institute are currently engaged in establishing and developing an Istitutional Biobank (BBIRE). The main function of the biobank is to collect tissue (T) and body fluids (LB) samples in accordance with standardized criteria and cryoconserve them in order to provide biological material for approved cancer research projects. The number of samples collected to date is 11350.

BBIRE includes a Steering Committee and an Operating Group. A broad Informed consent has been drawn up, submitted to the Ethics Committee, subsequently validated and added to the medical record.

Since 2016 IFO have become a European Referral Center for rare tumors (EURACAN), the BBIRE is involved in the collection of biological samples of rare tumors, such as sarcoma, thymoma, and neuroendocrine tumours. Moreover the BBIRE collaborate with ACC for translational research projects. The BBIRE is a member of the Biobanking and BioMolecular resources Research Infrastructure - European Research Infrastructure Consortium known as "BBMRI-ERIC".

**Radio-induced modifications of lymphoid subpopulations involved in resistance and escape mechanisms to the treatment of localized prostate cancer.**

PI Sanguineti G

Aim of the study is to evaluate the effect of radiotherapy (RT) on immuno-regulatory B and T lymphocyte subpopulations (Breg and Treg) and plasma cells and possible correlations with the clinical course of the disease and acute and late toxicity.

The flow cytometry characterization developed in our laboratory allowed the identification of Treg and Breg peripheral blood subpopulations through the acquisition of a high number (> 5000) of regulatory cells using innovative acquisition and analysis strategies. 14 patients were analyzed before treatment (T0), 3 hours after the first RT session (T1), after an average dose of 24 Gy (T2) and after the last RT session (T3). Analysis of the regulatory sub-populations modifications are ongoing.

## *Publications*


1. Allegretti M, Casini B, Mandoj C, Benini S, Alberti L, Novello M, Melucci E, Conti L, Covello R, Pescarmona E, Milano GM, Annovazzi A, Anelli V, Ferraresi V, Biagini R, Giacomini P. Precision Diagnostics of Ewing's Sarcoma by Liquid Biopsy: Circulating EWS-FLI1 Fusion Transcripts. *Ther. Adv. Med. Oncol.* 2018 Jun 1; 10: 1758835918774337a

2. Allegretti M, Fabi A, Buglioni S, Martayan A, Conti L, Pescarmona E, Ciliberto G, Giacomini P. Tearing Down the Walls: FDA Approves Next Generation Sequencing (NGS) Assays for Actionable Cancer Genomic Aberrations. *J. Exp. Clin. Cancer Res.* 2018 Mar 5; 37(1): 47a

3. Bailey MH, Tokheim C, Porta-Pardo E, Sengupta S, Bertrand D, Weerasinghe A, Colaprico A, Wendl MC, Kim J, Reardon B, Ng PK, Jeong KJ, Cao S, Wang Z, Gao J, Gao Q, Wang F, Liu EM, Mularoni L, Rubio-Perez C, Nagarajan N, Cortes-Ciriano I, Zhou DC, Liang WW, Hess JM, Yellapantula VD, Tamborero D, Gonzalez-Perez A, Suphavilai C, Ko JY, Khurana E, Park PJ, Van Allen EM, Liang H, MC3 Working Group, Cancer Genome Atlas Research Network, Lawrence MS, Godzik A, Lopez-Bigas N, Stuart J, Wheeler D, Getz G, Chen K, Lazar AJ, Mills GB, Karchin R, Ding L, Merola R (c), Antenucci A(c). Comprehensive Characterization of Cancer Driver Genes and Mutations. *Cell.* 2018 Apr 5; 173(2): 371a

4. Barnabei A, Strigari L, Persichetti A, Baldelli R, Rizza L, Annoscia C, Lauretta R, Cigliana G, Barba M, De Leo A, Appetecchia M, Torino F. Indirect Basal Metabolism Estimation in Tailoring Recombinant Human TSH Administration in Patients Affected by Differentiated Thyroid Cancer: A Hypothesis-Generating Study. *Front. Endocrinol. (Lausanne)*. 2018 Feb 15; 9: 37a

5. Berger AC, Korkut A, Kanchi RS, Hegde AM, Lenoir W, Liu W, Liu Y, Fan H, Shen H, Ravikumar V, Rao A, Schultz A, Li X, Sumazin P, Williams C, Mestdagh P, Gunaratne PH, Yau C, Bowlby R, Robertson AG, Tiezzi DG, Wang C, Cherniack AD, Godwin AK, Kuderer NM, Rader JS, Zuna RE, Sood AK, Lazar AJ, Ojesina AI, Adebamowo C, Adebamowo SN, Baggerly KA, Chen TW, Chiu HS, Lefever S, Liu L, MacKenzie K, Orsulic S, Roszik J, Shelley CS, Song Q, Vellano CP, Wentzensen N, Cancer Genome Atlas Research Network, Weinstein JN, Mills GB, Levine DA, Akbani R. Merola R (c), Antenucci A(c). A Comprehensive Pan-Cancer Molecular Study of Gynecologic and Breast Cancers. *Cancer Cell*. 2018 Apr 9; 33(4): 690a

6. Campbell JD, Yau C, Bowlby R, Liu Y, Brennan K, Fan H, Taylor AM, Wang C, Walter V, Akbani R, Byers LA, Creighton CJ, Coarfa C, Shih J, Cherniack AD, Gevaert O, Prunello M, Shen H, Anur P, Chen J, Cheng H, Hayes DN, Bullman S, Pedamallu CS, Ojesina AI, Sadeghi S, Mungall KL, Robertson AG, Benz C, Schultz A, Kanchi RS, Gay CM, Hegde A, Diao L, Wang J, Ma W, Sumazin P, Chiu HS, Chen TW, Gunaratne P, Donehower L, Rader JS, Zuna R, Al-Ahmadie H, Lazar AJ, Flores ER, Tsai KY, Zhou JH, Rustgi AK, Drill E, Shen R, Wong CK, Cancer Genome Atlas Research Network, Stuart JM, Laird PW, Hoadley KA, Weinstein JN, Peto M, Pickering CR, Chen Z, Van Waes C. Merola R (c), Antenucci A(c). Genomic, Pathway Network, and Immunologic Features Distinguishing Squamous Carcinomas. *Cell. Rep.* 2018 Apr 3; 23(1): 194a

7. Chen H, Li C, Peng X, Zhou Z, Weinstein JN, Cancer Genome Atlas Research Network, Liang H. Merola R (c), Antenucci A(c). A Pan-Cancer Analysis of Enhancer Expression in nearly 9000 Patient Samples. *Cell*. 2018 Apr 5; 173(2): 386a

8. Chiu HS, Somvanshi S, Patel E, Chen TW, Singh VP, Zorman B, Patil SL, Pan Y, Chatterjee SS, Cancer Genome Atlas Research Network, Sood AK, Gunaratne PH, Sumazin P. Merola R (c), Antenucci A(c). Pan-Cancer Analysis of lncRNA Regulation Supports their Targeting of Cancer Genes in each Tumor Context. *Cell. Rep.* 2018 Apr 3; 23(1): 297a

9. Cigliana G, Gulli F, Napodano C, Pocino K, De Santis E, Colacicco L, Cordone I, Conti L, Basile U. Serum Free Light Chain Quantitative Assays: Dilemma of a Biomarker. *J. Clin. Lab. Anal*. 2018 Feb;32(2)

10. Ding L, Bailey MH, Porta-Pardo E, Thorsson V, Colaprico A, Bertrand D, Gibbs DL, Weerasinghe A, Huang KL, Tokheim C, Cortes-Ciriano I, Jayasinghe R, Chen F, Yu L, Sun S, Olsen C, Kim J, Taylor AM, Cherniack AD, Akbani R, Suphavilai C, Nagarajan N, Stuart JM, Mills GB, Wyczalkowski MA, Vincent BG, Hutter CM, Zenklusen JC, Hoadley KA, Wendl MC, Shmulevich L, Lazar AJ, Wheeler DA, Getz G, Cancer Genome Atlas Research Network, Merola R (c), Antenucci A(c). Perspective on Oncogenic Processes at the End of the Beginning of Cancer Genomics. *Cell*. 2018 Apr 5; 173(2): 305a

11. Ellrott K, Bailey MH, Saksena G, Covington KR, Kandoth C, Stewart C, Hess J, Ma S, Chiotti KE, McLellan M, Sofia HJ, Hutter C, Getz G, Wheeler D, Ding L, MC3 Working Group, Cancer Genome Atlas Research Network. Merola R (c), Antenucci A(c). Scalable Open Science Approach for Mutation Calling of Tumor Exomes using Multiple Genomic Pipelines. *Cell. Syst*. 2018 Mar 28; 6(3): 271a

12. Gao Q, Liang WW, Foltz SM, Mutharasu G, Jayasinghe RG, Cao S, Liao WW, Reynolds SM, Wyczalkowski MA, Yao L, Yu L, Sun SQ, Fusion Analysis Working Group, Cancer Genome Atlas Research Network, Chen K, Lazar AJ, Fields RC, Wendl MC, Van Tine BA, Vij R, Chen F, Nykter M, Shmulevich I, Ding L. Merola R (c), Antenucci A(c). Driver Fusions and their Implications in the Development and Treatment of Human Cancers. *Cell. Rep.* 2018 Apr 3; 23(1): 227a

13. Ge Z, Leighton JS, Wang Y, Peng X, Chen Z, Chen H, Sun Y, Yao F, Li J, Zhang H, Liu J, Shriver CD, Hu H, Cancer Genome Atlas Research Network, Piwnica-Worms H, Ma L, Liang H. Merola R (c), Antenucci A(c). Integrated Genomic Analysis of the Ubiquitin Pathway Across Cancer Types. *Cell. Rep.* 2018 Apr 3; 23(1): 213a

14. Giuffrida MC, Cigliana G, Spoto G. Ultrasensitive Detection of Lysozyme in Droplet-Based Microfluidic Devices. *Biosens. Bioelectron*. 2018 May 1; 104: 8a

15. Hoadley KA, Yau C, Hinoue T, Wolf DM, Lazar AJ, Drill E, Shen R, Taylor AM, Cherniack AD, Thorsson V, Akbani R, Bowlby R, Wong CK, Wiznerowicz M, Sanchez-Vega F, Robertson AG, Schneider BG, Lawrence MS, Noushmehr H, Malta TM, Cancer Genome Atlas Network, Stuart JM, Benz CC, Laird PW. Merola R (c), Antenucci A(c). Cell-of-Origin Patterns Dominate the Molecular Classification of 10,000 Tumors from 33 Types of Cancer. *Cell.* 2018 Apr 5; 173(2): 291a

16. Huang KL, Mashl RJ, Wu Y, Ritter DI, Wang J, Oh C, Paczkowska M, Reynolds S, Wyczalkowski MA, Oak N, Scott AD, Krassowski M, Cherniack AD, Houlahan KE, Jayasinghe R, Wang LB, Zhou DC, Liu D, Cao S, Kim YW, Koire A, McMichael JF, Hucthagowder V, Kim TB, Hahn A, Wang C, McLellan MD, Al-Mulla F, Johnson KJ, Cancer Genome Atlas Research Network, Lichtarge O, Boutros PC, Raphael B, Lazar AJ, Zhang W, Wendl MC, Govindan R, Jain S, Wheeler D, Kulkarni S, Dipersio JF, Reimand J, Meric-Bernstam F, Chen K, Shmulevich I, Plon SE, Chen F, Ding L. Merola R (c), Antenucci A(c). Pathogenic Germline Variants in 10,389 Adult Cancers. *Cell.* 2018 Apr 5; 173(2): 355a

17. Jayasinghe RG, Cao S, Gao Q, Wendl MC, Vo NS, Reynolds SM, Zhao Y, Climente-Gonzalez H, Chai S, Wang F, Varghese R, Huang M, Liang WW, Wyczalkowski MA, Sengupta S, Li Z, Payne SH, Fenyo D, Miner JH, Walter MJ, Cancer Genome Atlas Research Network, Vincent B, Eyras E, Chen K, Shmulevich I, Chen F, Ding L. Merola R (c), Antenucci A(c). Systematic Analysis of Splice-Site-Creating Mutations in Cancer. *Cell.Rep.* 2018 Apr 3; 23(1): 270a

18. Kahles A, Lehmann KV, Toussaint NC, Huser M, Stark SG, Sachsenberg T, Stegle O, Kohlbacher O, Sander C, Cancer Genome Atlas Research Network, Ratsch G. Merola R (c), Antenucci A(c). Comprehensive Analysis of Alternative Splicing Across Tumors from 8,705 Patients. *Cancer.Cell.* 2018 Aug 13; 34(2): 211a

19. Knijnenburg TA, Wang L, Zimmermann MT, Chambwe N, Gao GF, Cherniack AD, Fan H, Shen H, Way GP, Greene CS, Liu Y, Akbani R, Feng B, Donehower LA, Miller C, Shen Y, Karimi M, Chen H, Kim P, Jia P, Shinbrot E, Zhang S, Liu J, Hu H, Bailey MH, Yau C, Wolf D, Zhao Z, Weinstein JN, Li L, Ding L, Mills GB, Laird PW, Wheeler DA, Shmulevich I, Cancer Genome Atlas Research Network, Monnat RJ,Jr, Xiao Y, Wang C. Merola R (c), Antenucci A(c). Genomic and Molecular Landscape of DNA Damage Repair Deficiency Across the Cancer Genome Atlas. *Cell.Rep.* 2018 Apr 3; 23(1): 239a

20. Korkut A, Zaidi S, Kanchi RS, Rao S, Gough NR, Schultz A, Li X, Lorenzi PL, Berger AC, Robertson G, Kwong LN, Datto M, Roszik J, Ling S, Ravikumar V, Manyam G, Rao A, Shelley S, Liu Y, Ju Z, Hansel D, de Velasco G, Pennathur A, Andersen JB, O'Rourke CJ, Ohshiro K, Jogunoori W, Nguyen BN, Li S, Osmanbeyoglu HU, Ajani JA, Mani SA, Houseman A, Wiznerowicz M, Chen J, Gu S, Ma W, Zhang J, Tong P, Cherniack AD, Deng C, Resar L, Cancer Genome Atlas Research Network, Weinstein JN, Mishra L, Akbani R. Merola R (c), Antenucci A(c). A Pan-Cancer Analysis Reveals High-Frequency Genetic Alterations in Mediators of Signaling by the TGF-Beta Superfamily. *Cell.Syst.* 2018 Oct 24; 7(4): 422a

21. Liu J, Lichtenberg T, Hoadley KA, Poisson LM, Lazar AJ, Cherniack AD, Kovatich AJ, Benz CC, Levine DA, Lee AV, Omberg L, Wolf DM, Shriver CD, Thorsson V, Cancer Genome Atlas Research Network, Hu H. Merola R (c), Antenucci A(c). An Integrated TCGA Pan-Cancer Clinical Data Resource to Drive High-Quality Survival Outcome Analytics. *Cell.* 2018 Apr 5; 173(2): 400a

22. Liu Y, Sethi NS, Hinoue T, Schneider BG, Cherniack AD, Sanchez-Vega F, Seoane JA, Farshidfar F, Bowlby R, Islam M, Kim J, Chatila W, Akbani R, Kanchi RS, Rabkin CS, Willis JE, Wang KK, McCall SJ, Mishra L, Ojesina AI, Bullman S, Pedamallu CS, Lazar AJ, Sakai R, Cancer Genome Atlas Research Network, Thorsson V, Bass AJ, Laird PW. Merola R (c), Antenucci A(c). Comparative Molecular Analysis of Gastrointestinal Adenocarcinomas. *Cancer.Cell.* 2018 Apr 9; 33(4): 721a

23. Malta TM, Sokolov A, Gentles AJ, Burzykowski T, Poisson L, Weinstein JN, Kaminska B, Huelsken J, Omberg L, Gevaert O, Colaprico A, Czerwinska P, Mazurek S, Mishra L, Heyn H, Krasnitz A, Godwin AK, Lazar AJ, Cancer Genome Atlas Research Network, Stuart JM, Hoadley KA, Laird PW, Noushmehr H, Wiznerowicz M. Merola R (c), Antenucci A(c). Machine Learning Identifies Stemness Features Associated with Oncogenic Dedifferentiation. *Cell.* 2018 Apr 5; 173(2): 338a

24. Mandoj C, Pizzuti L, Sergi D, Sperduti I, Mazzotta M, Di Lauro L, Amodio A, Carpano S, Di Benedetto A, Botti C,

Ferranti F, Antenucci A, D'Alessandro MG, Marchetti P, Tomao S, Sanguineti G, Giordano A, Maugeri-Sacca M, Ciliberto G, Conti L, Vici P, Barba M. Observational Study of Coagulation Activation in Early Breast Cancer: Development of a Prognostic Model Based on Data from the Real World Setting. *J. Transl. Med.* 2018 May 16; 16(1): 129a

25. Pace A, Mandoj C, Antenucci A, Villani V, Sperduti I, Casini B, Carosi M, Fabi A, Vidiri A, Koudriavtseva T, Conti L. A Predictive Value of Von Willebrand Factor for Early Response to Bevacizumab Therapy in Recurrent Glioma. *J. Neurooncol.* 2018 Jul; 138(3): 527a

26. Peng X, Chen Z, Farshidfar F, Xu X, Lorenzi PL, Wang Y, Cheng F, Tan L, Mojumdar K, Du D, Ge Z, Li J, Thomas GV, Birsoy K, Liu L, Zhang H, Zhao Z, Marchand C, Weinstein JN, Cancer Genome Atlas Research Network, Bathe OF, Liang H. Merola R (c), Antenucci A(c). Molecular Characterization and Clinical Relevance of Metabolic Expression Subtypes in Human Cancers. *Cell. Rep.* 2018 Apr 3; 23(1): 255a

27. Pizzuti L, Sergi D, Mandoj C, Antoniani B, Sperati F, Chirico A, Di Lauro L, Valle M, Garofalo A, Vizza E, Corrado G, Tomao F, Rinaldi M, Carpano S, Maugeri-Sacca M, Conti L, Digiesi G, Marchetti P, De Maria R, Giordano A, Barba M, Carosi MA, Vici P. GLUT 1 Receptor Expression and Circulating Levels of Fasting Glucose in High Grade Serous Ovarian Cancer. *J. Cell. Physiol.* 2018 233(2): 1396a

28. Ricketts CJ, De Cubas AA, Fan H, Smith CC, Lang M, Reznik E, Bowlby R, Gibb EA, Akbani R, Beroukhim R, Bottaro DP, Choueiri TK, Gibbs RA, Godwin AK, Haake S, Hakimi AA, Henske EP, Hsieh JJ, Ho TH, Kanchi RS, Krishnan B, Kwiatkowski DJ, Lui W, Merino MJ, Mills GB, Myers J, Nickerson ML, Reuter VE, Schmidt LS, Shelley CS, Shen H, Shuch B, Signoretti S, Srinivasan R, Tamboli P, Thomas G, Vincent BG, Vocke CD, Wheeler DA, Yang L, Kim WY, Robertson AG, Cancer Genome Atlas Research Network, Spellman PT, Rathmell WK, Linehan WM. Merola R (c), Antenucci A(c). The Cancer Genome Atlas Comprehensive Molecular Characterization of Renal Cell Carcinoma. *Cell. Rep.* 2018 Apr 3; 23(1): 313a

29. Saltz J, Gupta R, Hou L, Kurc T, Singh P, Nguyen V, Samaras D, Shroyer KR, Zhao T, Batiste R, Van Arnam J, Cancer Genome Atlas Research Network, Shmulevich I, Rao AUK, Lazar AJ, Sharma A, Thorsson V. Merola R (c), Antenucci A(c). Spatial Organization and Molecular Correlation of Tumor-Infiltrating Lymphocytes using Deep Learning on Pathology Images. *Cell. Rep.* 2018 Apr 3; 23(1): 181a

30. Sanchez-Vega F, Mina M, Armenia J, Chatila WK, Luna A, La KC, Dimitriadoy S, Liu DL, Kantheti HS, Saghafinia S, Chakravarty D, Daian F, Gao Q, Bailey MH, Liang WW, Foltz SM, Shmulevich I, Ding L, Heins Z, Ochoa A, Gross B, Gao J, Zhang H, Kundra R, Kandoth C, Bahceci I, Dervishi L, Dogrusoz U, Zhou W, Shen H, Laird PW, Way GP, Greene CS, Liang H, Xiao Y, Wang C, Iavarone A, Berger AH, Bivona TG, Lazar AJ, Hammer GD, Giordano T, Kwong LN, McArthur G, Huang C, Tward AD, Frederick MJ, McCormick F, Meyerson M, Cancer Genome Atlas Research Network, Van Allen EM, Cherniack AD, Ciriello G, Sander C, Schultz N. Merola R (c), Antenucci A(c). Oncogenic Signaling Pathways in the Cancer Genome Atlas. *Cell.* 2018 Apr 5; 173(2): 321a

31. Schaub FX, Dhankani V, Berger AC, Trivedi M, Richardson AB, Shaw R, Zhao W, Zhang X, Ventura A, Liu Y, Ayer DE, Hurlin PJ, Cherniack AD, Eisenman RN, Bernard B, Grandori C, Cancer Genome Atlas Network. Merola R (c), Antenucci A(c). Pan-Cancer Alterations of the MYC Oncogene and its Proximal Network Across the Cancer Genome Atlas. *Cell. Syst.* 2018 Mar 28; 6(3): 282a

32. Seiler M, Peng S, Agrawal AA, Palacino J, Teng T, Zhu P, Smith PG, Cancer Genome Atlas Research Network, Buonamici S, Yu L. Merola R (c), Antenucci A(c). Somatic Mutational Landscape of Splicing Factor Genes and their Functional Consequences Across 33 Cancer Types. *Cell. Rep.* 2018 Apr 3; 23(1): 282a

33. Taylor AM, Shih J, Ha G, Gao GF, Zhang X, Berger AC, Schumacher SE, Wang C, Hu H, Liu J, Lazar AJ, Cancer Genome Atlas Research Network, Cherniack AD, Beroukhim R, Meyerson M. Merola R (c), Antenucci A(c). Genomic and Functional Approaches to Understanding Cancer Aneuploidy. *Cancer. Cell.* 2018 Apr 9; 33(4): 676a

34. Terrenato I, Sperati F, Musicco F, Pozzi AF, di Turi A, Caterino M, de Lutio di Castelguidone E, Setola SV, Bellomi M, Neumaier CE, Conti L, Cigliana G, Merola R, Antenucci A, Orlandi G, Giordano A, Barba M, Canitano S. Iodixanol Versus Iopromide in Cancer Patients: Evidence from a Randomized Clinical Trial. *J. Cell. Physiol.* 2018 Mar; 233(3): 2572a

35. Thorsson V, Gibbs DL, Brown SD, Wolf D, Bortone DS, Ou Yang TH, Porta-Pardo E, Gao GF, Plaisier CL, Eddy JA, Ziv E, Culhane AC, Paull EO, Sivakumar IKA, Gentles AJ, Malhotra R, Farshidfar F, Colaprico A, Parker JS, Mose LE, Vo NS, Liu J, Liu Y, Rader J, Dhankani V, Reynolds SM, Bowlby R, Califano A, Cherniack AD, Anastassiou D, Bedognetti D, Rao A, Chen K, Krasnitz A, Hu H, Malta TM, Noushmehr H, Pedamallu CS, Bullman S, Ojesina AI, Lamb A, Zhou W, Shen H, Choueiri TK, Weinstein JN, Guinney J, Saltz J, Holt RA, Rabkin CE, Cancer Genome Atlas Research Network, Lazar AJ, Serody JS, Demicco EG, Disis ML, Vincent BG, Shmulevich L. Merola R (c), Antenucci A(c). The Immune Landscape of Cancer. *Immunity.* 2018 Apr 17; 48(4): 812a

36. Wang Y, Xu X, Maglic D, Dill MT, Mojumdar K, Ng PK, Jeong KJ, Tsang YH, Moreno D, Bhavana VH, Peng X, Ge Z, Chen H, Li J, Chen Z, Zhang H, Han L, Du D, Creighton CJ, Mills GB, Cancer Genome Atlas Research Network, Camargo F, Liang H. Merola R (c), Antenucci A(c). Comprehensive Molecular Characterization of the Hippo Signaling Pathway in Cancer. *Cell.Rep.* 2018 Oct 30; 25(5): 1304a

37. Wang Z, Yang B, Zhang M, Guo W, Wu Z, Wang Y, Jia L, Li S, Cancer Genome Atlas Research Network, Xie W, Yang D. Merola R (c), Antenucci A(c). LncRNA Epigenetic Landscape Analysis Identifies EPIC1 as an Oncogenic lncRNA that Interacts with MYC and Promotes Cell-Cycle Progression in Cancer. *Cancer.Cell.* 2018 Apr 9; 33(4): 706a

38. Way GP, Sanchez-Vega F, La K, Armenia J, Chatila WK, Luna A, Sander C, Cherniack AD, Mina M, Ciriello G, Schultz N, Cancer Genome Atlas Research Network, Sanchez Y, Greene CS. Merola R (c), Antenucci A(c). Machine Learning Detects Pan-Cancer Ras Pathway Activation in the Cancer Genome Atlas. *Cell.Rep.* 2018 Apr 3; 23(1): 172a

# PATHOLOGY UNIT

*Head: Edoardo Pescarmona, MD*

## STAFF

| | |
|---|---|
| Mariantonia Carosi, M.D. Pathologist | Paola Canalini, Technical Coordinator |
| Renato Covello, M.D. Pathologist | Beatrice Casini, Technician |
| Maria Diodoro, M.D. Pathologist | Stefania Filippi, Technician |
| Ferdinando Marandino, M.D. Pathologist | Angela Lattanzi, Technician |
| Mirella Marino, M.D. Pathologist | Barbara Frollano, Technician |
| Letizia Perracchio, M.D. Pathologist | Sabrina Lori, Technician |
| Andrea Russo, M.D. Pathologist | Patrizia Palmarelli, Technician |
| Paolo Visca, M.D. Pathologist | Arianna Papadantonakis, Technician |
| Maria Benevolo, Biologist | Annarita Pennetti, Technician |
| Simonetta Buglioni, Biologist | Patrizia Scordati, Technician |

| Research fellowships |
|---|
| **Anna Di Benedetto, Biologist** |
| **Cristiana Ercolani, Biologist** |
| **Enzo Gallo, Biologist** |
| **Carla Azzurra Amoreo, Biologist** |

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| **Francesca Rollo, Biologist** |
| **Simona di Martino, Biologist (Biobank IRE)** |
| **Valentina Laquintana, Biologist (Biobank IRE)** |
| **Barbara Antoniani, Technician** |
| **Claudia Bonomo, Technician** |

## Mission

The Pathology Unit, which represents a pivotal hub for innovative diagnostic services and research programs, has the following missions :

- To provide the 'state of the art' in pathology, that is crucial for patients' care, allowing disease prevention and treatment in a comprehensive, coordinated and cost-effective manner.
- To implement the diagnostic expertise setting up novel molecular assays to be applied to diagnosis and care of tumours, facilitating collaborations with the other clinical units.
- To promote innovative scientific programs, spanning the spectrum from basic to translational disease-oriented research. The participation to multidisciplinary and multicentric research is an essential component of the overall clinical and research mission. Furthermore, as custodians of tumour tissue Biobank, an important role of the Pathology Unit research mission is the proper and authorized use of tumour tissue samples.

## Clinical Activity

In 2018 the clinical activities have included as a rule macroscopy and conventional histopathology on biopsy and surgical samples (surgical pathology), cytology on cytological samples (diagnostic cytology), and clinical necroscopy (autopsy). Furthermore, immunohistochemistry, FISH/SISH analysis, HPV detection a/o genotyping, and gene mutational status analysis (by NGS a/o real time PCR analysis) were also routinely performed. In 2018 surgical or biopsy samples from about 11.000 patients have been studied, encompassing the whole spectrum of the main human tumours (in particular urological, lung, breast, head & neck, and colorectal cancers). All cases of malignant tumours have been histologically typed and graded according to the more recent WHO classifications, and pathologically staged (pTNM) according to the latest TNM/UICC edition. Whenever required, ancillary (histochemistry, immunohistochemistry and molecular) studies were performed. In 2018 cytological samples from about 8.500 patients have been studied, including FNAC, effusions, urine and cervico—vaginal cytology. In 2018 about 20.000 tests of diagnostic immunohistochemistry have been performed, including mainly tumour immunohistological typing and assessment of tumour prognostic and/or predictive factors. In 2018 about 500 FISH/SISH tests have been performed, mainly in cases of breast and gastric carcinoma (HER2 gene), in cases of lung adenocarcinoma (ALK and ROS1 genes), and in selected cases of 'aggressive' B-cell lymphomas (Bcl2, Bcl6, and c-MYC genes), sarcomas, and primary CNS tumours. In 2018 the mutational status of about 1000 patients with lung adenocarcinomas, colorectal adenocarcinomas, metastatic melanoma, 'undefined' (THY3B) thyroid lesions, and GastroIntestinal Stromal Tumours (GIST) has been studied by a NGS procedure, mainly based on a panel of 22 different 'target' genes ('ONCOMINE'). Furthermore, in 2018 about 500 molecular tests for MGMT promoter gene metilation status and IDH1-IDH2 genes mutational status in primary CNS tumours, and MSI evaluation, mainly in colorectal cancer, have been performed.

## Research Activity

**Colorectal cancer.** We have investigated the role of deep sequencing and pathway-focused analysis in predicting patients survival in advanced colorectal cancer, and the clinical significance of EphB2 stem-related and EphA2 progression-related miRNA-based networks in colorectal cancer progression/evolution. In addition, we have also studied the immune profile of premalignant lesions in patients with Lynch syndrome.
**Gastric cancer.** We have studied the prognostic impact of the expression of the Hippo transducer TAZ in association with WNT pathway mutations in advanced

gastric cancer patients and, in the same setting, we have shown that the clinical significance of PDL1 is dependent on ARID1A mutations and ATM expression, and that coexisting YAP expression and TP53 missense mutations are associated with better survival.

**Breast cancer.** We have investigated the role of Akt down modulation induced by Vav1, and the role of stanniocalcin 2 expression in the outcome of breast cancer patients. Furthermore, we have shown that the expression of ID4 protein in breast cancer cells induces reprogramming of tumour-associated macrophages, and we have also studied the genomic profile and the implication for treatment of HER2 double-equivocal breast cancer cases.

**Lung cancer.** We have demonstrated that microRNA-128-3p-mediated depletion of Drosha promotes lung cancer cell migration, and that hMENA isoforms impact NSCLC patient outcome through fibronectin/beta1 integrin axis.

**Sarcomas.** We have studied the role of the histone deacetylase inhibitor ITF2357 in apoptosis and doxorubicin cytotoxicyty in preclinical models of human sarcomas, and the role of HMGA1/E2F1 axis and of NFkB pathways in liposarcoma progression and trabectidin resistance. Furthermore, we have demonstrated the presence of circulating EWS-FLI1 fusion transcripts in Ewing sarcoma.

**Gynecological tumours.** We have evaluated serum DNA integrity index as a potential molecular biomarker in endometrial cancer, and GLUT1 receptor expression and circulating levels of fasting glucose in high grade serous ovarian cancer. Furthermore, we have shown that endometrial cancer prognosis correlates with the expression of L1CAM and miR34a biomarkers.

**HPV related tumours.** We have investigated by cytology the HPV related anal lesions in individuals at increased risk for anal cancer, and have tested HPV on fine needle aspirates from cervical lymph node metastases of oropharyngeal squamous cell carcinoma or occult primary.

**Thymic epithelial tumours.** In the context of the TCGA research network we have investigated the integrated genomic landscape of thymic epithelial tumours.

**Central nervous system tumours.** We have shown that circulating microRNAs predict survival of patients with tumours of glial origin.

## Publications


1. Allegretti M, Casini B, Mandoj C, Benini S, Alberti L, Novello M, Melucci E, Conti L, Covello R, Pescarmona E, Milano GM, Annovazzi A, Anelli V, Ferraresi V, Biagini R, Giacomini P. Precision Diagnostics of Ewing's Sarcoma by Liquid Biopsy: Circulating EWS-FLI1 Fusion Transcripts. *Ther.Adv.Med.Oncol.* 2018 Jun 1; 10: 1758835918774337a

2. Allegretti M, Fabi A, Buglioni S, Martayan A, Conti L, Pescarmona E, Ciliberto G, Giacomini P. Tearing Down the Walls: FDA Approves Next Generation Sequencing (NGS) Assays for Actionable Cancer Genomic Aberrations. J.Exp.Clin. Cancer Res. 2018 Mar 5; 37(1): 47a

3. Bailey MH, Tokheim C, Porta-Pardo E, Sengupta S, Bertrand D, Weerasinghe A, Colaprico A, Wendl MC, Kim J, Reardon B, Ng PK, Jeong KJ, Cao S, Wang Z, Gao J, Gao Q, Wang F, Liu EM, Mularoni L, Rubio-Perez C, Nagarajan N, Cortes-Ciriano I, Zhou DC, Liang WW, Hess JM, Yellapantula VD, Tamborero D, Gonzalez-Perez A, Suphavilai C, Ko JY, Khurana E, Park PJ, Van Allen EM, Liang H, MC3 Working Group, Cancer Genome Atlas Research Network, Lawrence MS, Godzik A, Lopez-Bigas N, Stuart J, Wheeler D, Getz G, Chen K, Lazar AJ, Mills GB, Karchin R, Ding L, Marino M(c. Comprehensive Characterization of Cancer Driver Genes and Mutations. Cell. 2018 Apr 5; 173(2): 371a

4. Berger AC, Korkut A, Kanchi RS, Hegde AM, Lenoir W, Liu W, Liu Y, Fan H, Shen H, Ravikumar V, Rao A, Schultz A, Li X, Sumazin P, Williams C, Mestdagh P, Gunaratne PH, Yau C, Bowlby R, Robertson AG, Tiezzi DG, Wang C, Cherniack AD, Godwin AK, Kuderer NM, Rader JS, Zuna RE, Sood AK, Lazar AJ, Ojesina AI, Adebamowo C, Adebamowo SN, Baggerly KA, Chen TW, Chiu HS, Lefever S, Liu L, MacKenzie K, Orsulic S, Roszik J, Shelley CS, Song Q, Vellano CP, Wentzensen N, Cancer Genome Atlas Research Network, Weinstein JN, Mills GB, Levine DA, Akbani R. A Comprehensive Pan-Cancer Molecular Study of Gynecologic and Breast Cancers. Cancer.Cell. 2018 Apr 9; 33(4): 690a

5. Buglioni S, Melucci E, Sperati F, Pallocca M, Terrenato I, De Nicola F, Goeman F, Casini B, Amoreo CA, Gallo E, Diodoro MG, Pescarmona E, Vici P, Sergi D, Pizzuti L, Di Lauro L, Mazzotta M, Barba M, Fanciulli M, Vitale I, De Maria

R, Ciliberto G, Maugeri-Saccà M. The Clinical Significance of PD-L1 in Advanced Gastric Cancer is Dependent on ARID1A Mutations and ATM Expression. Oncoimmunology. 2018 03/27; 7(8): e1457602a

6. Campbell JD, Yau C, Bowlby R, Liu Y, Brennan K, Fan H, Taylor AM, Wang C, Walter V, Akbani R, Byers LA, Creighton CJ, Coarfa C, Shih J, Cherniack AD, Gevaert O, Prunello M, Shen H, Anur P, Chen J, Cheng H, Hayes DN, Bullman S, Pedamallu CS, Ojesina AI, Sadeghi S, Mungall KL, Robertson AG, Benz C, Schultz A, Kanchi RS, Gay CM, Hegde A, Diao L, Wang J, Ma W, Sumazin P, Chiu HS, Chen TW, Gunaratne P, Donehower L, Rader JS, Zuna R, Al-Ahmadie H, Lazar AJ, Flores ER, Tsai KY, Zhou JH, Rustgi AK, Drill E, Shen R, Wong CK, Cancer Genome Atlas Research Network, Stuart JM, Laird PW, Hoadley KA, Weinstein JN, Peto M, Pickering CR, Chen Z, Van Waes C. Genomic, Pathway Network, and Immunologic Features Distinguishing Squamous Carcinomas. Cell.Rep. 2018 Apr 3; 23(1): 194a

7. Carboni F, Federici O, Giofre M, Diodoro M, Valle M. Recurrence of Gallbladder Carcinoma 12 Years After Laparoscopic Cholecystectomy. Clin.Res.Hepatol.Gastroenterol. 2018 Aug 30 [Epub ahead of print]Carboni F, Marandino F, Valle M. Late Isolated Subcutaneous Metastasis from Colon Cancer. ANZ J.Surg. 2018 Oct 22;

8. Carboni F, Valle M, Federici O, Covello R, Garofalo A. Giant Primary Retroperitoneal Dedifferentiated Liposarcoma. J.Gastrointest.Surg. 2018 Jun 29; a

9. Chang K, Taggart MW, Reyes-Uribe L, Borras E, Riquelme E, Barnett RM, Leoni G, San Lucas FA, Catanese MT, Mori F, Diodoro MG, You YN, Hawk ET, Roszik J, Scheet P, Kopetz S, Nicosia A, Scarselli E, Lynch PM, McAllister F, Vilar E. Immune Profiling of Premalignant Lesions in Patients with Lynch Syndrome. JAMA Oncol. 2018 Aug; a

10. Chen H, Li C, Peng X, Zhou Z, Weinstein JN, Cancer Genome Atlas Research Network, Liang H. A Pan-Cancer Analysis of Enhancer Expression in nearly 9000 Patient Samples. Cell. 2018 Apr 5; 173(2): 386a

11. Chiappetta M, Marino M, Facciolo F. Unique Case of Atypical Type A Thymoma with Vertebral Metastasis and High 18-Fluorodeoxyglucose Avidity. ANZ J.Surg. 2018 Aug 17; a

12. Chiu HS, Somvanshi S, Patel E, Chen TW, Singh VP, Zorman B, Patil SL, Pan Y, Chatterjee SS, Cancer Genome Atlas Research Network, Sood AK, Gunaratne PH, Sumazin P, Marino M(c. Pan-Cancer Analysis of lncRNA Regulation Supports their Targeting of Cancer Genes in each Tumor Context. Cell.Rep. 2018 Apr 3; 23(1): 297a

13. Corrado G, Laquintana V, Loria R, Carosi M, de Salvo L, Sperduti I, Zampa A, Cicchillitti L, Piaggio G, Cutillo G, Falcioni R, Vizza E. Endometrial Cancer Prognosis Correlates with the Expression of L1CAM and miR34a Biomarkers. J.Exp.Clin.Cancer Res. 2018 Jul 6; 37(1): 139a

14. Coulson-Gilmer C, Humphries MP, Sundara Rajan S, Droop A, Jackson S, Condon A, Cserni G, Jordan LB, Jones JL, Kanthan R, Di Benedetto A, Mottolese M, Provenzano E, Kulka J, Shaaban AM, Hanby AM, Speirs V. Stanniocalcin 2 Expression is Associated with a Favourable Outcome in Male Breast Cancer. J.Pathol.Clin.Res. 2018 4(4): 241-249a .

15. D'Aguanno S, Valentini E, Tupone MG, Desideri M, Di Martile M, Spagnuolo M, Buglioni S, Ercolani C, Falcone I, De Dominici M, Milella M, Rizzo MG, Calabretta B, Cota C, Anichini A, Trisciuoglio D, Del Bufalo D. Semaphorin 5A Drives Melanoma Progression: Role of Bcl-2, miR-204 and c-Myb. J.Exp.Clin.Cancer Res. 2018 Nov 19; 37(1): 278a

16. De Nicola F, Goeman F, Pallocca M, Sperati F, Pizzuti L, Melucci E, Casini B, Amoreo CA, Gallo E, Diodoro MG, Buglioni S, Mazzotta M, Vici P, Sergi D, Di Lauro L, Barba M, Pescarmona E, Ciliberto G, De Maria R, Fanciulli M, Maugeri-Sacca M. Deep Sequencing and Pathway-Focused Analysis Revealed Multigene Oncodriver Signatures Predicting Survival Outcomes in Advanced Colorectal Cancer. Oncogenesis. 2018 Jul 22; 7(7): 55a

17. De Robertis M, Mazza T, Fusilli C, Loiacono L, Poeta ML, Sanchez M, Massi E, Lamorte G, Diodoro MG, Pescarmona E, Signori E, Pesole G, Vescovi AL, Garcia-Foncillas J, Fazio VM. EphB2 Stem-Related and EphA2 Progression-Related miRNA-Based Networks in Progressive Stages of CRC Evolution: Clinical Significance and Potential miRNA Drivers. Mol.Cancer. 2018 Nov 30; 17(1): 169a

18. Di Martile M, Desideri M, Tupone MG, Buglioni S, Antoniani B, Mastroiorio C, Falcioni R, Ferraresi V, Baldini N, Biagini R, Milella M, Trisciuoglio D, Del Bufalo D. Histone Deacetylase Inhibitor ITF2357 Leads to Apoptosis and Enhances Doxorubicin Cytotoxicity in Preclinical Models of Human Sarcoma. Oncogenesis. 2018 Feb 23; 7(2): 20a

19. di Martino S, De Luca G, Grassi L, Federici G, Alfonsi R, Signore M, Addario A, De Salvo L, Francescangeli F, Sanchez M, Tirelli V, Muto G, Sperduti I, Sentinelli S, Costantini M, Pasquini L, Milella M, Haoui M, Simone G, Gallucci M, De Maria R, Bonci D. Renal Cancer: New Models and Approach for Personalizing Therapy. J.Exp.Clin.Cancer Res. 2018 Sep 5; 37(1): 217a

20. Di Modugno F, Spada S, Palermo B, Visca P, Iapicca P, Di Carlo A, Antoniani B, Sperduti I, Di Benedetto A, Terrenato I, Mottolese M, Gandolfi F, Facciolo F, Chen EI, Schwartz MA, Santoni A, Bissell MJ, Nistico P. HMENA Isoforms Impact NSCLC Patient Outcome through fibronectin/beta1 Integrin Axis. Oncogene. 2018 Oct; 37(42): 5605-5617a

21. Ding L, Bailey MH, Porta-Pardo E, Thorsson V, Colaprico A, Bertrand D, Gibbs DL, Weerasinghe A, Huang KL, Tokheim C, Cortes-Ciriano I, Jayasinghe R, Chen F, Yu L, Sun S, Olsen C, Kim J, Taylor AM, Cherniack AD, Akbani R, Suphavilai C, Nagarajan N, Stuart JM, Mills GB, Wyczalkowski MA, Vincent BG, Hutter CM, Zenklusen JC, Hoadley KA, Wendl MC, Shmulevich L, Lazar AJ, Wheeler DA, Getz G, Cancer Genome Atlas Research Network, Marino M(c. Perspective on Oncogenic Processes at the End of the Beginning of Cancer Genomics. Cell. 2018 Apr 5; 173(2): 305a

22. Donà MG, Benevolo M, Latini A, Rollo F, Colafigli M, Frasca M, Zaccarelli M, Giglio A, Moretto D, Pescarmona E, Cristaudo A, Giuliani M. Anal Cytological Lesions and HPV Infection in Individuals at Increased Risk for Anal Cancer. Cancer.Cytopathol. 2018 Jul; 126(7): 461a

23. Donzelli S, Milano E, Pruszko M, Sacconi A, Masciarelli S, Iosue I, Melucci E, Gallo E, Terrenato I, Mottolese M, Zylicz M, Zylicz A, Fazi F, Blandino G, Fontemaggi G. Expression of ID4 Protein in Breast Cancer Cells Induces Reprogramming of Tumour-Associated Macrophages. Breast Cancer Res. 2018 Jun 19; 20(1): 59a

24. Drusco A, Fadda P, Nagita G, Fassan N, Bottoni A, Gardigam MM, Sacchi D, Calore F, Carosi M, Antenucci A, Casini B, Kelani H, Pescarmona E, Di Leva G, Zanesi N, Berger MC, Croce CM. Circulating Micrornas Predict Survival of Patients with Tumors of Glial Origin. Ebiomedicine. 2018 Apr; 30: 105a

25. Ellrott K, Bailey MH, Saksena G, Covington KR, Kandoth C, Stewart C, Hess J, Ma S, Chiotti KE, McLellan M, Sofia HJ, Hutter C, Getz G, Wheeler D, Ding L, MC3 Working Group, Cancer Genome Atlas Research Network. Scalable Open Science Approach for Mutation Calling of Tumor Exomes using Multiple Genomic Pipelines. Cell.Syst. 2018 Mar 28; 6(3): 271a

26. Ferrara M, Sessa G, Fiore M, Bernard F, Asteriti IA, Cundari E, Colotti G, Ferla S, Desideri M, Buglioni S, Trisciuoglio D, Del Bufalo D, Brancale A, Degrassi F. Small Molecules Targeted to the Microtubule-Hec1 Interaction Inhibit Cancer Cell Growth through Microtubule Stabilization. Oncogene. 2018 37(2): 231a

27. Frixa T, Sacconi A, Cioce M, Roscilli G, Ferrara FF, Aurisicchio L, Pulito C, Telera S, Carosi M, Muti P, Strano S, Donzelli S, Blandino G. MicroRNA-128-3p-Mediated Depletion of Drosha Promotes Lung Cancer Cell Migration. Carcinogenesis. 2018 Feb 9; 39(2): 293a

28. Gasparello J, Allegretti M, Tremante E, Fabbri E, Amoreo CA, Romania P, Melucci E, Messana K, Borgatti M, Giacomini P, Gambari R, Finotti A. Liquid Biopsy in Mice Bearing Colorectal Carcinoma Xenografts: Gateways Regulating the Levels of Circulating Tumor DNA (ctDNA) and miRNA (ctmiRNA). J.Exp.Clin.Cancer Res. 2018 Jun 26; 37(1): 124a

29. Ge Z, Leighton JS, Wang Y, Peng X, Chen Z, Chen H, Sun Y, Yao F, Li J, Zhang H, Liu J, Shriver CD, Hu H, Cancer Genome Atlas Research Network, Piwnica-Worms H, Ma L, Liang H, Marino M(c. Integrated Genomic Analysis of the Ubiquitin Pathway Across Cancer Types. Cell.Rep. 2018 Apr 3; 23(1): 213a

30. Giuliani M, Latini A, Colafigli M, Benevolo M, Rollo F, Zaccarelli M, Giuliani E, Moretto D, Giglio A, Rezza G, Cristaudo A, Dona MG. Vaccine-Preventable Anal Infections by Human Papillomavirus among HIV-Infected Men Who have Sex with Men. Future Microbiol. 2018 Oct; 13: 1463a

31. Grassilli S, Brugnoli F, Lattanzio R, Marchisio M, Perracchio L, Piantelli M, Bavelloni A, Capitani S, Bertagnolo V. Vav1 Downmodulates Akt in Different Breast Cancer Subtypes: A New Promising Chance to Improve Breast Cancer Outcome. Mol.Oncol. 2018 Jun; 12(7): 1012a

32. Hoadley KA, Yau C, Hinoue T, Wolf DM, Lazar AJ, Drill E, Shen R, Taylor AM, Cherniack AD, Thorsson V, Akbani R,

Bowlby R, Wong CK, Wiznerowicz M, Sanchez-Vega F, Robertson AG, Schneider BG, Lawrence MS, Noushmehr H, Malta TM, Cancer Genome Atlas Network, Stuart JM, Benz CC, Laird PW, Marino M(c. Cell-of-Origin Patterns Dominate the Molecular Classification of 10,000 Tumors from 33 Types of Cancer. Cell. 2018 Apr 5; 173(2): 291a

33. Huang KL, Mashl RJ, Wu Y, Ritter DI, Wang J, Oh C, Paczkowska M, Reynolds S, Wyczalkowski MA, Oak N, Scott AD, Krassowski M, Cherniack AD, Houlahan KE, Jayasinghe R, Wang LB, Zhou DC, Liu D, Cao S, Kim YW, Koire A, McMichael JF, Hucthagowder V, Kim TB, Hahn A, Wang C, McLellan MD, Al-Mulla F, Johnson KJ, Cancer Genome Atlas Research Network, Lichtarge O, Boutros PC, Raphael B, Lazar AJ, Zhang W, Wendl MC, Govindan R, Jain S, Wheeler D, Kulkarni S, Dipersio JF, Reimand J, Meric-Bernstam F, Chen K, Shmulevich I, Plon SE, Chen F, Ding L, Marino M(c. Pathogenic Germline Variants in 10,389 Adult Cancers. Cell. 2018 Apr 5; 173(2): 355a

34. Imbimbo M, Ottaviano M, Vitali M, Fabbri A, Leuzzi G, Fiore M, Franceschini D, Pasello G, Perrino M, Schiavon M, Pruneri G, Dei Tos AP, Sangalli C, Garassino MC, Berardi R, Alessi A, Calareso G, Petrini I, Scorsetti M, Scotti V, Rosso L, Rea F, Pastorino U, Casali PG, Ramella S, Ricardi U, Abate-Daga L, Torri V, Trama A, Palmieri G, Marino M, Zucali PA, TYME network collaborators. Best Practices for the Management of Thymic Epithelial Tumors: A Position Paper by the Italian Collaborative Group for ThYmic MalignanciEs (TYME). Cancer Treat.Rev. 2018 Dec; 71: 76a

35. Imbimbo M, Vitali M, Fabbri A, Ottaviano M, Pasello G, Petrini I, Palmieri G, Berardi R, Zucali P, Ganzinelli M, Marabese M, Broggini M, Marino M, Trama A, Rulli E, Hollander L, Pruneri G, Torri V, Garassino MC. RELEVENT Trial: Phase II Trial of Ramucirumab, Carboplatin, and Paclitaxel in Previously Untreated Thymic Carcinoma/B3 Thymoma with Area of Carcinoma. Clin.Lung Cancer. 2018 Sep; 19(5): e811a

36. Jayasinghe RG, Cao S, Gao Q, Wendl MC, Vo NS, Reynolds SM, Zhao Y, Climente-Gonzalez H, Chai S, Wang F, Varghese R, Huang M, Liang WW, Wyczalkowski MA, Sengupta S, Li Z, Payne SH, Fenyo D, Miner JH, Walter MJ, Cancer Genome Atlas Research Network, Vincent B, Eyras E, Chen K, Shmulevich I, Chen F, Ding L. Systematic Analysis of Splice-Site-Creating Mutations in Cancer. Cell.Rep. 2018 Apr 3; 23(1): 270a

37. Kahles A, Lehmann KV, Toussaint NC, Huser M, Stark SG, Sachsenberg T, Stegle O, Kohlbacher O, Sander C, Cancer Genome Atlas Research Network, Ratsch G. Comprehensive Analysis of Alternative Splicing Across Tumors from 8,705 Patients. Cancer.Cell. 2018 Aug 13; 34(2): 211a

38. Knijnenburg TA, Wang L, Zimmermann MT, Chambwe N, Gao GF, Cherniack AD, Fan H, Shen H, Way GP, Greene CS, Liu Y, Akbani R, Feng B, Donehower LA, Miller C, Shen Y, Karimi M, Chen H, Kim P, Jia P, Shinbrot E, Zhang S, Liu J, Hu H, Bailey MH, Yau C, Wolf D, Zhao Z, Weinstein JN, Li L, Ding L, Mills GB, Laird PW, Wheeler DA, Shmulevich I, Cancer Genome Atlas Research Network, Monnat RJ,Jr, Xiao Y, Wang C, Marino M(c. Genomic and Molecular Landscape of DNA Damage Repair Deficiency Across the Cancer Genome Atlas. Cell.Rep. 2018 Apr 3; 23(1): 239a

39. Korkut A, Zaidi S, Kanchi RS, Rao S, Gough NR, Schultz A, Li X, Lorenzi PL, Berger AC, Robertson G, Kwong LN, Datto M, Roszik J, Ling S, Ravikumar V, Manyam G, Rao A, Shelley S, Liu Y, Ju Z, Hansel D, de Velasco G, Pennathur A, Andersen JB, O'Rourke CJ, Ohshiro K, Jogunoori W, Nguyen BN, Li S, Osmanbeyoglu HU, Ajani JA, Mani SA, Houseman A, Wiznerowicz M, Chen J, Gu S, Ma W, Zhang J, Tong P, Cherniack AD, Deng C, Resar L, Cancer Genome Atlas Research Network, Weinstein JN, Mishra L, Akbani R. A Pan-Cancer Analysis Reveals High-Frequency Genetic Alterations in Mediators of Signaling by the TGF-Beta Superfamily. Cell.Syst. 2018 Oct 24; 7(4): 422a

40. Lamberti D, Cristinziano G, Porru M, Leonetti C, Egan JB, Shi CX, Buglioni S, Amoreo CA, Castellani L, Borad MJ, Alema S, Anastasi S, Segatto O. HSP90 Inhibition Drives Degradation of FGFR2 Fusion Proteins: Implications for Treatment of Cholangiocarcinoma. Hepatology. 2018 Aug 1[Epub ahead of print]

41. Liu J, Lichtenberg T, Hoadley KA, Poisson LM, Lazar AJ, Cherniack AD, Kovatich AJ, Benz CC, Levine DA, Lee AV, Omberg L, Wolf DM, Shriver CD, Thorsson V, Cancer Genome Atlas Research Network, Hu H, Marino M(c. An Integrated TCGA Pan-Cancer Clinical Data Resource to Drive High-Quality Survival Outcome Analytics. Cell. 2018 Apr 5; 173(2): 400a

42. Liu Y, Sethi NS, Hinoue T, Schneider BG, Cherniack AD, Sanchez-Vega F, Seoane JA, Farshidfar F, Bowlby R, Islam M, Kim J, Chatila W, Akbani R, Kanchi RS, Rabkin CS, Willis JE, Wang KK, McCall SJ, Mishra L, Ojesina AI, Bullman S, Pedamallu CS, Lazar AJ, Sakai R, Cancer Genome Atlas Research Network, Thorsson V, Bass AJ, Laird PW, Marino M(c. Comparative Molecular Analysis of Gastrointestinal Adenocarcinomas. Cancer.Cell. 2018 Apr 9; 33(4): 721a

43. Loria R, Laquintana V, Bon G, Trisciuoglio D, Frapolli R, Covello R, Amoreo CA, Ferraresi V, Zoccali C, Novello M, Del Bufalo D, Milella M, Biagini R, D'Incalci M, Falcioni R. HMGA1/E2F1 Axis and NFkB Pathways Regulate LPS Progression and Trabectedin Resistance. Oncogene. 2018 Nov; 37(45): 5926a

44. Malta TM, Sokolov A, Gentles AJ, Burzykowski T, Poisson L, Weinstein JN, Kaminska B, Huelsken J, Omberg L, Gevaert O, Colaprico A, Czerwinska P, Mazurek S, Mishra L, Heyn H, Krasnitz A, Godwin AK, Lazar AJ, Cancer Genome Atlas Research Network, Stuart JM, Hoadley KA, Laird PW, Noushmehr H, Wiznerowicz M, Marino M(c. Machine Learning Identifies Stemness Features Associated with Oncogenic Dedifferentiation. Cell. 2018 Apr 5; 173(2): 338a

45. Mancini R, Pattaro G, Diodoro MG, Sperduti I, Garufi C, Stigliano V, Perri P, Grazi GL, Cosimelli M. Tumor Regression Grade After Neoadjuvant Chemoradiation and Surgery for Low Rectal Cancer Evaluated by Multiple Correspondence Analysis: Ten Years as Minimum Follow-Up. Clin.Colorectal Cancer. 2018 Mar; 17(1): e13a

46. Mandoj C, Pizzuti L, Sergi D, Sperduti I, Mazzotta M, Di Lauro L, Amodio A, Carpano S, Di Benedetto A, Botti C, Ferranti F, Antenucci A, D'Alessandro MG, Marchetti P, Tomao S, Sanguineti G, Giordano A, Maugeri-Sacca M, Ciliberto G, Conti L, Vici P, Barba M. Observational Study of Coagulation Activation in Early Breast Cancer: Development of a Prognostic Model Based on Data from the Real World Setting. J.Transl.Med. 2018 May 16; 16(1): 129a

47. Manic G, Signore M, Sistigu A, Russo G, Corradi F, Siteni S, Musella M, Vitale S, De Angelis ML, Pallocca M, Amoreo CA, Sperati F, Di Franco S, Barresi S, Policicchio E, De Luca G, De Nicola F, Mottolese M, Zeuner A, Fanciulli M, Stassi G, Maugeri-Sacca M, Baiocchi M, Tartaglia M, Vitale I, De Maria R. CHK1-Targeted Therapy to Deplete DNA Replication-Stressed, p53-Deficient, Hyperdiploid Colorectal Cancer Stem Cells. Gut. 2018 May; a

48. Marchesi F, Regazzo G, Palombi F, Terrenato I, Sacconi A, Spagnuolo M, Donzelli S, Marino M, Ercolani C, Di Benedetto A, Blandino G, Ciliberto G, Mengarelli A, Rizzo MG. Serum miR-22 as Potential Non-Invasive Predictor of Poor Clinical Outcome in Newly Diagnosed, Uniformly Treated Patients with Diffuse Large B-Cell Lymphoma: An Explorative Pilot Study. J.Exp.Clin.Cancer Res. 2018 May 2; 37(1): 95a

49. Marchiò C, Dell'Orto P, Annaratone L, Geyer FC, Venesio T, Berrino E, Verdun di Cantogno L, Garofoli A, Rangel N, Casorzo L, dell'Aglio C, Gugliotta P, Trisolini E, Beano A, Pietribiasi F, Orlassino R, Cassoni P, Pich A, Montemurro F, Mottolese M, Vincent-Salomon A, Penault-Llorca F, Medico E, Ng CKY, Viale G, Sapino A. The Dilemma of HER2 Double-Equivocal Breast Carcinomas: Genomic Profiling and Implications for Treatment. Am.J.Surg.Pathol. 2018 Sep; 42(9): 1190a

50. Marino M, Visca P, Ottaviano M. PD-L1 Testing in Lung Cancer: An International Pathologist's Initiative in an Unknown "Middle Earth". J.Thorac.Oncol. 2018 Sep; 13(9): 1239a

51. Melucci E, Casini B, Ronchetti L, Pizzuti L, Sperati F, Pallocca M, De Nicola F, Goeman F, Gallo E, Amoreo CA, Sergi D, Terrenato I, Vici P, Di Lauro L, Diodoro MG, Pescarmona E, Barba M, Mazzotta M, Mottolese M, Fanciulli M, Ciliberto G, De Maria R, Buglioni S, Maugeri-Sacca M. Expression of the Hippo Transducer TAZ in Association with WNT Pathway Mutations Impacts Survival Outcomes in Advanced Gastric Cancer Patients Treated with First-Line Chemotherapy. J.Transl.Med. 2018 Feb 5; 16(1): 22a

52. Nicholson AG, Tsao MS, Travis WD, Patil DT, Galateau-Salle F, Marino M, Dacic S, Beasley MB, Butnor KJ, Yatabe Y, Pass HI, Rusch VW, Detterbeck FC, Asamura H, Rice TW, Rami-Porta R. Eighth Edition Staging of Thoracic Malignancies: Implications for the Reporting Pathologist. Arch.Pathol.Lab.Med. 2018 May; 142(5): 645a.

53. Pace A, Mandoj C, Antenucci A, Villani V, Sperduti I, Casini B, Carosi M, Fabi A, Vidiri A, Koudriavtseva T, Conti L. A Predictive Value of Von Willebrand Factor for Early Response to Bevacizumab Therapy in Recurrent Glioma. J.Neurooncol. 2018 Jul; 138(3): 527a

54. Pallocca M, Goeman F, De Nicola F, Melucci E, Sperati F, Terrenato I, Pizzuti L, Casini B, Gallo E, Amoreo CA, Vici P, Di Lauro L, Buglioni S, Diodoro MG, Pescarmona E, Mazzotta M, Barba M, Fanciulli M, De Maria R, Ciliberto G, Maugeri-Sacca M. Coexisting YAP Expression and TP53 Missense Mutations Delineates a Molecular Scenario Unexpectedly Associated with Better Survival Outcomes in Advanced Gastric Cancer. J.Transl.Med. 2018 Sep 4; 16(1): 247a

55. Peng X, Chen Z, Farshidfar F, Xu X, Lorenzi PL, Wang Y, Cheng F, Tan L, Mojumdar K, Du D, Ge Z, Li J, Thomas GV, Birsoy K, Liu L, Zhang H, Zhao Z, Marchand C, Weinstein JN, Cancer Genome Atlas Research Network, Bathe OF, Liang H. Molecular Characterization and Clinical Relevance of Metabolic Expression Subtypes in Human Cancers. Cell.Rep. 2018 Apr 3; 23(1): 255a

56. Piludu F, Gangemi E, Marucci L, Guerrisi A, Pellini R, Covello R, Carlini P, Spriano G, Sanguineti G, Marzi S, Vidiri A. MRI Evaluation using DWI and T2WI of Residual Lymph Nodes in Patients Affected by Head and Neck Squamous Cell Carcinoma Treated with Chemo-Radiotherapy. Curr.Med.Imaging Rev. 2018 14(4): 599a

57. Pizzuti L, Sergi D, Mandoj C, Antoniani B, Sperati F, Chirico A, Di Lauro L, Valle M, Garofalo A, Vizza E, Corrado G, Tomao F, Rinaldi M, Carpano S, Maugeri-Sacca M, Conti L, Digiesi G, Marchetti P, De Maria R, Giordano A, Barba M, Carosi MA, Vici P. GLUT 1 Receptor Expression and Circulating Levels of Fasting Glucose in High Grade Serous Ovarian Cancer. J.Cell.Physiol. 2018 233(2): 1396a

58. Prieto-Potin I, Montagut C, Bellosillo B, Evans M, Smith M, Melchior L, Reiltin W, Bennett M, Pennati V, Castiglione F, Burrig KF, Cooper U, Dockhorn-Dworniczak B, Rossenbach C, Luna-Aguirre CM, Barrera-Saldana HA, Machado JC, Costa JL, Yacobi R, Tabibian-Keissar H, Buglioni S, Ronchetti L, Douglas-Berger L, Dubbink HJ, Alorini M, Sabourin JC, Rojo F. Multicenter Evaluation of the Idylla NRAS-BRAF Mutation Test in Metastatic Colorectal Cancer. J.Mol. Diagn. 2018 20(5): 664-676a IF:4.880.

59. Radovich M, Pickering CR, Felau I, Ha G, Zhang H, Jo H, Hoadley KA, Anur P, Zhang J, McLellan M, Bowlby R, Matthew T, Danilova L, Hegde AM, Kim J, Leiserson MDM, Sethi G, Lu C, Ryan M, Su X, Cherniack AD, Robertson G, Akbani R, Spellman P, Weinstein JN, Hayes DN, Raphael B, Lichtenberg T, Leraas K, Zenklusen JC, Cancer Genome Atlas Network, Fujimoto J, Scapulatempo-Neto C, Moreira AL, Hwang D, Huang J, Marino M, Korst R, Giaccone G, Gokmen-Polar Y, Badve S, Rajan A, Strobel P, Girard N, Tsao MS, Marx A, Tsao AS, Loehrer PJ. The Integrated Genomic Landscape of Thymic Epithelial Tumors. Cancer.Cell. 2018 Feb 12; 33(2): 244a

60. Ricketts CJ, De Cubas AA, Fan H, Smith CC, Lang M, Reznik E, Bowlby R, Gibb EA, Akbani R, Beroukhim R, Bottaro DP, Choueiri TK, Gibbs RA, Godwin AK, Haake S, Hakimi AA, Henske EP, Hsieh JJ, Ho TH, Kanchi RS, Krishnan B, Kwiatkowski DJ, Lui W, Merino MJ, Mills GB, Myers J, Nickerson ML, Reuter VE, Schmidt LS, Shelley CS, Shen H, Shuch B, Signoretti S, Srinivasan R, Tamboli P, Thomas G, Vincent BG, Vocke CD, Wheeler DA, Yang L, Kim WY, Robertson AG, Cancer Genome Atlas Research Network, Spellman PT, Rathmell WK, Linehan WM. The Cancer Genome Atlas Comprehensive Molecular Characterization of Renal Cell Carcinoma. Cell.Rep. 2018 Apr 3; 23(1): 313a

61. Rollo F, Donà MG, Pellini R, Pichi B, Marandino F, Covello R, Benevolo M. Cytology and Direct Human Papillomavirus Testing on Fine Needle Aspirates from Cervical Lymph Node Metastases of Patients with Oropharyngeal Squamous Cell Carcinoma Or Occult Primary. Cytopathology. 2018 Oct; 29(5): 449-454a

62. Saltz J, Gupta R, Hou L, Kurc T, Singh P, Nguyen V, Samaras D, Shroyer KR, Zhao T, Batiste R, Van Arnam J, Cancer Genome Atlas Research Network, Shmulevich I, Rao AUK, Lazar AJ, Sharma A, Thorsson V. Spatial Organization and Molecular Correlation of Tumor-Infiltrating Lymphocytes using Deep Learning on Pathology Images. Cell.Rep. 2018 Apr 3; 23(1): 181a

63. Sanchez-Vega F, Mina M, Armenia J, Chatila WK, Luna A, La KC, Dimitriadoy S, Liu DL, Kantheti HS, Saghafinia S, Chakravarty D, Daian F, Gao Q, Bailey MH, Liang WW, Foltz SM, Shmulevich I, Ding L, Heins Z, Ochoa A, Gross B, Gao J, Zhang H, Kundra R, Kandoth C, Bahceci I, Dervishi L, Dogrusoz U, Zhou W, Shen H, Laird PW, Way GP, Greene CS, Liang H, Xiao Y, Wang C, Iavarone A, Berger AH, Bivona TG, Lazar AJ, Hammer GD, Giordano T, Kwong LN, McArthur G, Huang C, Tward AD, Frederick MJ, McCormick F, Meyerson M, Cancer Genome Atlas Research Network, Van Allen EM, Cherniack AD, Ciriello G, Sander C, Schultz N, Marino M(c. Oncogenic Signaling Pathways in the Cancer Genome Atlas. Cell. 2018 Apr 5; 173(2): 321a

64. Schaub FX, Dhankani V, Berger AC, Trivedi M, Richardson AB, Shaw R, Zhao W, Zhang X, Ventura A, Liu Y, Ayer DE, Hurlin PJ, Cherniack AD, Eisenman RN, Bernard B, Grandori C, Cancer Genome Atlas Network. Pan-Cancer Alterations of the MYC Oncogene and its Proximal Network Across the Cancer Genome Atlas. Cell.Syst. 2018 Mar 28; 6(3): 282a

65. Sponziello M, Benvenuti S, Gentile A, Pecce V, Rosignolo F, Virzi AR, Milan M, Comoglio PM, Londin E, Fortina P, Barnabei A, Appetecchia M, Marandino F, Russo D, Filetti S, Durante C, Verrienti A. Whole Exome Sequencing Identifies a Germline MET Mutation in Two Siblings with Hereditary Wild-Type RET Medullary Thyroid Cancer. Hum.Mutat. 2018 Mar; 39(3): 371a

66. Taylor AM, Shih J, Ha G, Gao GF, Zhang X, Berger AC, Schumacher SE, Wang C, Hu H, Liu J, Lazar AJ, Cancer Genome Atlas Research Network, Cherniack AD, Beroukhim R, Meyerson M, Marino M(c. Genomic and Functional Approaches to Understanding Cancer Aneuploidy. Cancer.Cell. 2018 Apr 9; 33(4): 676a

67. Thorsson V, Gibbs DL, Brown SD, Wolf D, Bortone DS, Ou Yang TH, Porta-Pardo E, Gao GF, Plaisier CL, Eddy JA, Ziv E, Culhane AC, Paull EO, Sivakumar IKA, Gentles AJ, Malhotra R, Farshidfar F, Colaprico A, Parker JS, Mose LE, Vo NS, Liu J, Liu Y, Rader J, Dhankani V, Reynolds SM, Bowlby R, Califano A, Cherniack AD, Anastassiou D, Bedognetti D, Rao A, Chen K, Krasnitz A, Hu H, Malta TM, Noushmehr H, Pedamallu CS, Bullman S, Ojesina AI, Lamb A, Zhou W, Shen H, Choueiri TK, Weinstein JN, Guinney J, Saltz J, Holt RA, Rabkin CE, Cancer Genome Atlas Research Network, Lazar AJ, Serody JS, Demicco EG, Disis ML, Vincent BG, Shmulevich L, Marino M(c. The Immune Landscape of Cancer. Immunity. 2018 Apr 17; 48(4): 812°

68. Vidiri A, Minosse S, Piludu F, Pellini R, Cristalli G, Kayal R, Carlino G, Renzi D, Covello R, Marzi S. Cervical Lymphadenopathy: Can the Histogram Analysis of Apparent Diffusion Coefficient Help to Differentiate between Lymphoma and Squamous Cell Carcinoma in Patients with Unknown Clinical Primary Tumor? Radiol.Med. 2018 Sep 8 [Epub ahead of print]

69. Vizza E, Corrado G, De Angeli M, Carosi M, Mancini E, Baiocco E, Chiofalo B, Patrizi L, Zampa A, Piaggio G, Cicchillitti L. Serum DNA Integrity Index as a Potential Molecular Biomarker in Endometrial Cancer. J.Exp.Clin. Cancer Res. 2018 Jan 30; 37(1): 16a

70. Wang Y, Xu X, Maglic D, Dill MT, Mojumdar K, Ng PK, Jeong KJ, Tsang YH, Moreno D, Bhavana VH, Peng X, Ge Z, Chen H, Li J, Chen Z, Zhang H, Han L, Du D, Creighton CJ, Mills GB, Cancer Genome Atlas Research Network, Camargo F, Liang H. Comprehensive Molecular Characterization of the Hippo Signaling Pathway in Cancer. Cell.Rep. 2018 Oct 30; 25(5): 1304a

71. Wang Z, Yang B, Zhang M, Guo W, Wu Z, Wang Y, Jia L, Li S, Cancer Genome Atlas Research Network, Xie W, Yang D, Marino M(c. LncRNA Epigenetic Landscape Analysis Identifies EPIC1 as an Oncogenic lncRNA that Interacts with MYC and Promotes Cell-Cycle Progression in Cancer. Cancer.Cell. 2018 Apr 9; 33(4): 706a.

72. Way GP, Sanchez-Vega F, La K, Armenia J, Chatila WK, Luna A, Sander C, Cherniack AD, Mina M, Ciriello G, Schultz N, Cancer Genome Atlas Research Network, Sanchez Y, Greene CS, Marino M(c. Machine Learning Detects Pan-Cancer Ras Pathway Activation in the Cancer Genome Atlas. Cell.Rep. 2018 Apr 3; 23(1): 172a

# MEDICAL PHYSICS AND EXPERT SYSTEMS UNIT

*Head: Lidia Strigari, Medical Physicist*

## STAFF

| |
|---|
| Vicente Bruzzaniti, Medical Physicist |
| Marco D'Andrea, Medical Physicist |
| Giuseppe Iaccarino, Medical Physicist |
| Valeria Landoni, Medical Physicist |
| Simona Marzi, Medical Physicist |
| Luis Pedro Ordonez, Medical Physicist |
| Antonella Soriani, Medical Physicist |
| Giampiero Carlino, Technician p.i. |
| Sandro Carpino, Technician p.i. |
| Stefano Luppino, Technician p.i. |
| Sandro Nocentini, Technician p.i. |
| Francesco Quagliani, Technician p.i. |

| Research |
|---|
| Gianluca Bossi, Biologist Ph.D. |
| Silvia De Stefano, Physicist in training |
| Emiliano Loi, Physicist in training |
| Raffaella Marconi, Biologist Ph.D |
| Marica Masi, Physicist in training |
| Angelina Pranteda, Biologist Ph.D. student |
| Annalisa Serafini, Biologist Ph.D. |
| Elena Solfaroli Camillocci, PhD, Physicist in training |
| Lorenzo Stramucci, Biologist Ph.D. |
| Arianna Stravato, Biologist Ph.D. student |
| Sara Ungania, Medical Physicist |

## Mission

The Laboratory of Medical Physics and Expert Systems (in the following named Lab) technically supports different Departments within the IRE-ISG using physical agents, such as ionizing radiation (IR), ultrasounds, magnetic resonance, laser, etc.
The Lab's mission aims at reducing the undue dose to patients and environment through specific procedures in compliance with the national and international legislation. In particular, the Lab provides daily assistance for the identification, installation, commissioning, acceptance testing, maintenance and quality assurance of high technology equipment within the Institute. The Lab conducts basic and translational researches focusing on novel applications of medical physics in the image-based diagnosis and treatment of oncological disease by using minimally invasive strategies for treatment personalization. The Lab develops tools and methods for improving treatment precision and accuracy, performing automatic controls, analyzing the implemented procedures and modifying them accordingly. The Lab ensures patient care and safety reducing the clinical risk.

## Clinical Activities

The Lab implements quality assurance protocols to perform diagnosis and therapies efficiently and safely. In particular it daily develops personalized treatment plans for cancer patients including: conventional Radiation Therapy (RT); intra-operative RT; intensity modulated RT, also including gating deep inspiration breath hold (DIBH) treatments and nuclear medicine patient-specific dosimetry with the aim of improving tumor control, sparing normal tissues. The Lab monitors devices, perform patient-specific dosimetry, guarantees the accuracy of image fusion from multimodality devices and develops radiobiological models. The Lab cooperates with the Departments of Imaging Diagnostic for image analysis in order to identify novel image-based predictors of patients' outcome.
The Lab ensures radioprotection of patients and workers, thirdly part (familiars, care givers and population in general) and environment from physical agents. Main aim of this activity is reducing the clinical risk maintaining the level of security at the standard request by technical regulation. Moreover, the Lab provides educational programs. Since 2009, the Lab is ISO 9001 certified.

## Research Activities

Main ongoing research projects of the Lab are: dosimetry in diagnostics and treatments, medical imaging applications, mathematical modeling of biological systems.
The Lab participates to clinical trials and performs data analysis of clinical and dosimetric results, such as:

- implementation of strategies for dose tracking/adaptive/-omics for assessment of dosimetric predictors in oncological patients undergoing various therapies;
- investigation of toxicity after hypofractionated treatments in prostate and breast cancer patients;
- acquisition protocol optimization of advanced magnetic resonance imaging (MRI) techniques and the subsequent quantitative image analysis, by developing dedicated home-made software. This allows the quantification of biophysical parameters derived from multi-modal images, which are potentially useful for tumor characterization and staging, and for detection of residual disease after treatment (chemotherapy or RT);
- evaluation of the relationship between the perfusion parameters measured by IVIM DWI and the perfusion measured by conventional perfusion MRI techniques in soft tissue tumors;
- studying the impact of molecular markers (prognostic gene/miRNA) and/or radiobiological modeling to predict patient' outcome;
- exploring MAP2K3 targeting as novel anti-cancer therapeutical strategy;
- studying of the wtp53 roles in RT induced abscopal effects;
- plan comparison, robustness and quality in multicentric setting;
- Monte Carlo simulations;
- development of specific tools for predicting effects of ablative microwaves in liver disease;
- implementation of tool for studying the normal tissues effects using neurological imaging.

Dr. Strigari is the PI of several national and international project, most important are: the project: "Accurate dosimetry and biomarkers improve survival in HCC patients treated with resin 90Y-μspheres: a randomized trial" funded by AIRC; the project "Development and optimisation of a dedicated system for hyperthermia treatments for patients with superficial and/or semi-

deep sarcomas – OTIS" (project code 85-2017-15264) funded by Regione Lazio (2018); the project "Reduction of the undue dose in nuclear medicine diagnostic study including PET" (Project Code: B N.17/DIPIA/09 - funded by INAIL); the project "TOP-IMPLART: Development of a new accelerator proton therapy facility" funded by Regione Lazio 2011; the project: "A panel of biomarkers as novel tool for early detection of radiation exposure" founded by NATO within the program Science for Peace programme (SPS n. 984815), in collaboration with ENEA and University of Alexandria (Egypt). The results of this project will also improve the patients' treatment, by the knowledge of the individual radio-sensitivity. Dr. Strigari is also member of Dosimetry Committee of EANM developing European guidelines on NM dosimetry and member of the ICRU Committee 31.

## Publications


1. Arcangeli G, Arcangeli S, Pinzi V, Benassi M, Benassi M, Strigari L. Optimal Scheduling of Hypofractionated Radiotherapy for Localized Prostate Cancer: A Systematic Review and Metanalysis of Randomized Clinical Trials. Cancer Treatment Reviews. 2018 November 2018; 70: 22a

2. Barnabei A, Strigari L, Persichetti A, Baldelli R, Rizza L, Annoscia C, Lauretta R, Cigliana G, Barba M, De Leo A, Appetecchia M, Torino F. Indirect Basal Metabolism Estimation in Tailoring Recombinant Human TSH Administration in Patients Affected by Differentiated Thyroid Cancer: A Hypothesis-Generating Study. Front.Endocrinol.(Lausanne). 2018 Feb 15; 9: 37a

3. Clemente S, Masi L, Fiandra C, Cagni E, Villaggi E, Esposito M, Giglioli FR, Marino C, Strigari L, Garibaldi C, Stasi M, Mancosu P, Russo S. A Multi-Center Output Factor Intercomparison to Uncover Systematic Inaccuracies in Small Field Dosimetry. Physics and Imaging in Radiation Oncology. 2018 January 2018; 5: 93a

4. Cremonesi M, Ferrari ME, Bodei L, Chiesa C, Sarnelli A, Garibaldi C, Pacilio M, Strigari L, Summers PE, Orecchia R, Grana CM, Botta F. Correlation of Dose with Toxicity and Tumour Response to (90)Y- and (177)Lu-PRRT Provides the Basis for Optimization through Individualized Treatment Planning. Eur.J.Nucl.Med.Mol.Imaging. 2018 Dec;45(13):2426-2441

5. D'Andrea M, Strolin S, Ungania S, Cacciatore A, Bruzzaniti V, Marconi R, Benassi M, Strigari L. Radiobiological Optimization in Lung Stereotactic Body Radiation Therapy: Are we Ready to Apply Radiobiological Models? Front. Oncol. 2018 Jan 8; 7: 321a

6. Daniela Falco M, Giancaterino S, D'Andrea M, Gimenez De Lorenzo R, Trignani M, Caravatta L, Di Carlo C, Di Biase S, Allajbej A, Genovesi D. Hippocampal Sparing Approach in Fractionated Stereotactic Brain VMAT Radio Therapy: A Retrospective Feasibility Analysis. J.Appl.Clin.Med.Phys. 2018 Jan; 19(1): 86a

7. De Angelis C, Ampollini A, Basile E, Cisbani E, Della Monaca S, Ghio F, Montereali RM, Picardi L, Piccinini M, Placido C, Ronsivalle C, Soriani A, Strigari L, Trinca E, Vadrucci M. Characterization of 27 Mev Proton Beam Generated by Top-Implart Linear Accelerator. Radiat.Prot.Dosimetry. 2018 Aug 1;180(1-4):329-333

8. Esposito M, Masi L, Zani M, Doro R, Fedele D, Garibaldi C, Clemente S, Fiandra C, Giglioli FR, Marino C, Orsingher L, Russo S, Stasi M, Strigari L, Villaggi E, Mancosu P. SBRT Planning for Spinal Metastasis: Indications from a Large Multicentric Study. Strahlenther.Onkol. 2018 Oct 23;

9. Fedeli L, Belli G, Ciccarone A, Coniglio A, Esposito M, Giannelli M, Mazzoni LN, Nocetti L, Sghedoni R, Tarducci R, Altabella L, Belligotti E, Benelli M, Betti M, Caivano R, Carni' M, Chiappiniello A, Cimolai S, Cretti F, Fulcheri C, Gasperi C, Giacometti M, Levrero F, Lizio D, Maieron M, Marzi S, Mascaro L, Mazzocchi S, Meliado' G, Morzenti S, Noferini L, Oberhofer N, Quattrocchi MG, Ricci A, Taddeucci A, Tenori L, Luchinat C, Gobbi G, Gori C, Busoni S, Italian Association of Physics in Medicine (AIFM) Working Group on MR Intercomparison. Dependence of Apparent Diffusion Coefficient Measurement on Diffusion Gradient Direction and Spatial Position - A Quality Assurance Intercomparison Study of Forty-Four Scanners for Quantitative Diffusion-Weighted Imaging. Phys.Med. 2018 Nov; 55: 135a

10. Flux GD, Sjogreen Gleisner K, Chiesa C, Lassmann M, Chouin N, Gear J, Bardies M, Walrand S, Bacher K, Eberlein U, Ljungberg M, Strigari L, Visser E, Konijnenberg MW. From Fixed Activities to Personalized Treatments in Radionuclide Therapy: Lost in Translation? Eur.J.Nucl.Med.Mol.Imaging. 2018 Jan; 45(1): 152a

11. Kok HP, Navarro F, Strigari L, Cavagnaro M, Crezee J. Locoregional Hyperthermia of Deep-Seated Tumours Applied with Capacitive and Radiative Systems: A Simulation Study. Int.J.Hyperthermia. 2018 Apr 18; : 1a

12. Loi G, Fusella M, Lanzi E, Cagni E, Garibaldi C, Iacoviello G, Lucio F, Menghi E, Miceli R, Orlandini LC, Roggio A, Rosica F, Stasi M, Strigari L, Strolin S, Fiandra C. Performance of Commercially Available Deformable Image Registration Platforms for Contour Propagation using Patient-Based Computational Phantoms: A Multi-Institutional Study. Med. Phys. 2018 Feb; 45(2): 748a

13. Lopresto V, Strigari L, Farina L, Minosse S, Pinto R, Dâ€™Alessio D, Cassano B, Cavagnaro M. CT-Based Investigation of the Contraction of Ex Vivo Tissue Undergoing Microwave Thermal Ablation. Physics in Medicine & Biology. 2018 63(5): 055019a

14. Marzi S, Farneti A, Vidiri A, Di Giuliano F, Marucci L, Spasiano F, Terrenato I, Sanguineti G. Radiation-Induced Parotid Changes in Oropharyngeal Cancer Patients: The Role of Early Functional Imaging and Patient-/treatment-Related Factors. Radiat.Oncol. 2018 Oct 1; 13(1): 189a

15. Marzi S, Minosse S, Vidiri A, Piludu F, Giannelli M. Diffusional Kurtosis Imaging in Head and Neck Cancer: On the use of Trace-Weighted Images to Estimate Indices of Non-Gaussian Water Diffusion. Med.Phys. 2018 Dec;45(12):5411-5419

16. Mazzuca F, Onesti CE, Roberto M, Di Girolamo M, Botticelli A, Begini P, Strigari L, Marchetti P, Muscaritoli M. Lean Body Mass Wasting and Toxicity in Early Breast Cancer Patients Receiving Anthracyclines. Oncotarget. 2018 May 22; 9(39): 25714a

17. Piludu F, Gangemi E, Marucci L, Guerrisi A, Pellini R, Covello R, Carlini P, Spriano G, Sanguineti G, Marzi S, Vidiri A. MRI Evaluation using DWI and T2WI of Residual Lymph Nodes in Patients Affected by Head and Neck Squamous Cell Carcinoma Treated with Chemo-Radiotherapy. Curr.Med.Imaging Rev. 2018 14(4): 599a

18. Roberto M, Botticelli A, Strigari L, Ghidini M, Onesti CE, Ratti M, Benzoni I, Pizzo C, Falcone R, Lomiento D, Donida BM, Totaro L, Mazzuca F, Marchetti P. Prognosis of Elderly Gastric Cancer Patients After Surgery: A Nomogram to Predict Survival. Med.Oncol. 2018 Jun 19; 35(7): 111a

19. Stramucci L, Pranteda A, Bossi G. Insights of Crosstalk between p53 Protein and the MKK3/MKK6/p38 MAPK Signaling Pathway in Cancer. Cancers (Basel). 2018 May 3; 10(5): E131

20. Strigari L, Torriani F, Manganaro L, Inaniwa T, Dalmasso F, Cirio R, Attili A. Tumour Control in Ion Beam Radiotherapy with Different Ions in the Presence of Hypoxia: An Oxygen Enhancement Ratio Model Based on the Microdosimetric Kinetic Model. Phys.Med.Biol. 2018 Mar 16; 63(6): 065012a

# NUCLEAR MEDICINE UNIT

## *Head: Rosa Sciuto, MD*

## STAFF

| |
|---|
| **Alessio Annovazzi, MD** |
| **Serenella Bergomi, MD** |
| **Pasquale Iannantuono, MD** |
| **Costanza Mazzone, MD** |
| **Rosella Pasqualoni, MD** |
| **Sandra Rea, MD** |
| **Luisa Romano, MD** |
| **Silvia Di Traglia, Fellow** |
| **Salvatore Annunziata, Fellow** |
| **Aura D'Arcangeli, Head Nurse** |
| **Gaetano Salviati, Chief Technician** |

### *Mission*

The mission of the Nuclear Medicine Unit is to perform clinical and research activities in nuclear oncology aiming to the following main objectives:

- achieve professional exellence both in nuclear diagnostics and in nuclear therapy according national and international standards
- develope and validate innovative technologies and new radiopharmaceuticals for molecular imaging and molecular target therapy in the context of theranostic models
- transfer research results into clinical practice and national health system program
- monitor process influence on final outcome according to a vision of a process-oriented culture and patient's centered care

## Clinical Activity

The activities of the Nuclear Medicine Unit focus on clinical research directed towards **therapy and diagnostics in main oncology fields.** In 2018 over 16.000 therapeutic and diagnostic procedures were performed with approximately 300 cancer radionuclide treatments. Standard of all diagnostic and therapy activities are assured by ISO 9000 and professional quality certification is assured by AIMN-Bureau Veritas.

12. **Therapy**, as the main field of clinical activities, includes the radionuclide treatment of thyroid carcinoma, liver tumors and bone metastases using both beta emitters and alfa-emitters. The Centre is leader in Italy and Europe in the field of selective internal radiation therapy of liver tumors with more than 950 treatment performed and followed. Biological optimization of radiation dose studies have been performed using new algorithms and integrated imaging to evaluate heterogeneous dose distribution in tumor lesions and to develop personalized therapy plans. Training on innovative treatments with new alfa-emitters radiopharmaceuticals were performed and clinical protocols validated
13. **Diagnostics includes**: - PET / CT imaging with FDG and non FDG tracer and in particular the Centre is leader in F-Choline PET imaging of prostate cancer and FDG PET imaging of musculoskeletal tumors ; - all traditional planar and SPET oncological scan (mainly sentinel node mapping, cardiac gated-SPET and 131I whole –body scan) and state of art SPET/CT imaging.

## Research Activity

Research activities of the Nuclear Medicine Unit focus on radionuclide therapy and molecular imaging SPET/CT and PET/CT in different tumors (thyroid, head and neck, sarcoma, gynecological and urological tumors, lymphoma, breast and lung cancer, liver tumors) aiming to improve early diagnosis, biological characterization and response monitoring, biological volume contouring to guide radiotherapy.

Main currently specific topic of research includes:

- new PET radiopharmaceuticals (64-Cu and 64 Cu-PSMA) performance and safety evaluation in prostate cancer
- F-choline diagnostic performance in early prostate cancer recurrence detection at low PSA values
- clinical impact of SPET/CT vs. to standard planar or SPET protocols in oncology
- comparison of clinical impact and cost-effectiveness of different available diagnostic technologies of bone imaging (bone scintigraphy vs. F-choline PET)
- role of FDG PET in clinical management of musculoskeletal tumors
- biodistribution, radiobiological effects and long – term safety studies after treatment with alfa –emitter (223-radium) in metastatic prostate cancer patients and adapted protocols
- role of integrated imaging with $^{131}$I SPET/CT and $^{18}$F-FDG PET/CT in advanced thyroid carcinoma both for diagnosis than for biological and dosimetric optimization
- identification of specific selective internal radiation therapy with 90Y-microspheres indications in the context of the standard HCC guidelines
- quantitative 3D dosimetry based on hybrid imaging and biomarkers correlation to optimize therapy in HCC patients treated with 90Y-microspheres
- Early salvage with high-dose chemotherapy and stem cell transplantation in advanced stage Hodgkin's lymphoma patients with positive PET after two courses of ABVD (PET-2 positive) and comparison of radiotherapy versus no radiotherapy in PET-2 negative patients.

## Pubblications

1. Allegretti M, Casini B, Mandoj C, Benini S, Alberti L, Novello M, Melucci E, Conti L, Covello R, Pescarmona E, Milano GM, Annovazzi A, Anelli V, Ferraresi V, Biagini R, Giacomini P. Precision Diagnostics of Ewing's Sarcoma by Liquid Biopsy: Circulating EWS-FLI1 Fusion Transcripts. *Fher.Adv.Med.Oncol.* 2018 Jun 1; 10: 1758835918774337a

2. Annovazzi A, Rea S, Vici P, Fabi A, Sciuto R. Dual-Time 18F-FDG PET/CT for the Detection of Liver Metastases in Breast Cancer. *Nucl.Med.Commun.* 2018 Dec; 39(12): 1183-1189a

3. Sangro B, Maini CL, Ettorre GM, Cianni R, Golfieri R, Gasparini D, Ezziddin S, Paprottka PM, Fiore F, Van Buskirk M, Bilbao JI, Salvatori R, Giampalma E, Geatti O, Wilhelm K, Hoffmann RT, Izzo F, Inarrairaegui M, Urigo C, Cappelli A, Vit A, Ahmadzadehfar H, Jakobs TF, Sciuto R, Pizzi G, Lastoria S, European Network on Radioembolization with Yttrium-90 resin microspheres (ENRY). Radioembolisation in Patients with Hepatocellular Carcinoma that have Previously Received Liver-Directed Therapies. *Eur. J. Nucl. Med. Mol. Imaging.* 2018 Sep;45(10):1721-1730

4. Zoccali C, Baldi J, Attala D, Rossi B, Anelli V, Annovazzi A, Ferraresi V. Intralesional Vs. Extralesional Procedures for Low-Grade Central Chondrosarcoma: A Systematic Review of the Literature. *Arch. Orthop. Trauma Surg.* 2018 Jul; 138(7): 929a

# RADIOTHERAPY UNIT

*Head: Sanguineti Giuseppe, MD*

## STAFF

| |
|---|
| **Pinnarò Paola, MD** |
| **Saracino Bianca Maria, MD** |
| **Marucci Laura, MD** |
| **Petrongari Maria Grazia, MD** |
| **Farneti Alessia, MD** |
| **Giordano Carolina, MD** |
| **Faiella Adriana, MD** |
| **Genoveva Ionela Boboc, MD** |
| Nurse coordinator |
| **Di Ridolfi Paolo** |
| Nurse |
| **Caramadre Lucia** |
| **Bigiarini Luciano** |
| **Mondati Mara** |
| **Petitti Patrizia** |
| **Giardina Giuseppa Barbara.** |
| Therapist coordinator |
| **Lunghi Vincenzo** |

| Therapist |
|---|
| **Bedini Fabio** |
| **Canciani Laura** |
| **De Luca Francesco** |
| **Di Giammaria Flavio** |
| **Gabriele Teresa** |
| **Labonia Alessandro** |
| **Mafrica Carmelo** |
| **Marcelli Francesca** |
| **Marini Roberto** |
| **Mei Stefano** |
| **Minutello Martino** |
| **Monetti Flavio** |
| **Musella Giuseppe** |
| **Pepe Stefano** |
| **Rispoli Antonio** |
| **Trotta Simone** |
| **Vorzillo Maria** |
| Administrative collaboratror |
| **Parodi Laura** |
| **Moretti Luisa** |
| Data Manager |
| **Spasiano Filomena** |

## *Mission*

Department of Radiotherapy is characterized experience and technology that allow the realization of high-precision irradiation techniques such as Intensity Modulated Radiotherapy (IMRT) and Rapid Arc (RA)/Volumetric Modulated Arc Therapy (VMAT), Stereotactic Radiotherapy Surgery (SRS), Stereotactic Body Radiotherapy (SBRT), Image-Guided Radiation Therapy (IGRT). Moreover, respiratory movement control techniques are available to reduce the confounding effect of the position of the target to be irradiated, as well as 'tracking' techniques through the placement of radiopaque fiducials and Cyberknife irradiation. A constant collaboration with the Radiology and Nuclear Medicine allows us to have access to advanced imaging solutions to correctly identify the location of the disease prior to treatment planning, such as multiparametric MRI and novel tracer PET-CT.

Clinical Activity: Clinical activity covers all options of photon-based external beam radiotherapy including IMRT, VMAT, SRS, SBRT, IORT. Moreover, the

recent introduction of Cyberknife (CK) allows SRS/SBRT of both intracranial and extracranial lesions (both malignant and benign) with high precision and live motion tracking.

## Research Activity

1. Early Diffusion Weighted Magnetic Resonance Imaging Changes to Predict Tumor Response to Chemoradiotherapy in HN Cancer. Primary Objective: To prospectively evaluate the predictive value of novel MR biomarker (DWI, DCE-MRI and IVIM-MRI) changes early during CRT to assess therapy outcome in advanced HNSCC undergoing CRT.
2. Phase I-II study to evaluated feasibility and the effectiveness of SBRT with Linear Accelerator in 3 fractions for low/intermediate risk Prostate cancer: evaluate the feasibility and locoregional toxicity of SBRT in 3 fractions using LINAC; evaluate the effectiveness hypofractionated "extreme" (3 fractions) delivered using SBRT for low /intermediate risk localized prostate cancer.
3. Single vocal cord stereotactic Radiotherapy for early stage glottis cancer (cTis-1): Prospective phase I-II study to evaluated feasibility and the effectiveness of SBRT for early stage (cTis-1N0M0) glottic cancer.
4. Short-Course Hypofractionated Whole-Breast Radiation Therapy After Conservative Surgery: A Single-Institution Prospective Study: To assess the oncologic outcomes of an accelerated and hypofractionated whole breast irradiation (AH-WBI) schedule in which therapy was completed in 11 fractions over 3 weeks inclusive of a sequential boost.
5. Accelerated Hypofractionated radiotherapy inclusive of nodal radiation after conservative surgery for women whit node-positive breast cancer. Feasibility study. To evaluated acute toxicity of radiotherapy schedule in which therapy was completed in 11 fractions over 3 weeks inclusive of a sequential boos.
6. Neurocognitive assessment for cancer patient whit 1-3 brain metastatis treated with stereotactic Radiotherapy or iphocampal sparing whole brain radiotherapy: Observation study to evaluated the different preservation of neurocognitive function between the two radiotherapic treatements.
7. Longitudinal Evaluation of Intestinal, Haematological

and Urinary Toxicity From Pelvic Irradiation for Prostate Cancer (IHU-WPRT-TOX): The aim of this study is to develop predictive models of IMRT-WPRT induced patient-reported intestinal, hematologic and urinary toxicity in PCa treatment. The rationale of the prophylactic irradiation of pelvic lymph-nodes by means of Whole-Pelvis Radiotherapy (WPRT) in prostate cancer (PCa) is to eradicate subclinical lymph-nodal involvement. Even though delivered by means of modern Intensity-Modulated Radiotherapy techniques,WPRT may result in intestinal, hematologic and urinary toxicity severely affecting patients' daily health-related quality-of-life (HRQoL) within the so-called and inadequately investigated Pelvic Radiation Disease.

8. Radiation Therapy in the initial stages of hodgkin's lymphoma: Impact of use of pet-ct performed in position of treatment on target delineation. Observational Study. The *aim* of study is to determine the impact of co-registration of CT-PET images of staging performed with the patient in the treatment position with the simulation TC in definition and delineation of the target volume and, consequently, in radiotherapy treatment planning of initial stages of hodgkin's lymphoma. The *primary endpoint* will be the evaluation of the modification of treatment volume as a result of the co-registration process; the secondary end point will consist in evaluating the impact of process on the dose deposited in specific and significant volumes of healthy tissue.
9. A Randomized, Double-blind, Placebo-controlled Phase 3 Study of JNJ-56021927 in Subjects with High-risk, Localized or Locally Advanced Prostate Cancer Receiving Treatment with Primary Radiation Therapy: To determine if JNJ-56021927 plus gonadotropin releasing hormone (GnRH) agonist in subjects with high-risk, localized or locally advanced prostate cancer receiving primary radiation therapy (RT) results in an improvement of metastasis-free survival (MFS) evaluated by blinded independent central review (BICR)
10. A multicenter randomized, open-label phase ii/iii study, to compare the efficacy of nbtxr3, implanted as intratumor injection and activated by radiotherapy, versus radiotherapy alone in patients with locally advanced soft tissue sarcoma of the extremity and trunk wall: To compare the antitumor activity in terms of Pathological complete response rate (pCRR) of intratumor injection of NBTXR3 activated by external beam radiation therapy (EBRT), versus EBRT alone, in patients with locally advanced soft tissue sarcoma (STS) of the extremity and trunk wall.
11. DUE02 - Urinary and Erectile Dysfunction – 02. Validation of predictive toxicity models after radiotherapy treatment for prostate cancer: The prospective observational study (DUE02) proposes to enroll patients with prostate cancer treated with high-dose external radiotherapy and to follow them during follow-up, in order to be able to validate the models developed in the previous study DUE01 on an independent population.
12. Acral Chordoma: a Randomized & Observational study on surgery versus definitive radiation therapy in primary localized disease (SACRO):This study is aimed at estimating the effectiveness of definitive radiotherapy as compared to standard surgical treatment for patients with primary sacral chordoma who are candidates to a complete en-bloc resection, in term of relapse-free-survival (RFS).

## Publications

1. Bossi P, Miceli R, Benasso M, Corvo R, Bacigalupo A, Sanguineti G, Fallai C, Merlano MC, Infante G, Dani C, Di Giannantonio V, Licitra L. Impact of Treatment Expertise on the Outcome of Patients with Head and Neck Cancer Treated within 6 Randomized Trials. *Head Neck*. 2018 Dec; 40(12): 2648a.

2. Gamucci T, Pizzuti L, Natoli C, Mentuccia L, Sperduti I, Barba M, Sergi D, Iezzi L, Maugeri-Sacca M,Vaccaro A, Magnolfi E, Gelibter A, Barchiesi G, Magri V, D'Onofrio L, Cassano A, Rossi E, Botticelli A, Moscetti L, Omarini C, Fabbri MA, Scinto AF, Corsi D, Carbognin L, Mazzotta M, Bria E, Foglietta J, Samaritani R, Garufi C, Mariani L, Barni S, Mirabelli R, Sarmiento R, Graziano V, Santini D, Marchetti P, Tonini G, Di Lauro L, Sanguineti G, Paoletti G, Tomao S, De Maria R, Veltri E, Paris I, Giotta F, Latorre A, Giordano A, Ciliberto G,Vici P. A Multicenter REtrospective Observational Study of First-Line Treatment with PERtuzumab, Trastuzumab and Taxanes for Advanced HER2 Positive Breast Cancer Patients. RePer Study. *Cancer Biol Ther.* 2018 Nov 7 [Epub ahead of print]

3. Gamucci T, Pizzuti L, Sperduti I, Mentuccia L, Vaccaro A, Moscetti L, Marchetti P, Carbognin L, Michelotti A, Iezzi L, Cassano A, Grassadonia A, Astone A, Botticelli A, Magnolfi E, Di Lauro L, Sergi D, Fuso P, Tinari N, Barba M, Maugeri-Sacca M, Landucci E, Conti F, Sanguineti G, De Tursi M, Iafrate G, Giordano A, Ciliberto G, Natoli C, Vici P. Neoadjuvant Chemotherapy in Triple-Negative Breast Cancer: A Multicentric Retrospective Observational Study in Real-Life Setting. *J. Cell. Physiol.* 2018 Mar; 233(3): 2313a.

4. Licitra L, Bonomo P, Sanguineti G, Bacigalupo A, Baldi GG, Valerini S, Bruzzi P. Different View on Larynx Preservation Evidence-Based Treatment Recommendations. *J. Clin. Oncol.* 2018 May 1; 36(13): 1376a

5. Mandoj C, Pizzuti L, Sergi D, Sperduti I, Mazzotta M, Di Lauro L, Amodio A, Carpano S, Di Benedetto A, Botti C, Ferranti F, Antenucci A, D'Alessandro MG, Marchetti P, Tomao S, Sanguineti G, Giordano A, Maugeri-Sacca M, Ciliberto G, Conti L, Vici P, Barba M. Observational Study of Coagulation Activation in Early Breast Cancer: Development of a Prognostic Model Based on Data from the Real World Setting. *J. Transl. Med.* 2018 May 16; 16(1): 129a

6. Marzi S, Farneti A, Vidiri A, Di Giuliano F, Marucci L, Spasiano F, Terrenato I, Sanguineti G. Radiation-Induced Parotid Changes in Oropharyngeal Cancer Patients: The Role of Early Functional Imaging and Patient-/treatment-Related Factors. *Radiat. Oncol.* 2018 Oct 1; 13(1): 189a

7. Piludu F, Gangemi E, Marucci L, Guerrisi A, Pellini R, Covello R, Carlini P, Spriano G, Sanguineti G, Marzi S, Vidiri A. MRI Evaluation using DWI and T2WI of Residual Lymph Nodes in Patients Affected by Head and Neck Squamous Cell Carcinoma Treated with Chemo-Radiotherapy. *Curr. Med. Imaging Rev.* 2018 14(4): 599a

# RADIOLOGY UNIT

*interim head: Maurizio Caterino, MD*

## STAFF

| |
|---|
| **Anelli Vincenzo MD** |
| **Bertini Luca MD** |
| **Ferranti Francesca Romana MD** |
| **Greco Marcello MD** |
| **Kayal Ramy MD** |
| **Marsella Annelisa MD** |
| **Piacentini Francesca MD** |
| **Pizzi Giuseppe MD** |
| **Saracca Elena MD** |
| **Vallati Giulio MD** |
| **Vidiri Antonello MD** |
| Radiology Techinician Coordinator |
| **D'Auria Lorenzo** |
| **Fodde Francesca** |
| Radiology Technician |
| **Abrugia Maurizio** |
| **Baldolini Roberto** |
| **De Leo Rodolfo** |
| **Dominici Fabrizio** |
| **Farella Michele** |
| **Fetonti Gaetano** |
| **Fringuelli Stefania** |
| **Lattanzi Gianluca** |
| **Longo Anna** |
| **Morelli Graziella** |
| **Pandini Roberto** |
| **Pasqualucci Rita** |
| **Portieri Fabio** |
| **Rea Franco** |
| **Rinaldi Francesco** |
| **Tomassini Elisa** |
| **Trotta Simone** |
| **Strino Giulio** |

| |
|---|
| Nurse Coordinator |
| **Colucci Pasquale** |
| Nurse |
| **Annibali Cristina** |
| **Cicconardi Alba** |
| **Del Vecchio Serena** |
| **Desideri Manuela** |
| **Fantozzi Roberto** |
| **Guido Franco** |
| **Rosi Fabio** |
| **Schiavone Raffaella** |
| **Tolu Sebastiano** |
| **Vita Silvano** |
| Administrative Collaborator |
| **Boi Cristina** |
| **Giacinti Fausto** |
| **Settembrini Cristina** |

## *Mission*

The Radiology Unit main mission is to perform diagnosis, staging and follow-up of neoplasms through state of the art medical equipment such as: 3T superconductive scanner in MR, multidetector CT at 128Layer, Ultrasound with color-doppler and through the use of contrast-medium, Digital Mammography, Mammotome for biopsy and Contrast Enhanced Mammography (CESM). The Radiology Unit also offers image-guided Interventional Services for diagnosis and treatment of neoplasms. More specifically, the radiology service is specialized in the evaluation of head-neck tumors, pleural mesothelioma, prostate cancer with multiparametric approaches and integrated breast diagnostic through ultrasound, mammography, mammotome biopsy, CESM and MR. We also focus on performing neuro-oncology with 3T MR, where is possible to obtain morphological

and non-morphological (diffusion, perfusion, functional, tractography and spectroscopy) imaging, soft and osseous tumors. In addition, neoplasms of the female pelvic, lung, colon-rectum and onco-hematologic tumors are also assessed by various imaging techniques. The department is also involved in all diagnostic therapeutic care (PDTA) and participates in all Disease Management Team (DMT) meetings.

## Clinical Activity

Clinical diagnostic activity includes: traditional X-ray, ultrasound, CT, MR, and mammography and is performed every day (morning and afternoon) except Saturday afternoon. The Interventional service is open from Monday to Friday (morning and afternoon) except on Wednesdays, when the Radiology Unit is reserved to Gastroenterology unit. The MR unit offers services such as functional imaging, image-guided breast unit biopsy with mammotome, in US is possible to perform exam with contrast medium infusion, while the Interventional unit service biopsy and treatment of neoplasms with thermoablation, radiofrequences, radionuclide (Sirtex).

## Research Activity

Research activities of the Radiology Unit, focus on the detection of new imaging biomarkers that can be used as prognostic and teranostic markers; these will be correlated with histopathological and immunohistochemical data. Main currently specific topics of research include:

- **Radiomics:** A hot topic in modern diagnostic imaging. Radiomics basically consists in performing cross-sectional scanninng in order to extract quantitative information hidden in the texture of images, which goes far beyond the detection of the human eye. Such process, powered by dedicated software, enables to convert digital diagnostic images into big-data that can be used to investigate correlations between imaging-related parameters, genomic profile and metabolism of tumors. In the era of precision medicine, this technique promises to assist in the selection of the right treatment for the right patient in the right clinical context. We use Radiomics in the evaluation of parotid tumors, breast cancer, lung cancer and lymphoma.
- Correlate the set of identified imaging biomarkers – with diffusion and perfusion MR in head-neck tumors – with those related to tissue architecture analyzed by immunohistochemistry and 'digital pathology'. Identify a panel of baseline imaging biomarkers before surgery that can be used as prognostic and theragnostic markers.
- Early diffusion and perfusion MR to predict tumor response to chemo-radiation therapy in head-neck cancers. The aim of this study is to investigate the possibility to obtain a differentiation between responder and non-responder patients before treatment.
- Ongoing functional studies with MR to define the differential diagnosis on recurrence and radionecrosis in brain metastases undergoing cyber-knife treatment.
- Multiparametric-MR prostate studies before and after therapy, performed in particular for the evaluation of the alterations after radiotherapy compared with those performed with PET-CT scan.
- Neo-adjuvant treatments using 3T MR with functional sequences (diffusion and perfusion) in the sarcomas, osteosarcoma and Ewing sarcoma and evaluation of patient response to sarcomas treated with Trabectin.
- Carrying out an ongoing study on the use of iodinated contrast media in association with mammography (CESM) and digital mammography, comparing the results with those of MR.
- Evaluation of breast cancer before and after neoadjuvant chemotherapy with multiparametric MR.
- In the Interventional service we use targeted dosimetry-guided therapy aiming at significantly impact patient's specific therapy selection and treatment.

## Publications

1. Allegretti M, Casini B, Mandoj C, Benini S, Alberti L, Novello M, Melucci E, Conti L, Covello R, Pescarmona E, Milano GM, Annovazzi A, Anelli V, Ferraresi V, Biagini R, Giacomini P. Precision Diagnostics of Ewing's Sarcoma by Liquid Biopsy: Circulating EWS-FLI1 Fusion Transcripts. *Ther. Adv. Med. Oncol.* 2018 Jun 1; 10: 1758835918774337a

2. Catania G, Malaguti P, Gasparro S, Cognetti F, Vidiri A, Fabi A. Activity of Eribulin Mesylate in Brain Metastasis from Breast Cancer: A Stone in a Pond? *Oncology.* 2018 94(Suppl 1): 29a

3. Di Stefano AL, Berzero G, Ducray F, Eoli M, Pichiecchio A, Farina LM, Cuccarini V, Brunelli MC, Diamanti L, Condette Auliac S, Salmaggi A, Silvani A, Giometto B, Pace A, Vidiri A, Bourdain F, Bastianello S, Ceroni M, Marchioni E. "Stroke-Like" Events After Brain Radiotherapy: A Large Series with Long-Term Follow-Up. *Eur. J. Neurol.* 2018 Nov 24 [Epub ahead of print]

4. Mandoj C, Pizzuti L, Sergi D, Sperduti I, Mazzotta M, Di Lauro L, Amodio A, Carpano S, Di Benedetto A, Botti C, Ferranti F, Antenucci A, D'Alessandro MG, Marchetti P, Tomao S, Sanguineti G, Giordano A, Maugeri-Sacca M, Ciliberto G, Conti L, Vici P, Barba M. Observational Study of Coagulation Activation in Early Breast Cancer: Development of a Prognostic Model Based on Data from the Real World Setting. *J. Transl. Med.* 2018 May 16; 16(1): 129a

5. Marzi S, Farneti A, Vidiri A, Di Giuliano F, Marucci L, Spasiano F, Terrenato I, Sanguineti G. Radiation-Induced Parotid Changes in Oropharyngeal Cancer Patients: The Role of Early Functional Imaging and Patient-/treatment-Related Factors. *Radiat. Oncol.* 2018 Oct 1; 13(1): 189a

6. Marzi S, Minosse S, Vidiri A, Piludu F, Giannelli M. Diffusional Kurtosis Imaging in Head and Neck Cancer: On the use of Trace-Weighted Images to Estimate Indices of Non-Gaussian Water Diffusion. *Med. Phys.* 2018 Dec;45(12):5411-5419

7. Pace A, Mandoj C, Antenucci A, Villani V, Sperduti I, Casini B, Carosi M, Fabi A, Vidiri A, Koudriavtseva T, Conti L. A Predictive Value of Von Willebrand Factor for Early Response to Bevacizumab Therapy in Recurrent Glioma. *J. Neurooncol.* 2018 Jul; 138(3): 527a

8. Paladini A, Lucatelli P, Cappelli F, Pizzi G, Anelli V, Amodeo EM, Beomonte Zobel D, Paladini L, Biagini R, Attala D, Zoccali C, Vallati GE. Osteoid Osteoma Treated with Radiofrequency Ablation in Non-Operating Room Anesthesia. A Different Way of Approaching Ablative Therapy on Osteoid Osteoma. *Eur. Rev. Med. Pharmacol. Sci.* 2018 Sep; 22(17): 5438a

9. Piludu F, Gangemi E, Marucci L, Guerrisi A, Pellini R, Covello R, Carlini P, Spriano G, Sanguineti G, Marzi S, Vidiri A. MRI Evaluation using DWI and T2WI of Residual Lymph Nodes in Patients Affected by Head and Neck Squamous Cell Carcinoma Treated with Chemo-Radiotherapy. *Curr. Med. Imaging Rev.* 2018 14(4): 599a

10. Russillo M, Ferretti G, Vidiri A, Gasparro S, Cognetti F, Pellegrini D, Fabi A. Impressive Long-Term Response with Pertuzumab and Trastuzumab in HER2-Positive Breast Cancer with Brain Metastasis. *In Vivo.* 2018 Jul-Aug; 32(4): 839a

11. Sangro B, Maini CL, Ettorre GM, Cianni R, Golfieri R, Gasparini D, Ezziddin S, Paprottka PM, Fiore F, Van Buskirk M, Bilbao JI, Salvatori R, Giampalma E, Geatti O, Wilhelm K, Hoffmann RT, Izzo F, Inarrairaegui M, Urigo C, Cappelli A, Vit A, Ahmadzadehfar H, Jakobs TF, Sciuto R, Pizzi G, Lastoria S, European Network on Radioembolization with Yttrium-90 resin microspheres (ENRY). Radioembolisation in Patients with Hepatocellular Carcinoma that have Previously Received Liver-Directed Therapies. *Eur. J. Nucl. Med. Mol. Imaging.* 2018 Sep;45(10):1721-1730

12. Simone G, Papalia R, Misuraca L, Tuderti G, Minisola F, Ferriero M, Vallati G, Guaglianone S, Gallucci M. Robotic Intracorporeal Padua Ileal Bladder: Surgical Technique, Perioperative, Oncologic and Functional Outcomes. *Eur. Urol.* 2018 Jun; 73(6): 934a

13. Simone G, Tuderti G, Anceschi U, Ferriero M, Costantini M, Minisola F, Vallati G, Pizzi G, Guaglianone S, Misuraca L, Gallucci M. "Ride the Green Light": Indocyanine Green-Marked Off-Clamp Robotic Partial Nephrectomy for Totally Endophytic Renal Masses. *Eur. Urol.* 2018 Sep 24 [Epub ahead of print]

14. Terrenato I, Sperati F, Musicco F, Pozzi AF, di Turi A, Caterino M, de Lutio di Castelguidone E, Setola SV, Bellomi M, Neumaier CE, Conti L, Cigliana G, Merola R, Antenucci A, Orlandi G, Giordano A, Barba M, Canitano S. Iodixanol Versus Iopromide in Cancer Patients: Evidence from a Randomized Clinical Trial. *J. Cell. Physiol.* 2018 Mar; 233(3): 2572a

15. Zoccali C, Baldi J, Attala D, Rossi B, Anelli V, Annovazzi A, Ferraresi V. Intralesional Vs. Extralesional Procedures for Low-Grade Central Chondrosarcoma: A Systematic Review of the Literature. *Arch. Orthop. Trauma Surg.* 2018 Jul; 138(7): 929a

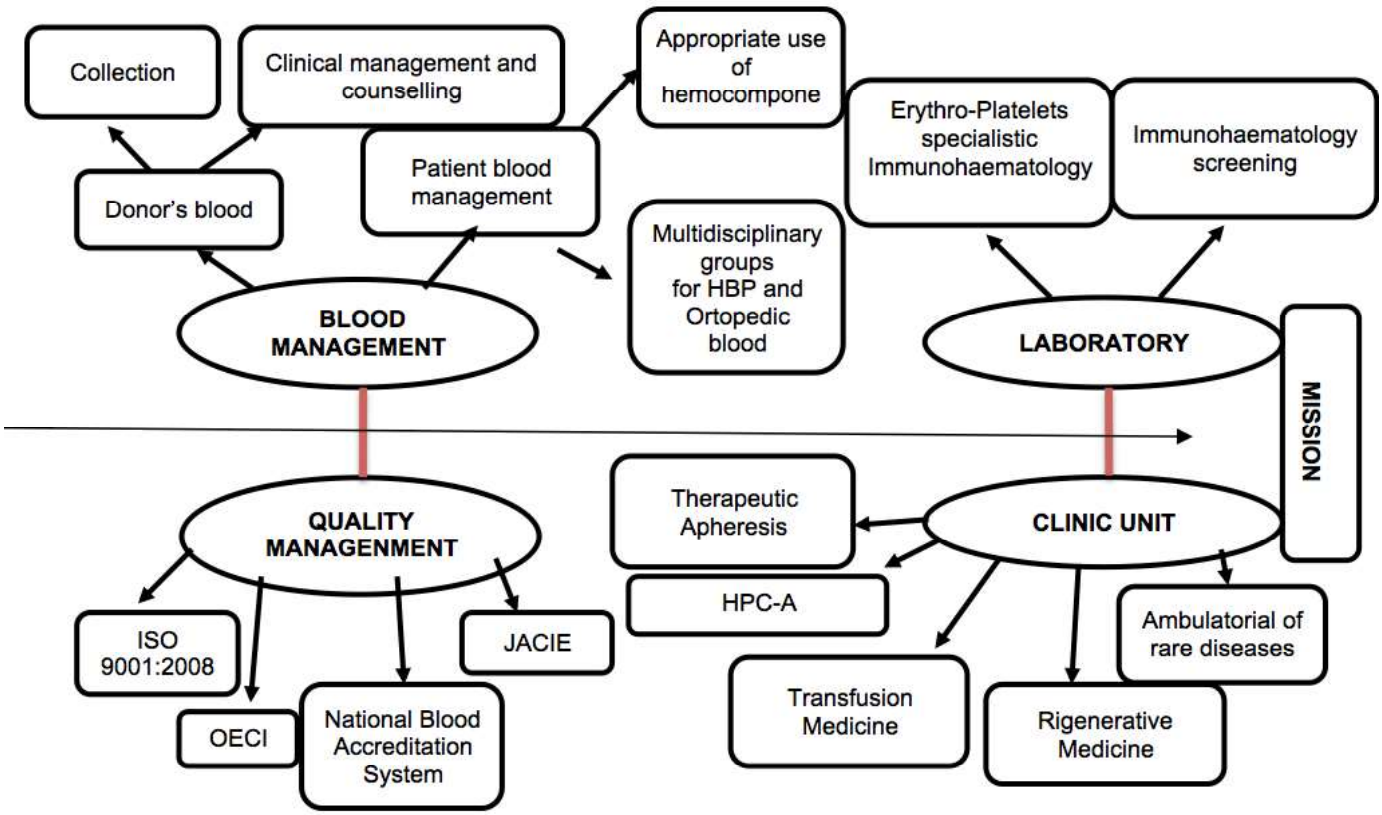
# TRANSFUSION MEDICINE UNIT

*Head: Maria Laura Foddai, MD*

## STAFF

| |
|---|
| Mafalda de Rienzo, MD |
| Stefano Iaboni, MD |
| Silvia De Matteis, MD |
| **Technicians** |
| Mara Battista, Coordinator |
| Tonino Federico |
| Nadia Coculo |
| Patrizio Ceccacci |
| Daniela Mozzetti |
| Emanuele Fazi |
| Maria Piedimonte |
| Daniela Di Mambro |

| |
|---|
| **Biologist** |
| Pina Chichierchia, |
| **Nurse** |
| Maria Rosa Piras, Nurse |
| Patrizia Comuzzi, Nurse |
| Ilenia Saladini, Nurse |



## Clinical Activity

The Immunohaematology and Trasfusion Medicine Service is an articulated structure that complies with specific tasks provided by the Italian Legislation in the field of transfusion and supports with diagnostics and therapeutic activities the clinical departments for the treatment of haematological, dermatological, oncological, internal and surgical diseases. The activities are mainly directed to:

- Ensure the constant availability of blood and hemocomponents for the departments' needs;
- Verify the appropriateness of blood and hemocomponents clinical use;
- Manage cryopreserved pheripheral blood stem cells
- Control the quality and safety requirements of the hemocomponents.

In the Unit, there are the following areas of excellence which are intended to be implemented: Therapeutic Apheresis, Regenerative Medicine and Erytro-Platelets Immunohaematology.

The unit of Therapeutic Apheresis relies on the latest generation cell separators that allow to perform plasma exchange and photopheresis procedures in autoimmune and dysimmune diseases, in particularly in dermatological patients affected by Pemphigus Vulgaris, Atopic Dermatitis, Mycosis Fungoid, Psoriasis, etc.

The Regenerative Medicine is a new therapeutic approach aimed at the biological regeneration of tissues instead of replacing them, and finds its most relevant applications in orthopedics, dermatology and corrective medicine.

The Immunohaematological diagnostic is important in oncologic and polytransfused patients to prevent alloimmunization and consist in typing of rare erythrocyte groups, research of anti-erythrocyte and anti-platelets antibodies and identification of auto and allo-antibodies.

## Research Activity

Blood derivatives ameliorate myogenic progenitor cells proliferation and differentiation:

In collaboration with Dr. Cesare Gargioli, researcher at the Department of Biology of Rome University Tor Vergata, we are developing a project regarding the effect of human blood derived serum and/or growth factor on human derived perivascular myogenic progenitor/stem cell, namely pericytes. So, the project purpose is to test human blood derivatives in order to supersede problems related to animal medium supplement and cell therapy for clinical application; moreover, working with human derived stem cells, we are analyzing the effect of human serum and growth factors on the myogenic capabilities of human skeletal muscle derived pericytes.

Bcl-2 promotes recruitment and differentiation of macrophages towards a M2-like phenotype:

In collaboration Dr. Donatella del Bufalo, preclinical models and new therapeutic agents unit – proposal AIRC investigator grant – Spanning bcl-2 functions in melanoma models from micro environment to microRNA modulation.

Evaluation of platelets-rich plasma effectiveness in vulvar lichen sclerosus in collaboration with plastic surgery unit IRCCS San Gallicano.

## Publications

1. Palermo B, Franzese O, Donna CD, Panetta M, Quintarelli C, Sperduti I, Gualtieri N, Foddai ML, Proietti E, Ferraresi V, Ciliberto G, Nisticò P. Antigen-Specificity and DTIC before Peptide-Vaccination Differently Shape Immune-Checkpoint Expression Pattern, Anti-Tumor Functionality and TCR Repertoire in Melanoma Patients. Oncoimmunology. 2018 Sep 11;7(12):e1465163

# PULMONARY PHYSIOPATHOLOGY UNIT

## *Head: Maria Papale, MD*


| STAFF |
|---|
| **Eliuccia Mastropasqua, MD** |
| **Giorgio Piperno, MD** |
| **Two nurses** |
| **Annalisa Carolina Damiani, doctor in teaching** |

### *Mission*

The Physiopathology Respiratory Unit has forwarded its traditional mission addressing and programming in research activity through useful objectives aimed at the prevention, diagnosis, cure and rehabilitation of pulmonary diseases, in particular oncology and smoke related diseases. The directives have been:

- primary and secondary prevention in the field of pneumology through education clinical-functional diagnostics
- respiratory therapy and rehabilitation for both inpatients and outpatients
- participation in research program
- participation and organization of courses, conferences and congresses both for reports as well as professional updating.

Regarding the activities and objectives the Unit confirm his commitment to respiratory rehabilitation activities with the aim to improve the quality of life and the respiratory functionality at the same time to reduce the days of stay. The Unit is also dedicate to patients suffering

from Interstitial lung disease and IPF (Idiopathic pulmonary fibrosis) rare diseases but frequently verified in our Institute as outcomes of administered therapies. In addition to early diagnosis and therapy of the IPF, it contributes to prevention of related lung cancer.
The smoking cessation clinic (referral Centre for the Observation of Smoke, Alcohol and Addiction,I.S.S.), appreciated and considered a strong point during Audit OECI, has continued its own activity helping patients quit smoking even with pharmacologic treatment. In regards to the effort to prevent smoking, the focus has been on educational and counseling for the staff of our Institute.

## Clinical Activity

During 2018 about 19.724 services (visits, consultations, instrumental tests and respiratory rehabilitation activity) have been conducted on patients coming from different Units of the Institute. Cooperation, above all, with Thoracic Surgery, for a more accurate identification of surgical risks, has been particularly intense.

There has been a total of 18.590 -services conducted for outpatients who came either for pulmonary oncology and other diseases or for to quit smoking or to run respiratory rehabilitation. We have increased our performance compared to 2017.
Respiratory rehabilitation activity is offered mainly to external patients who either have to undergo major thoracic or abdominal surgery, or have already undergone pulmonary resection for cancer and suffer from COPD. In 2018 , about 10.035 services of respiratory rehabilitation have been performed on 705 internal patients and 3779 services on external patients. In addition, about 50 patients were visited in the internal outpatient clinic of interstitial lung diseases and IPF.

## Research Activity

The Unit has taken part along with " Mario Negri Institute for Pharmacological Research" coordinated by the Italian Association of Hospital Pneumologists (AIPO) in : "Studio multicentrico osservazionale sull'utilizzo della sigaretta elettronica in Italia".

The Unit continued to participate in the study BR31 "A phase III prospective double blind placebo controlled randomized study of adjuvant medi4736 in completely resected non-small cell lung cancer".

The Unit has participated, about the research line 1 "Prevention and early diagnosis of Cancer", in study "Role of the estradiol axis in the carcinogenesis and prevention of mesothelioma".

The Unit has taken part in "Registro asma grave- Studio osservazionale e/o retrospettivo non interventistico, multicentrico, nazionale" coordinated by the Italian Association of Hospital Pneumologists (AIPO).

# EPIDEMIOLOGY AND CANCER REGISTRY UNIT

## *Head: Valerio Ramazzotti, MD*

### STAFF

| |
|---|
| **Maria Cecilia Cercato, MD** |
| **Marco Caperle, MD** (until 31.03.2018) |
| **Oreste Aronadio, MD** |
| **Teresa Borruso, nurse cancer registrar** (since 01.09.2018) |
| **Elisabetta Fragalà, nurse cancer registrar** |
| **Emma Santoro, nurse cancer registrar** |

## *Mission*

The 'Epidemiology and Cancer Registry' Unit – a branch of public health in the oncological discipline framework– aims at the monitoring, control and prevention of cancer. The unit is mainly involved in: descriptive epidemiology based on 'cancer registration'; evaluative epidemiology based on data from the 'regional and national programs for the evaluation of the health care interventions'; 'medical humanities and personalization of care'. Many activities are focused on the specific aims of the Organisation of European Cancer Institutes (OECI), that has recognized the National Cancer Institute 'Regina Elena' as a 'Comprehensive Cancer Centre' in 2015. The unit actively takes part in the ongoing projects included in the 'improvement action plan', and it contributes to the implementation of the Institute's Information and Communication Technology system, aiming at providing easy access and analysis of clinical and research data.

## *Activities*

### Cancer Registration

The Unit has implemented two main activities:

1.Since 2015, in accordance to a regional law establishing the Population Based Cancer Registry of the Lazio region (RTL), the Unit has assumed – under the coordinating action of the Department of Epidemiology Lazio Regional Health Service – the role of "functional unit" for the area of the 'Città metropolitana di Roma', covering a population of over 4.330.000 inhabitants and more than 24.000 estimated incident cases of malignant neoplasms per year.The ongoing registration activity has enabled to input over 26 thousands cases of malignant neoplasms in the RTL database at 31.12.2018.

2.The hospital-based cancer registry (RTO) of the National Cancer Institute 'Regina Elena' was established to define the number, the topography and the morphology of the treated cases per year; to provide statistical reports according to the OECI standards; as collaborative unit of the Clinical Trial Centre IFO, to estimate the number of eligible patients for the clinical trials by specific neoplastic features The ongoing registration activity has enabled to input almost 2,500 cases of breast, lung and colonrectum neoplasms at 31.12.2018. Based on the RTO data, 3 technical reports were submitted to the Scientific Director.

### Evaluative epidemiology.

The Unit was involved in the internal audit for: 1) the Regional Outcome Evaluation Program ( P.Re.Val.E.);

2) the National Outcome Evaluation Program (PNE). The main objectives are: observational assessment of the efficacy and the effectiveness of health-care interventions; identification of factors within the health-care delivery process that affect outcomes; monitoring levels of care. In this framework, on request from the **Department of Epidemiology of the Regional Health Service – Lazio,** the Unit coordinated the audit on "Mortality by 30 days after surgery for malignant neoplasms of lung and stomach" and on "Proportion of interventions for malignant breast cancer performed in wards with activity volume greater than 135 cases" at the National Cancer Institute "Regina Elena".

### European Network for European Rare Solid Cancer (EURACAN)

EURACAN will enable a major improvement in the access to excellence diagnosis and treatment for European patients. IFO has been recognized as a ERN member with expertise on more than one rare malignancies. The Unit was actively involved in the ongoing activities, particularly in designing and implementing an institutional database able to collect data from the rare solid cancer patients who are diagnosed and/or treated at the Institute. From 1 January to 31 Dicember 2018, 814 patients were registered.

### Patient Empowerment Network

The Unit has been involved in developing the project of a network for the empowerment and involvement of patients.The following has been conducted:identification of the ongoing services, processes and resources, aiming at supporting, educating, and empowering cancer patients and their families; promotion of humanistic and narrative medicine implementation.

### Narrative Medicine

Since 2009 the Unit has been involved in initiatives related to Narrative Medicine. In 2015 a multidisciplinary project named "Raccontami di te" based on the sharing of individual stories started. In order to increase efficacy of care, by improving narrative competence and careful listening, the ongoing project develops a strategy of communication based on promotion of reflexive writing among health care professionals, patients and caregivers, including training courses, text analysis and a story-sharing meeting. In 2017 started the first Italian project applying the DNM (Digital Narrative Medicine) diary in clinical practice for cancer patients: AMENO a pilot study addressing patients in chemotherapy treatment. In 2018 started AMENART study, addressing patients undergoing radiotherapy treatment. The preliminary results were published and reported by oral communications at national courses and meetings.

## *Publications*


1. Cercato M.C. Colella E., Fabi A, Bertazzi I, Scarinci V, Franceschini A, Cognetti F, Cenci C. Narrative Based Medicine: A Digital Diary during Chemotherapy Treatment to Personalize Patient Care (Pilot Study). *Tumori Journal.* 2018 104(4S): 194 (S40)a
2. Cercato MC. Narrative Medicine in the Oncological Clinical Practice: The Path from a Story-Telling Intervention to a Narrative Digital Diary. *Recenti Prog.Med.* 2018 Jun; 109(6): 324a
3. Cercato MC, Bertazzi I, Cognetti G, Colella E, Fabi A, Scarinci V, Servoli F. Raccontami Di Te - Il Quaderno Dei Racconti 2016-17 Di Pazienti, Familiari, Volontari e Operatori Sanitari. 2018 May; .
4. Stagnaro E, Parodi S, Costantini AS, Crosignani P, Miligi L, Nanni O, Piro S, Ramazzotti V, Rodella S, Tumino R, Vindigni C, Vineis P. Childhood Infectious Diseases and Risk of Multiple Myeloma: An Analysis of the Italian Multicentre Case-Control Study. *Epidemiol.Infect.* 2018 sep; 146(12): 1572a
5. Lapucci, E., C. Cercato, V. Ramazzotti, S. Busco, I. Cozzi, F. Santi, F. Pannozzo, P. Michelozzi, and P. Schifano. 2018. "Determinanti Della Qualità Della Codifica Automatica Dei Casi Incidenti Di Tumore: L'esempio Della Mammella " - Atti della XXII Riunione Scientifica Annuale Associazione Italiana registri Tumori. Venezia, 11-13 aprile.

# PUBLICATIONS

# PUBLICATIONS 2018


Allegretti M, Casini B, Mandoj C, Benini S, Alberti L, Novello M, Melucci E, Conti L, Covello R, Pescarmona E, Milano GM, Annovazzi A, Anelli V, Ferraresi V, Biagini R, Giacomini P. Precision Diagnostics of Ewing's Sarcoma by Liquid Biopsy: Circulating EWS-FLI1 Fusion Transcripts. Ther.Adv.Med.Oncol. 2018 Jun 1; 10: 1758835918774337a **IF 6.238**

Allegretti M, Fabi A, Buglioni S, Martayan A, Conti L, Pescarmona E, Ciliberto G, Giacomini P. Tearing Down the Walls: FDA Approves Next Generation Sequencing (NGS) Assays for Actionable Cancer Genomic Aberrations. J.Exp.Clin. Cancer Res. 2018 Mar 5; 37(1): 47a **IF 6.217**

Amato J, Platella C, Iachettini S, Zizza P, Musumeci D, Cosconati S, Pagano A, Novellino E, Biroccio A, Randazzo A, Pagano B, Montesarchio D. Tailoring a Lead-Like Compound Targeting Multiple G-Quadruplex Structures. Eur.J.Med. Chem. 2018 Nov 27 [Epub ahead of print] **IF 4.816**

Anceschi U, Tuderti G, Lugnani F, Biava P, Malossini G, Luciani L, Cai T, Marsiliani D, Filianoti A, Mattevi D, Costantini M, Misuraca L, Simone G. Novel Diagnostic Biomarkers of Prostate Cancer: An Update. Curr.Med.Chem. 2018 Sep 13; [Epub ahead of print] **IF 3.469**

Annaloro C, Airaghi L, Giannarelli D, Mometto G, Orsatti A, Saporiti G, Grifoni FI, Baldini M, Tagliaferri E, Vincenti D, Maira D, Onida F, Cortelezzi A. Prospective Evaluation of Metabolic Syndrome and its Features in a Single-Center Series of Hematopoietic Stem Cell Transplantation Recipients. Ann.Hematol. 2018 97(12): 2471-2478a **IF 2.845**

Annovazzi A, Rea S, Vici P, Fabi A, Sciuto R. Dual-Time 18F-FDG PET/CT for the Detection of Liver Metastases in Breast Cancer. Nucl.Med.Commun. 2018 Dec; 39(12): 1183-1189a **IF 1.495**

Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R, Kurata T, Chiappori A, Lee KH, de Wit M, Cho BC, Bourhaba M, Quantin X, Tokito T, Mekhail T, Planchard D, Kim YC, Karapetis CS, Hiret S, Ostoros G, Kubota K, Gray JE, Paz-Ares L, de Castro Carpeno J, Faivre-Finn C, Reck M, Vansteenkiste J, Spigel DR, Wadsworth C, Melillo G, Taboada M, Dennis PA, Ozguroglu M, PACIFIC Investigators. Milella M. (c.) Overall Survival with Durvalumab After Chemoradiotherapy in Stage III NSCLC. N.Engl.J.Med. 2018 Dec 13; 379(24): 2342. **IF 79.260**

Antonini G, De Berardinis E, Del Giudice F, Busetto GM, Lauretti S, Fragas R, Chung BI, Conti SL, Giannarelli D, Sperduti I, Gross MS, Perito PE. Inflatable Penile Prosthesis Placement, Scratch Technique and Postoperative Vacuum Therapy as a Combined Approach to Definitive Treatment of Peyronie's Disease. J.Urol. 2018 200(3): 642-647a **IF 5.381**

Appetecchia M, Lauretta R, Sperduti I, Gallucci M. Chromogranin A as a Biomarker for Prostate Cancer: Is it Actually Relevant for Clinical Practice? Future Oncol. 2018 Jun; 14(13):1233-1235 **IF 2.369**

Arcangeli G, Arcangeli S, Pinzi V, Benassi M, Benassi M, Strigari L. Optimal Scheduling of Hypofractionated Radiotherapy for Localized Prostate Cancer: A Systematic Review and Metanalysis of Randomized Clinical Trials. Cancer Treatment Reviews. 2018 November 2018; 70: 22a **IF 8.122**

Ascierto PA, Long GV, Robert C, Brady B, Dutriaux C, Di Giacomo AM, Mortier L, Hassel JC, Rutkowski P, McNeil C, Kalinka-Warzocha E, Savage KJ, Hernberg MM, Lebbe C, Charles J, Mihalcioiu C, Chiarion-Sileni V, Mauch C, Cognetti F, Ny L, Arance A, Svane IM, Schadendorf D, Gogas H, Saci A, Jiang J, Rizzo J, Atkinson V. Survival Outcomes in Patients with Previously Untreated BRAF Wild-Type Advanced Melanoma Treated with Nivolumab Therapy: Three-Year Follow-Up of a Randomized Phase 3 Trial. JAMA Oncol. 2018 Oct 25; [Epub ahead of print] **IF 20.871**

Ascierto PA, Puzanov I, Agarwala SS, Bifulco C, Botti G, Caraco C, Ciliberto G, Davies MA, Dummer R, Ferrone S, Gajewski TF, Garbe C, Luke JJ, Marincola FM, Masucci G, Mehnert JM, Mozzillo N, Palmieri G, Postow MA, Schoenberger SP, Wang E, Thurin M. Perspectives in Melanoma: Meeting Report from the Melanoma Bridge (30 November-2 December, 2017, Naples, Italy). J.Transl.Med. 2018 Jul 21; 16(1): 207a **IF 4.197**

Aurisicchio L, Pallocca M, Ciliberto G, Palombo F. The Perfect Personalized Cancer Therapy: Cancer Vaccines Against Neoantigens. J.Exp.Clin.Cancer Res. 2018 Apr 20; 37(1): 86a **IF 6.217**

Bagnato A, Rosano L. Endothelin-1 Receptor Drives Invadopodia: Exploiting how Beta-Arrestin-1 Guides the Way. Small GTPases. 2018 Sep 3; 9(5): 394a

Bailey MH, Tokheim C, Porta-Pardo E, Sengupta S, Bertrand D, Weerasinghe A, Colaprico A, Wendl MC, Kim J, Reardon B, Ng PK, Jeong KJ, Cao S, Wang Z, Gao J, Gao Q, Wang F, Liu EM, Mularoni L, Rubio-Perez C, Nagarajan N, Cortes-Ciriano I, Zhou DC, Liang WW, Hess JM, Yellapantula VD, Tamborero D, Gonzalez-Perez A, Suphavilai C, Ko JY, Khurana E, Park PJ, Van Allen EM, Liang H, MC3 Working Group, Cancer Genome Atlas Research Network, Lawrence MS, Godzik A, Lopez-Bigas N, Stuart J, Wheeler D, Getz G, Chen K, Lazar AJ, Mills GB, Karchin R, Ding L, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Comprehensive Characterization of Cancer Driver Genes and Mutations. Cell. 2018 Apr 5; 173(2): 371a **IF 31.398**

Baldi J, Attala D, Scotto di Uccio A, Laquintana V, Biagini R, Zoccali C. The Effectiveness of a Standard Drill Connected to a Core Biopsy Needle: How to Obtain Specimens in very Strong Bone Tumors. Injury. 2018 Aug; 49(8): 1612-1616a **IF 2.199**

Barnabei A, Strigari L, Persichetti A, Baldelli R, Rizza L, Annoscia C, Lauretta R, Cigliana G, Barba M, De Leo A, Appetecchia M, Torino F. Indirect Basal Metabolism Estimation in Tailoring Recombinant Human TSH Administration in Patients Affected by Differentiated Thyroid Cancer: A Hypothesis-Generating Study. Front.Endocrinol.(Lausanne). 2018 Feb 15; 9: 37a **IF 3.519**

Barni S, Livraghi L, Morritti M, Vici P, Michelotti A, Cinieri S, Fontanella C, Porcu L, Del Mastro L, Puglisi F, ESEMPiO Study Group. Eribulin in the Treatment of Advanced Breast Cancer: Real-World Scenario from 39 Italian Centers - ESEMPiO Study. Future Oncol. 2018 Nov 9 [Epub ahead of print] **IF 2.369**

Barros MR, Jr, de Melo CML, Barros MLCMGR, de Cassia Pereira de Lima, R., de Freitas AC, Venuti A. Activities of Stromal and Immune Cells in HPV-Related Cancers. J.Exp.Clin.Cancer Res. 2018 Jul 5; 37(1): 137a **IF 6.217**

Barros MR, Jr, de Oliveira THA, de Melo CML, Venuti A, de Freitas AC. Viral Modulation of TLRs and Cytokines and the Related Immunotherapies for HPV-Associated Cancers. J.Immunol.Res. 2018 May 2; 2018: 2912671a **IF 3.298**

Basile S, Pinelli S, Benedetti Panici P, Angioli R, Plotti F, Giannarelli D, Fossati R, Rosati CM, Salerno MG. Association between Helicobacter Pylori Infection and Vulvar Lichen Sclerosus: A Clinical Comparative Study. Eur.J.Dermatol. 2018 Jan 16; **IF 2.243**

Belloni L, Di Cocco S, Guerrieri F, Nunn ADG, Piconese S, Salerno D, Testoni B, Pulito C, Mori F, Pallocca M, Sacconi A, Vivoli E, Marra F, Strano S, Blandino G, Levrero M, Pediconi N. Targeting a Phospho-STAT3-miRNAs Pathway Improves Vesicular Hepatic Steatosis in an in Vitro and in Vivo Model. Sci.Rep. 2018 Sep 11; 8(1): 13638a **IF 4.122**

Benedetti S, Catalani S, Palma F, Canonico B, Luchetti F, Galati R, Papa S, Battistelli S. Acyclovir Induces Cell Cycle Perturbation and Apoptosis in Jurkat Leukemia Cells, and Enhances Chemotherapeutic Drug Cytotoxicity. Life Sci. 2018 Dec 15; 215: 80a **IF 3.234**

Bergamini A, Ferrandina G, Candiani M, Cormio G, Giorda G, Lauria R, Perrone AM, Scarfone G, Breda E, Savarese A, Frigerio L, Gadducci A, Mascilini F, Maneschi F, Cassani C, Marchetti C, Cecere SC, Biglia N, De Giorgi U, Raspagliesi F, Lorusso D, Mangili G. Laparoscopic Surgery in the Treatment of Stage I Adult Granulosa Cells Tumors of the Ovary: Results from the MITO-9 Study. Eur.J.Surg.Oncol. 2018 Jun;44(6):766-770 **IF 3.688**

Berger AC, Korkut A, Kanchi RS, Hegde AM, Lenoir W, Liu W, Liu Y, Fan H, Shen H, Ravikumar V, Rao A, Schultz A, Li X, Sumazin P, Williams C, Mestdagh P, Gunaratne PH, Yau C, Bowlby R, Robertson AG, Tiezzi DG, Wang C, Cherniack AD, Godwin AK, Kuderer NM, Rader JS, Zuna RE, Sood AK, Lazar AJ, Ojesina AI, Adebamowo C, Adebamowo SN, Baggerly KA, Chen TW, Chiu HS, Lefever S, Liu L, MacKenzie K, Orsulic S, Roszik J, Shelley CS, Song Q, Vellano CP, Wentzensen N, Cancer Genome Atlas Research Network, Weinstein JN, Mills GB, Levine DA, Akbani R, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). A Comprehensive Pan-Cancer Molecular Study of Gynecologic and Breast Cancers. Cancer.Cell. 2018 Apr 9; 33(4): 690a **IF 22.844**

Bersanelli M, Buti S, De Giorgi U, Di Maio M, Giannarelli D, Banna GL. Influenza Vaccination in Advanced Cancer Patients Undergoing Immunotherapy with Anti-PD-1/PD-L1 Immune Checkpoint Inhibitors: What Data do we have for the Clinical Recommendation? Recenti Prog.Med. 2018 Nov; 109(11): 540a

Bersanelli M, Giannarelli D, Castrignano P, Fornarini G, Panni S, Mazzoni F, Tiseo M, Rossetti S, Gambale E, Rossi E, Papa A, Cortellini A, Lolli C, Ratta R, Michiara M, Milella M, De Luca E, Soraru M, Mucciarini C, Atzori F, Banna GL, La Torre L, Vitale MG, Massari F, Rebuzzi SE, Facchini G, Schinzari G, Tomao S, Bui S, Vaccaro V, Procopio G, De Giorgi U, Santoni M, Ficorella C, Sabbatini R, Maestri A, Natoli C, De Tursi M, Di Maio M, Rapacchi E, Pireddu A, Sava T, Lipari H, Comito F, Verzoni E, Leonardi F, Buti S. INfluenza Vaccine Indication during Therapy with Immune Checkpoint Inhibitors: A Transversal Challenge. the INVIDIa Study. Immunotherapy. 2018 Oct; 10(14): 1229a **IF 3.461**

Bertolo R, Autorino R, Simone G, Derweesh I, Garisto JD, Minervini A, Eun D, Perdona S, Porter J, Rha KH, Mottrie A, White WM, Schips L, Yang B, Jacobsohn K, Uzzo RG, Challacombe B, Ferro M, Sulek J, Capitanio U, Anele UA, Tuderti G, Costantini M, Ryan S, Bindayi A, Mari A, Carini M, Keehn A, Quarto G, Liao M, Chang K, Larcher A, De Naeyer G, De Cobelli O, Berardinelli F, Zhang C, Langenstroer P, Kutikov A, Chen D, De Luyk N, Sundaram CP, Montorsi F, Stein RJ, Haber GP, Hampton LJ, Dasgupta P, Gallucci M, Kaouk J, Porpiglia F. Outcomes of Robot-Assisted Partial Nephrectomy for Clinical T2 Renal Tumors: A Multicenter Analysis (ROSULA Collaborative Group). Eur.Urol. 2018 Aug; 74(2): 226a **IF 17.581**

Bertolo R, Simone G, Garisto J, Nakhoul G, Armanyous S, Agudelo J, Costantini M, Tuderti G, Gallucci M, Kaouk J. Off-Clamp Vs on-Clamp Robotic Partial Nephrectomy: Perioperative, Functional and Oncological Outcomes from a Propensity-Score Matching between Two High-Volume Centers. Eur.J.Surg.Oncol. 2018 Dec 9; [Epub ahead of print] **IF 3.688**

Biagioli V, Piredda M, Annibali O, Tirindelli MC, Pignatelli A, Marchesi F, Mauroni MR, Soave S, Del Giudice E, Ponticelli E, Clari M, Cavallero S, Monni P, Ottani L, Sica S, Cioce M, Cappucciati L, Bonifazi F, Alvaro R, De Marinis MG, Gargiulo G. Development and Initial Validation of a Questionnaire to Assess Patients' Perception of Protective Isolation Following Haematopoietic Stem Cell Transplantation. Eur.J.Cancer.Care.(Engl). 2018 Oct 24; e12955a

Blandino G, Di Agostino S. New Therapeutic Strategies to Treat Human Cancers Expressing Mutant p53 Proteins. J.Exp.Clin.Cancer Res. 2018 Feb 15; 37(1): 30a **IF 6.217**

Bossi P, Miceli R, Benasso M, Corvo R, Bacigalupo A, Sanguineti G, Fallai C, Merlano MC, Infante G, Dani C, Di Giannantonio V, Licitra L. Impact of Treatment Expertise on the Outcome of Patients with Head and Neck Cancer Treated within 6 Randomized Trials. Head Neck. 2018 Dec; 40(12): 2648a. **IF 2.471**

Bracarda S, Galli L, Maruzzo M, Lo Re G, Buti S, Favaretto A, Di Costanzo F, Sacco C, Merlano M, Mucciarini C, Zafarana E, Romito S, Maestri A, Giorgio CG, Ionta MT, Turci D, De Giorgi U, Procopio G, Cortesi E, Giannarelli D, Porta C. Negative Prognostic Factors and Resulting Clinical Outcome in Patients with Metastatic Renal Cell Carcinoma Included in the Italian Nivolumab-Expanded Access Program. Future Oncol. 2018 Jun; 14(14): 1347a **IF 2.369**

Bringhen S, Offidani M, Palmieri S, Pisani F, Rizzi R, Spada S, Evangelista A, Di Renzo N, Musto P, Marcatti M, Vallone R, Storti S, Bernardini A, Centurioni R, Aitini E, Palmas A, Annibali O, Angelucci E, Ferrando P, Baraldi A, Rocco S, Andriani A, Siniscalchi A, De Stefano V, Meneghini V, Palumbo A, Grammatico S, Boccadoro M, Larocca A. Early Mortality in Myeloma Patients Treated with First-Generation Novel Agents Thalidomide, Lenalidomide, Bortezomib at Diagnosis: A Pooled Analysis. Crit.Rev.Oncol. 2018 130: 27a **IF 4.495**

Broccoli A, Casadei B, Morigi A, Sottotetti F, Gotti M, Spina M, Volpetti S, Ferrero S, Spina F, Pisani F, Merli M, Visco C, Paolini R, Zilioli VR, Baldini L, Di Renzo N, Tosi P, Cascavilla N, Molica S, Ilariucci F, Rigolin GM, D'Alo F, Vanazzi A, Santambrogio E, Marasca R, Mastrullo L, Castellino C, Desabbata G, Scortechini I, Trentin L, Morello L, Argnani L, Zinzani PL. Italian Real Life Experience with Ibrutinib: Results of a Large Observational Study on 77 relapsed/refractory Mantle Cell Lymphoma. Oncotarget. 2018 May 4; 9(34): 23443a

Brunetti O, Aprile G, Marchetti P, Vasile E, Casadei Gardini A, Scartozzi M, Barni S, Delfanti S, De Vita F, Di Costanzo F, Milella M, Cella CA, Berardi R, Cataldo I, Scarpa A, Basile D, Mazzuca F, Graziano G, Argentiero A, Santini D, Reni M, Cascinu S, Silvestris N. Systemic Chemotherapy for Advanced Rare Pancreatic Histotype Tumors: A Retrospective Multicenter Analysis. Pancreas. 2018 May 15; 47(6): 759-771a **IF 2.958**

Buglioni S, Melucci E, Sperati F, Pallocca M, Terrenato I, De Nicola F, Goeman F, Casini B, Amoreo CA, Gallo E, Diodoro MG, Pescarmona E, Vici P, Sergi D, Pizzuti L, Di Lauro L, Mazzotta M, Barba M, Fanciulli M, Vitale I, De Maria R, Ciliberto G, Maugeri-Saccà M. The Clinical Significance of PD-L1 in Advanced Gastric Cancer is Dependent on ARID1A Mutations and ATM Expression. Oncoimmunology. 2018 03/27; 7(8): e1457602a **IF 5.503**

Busca A, Cesaro S, Teofili L, Delia M, Cattaneo C, Criscuolo M, Marchesi F, Fracchiolla NS, Valentini CG, Farina F, Di Blasi R, Prezioso L, Spolzino A, Candoni A, Del Principe MI, Verga L, Nosari A, Aversa F, Pagano L, SEIFEM group (Sorveglianza Epidemiologica Infezioni Fungine in Ematologia). SEIFEM 2017: From Real Life to an Agreement on the use of Granulocyte Transfusions and Colony-Stimulating Factors for Prophylaxis and Treatment of Infectious Complications in Patients with Hematologic Malignant Disorders. Expert Rev.Hematol. 2018 Feb; 11(2): 155a **IF 1.937**

Caforio M, Sorino C, Iacovelli S, Fanciulli M, Locatelli F, Folgiero V. Recent Advances in Searching c-Myc Transcriptional Cofactors during Tumorigenesis. J.Exp.Clin.Cancer Res. 2018 Sep 27; 37(1): 239a **IF 6.217**

Calabrese V, Menna P, Annibali O, Armento G, Carpino A, Cerchiara E, Greco C, Marchesi F, Spallarossa P, Toglia G, Reggiardo G, Minotti G, Collaborators. (Fabi A.) Early Diastolic Dysfunction After Cancer Chemotherapy: Primary Endpoint Results of a Multicenter Cardio-Oncology Study. Chemotherapy. 2018 63(2): 55a **IF 2.000**

Calabro L, Morra A, Giannarelli D, Amato G, D'Incecco A, Covre A, Lewis A, Rebelatto MC, Danielli R, Altomonte M, Di Giacomo AM, Maio M. Tremelimumab Combined with Durvalumab in Patients with Mesothelioma (NIBIT-MESO-1): An Open-Label, Non-Randomised, Phase 2 Study. Lancet Respir.Med. 2018 Jun; 6(6): 451a **IF 21.466**

Callovini GM, Telera S, Sherkat S, Sperduti I, Callovini T, Carapella CM. How is Stereotactic Brain Biopsy Evolving? A Multicentric Analysis of a Series of 421 Cases Treated in Rome Over the Last Sixteen Years. Clin.Neurol.Neurosurg. 2018 174: 101-107a **IF 1.736**

Calzetta L, Matera MG, Facciolo F, Cazzola M, Rogliani P. Beclomethasone Dipropionate and Formoterol Fumarate Synergistically Interact in Hyperresponsive Medium Bronchi and Small Airways. Respir.Res. 2018 Apr 12; 19(1): 65a **IF 3.751**

Calzetta L, Rogliani P, Facciolo F, Rinaldi B, Cazzola M, Matera MG. N-Acetylcysteine Protects Human Bronchi by Modulating the Release of Neurokinin A in an Ex Vivo Model of COPD Exacerbation. Biomed.Pharmacother. 2018 Apr 7; 103: 1a **IF 3.457**

Campbell JD, Yau C, Bowlby R, Liu Y, Brennan K, Fan H, Taylor AM, Wang C, Walter V, Akbani R, Byers LA, Creighton CJ, Coarfa C, Shih J, Cherniack AD, Gevaert O, Prunello M, Shen H, Anur P, Chen J, Cheng H, Hayes DN, Bullman S, Pedamallu CS, Ojesina AI, Sadeghi S, Mungall KL, Robertson AG, Benz C, Schultz A, Kanchi RS, Gay CM, Hegde A, Diao L, Wang J, Ma W, Sumazin P, Chiu HS, Chen TW, Gunaratne P, Donehower L, Rader JS, Zuna R, Al-Ahmadie H, Lazar AJ, Flores ER, Tsai KY, Zhou JH, Rustgi AK, Drill E, Shen R, Wong CK, Cancer Genome Atlas Research Network, Stuart JM, Laird PW, Hoadley KA, Weinstein JN, Peto M, Pickering CR, Chen Z, Van Waes, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Genomic, Pathway Network, and Immunologic Features Distinguishing Squamous Carcinomas. Cell.Rep. 2018 Apr 3; 23(1): 194a **IF 8.032**

Capone M, Giannarelli D, Mallardo D, Madonna G, Festino L, Grimaldi AM, Vanella V, Simeone E, Paone M, Palmieri G, Cavalcanti E, Caraco C, Ascierto PA. Baseline Neutrophil-to-Lymphocyte Ratio (NLR) and Derived NLR could Predict overall Survival in Patients with Advanced Melanoma Treated with Nivolumab. J.Immunother.Cancer. 2018 Jul 16; 6(1): 74a **IF 8.374**

Caputo D, Cartillone M, Cascone C, Pozzi D, Digiacomo L, Palchetti S, Caracciolo G, Coppola R. Improving the Accuracy of Pancreatic Cancer Clinical Staging by Exploitation of Nanoparticle-Blood Interactions: A Pilot Study. Pancreatology. 2018 18(6): 661a **IF 2.763**

Carafa V, Nebbioso A, Cuomo F, Rotili D, Cobellis G, Bontempo P, Baldi A, Spugnini EP, Citro G, Chambery A, Russo R, Ruvo M, Ciana P, Maravigna L, Shaik J, Radaelli E, De Antonellis P, Tarantino D, Pirolli A, Ragno R, Zollo M, Stunnenberg HG, Mai A, Altucci L. RIP1-HAT1-SirT Complex Identification and Targeting in Treatment and Prevention of Cancer. Clin.Cancer Res. 2018 Jun 15; 24(12): 2886-2900a **IF 10.199**

Carapella CM, Gorgoglione N, Oppido PA. The Role of Surgical Resection in Patients with Brain Metastases. Curr. Opin.Oncol. 2018 Nov; 30(6): 390a **IF 3.653**

Carapella CM, Oppido PA. The Present Role of Surgery for Brain Metastases. World Neurosurg. 2018 Dec; 120: 423-425a **IF 1.924**

Carbone A, Sperduti I, De Simone P, Piemonte P, Ferrari A, Buccini P, Silipo V, Iorio A, Frascione P, Eibenschutz L. Daylight Photodynamic Therapy: Experience in the Treatment of Actinic Keratosis in San Gallicano Institute of Rome and a Review of Literature. G.Ital.Dermatol.Venereol. 2018 Jan 24; **IF 1.327**

Carboni F, Federici O, Giofre M, Diodoro M, Valle M. Recurrence of Gallbladder Carcinoma 12 Years After Laparoscopic Cholecystectomy. Clin.Res.Hepatol.Gastroenterol. 2018 Aug 30 [Epub ahead of print] **IF 2.623**

Carboni F, Marandino F, Valle M. Late Isolated Subcutaneous Metastasis from Colon Cancer. ANZ J.Surg. 2018 Oct 22; **IF 1.586**

Carboni F, Valle M, Federici O, Covello R, Garofalo A. Giant Primary Retroperitoneal Dedifferentiated Liposarcoma. J.Gastrointest.Surg. 2018 Jun 29; [Epub ahead of print] **IF 2.813**

Carnio S, Galetta D, Scotti V, Cortinovis DL, Antonuzzo A, Pisconti S, Rossi A, Martelli O, Cecere FL, Lunghi A, Del Conte A, Montagna ES, Topulli J, Pelizzoni D, Rapetti SG, Gianetta M, Pacchiana MV, Pegoraro V, Cataldo N, Bria E, Novello S. Chemotherapy-Induced Nausea and Vomiting (CINV) in Patients with Advanced Lung Cancer during the First-Line Treatment: Assessment by Physicians, Nurses, and Patients from an Italian Multicenter Survey. Support. Care Cancer. 2018 Jun; 26(6): 1841. **IF 2.676**

Caruso A, Vigna C, Gremigni P. The Cancer Worry Scale Revised for Breast Cancer Genetic Counseling. Cancer Nurs. 2018 Jul/Aug; 41(4): 311a **IF 1.844**

Casali PG, Abecassis N, Bauer S, Biagini R, Bielack S, Bonvalot S, Boukovinas I, Bovee JVMG, Brodowicz T, Broto JM, Buonadonna A, De Alava E, Dei Tos AP, Del Muro XG, Dileo P, Eriksson M, Fedenko A, Ferraresi V, Ferrari A, Ferrari S, Frezza AM, Gasperoni S, Gelderblom H, Gil T, Grignani G, Gronchi A, Hannu A, Hassan B, Hohenberger P, Issels R, Joensuu H, Jones RL, Judson I, Jutte P, Kaal S, Kasper B, Kopeckova K, Krakorova DA, Le Cesne A, Lugowska I, Merimsky O, Montemurro M, Pantaleo MA, Piana R, Picci P, Piperno-Neumann S, Pousa AL, Reichardt P, Robinson MH, Rutkovski P, Safwat AA, Schoffski P, Sleijfer S, Stacchiotti S, Sundby Hall K, Unk M, Van Coevorden F, Van der Graaf W, Whelan J, Wardelmann E, Zaikova O, Blay JY, ESMO Guidelines Committee and EURACAN. Gastrointestinal Stromal Tumours: ESMO-EURACAN Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. Ann. Oncol. 2018 Oct 1; 29(Supplement_4): iv68-iv78a **IF 13.930**

Casali PG, Abecassis N, Bauer S, Biagini R, Bielack S, Bonvalot S, Boukovinas I, Bovee JVMG, Brodowicz T, Broto JM, Buonadonna A, De Alava E, Dei Tos AP, Del Muro XG, Dileo P, Eriksson M, Fedenko A, Ferraresi V, Ferrari A, Ferrari S, Frezza AM, Gasperoni S, Gelderblom H, Gil T, Grignani G, Gronchi A, Hannu A, Hassan B, Hohenberger P, Issels R, Joensuu H, Jones RL, Judson I, Jutte P, Kaal S, Kasper B, Kopeckova K, Krakorova DA, Le Cesne A, Lugowska I, Merimsky O, Montemurro M, Pantaleo MA, Piana R, Picci P, Piperno-Neumann S, Pousa AL, Reichardt P, Robinson MH, Rutkovski P, Safwat AA, Schoffski P, Sleijfer S, Stacchiotti S, Sundby Hall K, Unk M, Van Coevorden F, Van der Graaf W, Whelan J, Wardelmann E, Zaikova O, Blay JY, ESMO Guidelines Committee and EURACAN. Soft Tissue and Visceral Sarcomas: ESMO-EURACAN Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. Ann. Oncol. 2018 Oct 1; 29(Supplement_4): iv51-iv67a **IF 13.930**

Casali PG, Bielack S, Abecassis N, Aro HT, Bauer S, Biagini R, Bonvalot S, Boukovinas I, Bovee JVMG, Brennan B, Brodowicz T, Broto JM, Brugieres L, Buonadonna A, De Alava E, Dei Tos AP, Del Muro XG, Dileo P, Dhooge C, Eriksson M, Fagioli F, Fedenko A, Ferraresi V, Ferrari A, Ferrari S, Frezza AM, Gaspar N, Gasperoni S, Gelderblom H, Gil T, Grignani G, Gronchi A, Haas RL, Hassan B, Hecker-Nolting S, Hohenberger P, Issels R, Joensuu H, Jones RL, Judson I, Jutte P, Kaal S, Kager L, Kasper B, Kopeckova K, Krakorova DA, Ladenstein R, Le Cesne A, Lugowska I, Merimsky O, Montemurro M, Morland B, Pantaleo MA, Piana R, Picci P, Piperno-Neumann S, Pousa AL, Reichardt P, Robinson MH, Rutkowski P, Safwat AA, Schoffski P, Sleijfer S, Stacchiotti S, Strauss SJ, Sundby Hall K, Unk M, Van Coevorden F, van der Graaf WTA, Whelan J, Wardelmann E, Zaikova O, Blay JY, ESMO Guidelines Committee, PaedCan and ERN EURACAN. Bone Sarcomas: ESMO-PaedCan-EURACAN Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. Ann. Oncol. 2018 Oct 1; 29(Supplement_4): iv79a **IF 13.930**

Castiello L, Sestili P, Schiavoni G, Dattilo R, Monque DM, Ciaffoni F, Iezzi M, Lamolinara A, Sistigu A, Moschella F, Pacca AM, Macchia D, Ferrantini M, Zeuner A, Biffoni M, Proietti E, Belardelli F, Arico E. Disruption of IFN-I Signaling Promotes HER2/Neu Tumor Progression and Breast Cancer Stem Cells. Cancer. Immunol. Res. 2018 Jun; 6(6): 658a **IF 9.188**

Catania G, Malaguti P, Gasparro S, Cognetti F, Vidiri A, Fabi A. Activity of Eribulin Mesylate in Brain Metastasis from Breast Cancer: A Stone in a Pond? Oncology. 2018 94(Suppl 1): 29a

Cattaneo C, Di Blasi R, Skert C, Candoni A, Martino B, Di Renzo N, Delia M, Ballanti S, Marchesi F, Mancini V, Orciuolo E, Cesaro S, Prezioso L, Fanci R, Nadali G, Chierichini A, Facchini L, Picardi M, Malagola M, Orlando V, Trecarichi EM, Tumbarello M, Aversa F, Rossi G, Pagano L, SEIFEM Group. Bloodstream Infections in Haematological Cancer Patients Colonized by Multidrug-Resistant Bacteria. Ann.Hematol. 2018 Sep; 97(9): 1717-1726a **IF 2.845**

Cazzaniga M, Verusio C, Ciccarese M, Fumagalli A, Sartori D, Ancona C, Airoldi M, Moretti G, Ficorella C, Arcangeli V, Diodati L, Zambelli A, Febbraro A, Generali D, Pistelli M, Garrone O, Musolino A, Vici P, Maur M, Mentuccia L, La Verde N, Bianchi G, Artale S, Blasi L, Piezzo M, Atzori F, Turletti A, Benedetto C, Cursano MC, Fabi A, Gebbia V, Schirone A, Palumbo R, Ferzi A, Frassoldati A, Scavelli C, Clivio L, Torri On Behalf Of The Eva Study Group, V. Everolimus (EVE) and Exemestane (EXE) in Patients with Advanced Breast Cancer Aged >/= 65 Years: New Lessons for Clinical Practice from the EVA Study. Oncotarget. 2018 Aug 7; 9(61): 31877a

Cazzaniga ME, Ciruelos E, Fabi A, Garcia-Saenz J, Lindman H, Mavroudis D, Schem C, Steger G, Timotheadou E, Zaman K, Torri V, MACBETH Group. Metastatic Or Locally Advanced Breast Cancer Patients: Towards an Expert Consensus on Nab-Paclitaxel Treatment in HER2-Negative Tumours-the MACBETH Project. Cancer Chemother. Pharmacol. 2018 Nov 20; [Epub ahead of print] **IF 2.808**

Cercato M.C. C, E., Fabi A, Bertazzi I, Scarinci V, Franceschini A, Cognetti F, Cenci C. Narrative Based Medicine: A Digital Diary during Chemotherapy Treatment to Personalize Patient Care (Pilot Study). Tumori Journal. 2018 104(4S): 194 (S40)a **IF 1.304**

Cercato MC, Bertazzi I, Cognetti G, Colella E, Fabi A, Scarinci V, Servoli F. Raccontami Di Te - Il Quaderno Dei Racconti 2016-17 Di Pazienti, Familiari, Volontari e Operatori Sanitari. 2018 May; .

Cercato MC. Narrative Medicine in the Oncological Clinical Practice: The Path from a Story-Telling Intervention to a Narrative Digital Diary. Recenti Prog.Med. 2018 Jun; 109(6): 324a

Chang K, Taggart MW, Reyes-Uribe L, Borras E, Riquelme E, Barnett RM, Leoni G, San Lucas FA, Catanese MT, Mori F, Diodoro MG, You YN, Hawk ET, Roszik J, Scheet P, Kopetz S, Nicosia A, Scarselli E, Lynch PM, McAllister F, Vilar E. Immune Profiling of Premalignant Lesions in Patients with Lynch Syndrome. JAMA Oncol. 2018 Aug; a **IF 20.871**

Chellini L, Caprara V, Spadaro F, Sestito R, Bagnato A, Rosano L. Regulation of Extracellular Matrix Degradation and Metastatic Spread by IQGAP1 through Endothelin-1 Receptor Signaling in Ovarian Cancer. Matrix Biol. 2018 Oct 24; a. **IF 8.136**

Chellini L, Monteleone V, Lombari M, Caldarola S, Loreni F. The Oncoprotein Myc Controls the Phosphorylation of S6 Kinase and AKT through Protein Phosphatase 2A. J.Cell.Biochem. 2018 Dec; 119(12): 9878-9887a **IF 2.959**

Chen H, Li C, Peng X, Zhou Z, Weinstein JN, Cancer Genome Atlas Research Network, Liang H. Grazi GL(c.) Facciolo F(c.) Merola R (c), Antenucci A(c). Marino M.(c). A Pan-Cancer Analysis of Enhancer Expression in nearly 9000 Patient Samples. Cell. 2018 Apr 5; 173(2): 386a **IF 31.398**

Chiappetta M, Facciolo F. Sternum Reconstruction using Titanium Plates Matched with "Sandwich" Gore-Tex Meshes. J.Vis.Surg. 2018 Mar 12; 4: 47a

Chiappetta M, Forcella D, Pierconti F, Facciolo F. Combined Treatment for Single Giant Pulmonary Metastasis from Osteosarcoma: From Inside to Outside. ANZ J.Surg. 2018 Nov; 88(11): E801a **IF 1.586**

Chiappetta M, Leuzzi G, Sperduti I, Bria E, Mucilli F, Lococo F, Spaggiari L, Ratto GB, Filosso PL, Facciolo F. Lymph-Node Ratio Predicts Survival among the Different Stages of Non-Small-Cell Lung Cancer: A Multicentre Analysis. Eur.J.Cardiothorac.Surg. 2018 Sep 6;

Chiappetta M, Marino M, Facciolo F. Unique Case of Atypical Type A Thymoma with Vertebral Metastasis and High 18-Fluorodeoxyglucose Avidity. ANZ J.Surg. 2018 Aug 17; **IF 1.586**

Chiu HS, Somvanshi S, Patel E, Chen TW, Singh VP, Zorman B, Patil SL, Pan Y, Chatterjee SS, Cancer Genome Atlas Research Network, Sood AK, Gunaratne PH, Sumazin P, Grazi GL(c.), Facciolo F(c.), Merola R (c), Antenucci A(c). Marino M.(c). Pan-Cancer Analysis of lncRNA Regulation Supports their Targeting of Cancer Genes in each Tumor Context. Cell.Rep. 2018 Apr 3; 23(1): 297a **IF 8.032**

Cianci S, Abatini C, Fagotti A, Chiofalo B, Tropea A, Biondi A, Scambia G, Pacelli F. Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for Peritoneal Malignancies using New Hybrid CO2 System: Preliminary Experience in Referral Center. Updates Surg. 2018 Aug 9;

Cigliana G, Gulli F, Napodano C, Pocino K, De Santis E, Colacicco L, Cordone I, Conti L, Basile U. Serum Free Light Chain Quantitative Assays: Dilemma of a Biomarker. J.Clin.Lab.Anal. 2018 Feb;32(2) **IF 1.303**

Claroni C, Covotta M, Torregiani G, Forastiere E. In Response. Anesth.Analg. 2018 Apr; 126(4): 1426a **IF 3.463**

Clemente S, Masi L, Fiandra C, Cagni E, Villaggi E, Esposito M, Giglioli FR, Marino C, Strigari L, Garibaldi C, Stasi M, Mancosu P, Russo S. A Multi-Center Output Factor Intercomparison to Uncover Systematic Inaccuracies in Small Field Dosimetry. Physics and Imaging in Radiation Oncology. 2018 January 2018; 5: 93a

Cognetti G. La chiave della salute sta in biblioteca. Biblioteche specializzate e Biblioteche di pubblica lettura al centro dell'informazione sanitaria per i professionisti ed i cittadini. Bibelot 24 (3), 2018

Cognetti G. La documentazione scientifica è la chiave per i professionisti della salute? In: Scuola di Ricerca. Corso di formazione specifica i n medicina generale. La medicina generale in ricerca "ci raccontiamo"VIII/2018 p. 34-38. Luglio 2018 http://www.omceo.bari.it/articoli/allegato/giornale-viii.-ediz.pdf

Cognetti, G. L'informazione sanitaria tra il dr Google e le risorse elettroniche di qualità. In: Ripensare la sanità ai tempi del digitale, a cura di G. Cosentino. Youcanprint, ISBN: 9788827848807, 2018

Conciatori F, Bazzichetto C, Falcone I, Pilotto S, Bria E, Cognetti F, Milella M, Ciuffreda L. Role of mTOR Signaling in Tumor Microenvironment: An Overview. Int.J.Mol.Sci. 2018 Aug 19; 19(8): E2453a **IF 3.687**

Conciatori F, Ciuffreda L, Bazzichetto C, Falcone I, Pilotto S, Bria E, Cognetti F, Milella M. MTOR Cross-Talk in Cancer and Potential for Combination Therapy. Cancers (Basel). 2018 Jan 19; 10(1): E23 **IF 5.326**

Connors JM, Jurczak W, Straus DJ, Ansell SM, Kim WS, Gallamini A, Younes A, Alekseev S, Illes A, Picardi M, Lech-Maranda E, Oki Y, Feldman T, Smolewski P, Savage KJ, Bartlett NL, Walewski J, Chen R, Ramchandren R, Zinzani PL, Cunningham D, Rosta A, Josephson NC, Song E, Sachs J, Liu R, Jolin HA, Huebner D, Radford J, ECHELON-1 Study Group. Mengarelli (c.) Brentuximab Vedotin with Chemotherapy for Stage III Or IV Hodgkin's Lymphoma. N.Engl.J.Med. 2018 Jan 25; 378(4): 331a **IF 79.258**

Cordeiro MN, De Lima RCP, Paolini F, Melo ARDS, Campos APF, Venuti A, De Freitas AC. Current Research into Novel Therapeutic Vaccines Against Cervical Cancer. Expert Rev.Anticancer Ther. 2018 Apr; 18(4): 365a **IF 2.347**

Corrado G, Calagna G, Cutillo G, Insinga S, Mancini E, Baiocco E, Zampa A, Bufalo A, Perino A, Vizza E. The Patient and Observer Scar Assessment Scale to Evaluate the Cosmetic Outcomes of the Robotic Single-Site Hysterectomy in Endometrial Cancer. Int.J.Gynecol.Cancer. 2018 Jan; 28(1): 194a **IF 2.192**

Corrado G, Laquintana V, Loria R, Carosi M, de Salvo L, Sperduti I, Zampa A, Cicchillitti L, Piaggio G, Cutillo G, Falcioni R, Vizza E. Endometrial Cancer Prognosis Correlates with the Expression of L1CAM and miR34a Biomarkers. J.Exp.Clin.Cancer Res. 2018 Jul 6; 37(1): 139a **IF 6.217**

Corrado G, Vizza E, Cela V, Mereu L, Bogliolo S, Legge F, Ciccarone F, Mancini E, Gallotta V, Baiocco E, Monterossi G, Perri MT, Zampa A, Pasciuto T, Scambia G. Laparoscopic Versus Robotic Hysterectomy in Obese and Extremely Obese Patients with Endometrial Cancer: A Multi-Institutional Analysis. Eur.J.Surg.Oncol. 2018 Dec; 44(12): 1935-1941a **IF 3.688**

Corrado G, Vizza E, Legge F, Pedone Anchora L, Sperduti I, Fagotti A, Mancini E, Gallotta V, Zampa A, Chiofalo B, Scambia G. Comparison of Different Surgical Approaches for Stage IB1 Cervical Cancer Patients: A Multi-Institution Study and a Review of the Literature. Int.J.Gynecol.Cancer. 2018 Jun; 28(5): 1020a **IF 2.192**

Corrado G, Zoccali C, Salducca N, Oddi A, Vizza E, Biagini R. Anterior Robotic Approach in En-Bloc Sacrectomy: A Preliminary Experience. Journal of Robotic Surgery. 2018 Mar; : 1a

Coulson-Gilmer C, Humphries MP, Sundara Rajan S, Droop A, Jackson S, Condon A, Cserni G, Jordan LB, Jones JL, Kanthan R, Di Benedetto A, Mottolese M, Provenzano E, Kulka J, Shaaban AM, Hanby AM, Speirs V. Stanniocalcin 2 Expression is Associated with a Favourable Outcome in Male Breast Cancer. J.Pathol.Clin.Res. 2018 4(4): 241-249a

Cremonesi M, Ferrari ME, Bodei L, Chiesa C, Sarnelli A, Garibaldi C, Pacilio M, Strigari L, Summers PE, Orecchia R, Grana CM, Botta F. Correlation of Dose with Toxicity and Tumour Response to (90)Y- and (177)Lu-PRRT Provides the Basis for Optimization through Individualized Treatment Planning. Eur.J.Nucl.Med.Mol.Imaging. 2018 Dec;45(13):2426-2441 **IF 7.704**

Cudillo L, Cerretti R, Picardi A, Mariotti B, De Angelis G, Cantonetti M, Postorino M, Ceresoli E, De Santis G, Nasso D, Pisani F, Scala E, Di Piazza F, Lanti A, William Arcese for the Rome Transplant Network. Allogeneic Hematopoietic Stem Cell Transplantation in Primary Cutaneous T Cell Lymphoma. Ann.Hematol. 2018 Jun; 97(6): 1041a **IF 2.845**

D'Aguanno S, Valentini E, Tupone MG, Desideri M, Di Martile M, Spagnuolo M, Buglioni S, Ercolani C, Falcone I, De Dominici M, Milella M, Rizzo MG, Calabretta B, Cota C, Anichini A, Trisciuoglio D, Del Bufalo D. Semaphorin 5A Drives Melanoma Progression: Role of Bcl-2, miR-204 and c-Myb. J.Exp.Clin.Cancer Res. 2018 Nov 19; 37(1): 278a **IF 6.217**

D'Andrea M, Strolin S, Ungania S, Cacciatore A, Bruzzaniti V, Marconi R, Benassi M, Strigari L. Radiobiological Optimization in Lung Stereotactic Body Radiation Therapy: Are we Ready to Apply Radiobiological Models? Front. Oncol. 2018 Jan 8; 7: 321a **IF 4.416**

Daniela Falco M, Giancaterino S, D'Andrea M, Gimenez De Lorenzo R, Trignani M, Caravatta L, Di Carlo C, Di Biase S, Allajbej A, Genovesi D. Hippocampal Sparing Approach in Fractionated Stereotactic Brain VMAT Radio Therapy: A Retrospective Feasibility Analysis. J.Appl.Clin.Med.Phys. 2018 Jan; 19(1): 86a **IF 1.301**

Danielli R, Cisternino F, Giannarelli D, Calabro L, Camerini R, Savelli V, Bova G, Dragonetti R, Di Giacomo AM, Altomonte M, Maio M. Long-Term Follow Up of Metastatic Melanoma Patients Treated with Thymosin Alpha-1: Investigating Immune Checkpoints Synergy. Expert Opin.Biol.Ther. 2018 Jul; 18(sup1): 77a **IF 3.974**

De Angelis C, Ampollini A, Basile E, Cisbani E, Della Monaca S, Ghio F, Montereali RM, Picardi L, Piccinini M, Placido C, Ronsivalle C, Soriani A, Strigari L, Trinca E, Vadrucci M. Characterization of 27 Mev Proton Beam Generated by Top-Implart Linear Accelerator. Radiat.Prot.Dosimetry. 2018 Aug 1;180(1-4):329-333 **IF 0.822**

De Giorgi U, Carteni G, Giannarelli D, Basso U, Galli L, Cortesi E, Caserta C, Pignata S, Sabbatini R, Bearz A, Buti S, Lo Re G, Berruti A, Bracarda S, Cognetti F, Rastelli F, Fornarini G, Porta C, Turci D, Sternberg CN, Procopio G, Italian Nivolumab Renal Cell Cancer Early Access Program Group. Safety and Efficacy of Nivolumab for Metastatic Renal Cell Carcinoma: Real-World Results from an Expanded Access Programme. BJU Int. 2018 Jun 29 [Epub ahead of print] **IF 4.688**

De Nicola F, Goeman F, Pallocca M, Sperati F, Pizzuti L, Melucci E, Casini B, Amoreo CA, Gallo E, Diodoro MG, Buglioni S, Mazzotta M, Vici P, Sergi D, Di Lauro L, Barba M, Pescarmona E, Ciliberto G, De Maria R, Fanciulli M, Maugeri-Sacca M. Deep Sequencing and Pathway-Focused Analysis Revealed Multigene Oncodriver Signatures Predicting Survival Outcomes in Advanced Colorectal Cancer. Oncogenesis. 2018 Jul 22; 7(7): 55a **IF 4.722**

De Nunzio C, Brassetti A, Simone G, Lombardo R, Mastroianni R, Collura D, Muto G, Gallucci M, Tubaro A. Metabolic Syndrome Increases the Risk of Upgrading and Upstaging in Patients with Prostate Cancer on Biopsy: A Radical Prostatectomy Multicenter Cohort Study. Prostate Cancer.Prostatic Dis. 2018 Sep; 21(3): 438a **IF 4.099**

De Nunzio C, Pastore AL, Lombardo R, Simone G, Leonardo C, Mastroianni R, Collura D, Muto G, Gallucci M, Carbone A, Fuschi A, Dutto L, Witt JH, De Dominicis C, Tubaro A. The New Epstein Gleason Score Classification significantly Reduces Upgrading in Prostate Cancer Patients. Eur.J.Surg.Oncol. 2018 Jun;44(6):835-839 **IF 3.688**

De Placido S, Gallo C, De Laurentiis M, Bisagni G, Arpino G, Sarobba MG, Riccardi F, Russo A, Del Mastro L, Cogoni AA, Cognetti F, Gori S, Foglietta J, Frassoldati A, Amoroso D, Laudadio L, Moscetti L, Montemurro F, Verusio C, Bernardo A, Lorusso V, Gravina A, Moretti G, Lauria R, Lai A, Mocerino C, Rizzo S, Nuzzo F, Carlini P, Perrone F, GIM Investigators. Adjuvant Anastrozole Versus Exemestane Versus Letrozole, Upfront Or After 2 Years of Tamoxifen, in Endocrine-Sensitive Breast Cancer (FATA-GIM3): A Randomised, Phase 3 Trial. Lancet Oncol. 2018 Apr; 19(4): 474a **IF 36.418**

De Placido S, Giuliano M, Schettini F, Von Arx C, Buono G, Riccardi F, Cianniello D, Caputo R, Puglisi F, Bonotto M, Fabi A, Bilancia D, Ciccarese M, Lorusso V, Michelotti A, Bruzzese D, Veneziani BM, Locci M, De Laurentiis M, Arpino G. Human Epidermal Growth Factor Receptor 2 Dual Blockade with Trastuzumab and Pertuzumab in Real Life: Italian Clinical Practice Versus the CLEOPATRA Trial Results. Breast. 2018 Apr; 38: 86a **IF 2.951**

De Robertis E, Caprino Miceli A, Colombo GL, Corcione A, Leykin Y, Scudeller L, Vizza E, Scollo P, Societa Italiana Ginecologia E Ostetricia, Societa Italiana Di Anestesia Analgesia Rianimazione E Terapia Intensiva. Effects of Deep Versus Moderate Neuromuscular Blockade in Laparoscopic Gynecologic Surgery on Postoperative Pain and Surgical Conditions: Protocol for a Randomized Controlled Trial. JMIR Res.Protoc. 2018 Jul 9; 7(7): e131a

De Robertis M, Mazza T, Fusilli C, Loiacono L, Poeta ML, Sanchez M, Massi E, Lamorte G, Diodoro MG, Pescarmona E, Signori E, Pesole G, Vescovi AL, Garcia-Foncillas J, Fazio VM. EphB2 Stem-Related and EphA2 Progression-Related miRNA-Based Networks in Progressive Stages of CRC Evolution: Clinical Significance and Potential miRNA Drivers. Mol.Cancer. 2018 Nov 30; 17(1): 169a **IF 7.776**

De Virgilio A, Pellini R, Mercante G, Cristalli G, Manciocco V, Giannarelli D, Spriano G. Supracricoid Partial Laryngectomy for Radiorecurrent Laryngeal Cancer: A Systematic Review of the Literature and Meta-Analysis. Eur. Arch.Otorhinolaryngol. 2018 Jul; 275(7): 1671-1680a **IF 1.546**

de Vita R, Buccheri EM, Villanucci A, Pozzi M. Breast Reconstruction Actualized in Nipple-Sparing Mastectomy and Direct-to-Implant, Prepectoral Polyurethane Positioning: Early Experience and Preliminary Results. Clin.Breast Cancer. 2018 Dec 27; **IF 2.703**

de Vita R, Buccheri EM. Nipple Sparing Mastectomy and Direct to Implant Breast Reconstruction, Validation of the Safe Procedure through the use of Laser Assisted Indocyanine Green Fluorescent Angiography. Gland Surg. 2018 Jun; 7(3): 258a

Del Bene G, Calabro F, Giannarelli D, Plimack ER, Harshman LC, Yu EY, Crabb SJ, Pal SK, Alva AS, Powles T, De Giorgi U, Agarwal N, Bamias A, Ladoire S, Necchi A, Vaishampayan UN, Niegisch G, Bellmunt J, Baniel J, Galsky MD, Sternberg CN. Neoadjuvant Vs. Adjuvant Chemotherapy in Muscle Invasive Bladder Cancer (MIBC): Analysis from the RISC Database. Front.Oncol. 2018 Nov 19; 8: 463a **IF 4.416**

Del Curatolo A, Conciatori F, Cesta Incani U, Bazzichetto C, Falcone I, Corbo V, D'Agosto S, Eramo A, Sette G, Sperduti I, De Luca T, Marabese M, Shirasawa S, De Maria R, Scarpa A, Broggini M, Del Bufalo D, Cognetti F, Milella M, Ciuffreda L. Therapeutic Potential of Combined BRAF/MEK Blockade in BRAF-Wild Type Preclinical Tumor Models. J.Exp.Clin.Cancer Res. 2018 Jul 9; 37(1): 140a **IF 6.217**

Di Agostino S, Valenti F, Sacconi A, Fontemaggi G, Pallocca M, Pulito C, Ganci F, Muti P, Strano S, Blandino G. Long Non-Coding MIR205HG Depletes Hsa-miR-590-3p Leading to Unrestrained Proliferation in Head and Neck Squamous Cell Carcinoma. Theranostics. 2018 Feb 12; 8(7): 1850a **IF 8.537**

Di Domenico EG, Cavallo I, Bordignon V, Prignano G, Sperduti I, Gurtner A, Trento E, Toma L, Pimpinelli F, Capitanio B, Ensoli F. Inflammatory Cytokines and Biofilm Production Sustain Staphylococcus Aureus Outgrowth and Persistence: A Pivotal Interplay in the Pathogenesis of Atopic Dermatitis. Sci.Rep. 2018 Jun 28; 8(1): 9573a **IF 4.122**

Di Domenico EG, Cavallo I, Bordignon V, D'Agosto G, Pontone M, Trento E, Gallo MT, Prignano G, Pimpinelli F, Toma L, Ensoli F. The emerging role of microbial biofilm in lyme neuroborreliosis. Front Neurol 2018;9:1048. **IF 4.122**

Di Domenico EG, Cavallo I, Guembe M, Prignano G, Gallo MT, Bordignon V, D'Agosto G, Sperduti I, Toma L, Ensoli F. The clinical biofilm ring test: A promising tool for the clinical assessment of biofilm-producing candida species. FEMS Yeast Res2018;18(3):10.1093/femsyr/foy025. **IF 3.508**

Di Leo L, Vegliante R, Ciccarone F, Salvatori I, Scimeca M, Bonanno E, Sagnotta A, Grazi GL, Aquilano K, Ciriolo MR. Forcing ATGL Expression in Hepatocarcinoma Cells Imposes Glycolytic Rewiring through PPAR-alpha/p300-Mediated Acetylation of p53. Oncogene. 2018 Oct 26; **IF 2.609**

Di Martile M, Desideri M, Tupone MG, Buglioni S, Antoniani B, Mastroiorio C, Falcioni R, Ferraresi V, Baldini N, Biagini R, Milella M, Trisciuoglio D, Del Bufalo D. Histone Deacetylase Inhibitor ITF2357 Leads to Apoptosis and Enhances Doxorubicin Cytotoxicity in Preclinical Models of Human Sarcoma. Oncogenesis. 2018 Feb 23; 7(2): 20a **IF 4.722**

Di Martino MT, Zazzeroni F, Donadelli M, Chiodoni C, Caraglia M, Scotlandi K, Meschini S, Leonetti C. Reprogramming Tumor-Immune Cell Interface in Solid and Hematological Malignancies to Enhance Response to Therapy. J.Exp.Clin. Cancer Res. 2018 Mar 5; 37(1): 48a **IF 6.217**

di Martino S, Amoreo CA, Nuvoli B, Galati R, Strano S, Facciolo F, Alessandrini G, Pass HI, Ciliberto G, Blandino G, De Maria R, Cioce M. HSP90 Inhibition Alters the Chemotherapy-Driven Rearrangement of the Oncogenic Secretome. Oncogene. 2018 Mar; 37(10): 1369a **IF 6.854**

di Martino S, De Luca G, Grassi L, Federici G, Alfonsi R, Signore M, Addario A, De Salvo L, Francescangeli F, Sanchez M, Tirelli V, Muto G, Sperduti I, Sentinelli S, Costantini M, Pasquini L, Milella M, Haoui M, Simone G, Gallucci M, De Maria R, Bonci D. Renal Cancer: New Models and Approach for Personalizing Therapy. J.Exp.Clin.Cancer Res. 2018 Sep 5; 37(1): 217a **IF 6.217**

Di Modugno F, Caprara V, Chellini L, Tocci P, Spadaro F, Ferrandina G, Sacconi A, Blandino G, Nisticò P, Bagnato A, Rosano L. HMENA is a Key Regulator in Endothelin-1/beta-arrestin1-Induced Invadopodial Function and Metastatic Process. Proc.Natl.Acad.Sci.U.S.A. 2018 Mar 20; 115(12): 3132a **IF 9.504**

Di Modugno F, Spada S, Palermo B, Visca P, Iapicca P, Di Carlo A, Antoniani B, Sperduti I, Di Benedetto A, Terrenato I, Mottolese M, Gandolfi F, Facciolo F, Chen EI, Schwartz MA, Santoni A, Bissell MJ, Nistico P. HMENA Isoforms Impact NSCLC Patient Outcome through fibronectin/beta1 Integrin Axis. Oncogene. 2018 Oct; 37(42): 5605-5617a **IF 6.854**

Di Noia V, D'Argento E, Pilotto S, Ferrara MG, Milella M, Tortora G, Bria E. Exploiting MET Dysregulation in EGFR-Addicted Non-Small-Cell Lung Carcinoma: A further Step Toward Personalized Medicine. Transl.Lung Cancer.Res. 2018 Dec; 7(Suppl 4): S312.

Di Rita A, Peschiaroli A, D Acunzo P, Strobbe D, Hu Z, Gruber J, Nygaard M, Lambrughi M, Melino G, Papaleo E, Dengjel J, El Alaoui S, Campanella M, Dotsch V, Rogov VV, Strappazzon F, Cecconi F. HUWE1 E3 Ligase Promotes PINK1/PARKIN-Independent Mitophagy by Regulating AMBRA1 Activation Via IKKalpha. Nat.Commun. 2018 Sep 14; 9(1): 3755a **IF 12.353**

Di Rocco G, Baldari S, Gentile A, Capogrossi M, Toietta G. Protein Disulfide Isomerase as a Prosurvival Factor in Cell Therapy for Muscular and Vascular Diseases. Stem Cell.Res.Ther. 2018 Oct; 9(1): 250a **IF 4.963**

Di Rocco G, Baldari S, Pani G, Toietta G. Stem Cells Under the Influence of Alcohol: Effects of Ethanol Consumption on stem/progenitor Cells. Cell Mol.Life Sci. 2018 Oct 10 [Epub ahead of print] **IF 6.721**

Di Stefano AL, Berzero G, Ducray F, Eoli M, Pichiecchio A, Farina LM, Cuccarini V, Brunelli MC, Diamanti L, Condette Auliac S, Salmaggi A, Silvani A, Giometto B, Pace A, Vidiri A, Bourdain F, Bastianello S, Ceroni M, Marchioni E. "Stroke-Like" Events After Brain Radiotherapy: A Large Series with Long-Term Follow-Up. Eur.J.Neurol. 2018 Nov 24; [Epub ahead of print] **IF 4.621**

DiVeroli A, Buccisano F, Andriani A, Montanaro M, Latagliata R, Santoro C, Breccia M, Spirito F, Cedrone M, Anaclerico B, Leonetti Crescenzi S, Porrini R, De Muro M, Avvisati G, Tafuri A, Cimino G, Spadea A. Prognostic Factors for Thrombosis-Free Survival and overall Survival in Polycythemia Vera: A Retrospective Analysis of 623 PTS with Long Follow-Up. Leuk.Res. 2018 jun; 69: 18a **IF 2.319**

Di Veroli A, Campagna A, De Muro M, Maurillo L, Trawinska MM, LeonettiCrescenzi S, Petriccione L, Romano A, D'Addosio A, Cenfra A, Montanaro M, Felici S, Andriani A, Carmosino I, Niscola P, Montefusco E, Breccia M, Latagliata R. Deferasirox in the Treatment of Iron Overload during Myeloproliferative Neoplasms in Fibrotic Phase: Does Ferritin Decrement Matter? Leuk.Res. 2019 Jan; 76: 65a **IF 2.319**

Dianzani C, Paolini F, Conforti C, Silvestre M, Flagiello F, Venuti A. Human Papillomavirus in Skin Tags: A Case Series. Dermatol.Pract.Concept. 2018 Oct 31; 8(4): 295a

Ding L, Bailey MH, Porta-Pardo E, Thorsson V, Colaprico A, Bertrand D, Gibbs DL, Weerasinghe A, Huang KL, Tokheim C, Cortes-Ciriano I, Jayasinghe R, Chen F, Yu L, Sun S, Olsen C, Kim J, Taylor AM, Cherniack AD, Akbani R, Suphavilai C, Nagarajan N, Stuart JM, Mills GB, Wyczalkowski MA, Vincent BG, Hutter CM, Zenklusen JC, Hoadley KA, Wendl MC, Shmulevich L, Lazar AJ, Wheeler DA, Getz G, Cancer Genome Atlas Research Network, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Perspective on Oncogenic Processes at the End of the Beginning of Cancer Genomics. Cell. 2018 Apr 5; 173(2): 305a **IF 31.398**

Donà MG, Benevolo M, Latini A, Rollo F, Colafigli M, Frasca M, Zaccarelli M, Giglio A, Moretto D, Pescarmona E, Cristaudo A, Giuliani M. Anal Cytological Lesions and HPV Infection in Individuals at Increased Risk for Anal Cancer. Cancer.Cytopathol. 2018 Jul; 126(7): 461a **IF 1.376**

Donzelli S, Milano E, Pruszko M, Sacconi A, Masciarelli S, Iosue I, Melucci E, Gallo E, Terrenato I, Mottolese M, Zylicz M, Zylicz A, Fazi F, Blandino G, Fontemaggi G. Expression of ID4 Protein in Breast Cancer Cells Induces Reprogramming of Tumour-Associated Macrophages. Breast Cancer Res. 2018 Jun 19; 20(1): 59a **IF 6.142**

Drusco A, Fadda P, Nagita G, Fassan N, Bottoni A, Gardigam MM, Sacchi D, Calore F, Carosi M, Antenucci A, Casini B, Kelani H, Pescarmona E, Di Leva G, Zanesi N, Berger MC, Croce CM. Circulating Micrornas Predict Survival of Patients with Tumors of Glial Origin. Ebiomedicine. 2018 Apr; 30: 105a **IF 6.183**

Ellrott K, Bailey MH, Saksena G, Covington KR, Kandoth C, Stewart C, Hess J, Ma S, Chiotti KE, McLellan M, Sofia HJ, Hutter C, Getz G, Wheeler D, Ding L, MC3 Working Group, Cancer Genome Atlas Research Network. Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Scalable Open Science Approach for Mutation Calling of Tumor Exomes using Multiple Genomic Pipelines. Cell.Syst. 2018 Mar 28; 6(3): 271a **IF 8.982**

Esposito M, Masi L, Zani M, Doro R, Fedele D, Garibaldi C, Clemente S, Fiandra C, Giglioli FR, Marino C, Orsingher L, Russo S, Stasi M, Strigari L, Villaggi E, Mancosu P. SBRT Planning for Spinal Metastasis: Indications from a Large Multicentric Study. Strahlenther.Onkol. 2018 Oct 23; **IF 2.459**

Fabi A, Alesini D, Valle E, Moscetti L, Caputo R, Caruso M, Carbognin L, Ciccarese M, La Verde N, Arpino G, Cannita K, Paris I, Santini D, Montemurro F, Russillo M, Ferretti G, Filippelli G, Rossello R, Fabbri A, Zambelli A, Leonardi V, D'Ottavio AM, Nistico C, Stani S, Giampaglia M, Scandurra G, Catania G, Malaguti P, Giannarelli D, Cognetti F. T-DM1 and Brain Metastases: Clinical Outcome in HER2-Positive Metastatic Breast Cancer. Breast. 2018 Oct; 41: 137a **IF 2.951**

Falvo E, Malagrino F, Arcovito A, Fazi F, Colotti G, Tremante E, Di Micco P, Braca A, Opri R, Giuffre A, Fracasso G, Ceci P. The Presence of Glutamate Residues on the PAS Sequence of the Stimuli-Sensitive Nano-Ferritin Improves in Vivo Biodistribution and Mitoxantrone Encapsulation Homogeneity. J.Control.Release. 2018 Apr 10; 275: 177a **IF 7.877**

Fedeli L, Belli G, Ciccarone A, Coniglio A, Esposito M, Giannelli M, Mazzoni LN, Nocetti L, Sghedoni R, Tarducci R, Altabella L, Belligotti E, Benelli M, Betti M, Caivano R, Carni' M, Chiappiniello A, Cimolai S, Cretti F, Fulcheri C, Gasperi C, Giacometti M, Levrero F, Lizio D, Maieron M, Marzi S, Mascaro L, Mazzocchi S, Meliado' G, Morzenti S, Noferini L, Oberhofer N, Quattrocchi MG, Ricci A, Taddeucci A, Tenori L, Luchinat C, Gobbi G, Gori C, Busoni S, Italian Association of Physics in Medicine (AIFM) Working Group on MR Intercomparison. Dependence of Apparent Diffusion Coefficient Measurement on Diffusion Gradient Direction and Spatial Position - A Quality Assurance Intercomparison Study of Forty-Four Scanners for Quantitative Diffusion-Weighted Imaging. Phys.Med. 2018 Nov; 55: 135a **IF 2.240**

Ferraiuolo M, Pulito C, Finch-Edmondson M, Korita E, Maidecchi A, Donzelli S, Muti P, Serra M, Sudol M, Strano S, Blandino G. Agave Negatively Regulates YAP and TAZ Transcriptionally and Post-Translationally in Osteosarcoma Cell Lines. Cancer Lett. 2018 Oct 1; 433: 18a **IF 6.491**

Ferrara M, Sessa G, Fiore M, Bernard F, Asteriti IA, Cundari E, Colotti G, Ferla S, Desideri M, Buglioni S, Trisciuoglio D, Del Bufalo D, Brancale A, Degrassi F. Small Molecules Targeted to the Microtubule-Hec1 Interaction Inhibit Cancer Cell Growth through Microtubule Stabilization. Oncogene. 2018 37(2): 231a **IF 6.854**

Ferrara R, Pilotto S, Caccese M, Grizzi G, Sperduti I, Giannarelli D, Milella M, Besse B, Tortora G, Bria E. Do Immune Checkpoint Inhibitors Need New Studies Methodology? J.Thorac.Dis. 2018 May; 10(Suppl 13): S1564a **IF 1.804**

Ferrari S, Bielack SS, Smeland S, Longhi A, Egerer G, Sundby Hall K, Donati D, Kevric M, Brosjo O, Comandone A, Werner M, Monge O, Palmerini E, Berdel WE, Bjerkehagen B, Paioli A, Lorenzen S, Eriksson M, Gambarotti M, Tunn PU, Jebsen NL, Cesari M, von Kalle T, Ferraresi V, Schwarz R, Bertulli R, Kasparek AK, Grignani G, Krasniqi F, Sorg B, Hecker-Nolting S, Picci P, Reichardt P. EURO-B.O.S.S.: A European Study on Chemotherapy in Bone-Sarcoma Patients Aged Over 40: Outcome in Primary High-Grade Osteosarcoma. Tumori. 2018 Jan-Feb; 104(1): 30a **IF 1.304**

Filianoti A, Paganelli A, Bassi P, Simone G, Ranieri A. Leiomyoma of the Renal Capsule: Case Report and Literature Review. Urologia. 2018 Feb; 85(1): 34a

Finotti A, Allegretti M, Gasparello J, Giacomini P, Spandidos DA, Spoto G, Gambari R. Liquid Biopsy and PCR-Free Ultrasensitive Detection Systems in Oncology (Review). Int.J.Oncol. 2018 Oct; 53(4): 1395a **IF 3.333**

Flux GD, Sjogreen Gleisner K, Chiesa C, Lassmann M, Chouin N, Gear J, Bardies M, Walrand S, Bacher K, Eberlein U, Ljungberg M, Strigari L, Visser E, Konijnenberg MW. From Fixed Activities to Personalized Treatments in Radionuclide Therapy: Lost in Translation? Eur.J.Nucl.Med.Mol.Imaging. 2018 Jan; 45(1): 152a **IF 7.704**

Folgiero V, Sorino C, Locatelli F, Fanciulli M. A New Baby in the c-Myc-Directed Transcriptional Machinery: Che-1/AATF. Cell.Cycle. 2018 17(11): 1286-1290a. **IF 3.304**

Folgiero V, Sorino C, Pallocca M, De Nicola F, Goeman F, Bertaina V, Strocchio L, Romania P, Pitisci A, Iezzi S, Catena V, Bruno T, Strimpakos G, Passananti C, Mattei E, Blandino G, Locatelli F, Fanciulli M. Che-1 is Targeted by c-Myc to Sustain Proliferation in Pre-B-Cell Acute Lymphoblastic Leukemia. EMBO Rep. 2018 Mar; 19(3): e44871 **IF 8.749**

Franconi, R., E. Illiano, F. Paolini, S. Massa, A. Venuti, and O. C. Demurtas. 2018. "Rapid and Low-Cost Tools Derived from Plants to Face Emerging/Re-Emerging Infectious Diseases and Bioterrorism Agents." In Defence Against Bioterrorism: Springer.

Frixa T, Sacconi A, Cioce M, Roscilli G, Ferrara FF, Aurisicchio L, Pulito C, Telera S, Carosi M, Muti P, Strano S, Donzelli S, Blandino G. MicroRNA-128-3p-Mediated Depletion of Drosha Promotes Lung Cancer Cell Migration. Carcinogenesis. 2018 Feb 9; 39(2): 293a. **IF 5.072**

Gabellini C, Gomez-Abenza E, Ibanez-Molero S, Tupone MG, Perez-Oliva AB, de Oliveira S, Del Bufalo D, Mulero V. Interleukin 8 Mediates Bcl-xL-Induced Enhancement of Human Melanoma Cell Dissemination and Angiogenesis in a Zebrafish Xenograft Model. Int.J.Cancer. 2018 142(3): 584-596a **IF 7.360**

Galgani A, Palleria C, Iannone LF, De Sarro G, Giorgi FS, Maschio M, Russo E. Pharmacokinetic Interactions of Clinical Interest between Direct Oral Anticoagulants and Antiepileptic Drugs. Front.Neurol. 2018 Dec 7; 9: 1067a **IF 3.508**

Galluzzi L, Vitale I, Aaronson SA, Abrams JM, Adam D, Agostinis P, Alnemri ES, Altucci L, Amelio I, Andrews DW, Annicchiarico-Petruzzelli M, Antonov AV, Arama E, Baehrecke EH, Barlev NA, Bazan NG, Bernassola F, Bertrand MJM, Bianchi K, Blagosklonny MV, Blomgren K, Borner C, Boya P, Brenner C, Campanella M, Candi E, Carmona-Gutierrez D, Cecconi F, Chan FK, Chandel NS, Cheng EH, Chipuk JE, Cidlowski JA, Ciechanover A, Cohen GM, Conrad M, Cubillos-Ruiz JR, Czabotar PE, D'Angiolella V, Dawson TM, Dawson VL, De Laurenzi V, De Maria R, Debatin KM, DeBerardinis RJ, Deshmukh M, Di Daniele N, Di Virgilio F, Dixit VM, Dixon SJ, Duckett CS, Dynlacht BD, El-Deiry WS, Elrod JW, Fimia GM, Fulda S, Garcia-Saez AJ, Garg AD, Garrido C, Gavathiotis E, Golstein P, Gottlieb E, Green DR, Greene LA, Gronemeyer H, Gross A, Hajnoczky G, Hardwick JM, Harris IS, Hengartner MO, Hetz C, Ichijo H, Jaattela M, Joseph B, Jost PJ, Juin PP, Kaiser WJ, Karin M, Kaufmann T, Kepp O, Kimchi A, Kitsis RN, Klionsky DJ, Knight RA, Kumar S, Lee SW, Lemasters JJ, Levine B, Linkermann A, Lipton SA, Lockshin RA, Lopez-Otin C, Lowe SW, Luedde T, Lugli E, MacFarlane M, Madeo F, Malewicz M, Malorni W, Manic G, Marine JC, Martin SJ, Martinou JC, Medema JP, Mehlen P, Meier P, Melino S, Miao EA, Molkentin JD, Moll UM, Munoz-Pinedo C, Nagata S, Nunez G, Oberst A, Oren M, Overholtzer M, Pagano M, Panaretakis T, Pasparakis M, Penninger JM, Pereira DM, Pervaiz S, Peter ME, Piacentini M, Pinton P, Prehn JHM, Puthalakath H, Rabinovich GA, Rehm M, Rizzuto R, Rodrigues CMP, Rubinsztein DC, Rudel T, Ryan KM, Sayan E, Scorrano L, Shao F, Shi Y, Silke J, Simon HU, Sistigu A, Stockwell BR, Strasser A, Szabadkai G, Tait SWG, Tang D, Tavernarakis N, Thorburn A, Tsujimoto Y, Turk B, Vanden Berghe T, Vandenabeele P, Vander Heiden MG, Villunger A, Virgin HW, Vousden KH, Vucic D, Wagner EF, Walczak H, Wallach D, Wang Y, Wells JA, Wood W, Yuan J, Zakeri Z, Zhivotovsky B, Zitvogel L, Melino G, Kroemer G. Molecular Mechanisms of Cell Death: Recommendations of the Nomenclature Committee on Cell Death 2018. Cell Death Differ. 2018 Mar; 25(3): 486a **IF 8.000**

Galluzzi L, Vitale I. Oncogene-Induced Senescence and Tumour Control in Complex Biological Systems. Cell Death Differ. 2018 Jun; 25(6): 1005a **IF 8.000**

Gamucci T, Pizzuti L, Natoli C, Mentuccia L, Sperduti I, Barba M, Sergi D, Iezzi L, Maugeri-Sacca M, Vaccaro A, Magnolfi E, Gelibter A, Barchiesi G, Magri V, D'Onofrio L, Cassano A, Rossi E, Botticelli A, Moscetti L, Omarini C, Fabbri MA, Scinto AF, Corsi D, Carbognin L, Mazzotta M, Bria E, Foglietta J, Samaritani R, Garufi C, Mariani L, Barni S, Mirabelli R, Sarmiento R, Graziano V, Santini D, Marchetti P, Tonini G, Di Lauro L, Sanguineti G, Paoletti G, Tomao S, De Maria R, Veltri E, Paris I, Giotta F, Latorre A, Giordano A, Ciliberto G, Vici P. A Multicenter REtrospective Observational Study of First-Line Treatment with PERtuzumab, Trastuzumab and Taxanes for Advanced HER2 Positive Breast Cancer Patients. RePer Study. Cancer.Biol.Ther. 2018 Nov 7 : 1-9 [Epub ahead of print] **IF 3.373**

Gamucci T, Pizzuti L, Sperduti I, Mentuccia L, Vaccaro A, Moscetti L, Marchetti P, Carbognin L, Michelotti A, Iezzi L, Cassano A, Grassadonia A, Astone A, Botticelli A, Magnolfi E, Di Lauro L, Sergi D, Fuso P, Tinari N, Barba M, Maugeri-Sacca M, Landucci E, Conti F, Sanguineti G, De Tursi M, Iafrate G, Giordano A, Ciliberto G, Natoli C, Vici P. Neoadjuvant Chemotherapy in Triple-Negative Breast Cancer: A Multicentric Retrospective Observational Study in Real-Life Setting. J.Cell.Physiol. 2018 Mar; 233(3): 2313a **IF 3.923**

Gandhi L, Rodriguez-Abreu D, Gadgeel S, Esteban E, Felip E, De Angelis F, Domine M, Clingan P, Hochmair MJ, Powell SF, Cheng SY, Bischoff HG, Peled N, Grossi F, Jennens RR, Reck M, Hui R, Garon EB, Boyer M, Rubio-Viqueira B, Novello S, Kurata T, Gray JE, Vida J, Wei Z, Yang J, Raftopoulos H, Pietanza MC, Garassino MC, KEYNOTE-189 Investigators. Cognetti F. (c.) Pembrolizumab Plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer. N.Engl.J.Med. 2018 May 31; 378(22): 2078. **IF 79.260**

Gao Q, Liang WW, Foltz SM, Mutharasu G, Jayasinghe RG, Cao S, Liao WW, Reynolds SM, Wyczalkowski MA, Yao L, Yu L, Sun SQ, Fusion Analysis Working Group, Cancer Genome Atlas Research Network, Chen K, Lazar AJ, Fields RC, Wendl MC, Van Tine BA, Vij R, Chen F, Nykter M, Shmulevich I, Ding L, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Driver Fusions and their Implications in the Development and Treatment of Human Cancers. Cell.Rep. 2018 Apr 3; 23(1): 227a **IF 8.032**

Garassino MC, Cho BC, Kim JH, Mazieres J, Vansteenkiste J, Lena H, Corral Jaime J, Gray JE, Powderly J, Chouaid C, Bidoli P, Wheatley-Price P, Park K, Soo RA, Huang Y, Wadsworth C, Dennis PA, Rizvi NA, ATLANTIC Investigators, Milella M. collaborators. Durvalumab as Third-Line Or Later Treatment for Advanced Non-Small-Cell Lung Cancer (ATLANTIC): An Open-Label, Single-Arm, Phase 2 Study. Lancet Oncol. 2018 Apr; 19(4): 521a **IF 36.421**

Garassino MC, Crino L, Catino A, Ardizzoni A, Cortesi E, Cappuzzo F, Bordi P, Calabro L, Barbieri F, Santo A, Altavilla G, Ambrosio F, Mini E, Vasile E, Morgillo F, Scoppola A, Bengala C, Follador A, Tedde N, Giannarelli D, Lo Russo G, Vitiello F. Nivolumab in Never-Smokers with Advanced Squamous Non-Small Cell Lung Cancer: Results from the Italian Cohort of an Expanded Access Program. Tumour Biol. 2018 Nov; 40(11): 1010428318815047a **IF 3.650**

Garassino MC, Gelibter AJ, Grossi F, Chiari R, Soto Parra H, Cascinu S, Cognetti F, Turci D, Blasi L, Bengala C, Mini E, Baldini E, Quadrini S, Ceresoli GL, Antonelli P, Vasile E, Pinto C, Fasola G, Galetta D, Macerelli M, Giannarelli D, Lo Russo G, de Marinis F. Italian Nivolumab Expanded Access Program in Nonsquamous Non-Small Cell Lung Cancer Patients: Results in Never-Smokers and EGFR-Mutant Patients. J.Thorac.Oncol. 2018 Aug; 13(8): 1146a **IF 10.340**

Gasparello J, Allegretti M, Tremante E, Fabbri E, Amoreo CA, Romania P, Melucci E, Messana K, Borgatti M, Giacomini P, Gambari R, Finotti A. Liquid Biopsy in Mice Bearing Colorectal Carcinoma Xenografts: Gateways Regulating the Levels of Circulating Tumor DNA (ctDNA) and miRNA (ctmiRNA). J.Exp.Clin.Cancer Res. 2018 Jun 26; 37(1): 124a **IF 6.217**

Ge Z, Leighton JS, Wang Y, Peng X, Chen Z, Chen H, Sun Y, Yao F, Li J, Zhang H, Liu J, Shriver CD, Hu H, Cancer Genome Atlas Research Network, Piwnica-Worms H, Ma L, Liang H, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Integrated Genomic Analysis of the Ubiquitin Pathway Across Cancer Types. Cell.Rep. 2018 Apr 3; 23(1): 213a **IF 8.032**

Gelderblom H, Cropet C, Chevreau C, Boyle R, Tattersall M, Stacchiotti S, Italiano A, Piperno-Neumann S, Le Cesne A, Ferraresi V, Penel N, Duffaud F, Cassier P, Toulmonde M, Casali P, Taieb S, Guillemaut S, Metzger S, Perol D, Blay JY. Nilotinib in Locally Advanced Pigmented Villonodular Synovitis: A Multicentre, Open-Label, Single-Arm, Phase 2 Trial. Lancet Oncol. 2018 May; 19(5): 639a **IF 36.418**

Giarra S, Zappavigna S, Campani V, Abate M, Cossu AM, Leonetti C, Porru M, Mayol L, Caraglia M, De Rosa G. Chitosan-Based Polyelectrolyte Complexes for Doxorubicin and Zoledronic Acid Combined Therapy to Overcome Multidrug Resistance. Pharmaceutics. 2018 Oct 9; 10(4): 10.3390/pharmaceutics10040180a **IF 3.746**

Girmenia C, Annino L, Bertaina A, Mariotti B, Caselli D, Fanci R, Barberi W, Marchesi F, Carotti A, Ferrari A, Cerchiara E, Cupelli L, Arcioni F, Ribersani M, Proia A, Cartoni C, Girardi K, Venditti A, Cassetta MI, Fallani S, Novelli A. Voriconazole Treatment in Adults and Children with Hematological Diseases: Can it be used without Measurement of Plasma Concentration? Med.Mycol. 2018 56(3): 263a **IF 2.799**

Giuffrida MC, Cigliana G, Spoto G. Ultrasensitive Detection of Lysozyme in Droplet-Based Microfluidic Devices. Biosens.Bioelectron. 2018 May 1; 104: 8a **IF 8.173**

Giuliani M, Latini A, Colafigli M, Benevolo M, Rollo F, Zaccarelli M, Giuliani E, Moretto D, Giglio A, Rezza G, Cristaudo A, Dona MG. Vaccine-Preventable Anal Infections by Human Papillomavirus among HIV-Infected Men Who have Sex with Men. Future Microbiol. 2018 Oct; 13: 1463a **IF 3.190**

Gkountakos A, Pilotto S, Mafficini A, Vicentini C, Simbolo M, Milella M, Tortora G, Scarpa A, Bria E, Corbo V. Unmasking the Impact of Rictor in Cancer: Novel Insights of mTORC2 Complex. Carcinogenesis. 2018 Jun 28; [Epub ahead of print] **IF 5.072**

Gobbini E, Pilotto S, Pasello G, Polo V, Di Maio M, Arizio F, Galetta D, Petrillo P, Chiari R, Matocci R, Di Costanzo A, Di Stefano TS, Aglietta M, Cagnazzo C, Sperduti I, Bria E, Novello S. Effect of Contract Research Organization Bureaucracy in Clinical Trial Management: A Model from Lung Cancer. Clin.Lung Cancer. 2018 Mar; 19(2): 191a **IF 4.204**

Granato M, Gilardini Montani MS, Angiolillo C, D'Orazi G, Faggioni A, Cirone M. Cytotoxic Drugs Activate KSHV Lytic Cycle in Latently Infected PEL Cells by Inducing a Moderate ROS Increase Controlled by HSF1, NRF2 and p62/SQSTM1. Viruses. 2018 Dec 24; 11(1): pii: E8a **IF 3.761**

Grassadonia A, Sperduti I, Vici P, Iezzi L, Brocco D, Gamucci T, Pizzuti L, Maugeri-Sacca M, Marchetti P, Cognetti G, De Tursi M, Natoli C, Barba M, Tinari N. Effect of Gender on the Outcome of Patients Receiving Immune Checkpoint Inhibitors for Advanced Cancer: A Systematic Review and Meta-Analysis of Phase III Randomized Clinical Trials. J.Clin.Med. 2018 Dec 12; 7(12): 10.3390/jcm7120542a **IF 5.583**

Grassilli S, Brugnoli F, Lattanzio R, Marchisio M, Perracchio L, Piantelli M, Bavelloni A, Capitani S, Bertagnolo V. Vav1 Downmodulates Akt in Different Breast Cancer Subtypes: A New Promising Chance to Improve Breast Cancer Outcome. Mol.Oncol. 2018 Jun; 12(7): 1012a **IF 5.264**

Grossi F, Crino L, Logroscino A, Canova S, Delmonte A, Melotti B, Proto C, Gelibter A, Cappuzzo F, Turci D, Gamucci T, Antonelli P, Marchetti P, Santoro A, Giusti S, Di Costanzo F, Giustini L, Del Conte A, Livi L, Giannarelli D, de Marinis F. Use of Nivolumab in Elderly Patients with Advanced Squamous Non-Small-Cell Lung Cancer: Results from the Italian Cohort of an Expanded Access Programme. Eur.J.Cancer. 2018 Sep; 100: 126a **IF 7.191**

Gurnari C, Latagliata R, Buccisano F, Piciocchi A, Fenu S, Mancini S, Fianchi L, Criscuolo M, Sarlo C, Romano A, Falconi G, Niscola P, Di Veroli A, Breccia M, Piccioni A, Aloe-Spiriti MA, Lo-Coco F, Voso MT, GROM-L (Gruppo Romano-Laziale MDS), GROM-L (Gruppo Romano-Laziale MDS). Erythropoietin Levels and Erythroid Differentiation Parameters in Patients with Lower-Risk Myelodysplastic Syndromes. Leuk.Res. 2018 Jul 10; 71: 89a **IF 2.319**

Hakoum MB, Kahale LA, Tsolakian IG, Matar CF, Yosuico VE, Terrenato I, Sperati F, Barba M, Schunemann H, Akl EA. Anticoagulation for the Initial Treatment of Venous Thromboembolism in People with Cancer. Cochrane Database Syst.Rev. 2018 Jan 24; 1: CD006649a **IF 6.754**

Hardy L, Frison M, Campanella M. Breast Cancer Cells Exploit Mitophagy to Exert Therapy Resistance. Oncotarget. 2018 Feb 19; 9(18): 14040a

Heffler E, Malvezzi L, Boita M, Brussino L, De Virgilio A, Ferrando M, Puggioni F, Racca F, Stomeo N, Spriano G, Canonica GW. Immunological Mechanisms Underlying Chronic Rhinosinusitis with Nasal Polyps. Expert Rev.Clin. Immunol. 2018 Sep; 14(9): 731. **IF 3.436**

Hoadley KA, Yau C, Hinoue T, Wolf DM, Lazar AJ, Drill E, Shen R, Taylor AM, Cherniack AD, Thorsson V, Akbani R, Bowlby R, Wong CK, Wiznerowicz M, Sanchez-Vega F, Robertson AG, Schneider BG, Lawrence MS, Noushmehr H, Malta TM, Cancer Genome Atlas Network, Stuart JM, Benz CC, Laird PW. Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Cell-of-Origin Patterns Dominate the Molecular Classification of 10,000 Tumors from 33 Types of Cancer. Cell. 2018 Apr 5; 173(2): 291a **IF 31.398**

Hopkins BL, Nadler M, Skoko JJ, Bertomeu T, Pelosi A, Shafaei PM, Levine K, Schempf A, Pennarun B, Yang B, Datta D, Bucur O, Ndebele K, Oesterreich S, Yang D, Giulia Rizzo M, Khosravi-Far R, Neumann CA. A Peroxidase Peroxiredoxin 1-Specific Redox Regulation of the Novel FOXO3 microRNA Target Let-7. Antioxid.Redox Signal. 2018 Jan 1; 28(1): 62a **IF 6.530**

Huang KL, Mashl RJ, Wu Y, Ritter DI, Wang J, Oh C, Paczkowska M, Reynolds S, Wyczalkowski MA, Oak N, Scott AD, Krassowski M, Cherniack AD, Houlahan KE, Jayasinghe R, Wang LB, Zhou DC, Liu D, Cao S, Kim YW, Koire A, McMichael JF, Hucthagowder V, Kim TB, Hahn A, Wang C, McLellan MD, Al-Mulla F, Johnson KJ, Cancer Genome Atlas Research Network, Lichtarge O, Boutros PC, Raphael B, Lazar AJ, Zhang W, Wendl MC, Govindan R, Jain S, Wheeler D, Kulkarni S, Dipersio JF, Reimand J, Meric-Bernstam F, Chen K, Shmulevich I, Plon SE, Chen F, Ding L, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Pathogenic Germline Variants in 10,389 Adult Cancers. Cell. 2018 Apr 5; 173(2): 355a **IF 31.398**

Humeau J, Bravo-San Pedro JM, Vitale I, Nunez L, Villalobos C, Kroemer G, Senovilla L. Calcium Signaling and Cell Cycle: Progression Or Death. Cell Calcium. 2018 Mar; 70: 3a **IF 3.718**

Iachettini S, Trisciuoglio D, Rotili D, Lucidi A, Salvati E, Zizza P, Di Leo L, Del Bufalo D, Ciriolo MR, Leonetti C, Steegborn C, Mai A, Rizzo A, Biroccio A. Pharmacological Activation of SIRT6 Triggers Lethal Autophagy in Human Cancer Cells. Cell.Death Dis. 2018 Sep 24; 9(10): 996a **IF 5.638**

Iacobini C, Blasetti Fantauzzi C, Bedini R, Pecci R, Bartolazzi A, Amadio B, Pesce C, Pugliese G, Menini S. Galectin-3 is Essential for Proper Bone Cell Differentiation and Activity, Bone Remodeling and Biomechanical Competence in Mice. Metabolism. 2018 Jun; 83: 149a **IF 5.963**

Iacorossi L, Gambalunga F, Fabi A, Giannarelli D, Marchetti A, Piredda M, De Marinis MG. Adherence to Oral Administration of Endocrine Treatment in Patients with Breast Cancer: A Qualitative Study. Cancer Nurs. 2018 Jan/Feb; 41(1): E57a **IF 1.844**

Iacorossi L, Gambalunga F, Molinaro S, De Domenico R, Giannarelli D, Fabi A. The Effectiveness of the Sport "Dragon Boat Racing" in Reducing the Risk of Lymphedema Incidence: An Observational Study. Cancer Nurs. 2018 Jun 22; [Epub ahead of print] **IF 1.844**

Iacovelli R, De Giorgi U, Galli L, Zucali P, Nole F, Sabbatini R, Fraccon AP, Basso U, Mosca A, Atzori F, Santini D, Facchini G, Fornarini G, Pasini F, Masini C, Massari F, Buti S, Sava T, Sacco C, Ricotta R, Sperduti I, Tortora G, Porta C. Is it Possible to Improve Prognostic Classification in Patients Affected by Metastatic Renal Cell Carcinoma with an Intermediate Or Poor Prognosis? Clin.Genitourin.Cancer. 2018 Oct; 16(5): 355-359.e1. **IF 2.539**

Iannitto E, Bellei M, Amorim S, Ferreri AJM, Marcheselli L, Cesaretti M, Haioun C, Mancuso S, Bouabdallah K, Gressin R, Tripodo C, Traverse-Glehen A, Baseggio L, Zupo S, Stelitano C, Castagnari B, Patti C, Alvarez I, Liberati AM, Merli M, Gini G, Cabras MG, Dupuis J, Tessoulin B, Perrot A, Re F, Palombi F, Gulino A, Zucca E, Federico M, Thieblemont C. Efficacy of Bendamustine and Rituximab in Splenic Marginal Zone Lymphoma: Results from the Phase II BRISMA/IELSG36 Study. Br.J.Haematol. 2018 Dec; 183(5): 755a **IF 5.128**

Imbimbo M, Ottaviano M, Vitali M, Fabbri A, Leuzzi G, Fiore M, Franceschini D, Pasello G, Perrino M, Schiavon M, Pruneri G, Dei Tos AP, Sangalli C, Garassino MC, Berardi R, Alessi A, Calareso G, Petrini I, Scorsetti M, Scotti V, Rosso L, Rea F, Pastorino U, Casali PG, Ramella S, Ricardi U, Abate-Daga L, Torri V, Trama A, Palmieri G, Marino M, Zucali PA, TYME network collaborators. Best Practices for the Management of Thymic Epithelial Tumors: A Position Paper by the Italian Collaborative Group for ThYmic MalignanciEs (TYME). Cancer Treat.Rev. 2018 Dec; 71: 76a **IF 8.122**

Imbimbo M, Vitali M, Fabbri A, Ottaviano M, Pasello G, Petrini I, Palmieri G, Berardi R, Zucali P, Ganzinelli M, Marabese M, Broggini M, Marino M, Trama A, Rulli E, Hollander L, Pruneri G, Torri V, Garassino MC. RELEVENT Trial: Phase II Trial of Ramucirumab, Carboplatin, and Paclitaxel in Previously Untreated Thymic Carcinoma/B3 Thymoma with Area of Carcinoma. Clin.Lung Cancer. 2018 Sep; 19(5): e811a **IF 4.204**

Impellizeri JA, Gavazza A, Greissworth E, Crispo A, Montella M, Ciliberto G, Lubas G, Aurisicchio L. Tel-eVax: A Genetic Vaccine Targeting Telomerase for Treatment of Canine Lymphoma. J.Transl.Med. 2018 Dec 11; 16(1): 349a **IF 4.197**

Iocca O, Farcomeni A, Di Rocco A, Di Maio P, Golusinski P, Pardinas Lopez S, Savo A, Pellini R, Spriano G. Locally Advanced Squamous Cell Carcinoma of the Head and Neck: A Systematic Review and Bayesian Network Meta-Analysis of the Currently Available Treatment Options. Oral Oncol. 2018 May; 80: 40-51. **IF 4.636**

Jayasinghe RG, Cao S, Gao Q, Wendl MC, Vo NS, Reynolds SM, Zhao Y, Climente-Gonzalez H, Chai S, Wang F, Varghese R, Huang M, Liang WW, Wyczalkowski MA, Sengupta S, Li Z, Payne SH, Fenyo D, Miner JH, Walter MJ, Cancer Genome Atlas Research Network, Vincent B, Eyras E, Chen K, Shmulevich I, Chen F, Ding L. Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c)Systematic Analysis of Splice-Site-Creating Mutations in Cancer. Cell.Rep. 2018 Apr 3; 23(1): 270a **IF 8.032**

Kahale LA, Hakoum MB, Tsolakian IG, Matar CF, Terrenato I, Sperati F, Barba M, Yosuico VE, Schunemann H, Akl EA. Anticoagulation for the Long-Term Treatment of Venous Thromboembolism in People with Cancer. Cochrane Database Syst.Rev. 2018 Jun 19; 6: CD006650a **IF 6.754**

Kahale LA, Tsolakian IG, Hakoum MB, Matar CF, Barba M, Yosuico VE, Terrenato I, Sperati F, Schunemann H, Akl EA. Anticoagulation for People with Cancer and Central Venous Catheters. Cochrane Database Syst.Rev. 2018 Jun 1; 6: CD006468a **IF 6.754**

Kahles A, Lehmann KV, Toussaint NC, Huser M, Stark SG, Sachsenberg T, Stegle O, Kohlbacher O, Sander C, Cancer Genome Atlas Research Network, Ratsch G. Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Comprehensive Analysis of Alternative Splicing Across Tumors from 8,705 Patients. Cancer.Cell. 2018 Aug 13; 34(2): 211a **IF 22.844**

Kaufman HL, Russell JS, Hamid O, Bhatia S, Terheyden P, D'Angelo SP, Shih KC, Lebbe C, Milella M, Brownell I, Lewis KD, Lorch JH, von Heydebreck A, Hennessy M, Nghiem P. Updated Efficacy of Avelumab in Patients with Previously Treated Metastatic Merkel Cell Carcinoma After >/=1 Year of Follow-Up: JAVELIN Merkel 200, a Phase 2 Clinical Trial. J.Immunother.Cancer. 2018 Jan 19; 6(1): 7a **IF 8.374**

Knijnenburg TA, Wang L, Zimmermann MT, Chambwe N, Gao GF, Cherniack AD, Fan H, Shen H, Way GP, Greene CS, Liu Y, Akbani R, Feng B, Donehower LA, Miller C, Shen Y, Karimi M, Chen H, Kim P, Jia P, Shinbrot E, Zhang S, Liu J, Hu H, Bailey MH, Yau C, Wolf D, Zhao Z, Weinstein JN, Li L, Ding L, Mills GB, Laird PW, Wheeler DA, Shmulevich I, Cancer Genome Atlas Research Network, Monnat RJ,Jr, Xiao Y, Wang C, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Genomic and Molecular Landscape of DNA Damage Repair Deficiency Across the Cancer Genome Atlas. Cell.Rep. 2018 Apr 3; 23(1): 239a **IF 8.032**

Kok HP, Navarro F, Strigari L, Cavagnaro M, Crezee J. Locoregional Hyperthermia of Deep-Seated Tumours Applied with Capacitive and Radiative Systems: A Simulation Study. Int.J.Hyperthermia. 2018 Apr 18; 1a **IF 3.440**

Korkut A, Zaidi S, Kanchi RS, Rao S, Gough NR, Schultz A, Li X, Lorenzi PL, Berger AC, Robertson G, Kwong LN, Datto M, Roszik J, Ling S, Ravikumar V, Manyam G, Rao A, Shelley S, Liu Y, Ju Z, Hansel D, de Velasco G, Pennathur A, Andersen JB, O'Rourke CJ, Ohshiro K, Jogunoori W, Nguyen BN, Li S, Osmanbeyoglu HU, Ajani JA, Mani SA, Houseman A, Wiznerowicz M, Chen J, Gu S, Ma W, Zhang J, Tong P, Cherniack AD, Deng C, Resar L, Cancer Genome Atlas Research Network, Weinstein JN, Mishra L, Akbani R. Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). A Pan-Cancer Analysis Reveals High-Frequency Genetic Alterations in Mediators of Signaling by the TGF-Beta Superfamily. Cell.Syst. 2018 Oct 24; 7(4): 422a **IF 8.982**

La Torre M, Merigliano C, Burla R, Mottini C, Zanetti G, Del Giudice S, Carcuro M, Virdia I, Bucciarelli E, Manni I, Vinciguerra GR, Piaggio G, Riminucci M, Cumano A, Bartolazzi A, Verni F, Soddu S, Gatti M, Saggio I. Mice with Reduced Expression of the Telomere-Associated Protein Ft1 Develop p53-Sensitive Progeroid Traits. Aging Cell. 2018 Apr 10; 17(4): e12730a **IF 7.627**

Lai S, Molfino A, Mecarelli O, Pulitano P, Morabito S, Pistolesi V, Romanello R, Zarabla A, Galani A, Frassetti N, Aceto P, Lai C, Study Group on Geriatric Nephrology of the Italian Society of Nephrology. Neurological and Psychological Changes in Hemodialysis Patients before and After the Treatment. Ther.Apher.Dial. 2018 Oct; 22(5): 530a **IF 1.416**

Lamberti D, Cristinziano G, Porru M, Leonetti C, Egan JB, Shi CX, Buglioni S, Amoreo CA, Castellani L, Borad MJ, Alema S, Anastasi S, Segatto O. HSP90 Inhibition Drives Degradation of FGFR2 Fusion Proteins: Implications for Treatment of Cholangiocarcinoma. Hepatology. 2018 Aug 1 [Epub ahead of print] **IF 14.079**

Lapucci, E., C. Cercato, V. Ramazzotti, S. Busco, I. Cozzi, F. Santi, F. Pannozzo, P. Michelozzi, and P. Schifano. 2018. "Determinanti Della Qualità Della Codifica Automatica Dei Casi Incidenti Di Tumore: L'esempio Della Mammella " - Atti della XXII Riunione Scientifica Annuale Associazione Italiana registri Tumori. Venezia, 11-13 aprile.

Lasala R, Santoleri F, Romagnoli A, Musicco F, Alberto Costantini. The Economic Value of Clinical Benefit in Oncology: Economic Consideration According ESMO Evaluation. Giornale Italiano Di Farmacia Clinica. 2018 32(4): 160a

Lauretta R, Sansone M, Romanelli F, Appetecchia M. Gender in Endocrinological Diseases: Biological and Clinical Differences. Ital J Gender-Specific Med. 2017 3(3): 109a

Lauretta R, Sansone M, Sansone A, Romanelli F, Appetecchia M. Gender in Endocrine Diseases: Role of Sex Gonadal Hormones. Int.J.Endocrinol. 2018 Oct 21; 2018: 4847376a **IF 2.340**

Lazzaro C, Barone C, Caprioni F, Cascinu S, Falcone A, Maiello E, Milella M, Pinto C, Reni M, Tortora G. An Italian Cost-Effectiveness Analysis of Paclitaxel Albumin (Nab-Paclitaxel) + Gemcitabine Vs Gemcitabine Alone for Metastatic Pancreatic Cancer Patients: The APICE Study. Expert Rev.Pharmacoecon Outcomes Res. 2018 18(4): 435-446a **IF 1.797**

Levi Sandri GB, Ettorre GM, Aldrighetti L, Cillo U, Dalla Valle R, Guglielmi A, Mazzaferro V, Ferrero A, Di Benedetto F, Gruttadauria S, De Carlis L, Vennarecci G, I Go MILS Group on HCC, Grazi G. Laparoscopic Liver Resection of Hepatocellular Carcinoma Located in Unfavorable Segments: A Propensity Score-Matched Analysis from the I Go

MILS (Italian Group of Minimally Invasive Liver Surgery) Registry. Surg.Endosc. 2018 Sep 10; **IF 3.117**

Licitra L, Bonomo P, Sanguineti G, Bacigalupo A, Baldi GG, Valerini S, Bruzzi P. Different View on Larynx Preservation Evidence-Based Treatment Recommendations. J.Clin.Oncol. 2018 May 1; 36(13): 1376a **IF 26.303**

Liu J, Lichtenberg T, Hoadley KA, Poisson LM, Lazar AJ, Cherniack AD, Kovatich AJ, Benz CC, Levine DA, Lee AV, Omberg L, Wolf DM, Shriver CD, Thorsson V, Cancer Genome Atlas Research Network, Hu H, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). An Integrated TCGA Pan-Cancer Clinical Data Resource to Drive High-Quality Survival Outcome Analytics. Cell. 2018 Apr 5; 173(2): 400a **IF 31.398**

Liu Y, Sethi NS, Hinoue T, Schneider BG, Cherniack AD, Sanchez-Vega F, Seoane JA, Farshidfar F, Bowlby R, Islam M, Kim J, Chatila W, Akbani R, Kanchi RS, Rabkin CS, Willis JE, Wang KK, McCall SJ, Mishra L, Ojesina AI, Bullman S, Pedamallu CS, Lazar AJ, Sakai R, Cancer Genome Atlas Research Network, Thorsson V, Bass AJ, Laird PW, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Comparative Molecular Analysis of Gastrointestinal Adenocarcinomas. Cancer.Cell. 2018 Apr 9; 33(4): 721a **IF 22.844**

Lo Sardo F, Strano S, Blandino G. YAP and TAZ in Lung Cancer: Oncogenic Role and Clinical Targeting. Cancers (Basel). 2018 May 6; 10(5): 10.3390/cancers10050137a **IF 5.326**

Loi G, Fusella M, Lanzi E, Cagni E, Garibaldi C, Iacoviello G, Lucio F, Menghi E, Miceli R, Orlandini LC, Roggio A, Rosica F, Stasi M, Strigari L, Strolin S, Fiandra C. Performance of Commercially Available Deformable Image Registration Platforms for Contour Propagation using Patient-Based Computational Phantoms: A Multi-Institutional Study. Med.Phys. 2018 Feb; 45(2): 748a **IF 2.884**

Lombardi D, Accorona R, Lambert A, Mercante G, Coropciuc R, Paderno A, Lancini D, Spriano G, Nicolai P, Vander Poorten V. Long-Term Outcomes and Prognosis in Submandibular Gland Malignant Tumors: A Multicenter Study. Laryngoscope. 2018 Dec; 128(12): 2745a **IF 2.442**

Lombardi D, Paderno A, Giordano D, Barbieri D, Taboni S, Piazza C, Cappelli C, Bertagna F, Barbieri V, Piana S, Bellafiore S, Spriano G, Mercante G, Nicolai P. Therapeutic Lateral Neck Dissection in Well-Differentiated Thyroid Cancer: Analysis on Factors Predicting Distribution of Positive Nodes and Prognosis. Head Neck. 2018 Feb; 40(2): 242a **IF 2.471**

Lombardi G, De Salvo GL, Brandes AA, Eoli M, Ruda R, Faedi M, Lolli I, Pace A, Daniele B, Pasqualetti F, Rizzato S, Bellu L, Pambuku A, Farina M, Magni G, Indraccolo S, Gardiman MP, Soffietti R, Zagonel V. Regorafenib Compared with Lomustine in Patients with Relapsed Glioblastoma (REGOMA): A Multicentre, Open-Label, Randomised, Controlled, Phase 2 Trial. Lancet Oncol. 2018 Dec 3 [Epub ahead of print] **IF 36.421**

Lopresto V, Strigari L, Farina L, Minosse S, Pinto R, Dâ ™Alessio D, Cassano B, Cavagnaro M. CT-Based Investigation of the Contraction of Ex Vivo Tissue Undergoing Microwave Thermal Ablation. Physics in Medicine & Biology. 2018 63(5): 055019a **IF 2.665**

Loria R, Laquintana V, Bon G, Trisciuoglio D, Frapolli R, Covello R, Amoreo CA, Ferraresi V, Zoccali C, Novello M, Del Bufalo D, Milella M, Biagini R, D'Incalci M, Falcioni R. HMGA1/E2F1 Axis and NFkB Pathways Regulate LPS Progression and Trabectedin Resistance. Oncogene. 2018 Nov; 37(45): 5926a **IF 6.854**

Ludovini V, Ricciuti B, Tofanetti FR, Mencaroni C, Giannarelli D, Sidoni A, Reda MS, Siggillino A, Baglivo S, Crino L, Bellezza G, Chiari R, Metro G. KRAS Mutation and DNA Repair and Synthesis Genes in Non-Small-Cell Lung Cancer. Mol.Clin.Oncol. 2018 Dec; 9(6): 689a

Luminari S, Viel E, Ferreri AJM, Zaja F, Chimienti E, Musuraca G, Tucci A, Balzarotti M, Tani M, Salvi F, Pesce EA, Ferrari A, Liberati AM, Spadea A, Marino D, Bruno-Ventre M, Volpetti S, Bottelli C, Ravaioli E, Merli F, Spina M.

Nonpegylated liposomal doxorubicin combination regimen in patients with diffuse large B-cell lymphoma and cardiac comorbidity. results of the HEART01 phase II trial conducted by the fondazione italiana linfomi. Hematol Oncol 2018;36(1):68-75. **IF 3.193**

Madonna G, Ballesteros-Merino C, Feng Z, Bifulco C, Capone M, Giannarelli D, Mallardo D, Simeone E, Grimaldi AM, Caraco C, Botti G, Fox BA, Ascierto PA. PD-L1 Expression with Immune-Infiltrate Evaluation and Outcome Prediction in Melanoma Patients Treated with Ipilimumab. Oncoimmunology. 2018 Sep 5; 7(12): e1405206a. **IF 5.503**

Magnani C, Calvieri A, Giannarelli D, Espino M, Casale G. Peripherally Inserted Central Catheter, Midline, and "Short" Midline in Palliative Care: Patient-Reported Outcome Measures to Assess Impact on Quality of Care. J.Vasc.Access. 2018 Dec 3; 1129729818814732a **IF 1.306**

Magnani C, Giannarelli D, Calvieri A, Dardeli A, Eusepi G, Restuccia MR, Mastroianni C, Casale G. Breakthrough Cancer Pain Tailored Treatment: Which Factors Influence the Medication Choice? an Observational, Prospective and Cross-Sectional Study in Patients with Terminal Cancer. Postgrad.Med.J. 2018 Oct; 94(1116): 566a **IF 2.078**

Maio M, Lewis K, Demidov L, Mandala M, Bondarenko I, Ascierto PA, Herbert C, Mackiewicz A, Rutkowski P, Guminski A, Goodman GR, Simmons B, Ye C, Yan Y, Schadendorf D, BRIM8 Investigators. Cognetti F. (c.) Adjuvant Vemurafenib in Resected, BRAF(V600) Mutation-Positive Melanoma (BRIM8): A Randomised, Double-Blind, Placebo-Controlled, Multicentre, Phase 3 Trial. Lancet Oncol. 2018 Apr; 19(4): 510. **IF 36.421**

Malta TM, Sokolov A, Gentles AJ, Burzykowski T, Poisson L, Weinstein JN, Kaminska B, Huelsken J, Omberg L, Gevaert O, Colaprico A, Czerwinska P, Mazurek S, Mishra L, Heyn H, Krasnitz A, Godwin AK, Lazar AJ, Cancer Genome Atlas Research Network, Stuart JM, Hoadley KA, Laird PW, Noushmehr H, Wiznerowicz M, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c).Machine Learning Identifies Stemness Features Associated with Oncogenic Dedifferentiation. Cell. 2018 Apr 5; 173(2): 338a **IF 31.398**

Mancini R, Noto A, Pisanu ME, De Vitis C, Maugeri-Sacca M, Ciliberto G. Metabolic Features of Cancer Stem Cells: The Emerging Role of Lipid Metabolism. Oncogene. 2018 37(18): 2367-2378a **IF 6.854**

Mancini R, Pattaro G, Diodoro MG, Sperduti I, Garufi C, Stigliano V, Perri P, Grazi GL, Cosimelli M. Tumor Regression Grade After Neoadjuvant Chemoradiation and Surgery for Low Rectal Cancer Evaluated by Multiple Correspondence Analysis: Ten Years as Minimum Follow-Up. Clin.Colorectal Cancer. 2018 Mar; 17(1): e13a **IF 3.861**

Mandoj C, Pizzuti L, Sergi D, Sperduti I, Mazzotta M, Di Lauro L, Amodio A, Carpano S, Di Benedetto A, Botti C, Ferranti F, Antenucci A, D'Alessandro MG, Marchetti P, Tomao S, Sanguineti G, Giordano A, Maugeri-Sacca M, Ciliberto G, Conti L, Vici P, Barba M. Observational Study of Coagulation Activation in Early Breast Cancer: Development of a Prognostic Model Based on Data from the Real World Setting. J.Transl.Med. 2018 May 16; 16(1): 129a **IF 4.197**

Manic G, Signore M, Sistigu A, Russo G, Corradi F, Siteni S, Musella M, Vitale S, De Angelis ML, Pallocca M, Amoreo CA, Sperati F, Di Franco S, Barresi S, Policicchio E, De Luca G, De Nicola F, Mottolese M, Zeuner A, Fanciulli M, Stassi G, Maugeri-Sacca M, Baiocchi M, Tartaglia M, Vitale I, De Maria R. CHK1-Targeted Therapy to Deplete DNA Replication-Stressed, p53-Deficient, Hyperdiploid Colorectal Cancer Stem Cells. Gut. 2018 May;67(5):903-917 **IF 17.016**

Manic G, Sistigu A, Corradi F, Musella M, De Maria R, Vitale I. Replication Stress Response in Cancer Stem Cells as a Target for Chemotherapy. Semin.Cancer Biol. 2018 Dec; 53: 31-41a **IF 10.198**

Marchesi F, Capria S, Giannarelli D, Trisolini SM, Ansuinelli M, Caputo MD, Serrao A, Gumenyuk S, Renzi D, Pupo L, Palombi F, Provenzano I, Di Rocco A, Pisani F, Romano A, Spadea A, Papa E, Canfora M, Cantonetti M, Mengarelli A. BEAM Vs FEAM High-Dose Chemotherapy: Retrospective Study in Lymphoma Patients Undergoing Autologous Stem Cell Transplant. Bone Marrow Transplant. 2018 53(8): 1051-1054a **IF 4.497**

Marchesi F, Girmenia C, Goffredo BM, Salvatorelli E, Romano A, Mengarelli A, Minotti G, Menna P. Isavuconazole: Case Report and Pharmacokinetic Considerations. Chemotherapy. 2018 Nov 20; 63(5): 253a **IF 2.000**

Marchesi F, Pimpinelli F, Ensoli F, Mengarelli A. Cytomegalovirus Infection in Hematologic Malignancy Settings Other than the Allogeneic Transplant. Hematol.Oncol. 2018 Apr; 36(2): 381a **IF 3.193**

Marchesi F, Regazzo G, Palombi F, Terrenato I, Sacconi A, Spagnuolo M, Donzelli S, Marino M, Ercolani C, Di Benedetto A, Blandino G, Ciliberto G, Mengarelli A, Rizzo MG. Serum miR-22 as Potential Non-Invasive Predictor of Poor Clinical Outcome in Newly Diagnosed, Uniformly Treated Patients with Diffuse Large B-Cell Lymphoma: An Explorative Pilot Study. J.Exp.Clin.Cancer Res. 2018 May 2; 37(1): 95a **IF 6.217**

Marchesi F,Vacca M, Giannarelli D, Ipsevich F, Pandolfi A, Gumenyuk S, Renzi D, Palombi F, Pisani F, Romano A, Spadea A, Papa E, Canfora M, Pierelli L, Mengarelli A. Lenograstim 5 microg/kg is Not Superior to Biosimilar Filgrastim 10 microg/kg in Lymphoma Patients Undergoing Peripheral Blood Stem Cell Mobilization After Chemotherapy: Preliminary Results from a Prospective Randomized Study. Transfusion. 2018 Feb 15; **IF 3.423**

Marchiò C, Dell'Orto P, Annaratone L, Geyer FC, Venesio T, Berrino E, Verdun di Cantogno L, Garofoli A, Rangel N, Casorzo L, dell'Aglio C, Gugliotta P, Trisolini E, Beano A, Pietribiasi F, Orlassino R, Cassoni P, Pich A, Montemurro F, Mottolese M, Vincent-Salomon A, Penault-Llorca F, Medico E, Ng CKY, Viale G, Sapino A. The Dilemma of HER2 Double-Equivocal Breast Carcinomas: Genomic Profiling and Implications for Treatment. Am.J.Surg.Pathol. 2018 Sep; 42(9): 1190a **IF 5.878**

Marino M, Visca P, Ottaviano M. PD-L1 Testing in Lung Cancer: An International Pathologist's Initiative in an Unknown "Middle Earth". J.Thorac.Oncol. 2018 Sep; 13(9): 1239a **IF 10.336**

Martin-Jimenez R, Faccenda D, Allen E, Reichel HB, Arcos L, Ferraina C, Strobbe D, Russell C, Campanella M. Reduction of the ATPase Inhibitory Factor 1 (IF1) Leads to Visual Impairment in Vertebrates. Cell.Death Dis. 2018 Jun 4; 9(6): 669a **IF 5.638**

Marzi S, Farneti A, Vidiri A, Di Giuliano F, Marucci L, Spasiano F, Terrenato I, Sanguineti G. Radiation-Induced Parotid Changes in Oropharyngeal Cancer Patients: The Role of Early Functional Imaging and Patient-/treatment-Related Factors. Radiat.Oncol. 2018 Oct 1; 13(1): 189a **IF 2.862**

Marzi S, Minosse S, Vidiri A, Piludu F, Giannelli M. Diffusional Kurtosis Imaging in Head and Neck Cancer: On the use of Trace-Weighted Images to Estimate Indices of Non-Gaussian Water Diffusion. Med.Phys. 2018 Dec;45(12):5411-5419 **IF 2.884**

Maschio M, Mengarelli A, Zarabla A, Giannarelli D, Maialetti A, Gumenyuk S, Renzi D, Palombi F, Pisani F, Romano A, Spadea A, Galie E, Marchesi F. Role of Pregabalin in Treatment of Polyneuropathy in Multiple Myeloma Patients: A Retrospective Study. Clin.Neuropharmacol. 2018 Dec 17[Epub ahead of print] **IF 1.370**

Maschio M, Pauletto G, Zarabla A, Maialetti A, Ius T, Villani V, Fabi A, Koudriavtseva T, Giannarelli D. Perampanel in Patients with Brain Tumour-Related Epilepsy in Real-Life Clinical Practice: A Retrospective Analysis. Int.J.Neurosci. 2018 Dec 3; : 1a [Epub ahead of print] **IF 1.848**

Maschio M, Zarabla A, Maialetti A, Marchesi F, Giannarelli D, Gumenyuk S, Pisani F, Renzi D, Galie E, Mengarelli A. Prevention of Bortezomib-Related Peripheral Neuropathy with Docosahexaenoic Acid and Alpha-Lipoic Acid in Patients with Multiple Myeloma: Preliminary Data. Integr.Cancer.Ther. 2018 Dec; 17(4): 1115a **IF 2.657**

Maschio M, Zarabla A, Maialetti A, Sperati F, Dinapoli L, Dispenza S, Petreri G, Cantelmi T. Lacosamide on Background Eeg Activity in Brain Tumor-Related Epilepsy Patients: A Case Series Study. Brain Behav. 2018 Nov; 8(11): e01067a **IF 2.219**

Masciarelli S, Capuano E, Ottone T, Divona M, De Panfilis S, Banella C, Noguera NI, Picardi A, Fontemaggi G, Blandino G, Lo-Coco F, Fazi F. Retinoic Acid and Arsenic Trioxide Sensitize Acute Promyelocytic Leukemia Cells to ER Stress. Leukemia. 2018 Feb; 32(2): 285a **IF 10.023**

Matar CF, Kahale LA, Hakoum MB, Tsolakian IG, Etxeandia-Ikobaltzeta I, Yosuico VE, Terrenato I, Sperati F, Barba M, Schunemann H, Akl EA. Anticoagulation for Perioperative Thromboprophylaxis in People with Cancer. Cochrane Database Syst.Rev. 2018 Jul 11; 7: CD009447a **IF 6.754**

Mattioli E, Andrenacci D, Garofalo C, Prencipe S, Scotlandi K, Remondini D, Gentilini D, Di Blasio AM, Valente S, Scarano E, Cicchilitti L, Piaggio G, Mai A, Lattanzi G. Altered Modulation of Lamin A/C-HDAC2 Interaction and p21 Expression during Oxidative Stress Response in HGPS. Aging Cell. 2018 Oct; 17(5): e12824a **IF 7.627**

Maugeri-Sacca M, De Maria R. The Hippo Pathway in Normal Development and Cancer. Pharmacol.Ther. 2018 Jun; 186: 60a **IF 10.376**

Mazzuca F, Onesti CE, Roberto M, Di Girolamo M, Botticelli A, Begini P, Strigari L, Marchetti P, Muscaritoli M. Lean Body Mass Wasting and Toxicity in Early Breast Cancer Patients Receiving Anthracyclines. Oncotarget. 2018 May 22; 9(39): 25714a

Melucci E, Casini B, Ronchetti L, Pizzuti L, Sperati F, Pallocca M, De Nicola F, Goeman F, Gallo E, Amoreo CA, Sergi D, Terrenato I, Vici P, Di Lauro L, Diodoro MG, Pescarmona E, Barba M, Mazzotta M, Mottolese M, Fanciulli M, Ciliberto G, De Maria R, Buglioni S, Maugeri-Sacca M. Expression of the Hippo Transducer TAZ in Association with WNT Pathway Mutations Impacts Survival Outcomes in Advanced Gastric Cancer Patients Treated with First-Line Chemotherapy. J.Transl.Med. 2018 Feb 5; 16(1): 22a **IF 4.197**

Menini S, Iacobini C, de Latouliere L, Manni I, Ionta V, Blasetti Fantauzzi C, Pesce C, Cappello P, Novelli F, Piaggio G, Pugliese G. The Advanced Glycation End-Product N() -Carboxymethyllysine Promotes Progression of Pancreatic Cancer: Implications for Diabetes-Associated Risk and its Prevention. J.Pathol. 2018 Jun;245(2):197-208 **IF 6.253**

Menna P, Calabrese V, Armento G, Annibali O, Greco C, Salvatorelli E, Marchesi F, Reggiardo G, Minotti G. Pharmacology of Cardio-Oncology: Chronotropic and Lusitropic Effects of B-Type Natriuretic Peptide in Cancer Patients with Early Diastolic Dysfunction Induced by Anthracycline Or Nonanthracycline Chemotherapy. J.Pharmacol.Exp.Ther. 2018 Jul; 366(1): 158a **IF 3.706**

Menna P, Salvatorelli E, Armento G, Annibali O, Greco C, Marchesi F, Calabrese V, Reggiardo G, Minotti G. The Endogenous Lusitropic and Chronotropic Agent, B-Type Natriuretic Peptide, Limits Cardiac Troponin Release in Cancer Patients with an Early Impairment of Myocardial Relaxation Induced by Anthracyclines. J.Pharmacol.Exp. Ther. 2018 Dec; 367(3): 518a **IF 3.706**

Metro G, Giannarelli D, Sidoni A, Chiari R, Bellezza G. Anaplastic Lymphoma Kinase Immunohistochemistry Scores do Not Predict Sensitivity to Crizotinib in Fluorescence in Situ Hybridization-Positive Non-Small Cell Lung Cancer Patients. Int.J.Biol.Markers. 2018 33(4): 549-550a **IF 1.449**

Metro G, Passaro A, Lo Russo G, Bonanno L, Giusti R, Gregorc V, Capelletto E, Martelli O, Cecere FL, Giannarelli D, Luciani A, Bearz A, Tuzi A, Scotti V, Tonini G, Galetta D, Carta A, Soto Parra H, Rebonato A, Morabito A, Chiari R. Ceritinib Compassionate use for Patients with Crizotinib-Refractory, Anaplastic Lymphoma Kinase-Positive Advanced Non-Small-Cell Lung Cancer. Future Oncol. 2018 Feb; 14(4): 353a **IF 2.369**

Migliore C, Morando E, Ghiso E, Anastasi S, Leoni VP, Apicella M, Cora' D, Sapino A, Pietrantonio F, De Braud F, Columbano A, Segatto O, Giordano S. MiR-205 Mediates Adaptive Resistance to MET Inhibition Via ERRFI1 Targeting and Raised EGFR Signaling. EMBO Mol.Med. 2018 Sep; 10(9): 10.15252/emmm.201708746a **IF 10.293**

Molica S, Giannarelli D, Mirabelli R, Levato L, Kay NE, Shanafelt TD. Chronic Lymphocytic Leukemia International Prognostic Index: A Systematic Review and Meta-Analysis. Blood. 2018 Jan 18; 131(3): 365a **IF 15.132**

Molica S, Giannarelli D, Mirabelli R, Levato L, Shanafelt TD. Chronic Lymphocytic Leukemia International Prognostic Index (CLL-IPI) in Patients Receiving Chemoimmuno Or Targeted Therapy: A Systematic Review and Meta-Analysis. Ann.Hematol. 2018 Oct; 97(10): 2005a **IF 2.845**

Molica S, Giannarelli D, Mirabelli R, Levato L, Shanafelt TD. The Magnitude of Improvement in Progression-Free Survival with Targeted Therapy in relapsed/refractory Chronic Lymphocytic Leukemia Based on Prognostic Risk Category: A Systematic Review and Meta-Analysis. Leuk.Lymphoma. 2018 Dec 5; : 1a **IF 2.644**

Monaco G, La Rovere R, Karamanou S, Welkenhuyzen K, Ivanova H, Vandermarliere E, Di Martile M, Del Bufalo D, De Smedt H, Parys JB, Economou A, Bultynck G. A Double Point Mutation at Residues Ile14 and Val15 of Bcl-2 Uncovers a Role for the BH4 Domain in both Protein Stability and Function. Febs j. 2018 285(1): 127a **IF 4.530**

Monteonofrio L, Valente D, Ferrara M, Camerini S, Miscione R, Crescenzi M, Rinaldo C, Soddu S. HIPK2 and Extrachromosomal Histone H2B are Separately Recruited by Aurora-B for Cytokinesis. Oncogene. 2018 Jun; 37(26): 3562a **IF 6.854**

Moschini M, Soria F, Mathieu R, Xylinas E, D'Andrea D, Tan WS, Kelly JD, Simone G, Tuderti G, Meraney A, Krishna S, Konety B, Zamboni S, Baumeister P, Mattei A, Briganti A, Montorsi F, Galucci M, Rink M, Karakiewicz PI, Roupret M, Aziz A, Perry M, Rowe E, Koupparis A, Kassouf W, Scherr DS, Ploussard G, Boorjian SA, Sooriakumaran P, Shariat SF, European Association of Urology - Young Academic Urologists (EAU-YAU), Urothelial Carcinoma Working Group. Propensity-Score-Matched Comparison of Soft Tissue Surgical Margins Status between Open and Robotic-Assisted Radical Cystectomy. Urol.Oncol. 2018 Nov 13; [Epub ahead of print] **IF 3.397**

Muti P, Donzelli S, Sacconi A, Hossain A, Ganci F, Frixa T, Sieri S, Krogh V, Berrino F, Biagioni F, Strano S, Beyene J, Yarden Y, Blandino G. MiRNA-513a-5p Inhibits Progesterone Receptor Expression and Constitutes a Risk Factor for Breast Cancer: The hOrmone and Diet in the ETiology of Breast Cancer Prospective Study. Carcinogenesis. 2018 Feb 9; 39(2): 98a **IF 5.072**

Nava MB, Adams WP Jr, Botti G, Campanale A, Catanuto G, Clemens MW, Del Vecchio DA, De Vita R, Di Napoli A, Hall-Findlay E, Hammond D, Heden P, Mallucci P, Martin Del Yerro JL, Muti E, Rancati A, Randquist C, Salgarello M, Stan C, Rocco N. MBN 2016 Aesthetic Breast Meeting BIA-ALCL Consensus Conference Report. Plast.Reconstr. Surg. 2018 Jan; 141(1): 40a **IF 3.475**

Nicholson AG, Tsao MS, Travis WD, Patil DT, Galateau-Salle F, Marino M, Dacic S, Beasley MB, Butnor KJ, Yatabe Y, Pass HI, Rusch VW, Detterbeck FC, Asamura H, Rice TW, Rami-Porta R. Eighth Edition Staging of Thoracic Malignancies: Implications for the Reporting Pathologist. Arch.Pathol.Lab.Med. 2018 May; 142(5): 645a. **IF 3.658**

Nigri G, Petrucciani N, Pinna AD, Ravaioli M, Jovine E, Minni F, Grazi GL, Chirletti P, Balzano G, Ferla F, De Carlis L, Tisone G, Napoli N, Boggi U, Ramacciato G. Evolution of Pancreatectomy with En Bloc Venous Resection for Pancreatic Cancer in Italy. Retrospective Cohort Study on 425 Cases in 10 Pancreatic Referral Units. Int.J.Surg. 2018 Jul; 55: 103a **IF 2.693**

Nuvoli B, Camera E, Mastrofrancesco A, Briganti S, Galati R. Modulation of Reactive Oxygen Species Via ERK and STAT3 Dependent Signalling are Involved in the Response of Mesothelioma Cells to Exemestane. Free Radic.Biol. Med. 2018 Feb 1; 115: 266a **IF 6.020**

Oderda M, Marra G, Albisinni S, Altobelli E, Baco E, Beatrici V, Cantiani A, Carbone A, Ciccariello M, Descotes JL, Dubreuil-Chambardel M, Eldred-Evans D, Fasolis G, Ferriero M, Fiard G, Forte V, Giacobbe A, Kumar P, Lacetera V, Mozer P, Muto G, Papalia R, Pastore A, Peltier A, Piechaud T, Simone G, Roche JB, Roupret M, Rouviere O, Van Velthoven R, Gontero P. Accuracy of Elastic Fusion Biopsy in Daily Practice: Results of a Multicenter Study of 2115 Patients. Int.J.Urol. 2018 Dec; 25(12): 990a **IF 1.941**

Olivieri J, Attolico I, Nuccorini R, Pascale SP, Chiarucci M, Poiani M, Corradini P, Farina L, Gaidano G, Nassi L, Sica S, Piccirillo N, Pioltelli PE, Martino M, Moscato T, Pini M, Zallio F, Ciceri F, Marktel S, Mengarelli A, Musto P, Capria S, Merli F, Codeluppi K, Mele G, Lanza F, Specchia G, Pastore D, Milone G, Saraceni F, Di Nardo E, Perseghin P, Olivieri A. Predicting Failure of Hematopoietic Stem Cell Mobilization before it Starts: The Predicted Poor Mobilizer (pPM) Score. Bone Marrow Transplant. 2018 Apr; 53(4): 461a **IF 4.497**

Pace A, Mandoj C, Antenucci A, Villani V, Sperduti I, Casini B, Carosi M, Fabi A, Vidiri A, Koudriavtseva T, Conti L. A Predictive Value of Von Willebrand Factor for Early Response to Bevacizumab Therapy in Recurrent Glioma. J.Neurooncol. 2018 Jul; 138(3): 527a **IF 3.060**

Pace A, Villani V. 2018. "Palliative Care and Palliative Rehabilitation: Approaches to the End-of-Life." In Neurorehabilitation in Neuro-Oncology, edited by M. Bartolo, R. Soffietti and M. Klein. 1st ed.: Springer International Publishing.

Pace A, Villani V. Palliative and Supportive Care of Patients with Intracranial Glioma. Prog.Neurol.Surg. 2018 31: 229-237

Pace A, Walbert T. Simultaneous Care in Neuro-Oncology. Neuro Oncol. 2018 Feb 19; 20(3): 302a **IF 9.384**

Pages F, Mlecnik B, Marliot F, Bindea G, Ou FS, Bifulco C, Lugli A, Zlobec I, Rau TT, Berger MD, Nagtegaal ID, Vink-Borger E, Hartmann A, Geppert C, Kolwelter J, Merkel S, Grutzmann R, Van den Eynde M, Jouret-Mourin A, Kartheuser A, Leonard D, Remue C, Wang JY, Bavi P, Roehrl MHA, Ohashi PS, Nguyen LT, Han S, MacGregor HL, Hafezi-Bakhtiari S, Wouters BG, Masucci GV, Andersson EK, Zavadova E, Vocka M, Spacek J, Petruzelka L, Konopasek B, Dundr P, Skalova H, Nemejcova K, Botti G, Tatangelo F, Delrio P, Ciliberto G, Maio M, Laghi L, Grizzi F, Fredriksen T, Buttard B, Angelova M, Vasaturo A, Maby P, Church SE, Angell HK, Lafontaine L, Bruni D, El Sissy C, Haicheur N, Kirilovsky A, Berger A, Lagorce C, Meyers JP, Paustian C, Feng Z, Ballesteros-Merino C, Dijkstra J, van de Water C, van Lent-van Vliet S, Knijn N, Musina AM, Scripcariu DV, Popivanova B, Xu M, Fujita T, Hazama S, Suzuki N, Nagano H, Okuno K, Torigoe T, Sato N, Furuhata T, Takemasa I, Itoh K, Patel PS, Vora HH, Shah B, Patel JB, Rajvik KN, Pandya SJ, Shukla SN, Wang Y, Zhang G, Kawakami Y, Marincola FM, Ascierto PA, Sargent DJ, Fox BA, Galon J. International Validation of the Consensus Immunoscore for the Classification of Colon Cancer: A Prognostic and Accuracy Study. Lancet. 2018 May 26; 391(10135): 2128a **IF 53.254**

Paladini A, Lucatelli P, Cappelli F, Pizzi G, Anelli V, Amodeo EM, Beomonte Zobel D, Paladini L, Biagini R, Attala D, Zoccali C, Vallati GE. Osteoid Osteoma Treated with Radiofrequency Ablation in Non-Operating Room Anesthesia. A Different Way of Approaching Ablative Therapy on Osteoid Osteoma. Eur.Rev.Med.Pharmacol.Sci. 2018 Sep; 22(17): 5438a-5446 **IF 2.387**

Palermo B, Franzese O, Donna CD, Panetta M, Quintarelli C, Sperduti I, Gualtieri N, Foddai ML, Proietti E, Ferraresi V, Ciliberto G, Nisticò P. Antigen-Specificity and DTIC before Peptide-Vaccination Differently Shape Immune-Checkpoint Expression Pattern, Anti-Tumor Functionality and TCR Repertoire in Melanoma Patients. Oncoimmunology. 2018 Sep 11;7(12):e1465163 **IF 5.503**

Pallocca M, Goeman F, De Nicola F, Melucci E, Sperati F, Terrenato I, Pizzuti L, Casini B, Gallo E, Amoreo CA, Vici P, Di Lauro L, Buglioni S, Diodoro MG, Pescarmona E, Mazzotta M, Barba M, Fanciulli M, De Maria R, Ciliberto G, Maugeri-Sacca M. Coexisting YAP Expression and TP53 Missense Mutations Delineates a Molecular Scenario Unexpectedly Associated with Better Survival Outcomes in Advanced Gastric Cancer. J.Transl.Med. 2018 Sep 4; 16(1): 247a **IF 4.197**

Panebianco V, Barchetti G, Simone G, Del Monte M, Ciardi A, Grompone MD, Campa R, Indino EL, Barchetti F, Sciarra A, Leonardo C, Gallucci M, Catalano C. Negative Multiparametric Magnetic Resonance Imaging for Prostate Cancer: What's Next? Eur.Urol. 2018 Jul;74(1):48-54 **IF 17.581**

Pasero D, Sangalli F, Baiocchi M, Blangetti I, Cattaneo S, Paternoster G, Moltrasio M, Auci E, Murrino P, Forfori F, Forastiere E, De Cristofaro MG, Deste G, Feltracco P, Petrini F, Tritapepe L, Girardis M. Experienced use of Dexmedetomidine in the Intensive Care Unit: A Report of a Structured Consensus. Turk.J.Anaesthesiol.Reanim. 2018 Jun; 46(3): 176a

Pasqualetti F, Pace A, Gonnelli A, Villani V, Cantarella M, Delishaj D, Vivaldi C, Molinari A, Montrone S, Pellerino A, Franchino F, Baldaccini D, Lombardi G, Lolli I, Catania F, Bazzoli E, Morganti R, Fabi A, Zagonel V, Bocci G, Fabrini MG, Ruda R, Soffietti R, Paiar F. Single-Agent Bevacizumab in Recurrent Glioblastoma After Second-Line Chemotherapy with Fotemustine: The Experience of the Italian Association of Neuro-Oncology. Am.J.Clin.Oncol. 2018 Dec; 41(12): 1272a **IF 3.424**

Peng X, Chen Z, Farshidfar F, Xu X, Lorenzi PL, Wang Y, Cheng F, Tan L, Mojumdar K, Du D, Ge Z, Li J, Thomas GV, Birsoy K, Liu L, Zhang H, Zhao Z, Marchand C, Weinstein JN, Cancer Genome Atlas Research Network, Bathe OF, Liang H. Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Molecular Characterization and Clinical Relevance of Metabolic Expression Subtypes in Human Cancers. Cell.Rep. 2018 Apr 3; 23(1): 255a **IF 8.032**

Persichetti A, Bizzarri G, Guglielmi R, Barnabei A, Bianchini A, Coccaro C, Appetecchia M, Papini E. Ultrasound-Guided Laser Ablation for Local Control of Neck Recurrences of Medullary Thyroid Cancer. A Feasibility Study. Int.J.Hyperthermia. 2018 Sep 11; 1a **IF 3.440**

Petroni M, Sardina F, Infante P, Bartolazzi A, Locatelli E, Fabretti F, Di Giulio S, Capalbo C, Cardinali B, Coppa A, Tessitore A, Colicchia V, Sahun Roncero M, Belardinilli F, Di Marcotullio L, Soddu S, Comes Franchini M, Petricci E, Gulino A, Giannini G. MRE11 Inhibition Highlights a Replication Stress-Dependent Vulnerability of MYCN-Driven Tumors. Cell.Death Dis. 2018 Aug 30; 9(9): 895a **IF 5.638**

Pichi B, Pellini R, DE Virgilio A, Spriano G. Electrochemotherapy: A Well-Accepted Palliative Treatment by Patients with Head and Neck Tumours. Acta Otorhinolaryngol.Ital. 2018 Jun; 38(3): 181a **IF 1.196**

Pilotto S, Sperduti I, Leuzzi G, Chiappetta M, Mucilli F, Ratto GB, Lococo F, Filosso PL, Spaggiari L, Novello S, Milella M, Santo A, Scarpa A, Infante M, Tortora G, Facciolo F, Bria E. Prognostic Model for Resected Squamous Cell Lung Cancer: External Multicenter Validation and Propensity Score Analysis Exploring the Impact of Adjuvant and Neoadjuvant Treatment. J.Thorac.Oncol. 2018 Apr; 13(4): 568a **IF 10.336**

Piludu F, Gangemi E, Marucci L, Guerrisi A, Pellini R, Covello R, Carlini P, Spriano G, Sanguineti G, Marzi S, Vidiri A. MRI Evaluation using DWI and T2WI of Residual Lymph Nodes in Patients Affected by Head and Neck Squamous Cell Carcinoma Treated with Chemo-Radiotherapy. Curr.Med.Imaging Rev. 2018 14(4): 599a **IF 0.299**

Pinelli S, Artini PG, Basile S, Obino MER, Sergiampietri C, Giannarelli D, Simi G, Cela V. Estrogen Treatment in Infertile Women with Premature Ovarian Insufficiency in Transitional Phase: A Retrospective Analysis. J.Assist.Reprod. Genet. 2018 Mar; **IF 2.788**

Pisanu ME, Maugeri-Sacca M, Fattore L, Bruschini S, De Vitis C, Tabbi E, Bellei B, Migliano E, Kovacs D, Camera E, Picardo M, Jakopin Z, Cippitelli C, Bartolazzi A, Raffa S, Torrisi MR, Fulciniti F, Ascierto PA, Ciliberto G, Mancini R. Inhibition of Stearoyl-CoA Desaturase 1 Reverts BRAF and MEK Inhibition-Induced Selection of Cancer Stem Cells in BRAF-Mutated Melanoma. J.Exp.Clin.Cancer Res. 2018 Dec 17; 37(1): 318a **IF 6.217**

Pizzuti L, Giordano A, Michelotti A, Mazzotta M, Natoli C, Gamucci T, De Angelis C, Landucci E, Diodati L, Iezzi L, Mentuccia L, Fabbri A, Barba M, Sanguineti G, Marchetti P, Tomao S, Mariani L, Paris I, Lorusso V, Vallarelli S, Cassano A, Airoldi F, Orlandi A, Moscetti L, Sergi D, Sarobba MG, Tonini G, Santini D, Sini V, Veltri E, Vaccaro A, Ferrari L, De Tursi M, Tinari N, Grassadonia A, Greco F, Botticelli A, La Verde N, Zamagni C, Rubino D, Cortesi E, Magri V, Pomati G, Scagnoli S, Capomolla E, Kayal R, Scinto AF, Corsi D, Cazzaniga M, Laudadio L, Forciniti S, Mancini M, Carbognin L, Seminara P, Barni S, Samaritani R, Roselli M, Portarena I, Russo A, Ficorella C, Cannita K, Carpano S, Pistelli M, Berardi R, De Maria R, Sperduti I, Ciliberto G, Vici P. Palbociclib Plus Endocrine Therapy in HER2 Negative, Hormonal Receptor-Positive, Advanced Breast Cancer: A Real-World Experience. J.Cell.Physiol. 2018 Dec 10 [Epub ahead of print] **IF 3.923**

Pizzuti L, Sergi D, Mandoj C, Antoniani B, Sperati F, Chirico A, Di Lauro L, Valle M, Garofalo A, Vizza E, Corrado G, Tomao F, Rinaldi M, Carpano S, Maugeri-Sacca M, Conti L, Digiesi G, Marchetti P, De Maria R, Giordano A, Barba M, Carosi MA, Vici P. GLUT 1 Receptor Expression and Circulating Levels of Fasting Glucose in High Grade Serous Ovarian Cancer. J.Cell.Physiol. 2018 233(2): 1396a **IF 3.923**

Pizzuti L, Sergi D, Sperduti I, Lauro LD, Mazzotta M, Botti C, Izzo F, Marchetti L, Tomao S, Marchetti P, Natoli C, Grassadonia A, Gamucci T, Mentuccia L, Magnolfi E, Vaccaro A, Cassano A, Rossi E, Botticelli A, Sini V, Sarobba MG, Fabbri MA, Moscetti L, Astone A, Michelotti A, De Angelis C, Bertolini I, Angelini F, Ciliberto G, Maugeri-Sacca M, Giordano A, Barba M, Vici P. Body Mass Index in HER2-Negative Metastatic Breast Cancer Treated with First-Line Paclitaxel and Bevacizumab. Cancer.Biol.Ther. 2018 Apr 3; 19(4): 328a **IF 3.373**

Plantone D, Koudriavtseva T. Current and Future use of Chloroquine and Hydroxychloroquine in Infectious, Immune, Neoplastic, and Neurological Diseases: A Mini-Review. Clin.Drug Investig. 2018 Aug; 38(8): 653-671a **IF 1.918**

Policicchio D, Muggianu G, Dipellegrini G, Boccaletti R. Delayed Diagnosis of Post-Traumatic Aneurysm of Distal Anterior Cerebral Artery. Surg.Neurol.Int. 2018 Nov 1; 9: 222a

Polo A, Marchese S, De Petro G, Montella M, Ciliberto G, Budillon A, Costantini S. Identifying a Panel of genes/proteins/miRNAs Modulated by Arsenicals in Bladder, Prostate, Kidney Cancers. Sci.Rep. 2018 Jul 10; 8(1): 10395a **IF 4.122**

Porru M, Pompili L, Caruso C, Biroccio A, Leonetti C. Targeting KRAS in Metastatic Colorectal Cancer: Current Strategies and Emerging Opportunities. J.Exp.Clin.Cancer Res. 2018 Mar 13; 37(1): 57a **IF 6.217**

Porru M, Pompili L, Caruso C, Leonetti C. Xenograft as in Vivo Experimental Model. Methods Mol.Biol. 2018 1692: 97a

Prieto-Potin I, Montagut C, Bellosillo B, Evans M, Smith M, Melchior L, Reiltin W, Bennett M, Pennati V, Castiglione F, Burrig KF, Cooper U, Dockhorn-Dworniczak B, Rossenbach C, Luna-Aguirre CM, Barrera-Saldana HA, Machado JC, Costa JL, Yacobi R, Tabibian-Keissar H, Buglioni S, Ronchetti L, Douglas-Berger L, Dubbink HJ, Alorini M, Sabourin JC, Rojo F. Multicenter Evaluation of the Idylla NRAS-BRAF Mutation Test in Metastatic Colorectal Cancer. J.Mol.Diagn. 2018 20(5): 664-676a **IF: 4.880**

Procopio G, Prisciandaro M, Iacovelli R, Cortesi E, Fornarini G, Facchini G, Carteni G, Sabbatini R, Del Bene G, Galli L, Caserta C, Multari AG, Bregni M, Massari F, Buti S, De Giorgi U, Zustovich F, Milella M, Calabro F, Mancini ML, Tortora G, Vernieri C, Santini D, Soraru M, Ricotta R, Masini C, Tucci M, Fedeli SL, Ortega C, Mecozzi A, Ratta R, Sternberg CN, Verzoni E. Safety and Efficacy of Cabozantinib in Metastatic Renal-Cell Carcinoma: Real-World Data from an Italian Managed Access Program. Clin.Genitourin.Cancer. 2018 Apr 19; 16(4): e945-e951a **IF 2.539**

Pruszko M, Milano E, Zylicz A, Zylicz M, Blandino G, Fontemaggi G. Zebrafish as Experimental Model to Establish the Contribution of Mutant p53 and ID4 to Breast Cancer Angiogenesis in Vivo. J.Thorac.Dis. 2018 Mar; 10(3): E231a **IF 1.804**

Radovich M, Pickering CR, Felau I, Ha G, Zhang H, Jo H, Hoadley KA, Anur P, Zhang J, McLellan M, Bowlby R, Matthew T, Danilova L, Hegde AM, Kim J, Leiserson MDM, Sethi G, Lu C, Ryan M, Su X, Cherniack AD, Robertson G, Akbani R, Spellman P, Weinstein JN, Hayes DN, Raphael B, Lichtenberg T, Leraas K, Zenklusen JC, Cancer Genome Atlas Network, Fujimoto J, Scapulatempo-Neto C, Moreira AL, Hwang D, Huang J, Marino M, Korst R, Giaccone G, Gokmen-Polar Y, Badve S, Rajan A, Strobel P, Girard N, Tsao MS, Marx A, Tsao AS, Loehrer PJ. Blandino G (c.) The Integrated Genomic Landscape of Thymic Epithelial Tumors. Cancer.Cell. 2018 Feb 12; 33(2): 244a **IF 22.844**

Reda G, Fattizzo B, Cassin R, Mattiello V, Tonella T, Giannarelli D, Massari F, Cortelezzi A. Predictors of Atrial Fibrillation in Ibrutinib-Treated CLL Patients: A Prospective Study. J.Hematol.Oncol. 2018 Jun 11; 11(1): 79a **IF 7.333**

Reda G, Riva M, Fattizzo B, Cassin R, Giannarelli D, Pennisi M, Freyrie A, Cairoli R, Molteni A, Cortelezzi A. Bone Marrow Fibrosis and Early Hematological Response as Predictors of Poor Outcome in Azacitidine Treated High Risk-Patients with Myelodysplastic Syndromes Or Acute Myeloid Leukemia. Semin.Hematol. 2018 Oct; 55(4): 202a **IF 3.926**

Ricciardi S, Cardillo G, Zirafa CC, Carleo F, Facciolo F, Fontanini G, Mutti L, Melfi F. Surgery for Malignant Pleural Mesothelioma: An International Guidelines Review. J.Thorac.Dis. 2018 Jan; 10(Suppl 2): S285a **IF 1.804**

Ricketts CJ, De Cubas AA, Fan H, Smith CC, Lang M, Reznik E, Bowlby R, Gibb EA, Akbani R, Beroukhim R, Bottaro DP, Choueiri TK, Gibbs RA, Godwin AK, Haake S, Hakimi AA, Henske EP, Hsieh JJ, Ho TH, Kanchi RS, Krishnan B, Kwiatkowski DJ, Lui W, Merino MJ, Mills GB, Myers J, Nickerson ML, Reuter VE, Schmidt LS, Shelley CS, Shen H, Shuch B, Signoretti S, Srinivasan R, Tamboli P, Thomas G, Vincent BG, Vocke CD, Wheeler DA, Yang L, Kim WY, Robertson AG, Cancer Genome Atlas Research Network, Spellman PT, Rathmell WK, Linehan WM. Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). The Cancer Genome Atlas Comprehensive Molecular Characterization of Renal Cell Carcinoma. Cell.Rep. 2018 Apr 3; 23(1): 313a **IF 8.032**

Roberto M, Botticelli A, Strigari L, Ghidini M, Onesti CE, Ratti M, Benzoni I, Pizzo C, Falcone R, Lomiento D, Donida BM, Totaro L, Mazzuca F, Marchetti P. Prognosis of Elderly Gastric Cancer Patients After Surgery: A Nomogram to Predict Survival. Med.Oncol. 2018 Jun 19; 35(7): 111a **IF 2.920**

Roila F, Fumi G, Ruggeri B, Antonuzzo A, Ripamonti C, Fatigoni S, Cavanna L, Gori S, Fabi A, Marzano N, Graiff C, De Sanctis V, Mirabile A, Serpentini S, Bocci C, Pino MS, Cilenti G, Verusio C, Ballatori E, NICSO (Network Italiano per le Cure di Supporto in Oncologia). Prevalence, Characteristics, and Treatment of Fatigue in Oncological Cancer Patients in Italy: A Cross-Sectional Study of the Italian Network for Supportive Care in Cancer (NICSO). Support. Care Cancer. 2018 Aug 6 [Epub ahead of print] **IF 2.676**

Rollo F, Donà MG, Pellini R, Pichi B, Marandino F, Covello R, Benevolo M. Cytology and Direct Human Papillomavirus Testing on Fine Needle Aspirates from Cervical Lymph Node Metastases of Patients with Oropharyngeal Squamous Cell Carcinoma Or Occult Primary. Cytopathology. 2018 Oct; 29(5): 449-454° **IF 1.376**

Rosati J, Ferrari D, Altieri F, Tardivo S, Ricciolini C, Fusilli C, Zalfa C, Profico DC, Pinos F, Bernardini L, Torres B, Manni I, Piaggio G, Binda E, Copetti M, Lamorte G, Mazza T, Carella M, Gelati M, Valente EM, Simeone A, Vescovi AL. Establishment of Stable iPS-Derived Human Neural Stem Cell Lines Suitable for Cell Therapies. Cell.Death Dis. 2018 Sep 17; 9(10): 937a. **IF 5.638**

Rotte A, D'Orazi G, Bhandaru M. Nobel Committee Honors Tumor Immunologists. J.Exp.Clin.Cancer Res. 2018 Oct 30; 37(1): 262a **IF 6.217**

Russignan A, Spina C, Tamassia N, Cassaro A, Rigo A, Bagnato A, Rosano L, Bonalumi A, Gottardi M, Zanatta L, Giacomazzi A, Scupoli MT, Tinelli M, Salvadori U, Mosna F, Zamo A, Cassatella MA, Vinante F, Tecchio C. In reply to schafer et al: New evidence on the role of endothelin-1 axis as a potential therapeutic target in multiple myeloma. Br J Haemato l2019;184(6):1052-1055. **IF 5.128**

Russillo M, Ferretti G, Vidiri A, Gasparro S, Cognetti F, Pellegrini D, Fabi A. Impressive Long-Term Response with Pertuzumab and Trastuzumab in HER2-Positive Breast Cancer with Brain Metastasis. In Vivo. 2018 Jul-Aug; 32(4): 839a **IF 1.116**

Russo M, Villani V, Taga A, Genovese A, Terrenato I, Manzoni GC, Servadei F, Torelli P, Pace A. Headache as a Presenting Symptom of Glioma: A Cross-Sectional Study. Cephalalgia. 2018 Apr; 38(4): 730a **IF 3.886**

Saltz J, Gupta R, Hou L, Kurc T, Singh P, Nguyen V, Samaras D, Shroyer KR, Zhao T, Batiste R, Van Arnam J, Cancer Genome Atlas Research Network, Shmulevich I, Rao AUK, Lazar AJ, Sharma A, Thorsson V, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Spatial Organization and Molecular Correlation of Tumor-Infiltrating Lymphocytes using Deep Learning on Pathology Images. Cell.Rep. 2018 Apr 3; 23(1): 181a **IF 8.032**

Sanchez-Mete L, Stigliano V. Update on Small Bowel Surveillance in Hereditary Colorectal Cancer Syndromes. Tumori. 2018 Aug 17 [Epub ahead of print] **IF 1.304**

Sanchez-Vega F, Mina M, Armenia J, Chatila WK, Luna A, La KC, Dimitriadoy S, Liu DL, Kantheti HS, Saghafinia S, Chakravarty D, Daian F, Gao Q, Bailey MH, Liang WW, Foltz SM, Shmulevich I, Ding L, Heins Z, Ochoa A, Gross B, Gao J, Zhang H, Kundra R, Kandoth C, Bahceci I, Dervishi L, Dogrusoz U, Zhou W, Shen H, Laird PW, Way GP, Greene CS, Liang H, Xiao Y, Wang C, Iavarone A, Berger AH, Bivona TG, Lazar AJ, Hammer GD, Giordano T, Kwong LN, McArthur G, Huang C, Tward AD, Frederick MJ, McCormick F, Meyerson M, Cancer Genome Atlas Research Network, Van Allen EM, Cherniack AD, Ciriello G, Sander C, Schultz N. Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Oncogenic Signaling Pathways in the Cancer Genome Atlas. Cell. 2018 Apr 5; 173(2): 321a **IF 31.398**

Sangro B, Maini CL, Ettorre GM, Cianni R, Golfieri R, Gasparini D, Ezziddin S, Paprottka PM, Fiore F, Van Buskirk M, Bilbao JI, Salvatori R, Giampalma E, Geatti O, Wilhelm K, Hoffmann RT, Izzo F, Inarrairaegui M, Urigo C, Cappelli A, Vit A, Ahmadzadehfar H, Jakobs TF, Sciuto R, Pizzi G, Lastoria S, European Network on Radioembolization with Yttrium-90 resin microspheres (ENRY). Radioembolisation in Patients with Hepatocellular Carcinoma that have Previously Received Liver-Directed Therapies. Eur.J.Nucl.Med.Mol.Imaging. 2018 Sep;45(10):1721-1730 **IF 7.704**

Sansone A, Fegatelli DA, Pozza C, Fattorini G, Lauretta R, Minnetti M, Romanelli F, Lucatelli P, Corona M, Bezzi M, Lombardo F, Lenzi A, Gianfrilli D. Effects of Percutaneous Varicocele Repair on Testicular Volume: Results from a 12-Month Follow-Up. Asian J.Androl. 2018 Dec 25; [Epub ahead of print] **IF 3.259**

Sartori E, Franchi M, Capelli G, Cicinelli E, Colacurci N, De Vincenzo R, Landoni F, Maggino T, Masturzo B, Parazzini F, Scarfone G, Peccatori F, Romagnolo C, Scibilia G, Scollo P, Zola P, Garzon S, Raffaelli R, Busato E, Cetin I, Giovannini M, Zanni G C, Greggi S, Marconi A M, Rizzo N, Ruspa G, Meroni MG, Volpi EO, Simoncini T, Gadducci A, Ghezzi F, Laganà AS, Melis GB, Paoletti AM, Strobelt N, Spinillo A, Severi FM, Frusca T, Greco P, Nappi L, Ricci G, Vizza E, Papaccio M, Ratti M, Scambia G. Cancer in Pregnancy: Proposal of an Italian Multicenter Study. Gynecologic Oncology Group of the Italian Society of Gynæcology and Obstetrics (SIGO). Italian Journal of Gynæcology & Obstetrics. 2018; 30(3)

Sartori E, Ghezzi F, Cromi A, Miscioscia R, Laganà AS, Garzon S, Raffaelli R, Candiani M, Casarin J, Ciavattini A, Di Paola R, Greco P, Guaschino S, Marchesoni D, Milani R, Rizzo N, Venturini PL, Zullo F, Valente E, Vizza E, Scambia G, Franchi M. Learning Climate and Quality of Postgraduate Training in Gynecology and Obstetrics should be Assessed in Italian Training Courses. Italian Journal of Gynæcology & Obstetrics 2018; 30(3)

Scaglione A, Monteonofrio L, Parisi G, Cecchetti C, Siepi F, Rinaldo C, Giorgi A, Verzili D, Zamparelli C, Savino C, Soddu S, Vallone B, Montemiglio LC. Effects of Y361-Auto-Phosphorylation on Structural Plasticity of the HIPK2 Kinase Domain. Protein Sci. 21. Callovini GM, Telera S, Sherkat S, Sperduti I, Callovini T, Carapella CM. How is Stereotactic Brain Biopsy Evolving? A Multicentric Analysis of a Series of 421 Cases Treated in Rome Over the Last Sixteen Years. Clin.Neurol.Neurosurg. 2018 174: 101-107a **IF 2.410**

Scambia G, Raffaelli R, Baggio S, Garzon S, Laganà AS, Sartori E, Vanzo F, Vizza E, Angioli R, Benedetto C, Cagnacci A, Candiani M, Carta G, Caserta D, Cherchi PL, Ciavattini A, Cicinelli E, Cobellis L, Cosmi E, D'Anna R, De Leo V, Di Paola R, Di Pinto A, Ercoli A, Facchinetti F, Ferrazzi E, Frusca T, Ghezzi F, Greco P, Liberati M, Loverro G, Nappi L, Palumbo M, Neri M, Perino A, Clemenza S, Piccione E, Peterlunger I, Rizzo N, Negri B, Simoncini T, Spinillo A, Venturini P L, Vergani P, Zullo F, Chiantera A, Colacurci N, Viora E, Franchi M. Needlestick Injuries among Obstetrics and Gynecology Trainees: A Study Design to Investigate an Underestimated Priority. Italian Journal of Gynaecology & Obstetrics. 2018; 30(3)

Schaub FX, Dhankani V, Berger AC, Trivedi M, Richardson AB, Shaw R, Zhao W, Zhang X, Ventura A, Liu Y, Ayer DE, Hurlin PJ, Cherniack AD, Eisenman RN, Bernard B, Grandori C, Cancer Genome Atlas Network Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Pan-Cancer Alterations of the MYC Oncogene and its Proximal Network Across the Cancer Genome Atlas. Cell.Syst. 2018 Mar 28; 6(3): 282a **IF 8.982**

Schinzari V, Timperi E, Pecora G, Palmucci F, Gallerano D, Grimaldi A, Covino DA, Guglielmo N, Melandro F, Manzi E, Sagnotta A, Lancellotti F, Sacco L, Chirletti P, Grazi GL, Rossi M, Barnaba V. Wnt3a/beta-Catenin Signaling Conditions Differentiation of Partially Exhausted T-Effector Cells in Human Cancers. Cancer.Immunol.Res. 2018 Aug; 6(8): 941a **IF 9.188**

Scioli MG, Artuso S, D'Angelo C, Porru M, D'Amico F, Bielli A, Gentile P, Cervelli V, Leonetti C, Orlandi A. Adipose-Derived Stem Cell-Mediated Paclitaxel Delivery Inhibits Breast Cancer Growth. PLoS One. 2018 Sep 7; 13(9): e0203426a **IF 2.766**

Seiler M, Peng S, Agrawal AA, Palacino J, Teng T, Zhu P, Smith PG, Cancer Genome Atlas Research Network, Buonamici S, Yu L. Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Somatic Mutational Landscape of Splicing Factor Genes and their Functional Consequences Across 33 Cancer Types. Cell.Rep. 2018 Apr 3; 23(1): 282a **IF 8.032**

Sestito, R., Blandino, G., Bagnato, A. A Novel p53-Mediated miR-30a/ZEB2 Regulatory Network in the Control of Breast Cancer Progression. Non-Coding RNA Investigation. 2018 Jul 6; 2

Sette G, Salvati V, Giordani I, Pilozzi E, Quacquarini D, Duranti E, De Nicola F, Pallocca M, Fanciulli M, Falchi M, Pallini R, De Maria R, Eramo A. Conditionally Reprogrammed Cells (CRC) Methodology does Not Allow the in Vitro Expansion of Patient-Derived Primary and Metastatic Lung Cancer Cells. Int.J.Cancer. 2018 143(1):88-99 **IF 7.360**

Simon C, Caballero C, Gregoire V, Thurnher D, Koivunen P, Ceruse P, Spriano G, Nicolai P, Licitra L, Machiels JP, Hamoir M, Andry G, Mehanna H, Hunter KD, Dietz A, Rene Leemans C. Surgical Quality Assurance in Head and Neck Cancer Trials: An EORTC Head and Neck Cancer Group Position Paper Based on the EORTC 1420 'Best of' and 24954 'Larynx Preservation' Study. Eur.J.Cancer. 2018 Nov; 103: 69. **IF 2.409**

Simone G, Anceschi U, Tuderti G, Misuraca L, Celia A, De Concilio B, Costantini M, Stigliano A, Minisola F, Ferriero M, Guaglianone S, Gallucci M. Robot-Assisted Partial Adrenalectomy for the Treatment of Conn's Syndrome: Surgical Technique, and Perioperative and Functional Outcomes. Eur.Urol. 2018 Aug 1; [Epub ahead of print] **IF 17.581**

Simone G, Misuraca L, Anceschi U, Minisola F, Ferriero M, Guaglianone S, Tuderti G, Gallucci M. Urethra and Ejaculation Preserving Robot-Assisted Simple Prostatectomy: Near-Infrared Fluorescence Imaging-Guided Madigan Technique. Eur.Urol. 2018 Dec 12; [Epub ahead of print] **IF 17.581**

Simone G, Misuraca L, Tuderti G, Minisola F, Ferriero M, Romeo G, Costantini M, Al-Rawashdah SF, Guaglianone S, Gallucci M. Purely Off-Clamp Robotic Partial Nephrectomy: Preliminary 3-Year Oncological and Functional Outcomes. Int.J.Urol. 2018 Jun;25(6):606-614 **IF 1.941**

Simone G, Papalia R, Misuraca L, Tuderti G, Minisola F, Ferriero M, Vallati G, Guaglianone S, Gallucci M. Robotic Intracorporeal Padua Ileal Bladder: Surgical Technique, Perioperative, Oncologic and Functional Outcomes. Eur.Urol. 2018 Jun; 73(6): 934a **IF 17.581**

Simone G, Tuderti G, Anceschi U, Ferriero M, Costantini M, Minisola F, Vallati G, Pizzi G, Guaglianone S, Misuraca L, Gallucci M. "Ride the Green Light": Indocyanine Green-Marked Off-Clamp Robotic Partial Nephrectomy for Totally Endophytic Renal Masses. Eur.Urol. 2018 Sep 24 [Epub ahead of print] **IF 17.581**

Simone G, Tuderti G, Misuraca L, Anceschi U, Ferriero M, Minisola F, Guaglianone S, Gallucci M. Perioperative and Mid-Term Oncologic Outcomes of Robotic Assisted Radical Cystectomy with Totally Intracorporeal Neobladder: Results of a Propensity Score Matched Comparison with Open Cohort from a Single-Centre Series. Eur.J.Surg.Oncol. 2018 Sep; 44(9): 1432-1438a **IF 3.688**

Soria F, Moschini M, D'Andrea D, Abufaraj M, Foerster B, Mathieu R, Gust KM, Gontero P, Simone G, Meraney A, Krishna S, Konety B, Roupret M, Perry M, Rowe E, Ploussard G, Boorjian SA, Wiklund P, Sooriakumaran P, Shariat SF. Comparative Effectiveness in Perioperative Outcomes of Robotic Versus Open Radical Cystectomy: Results from a Multicenter Contemporary Retrospective Cohort Study. Eur.Urol.Focus. 2018 Nov 16; [Epub ahead of print]

Spadaccio C, Nappi F, De Marco F, Sedati P, Taffon C, Nenna A, Crescenzi A, Chello M, Trombetta M, Gambardella I, Rainer A. Implantation of a Poly-L-Lactide GCSF-Functionalized Scaffold in a Model of Chronic Myocardial Infarction. J.Cardiovasc.Transl.Res. 2017 Feb; 10(1): 47a **IF 2.337**

Spagnuolo M, Regazzo G, De Dominici M, Sacconi A, Pelosi A, Korita E, Marchesi F, Pisani F, Magenta A, Lulli V, Cordone I, Mengarelli A, Strano S, Blandino G, Rizzo MG, Calabretta B. Transcriptional Activation of the miR-17-92 Cluster is Involved in the Growth-Promoting Effects of MYB in Human Ph-Positive Leukemia Cells. Haematologica. 2018 Aug 3 [Epub ahead of print] **IF 16.138**

Sponziello M, Benvenuti S, Gentile A, Pecce V, Rosignolo F, Virzi AR, Milan M, Comoglio PM, Londin E, Fortina P, Barnabei A, Appetecchia M, Marandino F, Russo D, Filetti S, Durante C, Verrienti A. Whole Exome Sequencing Identifies a Germline MET Mutation in Two Siblings with Hereditary Wild-Type RET Medullary Thyroid Cancer. Hum.Mutat. 2018 Mar; 39(3): 371a **IF 5.359**

Spriano G, Mercante G, Pellini R, Ferreli F. Total Laryngectomy: A New Lateral Cervical Approach. Clin.Otolaryngol. 2018 Apr; 43(2): 784a **IF 2.697**

Spugnini EP, Logozzi M, Di Raimo R, Mizzoni D, Fais S. A Role of Tumor-Released Exosomes in Paracrine Dissemination and Metastasis. Int.J.Mol.Sci. 2018 Dec 10; 19(12): E3968a **IF 3.687**

Stagnaro E, Parodi S, Costantini AS, Crosignani P, Miligi L, Nanni O, Piro S, Ramazzotti V, Rodella S, Tumino R, Vindigni C, Vineis P. Childhood Infectious Diseases and Risk of Multiple Myeloma: An Analysis of the Italian Multicentre Case-Control Study. Epidemiol.Infect. 2018 sep; 146(12): 1572a **IF 2.044**

Stramucci L, Pranteda A, Bossi G. Insights of Crosstalk between p53 Protein and the MKK3/MKK6/p38 MAPK Signaling Pathway in Cancer. Cancers (Basel). 2018 May 3; 10(5): E131 **IF 5.326**

Strigari L, Torriani F, Manganaro L, Inaniwa T, Dalmasso F, Cirio R, Attili A. Tumour Control in Ion Beam Radiotherapy with Different Ions in the Presence of Hypoxia: An Oxygen Enhancement Ratio Model Based on the Microdosimetric Kinetic Model. Phys.Med.Biol. 2018 Mar 16; 63(6): 065012° **IF 2.665**

Strobbe D, Campanella M. Anxiolytic Therapy: A Paradigm of Successful Mitochondrial Pharmacology. Trends Pharmacol.Sci. 2018 May; 39(5): 437a **IF 12.108**

Strobbe D, Robinson AA, Harvey K, Rossi L, Ferraina C, de Biase V, Rodolfo C, Harvey RJ, Campanella M. Distinct Mechanisms of Pathogenic DJ-1 Mutations in Mitochondrial Quality Control. Front.Mol.Neurosci. 2018 Mar 15; 11: 68a **IF 3.902**

Tang GH, Satkunam M, Pond GR, Steinberg GR, Blandino G, Schunemann HJ, Muti P. Association of Metformin with Breast Cancer Incidence and Mortality in Patients with Type II Diabetes: A GRADE-Assessed Systematic Review and Meta-Analysis. Cancer Epidemiol.Biomarkers Prev. 2018 Jun; 27(6): 627a **IF 4.554**

Taralli S, Sollini M, Milella M, Perotti G, Filice A, Menga M, Versari A, Rufini V. (18)F-FDG and (68)Ga-Somatostatin Analogs PET/CT in Patients with Merkel Cell Carcinoma: A Comparison Study. EJNMMI Res. 2018 Jul 21; 8(1): 64a **IF 2.630**

Taylor AM, Shih J, Ha G, Gao GF, Zhang X, Berger AC, Schumacher SE, Wang C, Hu H, Liu J, Lazar AJ, Cancer Genome Atlas Research Network, Cherniack AD, Beroukhim R, Meyerson M, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). Genomic and Functional Approaches to Understanding Cancer Aneuploidy. Cancer. Cell. 2018 Apr 9; 33(4): 676a **IF 22.844**

Telera S, Pompili A, Crispo F, Giovannetti M, Pace A, Villani V, Fabi A, Sperduti I, Raus L. Kyphoplasty with Purified Silicone VK100 (Elastoplasty) to Treat Spinal Lytic Lesions in Cancer Patients: A Retrospective Evaluation of 41 Cases. Clin.Neurol.Neurosurg. 2018 Aug; 171: 184-189. **IF 1.736**

Tendas A, Malandruccolo L, Venditti D, Costa A, Volta L, Annibali O, Marchesi F, Saltarelli D, de Fabritiis P, Arcese W, Bondanini F, Niscola P, Palumbo R. Gender, Age and Diagnosis Effect on Self-Perceived Pain in Hematological Patients: Retrospective Analysis of Two Case Series. Ann.Palliat.Med. 2018 May 9;

Tendas A, Marchesi F, Annibali O, Saltarelli D, Niscola P, Perrotti AP, Arcese W, Rome Transplant Network. Chemotherapy-Induced Nausea and Vomiting Prophylaxis in High-Dose Melphalan and Autologous Stem Cell Transplantation. Clin. Lymphoma Myeloma Leuk. 2018 Feb; 18(2): 161a **IF 2.308**

Tendas A, Marchesi F, Mengarelli A, Annibali O, Tomarchio V, Saltarelli D, Chierichini A, Di Venanzio M, Sollazzo F, Piedimonte M, Cupelli L, Bruno A, De Angelis G, Delbono L, Niscola P, Perrotti AP, de Fabritiis P, Arcese W, Rome Transplant Network. Prevention of Chemotherapy-Induced Nausea and Vomiting After High-Dose Melphalan and Stem Cell Transplantation: Review of the Evidence and Suggestions. Support.Care Cancer. 2018 Dec18 [Epub ahead of print] **IF 2.676**

Terrenato I, Sperati F, Musicco F, Pozzi AF, di Turi A, Caterino M, de Lutio di Castelguidone E, Setola SV, Bellomi M, Neumaier CE, Conti L, Cigliana G, Merola R, Antenucci A, Orlandi G, Giordano A, Barba M, Canitano S. Iodixanol Versus Iopromide in Cancer Patients: Evidence from a Randomized Clinical Trial. J.Cell.Physiol. 2018 Mar; 233(3): 2572a **IF 3.923**

Thorsson V, Gibbs DL, Brown SD, Wolf D, Bortone DS, Ou Yang TH, Porta-Pardo E, Gao GF, Plaisier CL, Eddy JA, Ziv E, Culhane AC, Paull EO, Sivakumar IKA, Gentles AJ, Malhotra R, Farshidfar F, Colaprico A, Parker JS, Mose LE, Vo NS, Liu J, Liu Y, Rader J, Dhankani V, Reynolds SM, Bowlby R, Califano A, Cherniack AD, Anastassiou D, Bedognetti D, Rao A, Chen K, Krasnitz A, Hu H, Malta TM, Noushmehr H, Pedamallu CS, Bullman S, Ojesina AI, Lamb A, Zhou W, Shen H, Choueiri TK, Weinstein JN, Guinney J, Saltz J, Holt RA, Rabkin CE, Cancer Genome Atlas Research Network, Lazar AJ, Serody JS, Demicco EG, Disis ML, Vincent BG, Shmulevich L, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). The Immune Landscape of Cancer. Immunity. 2018 Apr 17; 48(4): 812a **IF 19.734**

Torregiani G, Claroni C, Covotta M, Naccarato A, Canfora M, Giannarelli D, Grazi GL, Tribuzi S, Forastiere E. Impact of a Goal-Directed Fluid Therapy on Length of Hospital Stay and Costs of Hepatobiliarypancreatic Surgery: A Prospective Observational Study. J.Comp.Eff.Res. 2018 Nov 19; **IF 1.906**

Trestini I, Carbognin L, Sperduti I, Bonaiuto C, Auriemma A, Melisi D, Salvatore L, Bria E, Tortora G. Prognostic Impact of Early Nutritional Support in Patients Affected by Locally Advanced and Metastatic Pancreatic Ductal Adenocarcinoma Undergoing Chemotherapy. Eur.J.Clin.Nutr. 2018 May; 72(5): 772a **IF 2.954**

Trimboli P, Lauretta R, Barnabei A, Valabrega S, Romanelli F, Giovanella L, Appetecchia M. Procalcitonin as a Postoperative Marker in the Follow-Up of Patients Affected by Medullary Thyroid Carcinoma. Int.J.Biol.Markers. 2018 May; 33(2): 156° **IF 1.449**

Trisciuoglio D, Di Martile M, Del Bufalo D. Emerging Role of Histone Acetyltransferase in Stem Cells and Cancer. Stem Cells Int. 2018 Dec 16; 2018: 8908751° **IF 3.989**

Uccella S, Falcone F, Greggi S, Fanfani F, De Iaco P, Corrado G, Ceccaroni M, Mandato VD, Bogliolo S, Casarin J, Monterossi G, Pinelli C, Mangili G, Cormio G, Roviglione G, Bergamini A, Pesci A, Frigerio L, Uccella S, Vizza E, Scambia G, Ghezzi F. Survival in Clinical Stage I Endometrial Cancer with Single Vs. Multiple Positive Pelvic Nodes: Results of a Multi-Institutional Italian Study. J.Gynecol.Oncol. 2018 Nov; 29(6): e100a **IF 3.340**

Uccella S, Malzoni M, Cromi A, Seracchioli R, Ciravolo G, Fanfani F, Shakir F, Gueli Alletti S, Legge F, Berretta R, Corrado G, Casarella L, Donarini P, Zanello M, Perrone E, Gisone B, Vizza E, Scambia G, Ghezzi F. Laparoscopic Vs Transvaginal Cuff Closure After Total Laparoscopic Hysterectomy: A Randomized Trial by the Italian Society of Gynecologic Endoscopy. Am.J.Obstet.Gynecol. 2018 May; 218(5): 500.e1a **IF 5.732**

van Leeuwen M, Husson O, Alberti P, Arraras JI, Chinot OL, Costantini A, Darlington AS, Dirven L, Eichler M, Hammerlid EB, Holzner B, Johnson CD, Kontogianni M, Kaer TK, Morag O, Nolte S, Nordin A, Pace A, Pinto M, Polz K, Ramage J, Reijneveld JC, Serpentini S, Tomaszewski KA, Vassiliou V, Verdonck-de Leeuw IM, Vistad I, Young TE, Aaronson NK, van de Poll-Franse LV, EORTC QLG. Understanding the Quality of Life (QOL) Issues in Survivors of Cancer: Towards the Development of an EORTC QOL Cancer Survivorship Questionnaire. Health.Qual.Life. Outcomes. 2018 Jun 4; 16(1): 114a **IF 2.278**

Vennarecci G, Ferraro D, Tudisco A, Sandri GBL, Guglielmo N, Berardi G, Sperduti I, Ettorre GM. The ALPPS Procedure: Hepatocellular Carcinoma as a Main Indication. an Italian Single-Center Experience. Updates Surg. 2018 Sep 25;

Vicini E, Invento A, Cuoghi M, Bafile A, Battaglia C, Biglia N, Busani M, Bussone R, Cianchetti E, Caruso F, Cucchi MC, Dessena M, Di Filippo F, Fabi A, Folli S, Friedman D, Macellari G, Mainente P, Murgo R, Neri A, Pollini GP, Palli D, Ricci F, Scalco G, Taffurelli M, Trunfio M, Galimberti V, Italian Society of Surgical Oncology (SICO) Breast Oncoteam. Neoadjuvant Systemic Treatment for Breast Cancer in Italy: The Italian Society of Surgical Oncology (SICO) Breast Oncoteam Survey. Eur.J.Surg.Oncol. 2018 Aug; 44(8): 1157a **IF 3.688**

Vitale I, Galluzzi L. Everybody in! no bouncers at tumor gates. Trends Genet2018;34(2):85-87. **IF 10.556**

Vidiri A, Minosse S, Piludu F, Pellini R, Cristalli G, Kayal R, Carlino G, Renzi D, Covello R, Marzi S. Cervical Lymphadenopathy: Can the Histogram Analysis of Apparent Diffusion Coefficient Help to Differentiate between Lymphoma and Squamous Cell Carcinoma in Patients with Unknown Clinical Primary Tumor? Radiol.Med. 2018 Sep 8 [Epub ahead of print] **IF 1.819**

Vizza E, Chiofalo B, Cutillo G, Mancini E, Baiocco E, Zampa A, Bufalo A, Corrado G. Robotic Single Site Radical Hysterectomy Plus Pelvic Lymphadenectomy in Gynecological Cancers. J.Gynecol.Oncol. 2018 Jan; 29(1): e2a **IF 3.340**

Vizza E, Corrado G, De Angeli M, Carosi M, Mancini E, Baiocco E, Chiofalo B, Patrizi L, Zampa A, Piaggio G, Cicchillitti L. Serum DNA Integrity Index as a Potential Molecular Biomarker in Endometrial Cancer. J.Exp.Clin. Cancer Res. 2018 Jan 30; 37(1): 16a **IF 6.217**

Wang Y, Xu X, Maglic D, Dill MT, Mojumdar K, Ng PK, Jeong KJ, Tsang YH, Moreno D, Bhavana VH, Peng X, Ge Z, Chen H, Li J, Chen Z, Zhang H, Han L, Du D, Creighton CJ, Mills GB, Cancer Genome Atlas Research Network, Camargo F, Liang H. Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c).Comprehensive Molecular Characterization of the Hippo Signaling Pathway in Cancer. Cell.Rep. 2018 Oct 30; 25(5): 1304a **IF 8.032**

Wang Z, Yang B, Zhang M, Guo W, Wu Z, Wang Y, Jia L, Li S, Cancer Genome Atlas Research Network, Xie W, Yang D, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c). LncRNA Epigenetic Landscape Analysis Identifies EPIC1 as an Oncogenic lncRNA that Interacts with MYC and Promotes Cell-Cycle Progression in Cancer. Cancer.Cell. 2018 Apr 9; 33(4): 706a **IF 22.844**

Way GP, Sanchez-Vega F, La K, Armenia J, Chatila WK, Luna A, Sander C, Cherniack AD, Mina M, Ciriello G, Schultz N, Cancer Genome Atlas Research Network, Sanchez Y, Greene CS, Merola R (c), Facciolo F(c.), Grazi GL (c.), Antenucci A(c), Marino M(c).Machine Learning Detects Pan-Cancer Ras Pathway Activation in the Cancer Genome Atlas. Cell.Rep. 2018 Apr 3; 23(1): 172a **IF 8.032**

Welcker D, Jain M, Khurshid S, Jokic M, Hohne M, Schmitt A, Frommolt P, Niessen CM, Spiro J, Persigehl T, Wittersheim M, Buttner R, Fanciulli M, Schermer B, Reinhardt HC, Benzing T, Hopker K. AATF Suppresses Apoptosis, Promotes Proliferation and is Critical for Kras-Driven Lung Cancer. Oncogene. 2018 Mar; 37(11): 1503° **IF 6.854**

Wu R, Paolini F, Frank D, Kamdar D, Curzio G, Pichi B, Pellini R, Spriano G, Bonagura VR, Venuti A, Steinberg BM. Latent Human Papillomavirus Type 16 Infection is Widespread in Patients with Oropharyngeal Cancers. Oral Oncol. 2018 Mar; 78: 222a **IF 4.636**

Zoccali C, Attala D, Rossi B, Zoccali G, Ferraresi V. Fibrous Dysplasia: An Unusual Case of a very Aggressive Form with Costo-Vertebral Joint Destruction and Invasion of the Contralateral D7 Vertebral Body. Skeletal Radiol. 2018 Nov;47(11):1571-1576 **IF 1.567**

Zoccali C, Baldi J, Attala D, Rossi B, Anelli V, Annovazzi A, Ferraresi V. Intralesional Vs. Extralesional Procedures for Low-Grade Central Chondrosarcoma: A Systematic Review of the Literature. Arch.Orthop.Trauma Surg. 2018 Jul; 138(7): 929a **IF 1.967**

Zoccali C, Baldi J, Catanea A, Calabrò F, Calabrò D. The Spine Deformities of the Adolescent: The Pediatrician's Approach. Quaderni ACP. 2018.

Zoccali, Carmine, Dario Attala, Alessandra Scotto, and Roberto Biagini. 2018. "Megaprosthesis for Metastasis of the Lower Limb." Chap. 14, In Management of Bone Metastases, 149-157: Springer.

**Fonte : Impact Factor (IF): JCR 2017**

# CLINICAL TRIALS

# CLINICAL TRIALS 2018

| BRAIN | | | | |
|---|---|---|---|---|
| **STATUS*** | **TITLE** | **DIVISION** | **Principal Investigator** | **Patients IRE 2018** |
| O | SPINAL FLUID MICRORNA AS NEW DIAGNOSTIC AND PROGNOSTIC BIOMARKERS IN CNS | Pathology | Mariantonia Carosi | 0 |
| C | EFLORNITHINE FOR THE TREATMENT OF PATIENTS WITH RECURRENT ANAPLASTIC ASTROCYTOMAS (AA) WHO HAVE PROGRESSED FOLLOWING IRRADIATION AND AN ADJUVANT TEMOZOLOMIDE REGIMEN | Neurosurgery | Carmine Carapella | 0 |
| C | EFFECT OF PERAMPANEL AS ADD-ON THERAPY ON SEIZURE CONTROL, COGNITION, QUALITY OF LIFE AND MOOD IN PATIENTS WITH BRAIN TUMOR RELATED EPILEPSY: AN OBSERVATIONAL PILOT STUDY | Neurology | Marta Maschio | 9 |
| C | *PERCORSO RIABILITATIVO INTEGRATO PER PAZIENTI AFFETTI DA EPILESSIA TUMORALE: LA RI-PARTENZA* | Neurology | Marta Maschio | 19 |
| C | RETROSPECTIVE MULTICENTER EUROPEAN STUDY ON THE EFFICACY OF ANTIEPILEPTIC DRUGS IN PATIENTS WITH GLIOBLASTOMA MULTIFORME AND TUMOR-RELATED EPILEPSY | Neurology | Marta Maschio | 50 |
| O | *ANDAMENTO DELLE CEFALEE PRIMARIE IN PAZIENTI CON GLIOMA AD ALTO GRADO, UNO STUDIO OSSERVAZIONALE MULTICENTRICO* | Neurology | Andrea Pace | 1 |
| O | *IL PROCESSO DECISIONALE RELATIVO AL TRATTAMENTO NEI PAZIENTI NEURONOCOLOGICI* | Neurology | Andrea Pace | 3 |
| O | LIQUID BIOPSY: CIRCULATING/BLOOD MICRORNAS AS NOVEL NON-INVASIVE DIAGNOSTIC BIOMARKERS IN BRAIN TUMOR (AN INTEGRATED PLATFORM FOR DEVELOPING BRAIN CANCER DIAGNOSTIC TECHNIQUES) | Oncogenomics and Epigenetics | Maria Giulia Rizzo | 0 |
| **BREAST** | | | | |
| **STATUS*** | **TITLE** | **DIVISION** | **Principal Investigator** | **Patients IRE 2018** |
| O | *ADERENZA ALLA TERAPIA ENDOCRINA NELLE DONNE CON TUMORE DELLA MAMMELLA: SVILUPPO E VALIDAZIONE DI UN QUESTIONARIO* | Nursing Direction | Laura Iacorossi | 0 |
| O | A DANGEROUS RNA:DNA AFFAIR: UNRAVELING R-LOOP MANAGEMENT IN BREAST CANCER GENOME INTEGRITY AND CHROMATID COHESION | Pathology | Simonetta Buglioni | 0 |
| C | OPEN-LABEL PHASE 2 STUDY EVALUATING EFFICACY AND SAFETY OF SAR566658 TREATMENT IN PATIENTS WITH CA6 POSITIVE METASTATIC TRIPLE NEGATIVE BREAST CANCER | Medical Oncology 1 | Francesco Cognetti | 1 |
| C | RANDOMIZED STUDY OF FULVESTRANT AS MAINTENANCE THERAPY AFTER FIRST-LINE CHEMOTHERAPY IN HER2 NEGATIVE POSTMENOPAUSAL METASTATIC BREAST CANCER PATIENTS | Medical Oncology 1 | Alessandra Fabi | 0 |

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| C | A PHASE II RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF RADIUM-223 DICHLORIDE IN COMBINATION WITH EXEMESTANE AND EVEROLIMUS VERSUS PLACEBO IN COMBINATION WITH EXEMESTANE AND EVEROLIMUS WHEN ADMINISTERED TO METASTATI HER2 NEGATIVE HORMONE REC | Medical Oncology 1 | Francesco Cognetti | 0 |
| C | A RANDOMIZED, OPEN-LABEL, PHASE 3 STUDY OF ABEMACICLIB COMBINED WITH STANDARD ADJUVANT ENDOCRINE THERAPY VERSUS STANDARD ADJUVANT ENDOCRINE THERAPY ALONE IN PATIENTS WITH HIGH RISK, NODE POSITIVE, EARLY STAGE, HORMONE RECEPTOR POSITIVE, HUMAN EPIDER | Medical Oncology 1 | Francesco Cognetti | 7 |
| C | *STUDIO OSSERVAZIONALE PROSPETTICO SULL'ADERENZA AL TRATTAMENTO CON EVEROLIMUS ED EXEMESTANE NELLE DONNE CON NEOPLASIA DELLA MAMMELLA IN FASE AVANZATA DI MALATTIA: STUDIO ADEVEX (GLI EFFETTI COLLATERALI ASSOCIATI AL TRATTAMENTO CON EVEROLIMUS ED EXEMESTANE IN PAZIENTI CON NEOPLASIA DELLA MAMMELLA EAVANZATA: STUDIO OSSERVAZIONALE SULL'ADERENZA ALLA TERAPIA)* | Medical Oncology 1 | Alessandra Fabi | 1 |
| C | MULTICENTER, INTERVENTIONAL. SINGLE-ARM, PHASE IV STUDY EVALUATING TOLERABILITY OF ERIBULIN AND ITS RELATIONSHIP WITH A SET OF POLYMORPHISMS IN AN UNSELECTED POPULATION OF FEMALE PATIENTS WITH METASTATIC BREAST CANCER | Medical Oncology 1 | Alessandra Fabi | 2 |
| C | *STUDIO OSSERVAZIONALE LONGITUDINALE DI COORTE SULLE SCELTE TERAPEUTICHE DEL CARCINOMA MAMMARIO METASTATICO HER2-NEGATIVO NELLA PRATICA CLINICA ITALIANA* | Medical Oncology 1 | Francesco Cognetti | 0 |
| C | IMPACT OF EVEROLIMUS-INDUCED PRECOCIOUS MODIFICATIONS OF SYSTEMIC METABOLISM ON THE PROGNOSIS OF POSTMENOPAUSAL WOMEN WITH ADVANCED HORMONE RECEPTOR-POSITIVE HER2 NEGATIVE BREAST CANCER: THE RETROSPECTIVE, MULTICENTER ITALIAN EVERMET STUDY | Medical Oncology 1 | Alessandra Fabi | 19 |
| C | A PHASE IIIB, OPEN-LABEL, LOCAL, MULTICENTER STUDY OF THE MOLECULAR FEATURES OF POSTMENOPAUSAL WOMEN WITH HORMONE RECEPTOR-POSITIVE (HR+) HER2-NEGATIVE ADVANCED BREAST CANCER ON FIRST-LINE TREATMENT WITH RIBOCICLIB AND LETROZOLE (BIOITALEE) | Medical Oncology 1 | Alessandra Fabi | 5 |
| C | LUCY - LYNPARZA BREAST CANCER REAL WORLD UTILITY, CLINICAL EFFECTIVENESS AND SAFETY STUDY. A PHASE IIIB, SINGLE-ARM, OPEN-LABEL MULTICENTRE STUDY OF OLAPARIB MONOTHERAPY IN THE TREATMENT OF HER2-VE METASTATIC BREAST CANCER PATIENTS WITH GERMLINE BRCA1/2 MUTATIONS | Medical Oncology 1 | Francesco Cognetti | 1 |
| O | A PHASE 3 OPEN-LABEL, RANDOMIZED, MULTICENTER STUDY OF NKTR-102 VERSUS TREATMENT OF PHYSICIAN'S CHOICE (TPC) IN PATIENTS WITH METASTATIC BREAST CANCER WHO HAVE STABLE BRAIN METASTASES AND HAVE BEEN PREVIOUSLY TREATED WITH AN ANTHRACYCLINE, A TAXANE, AND CAPECITABINE | Medical Oncology 1 | Francesco Cognetti | 0 |
| O | *STUDIO OSSERVAZIONALE PER LA VALUTAZIONE DELLA COMPLIANCE AL TRATTAMENTO A BASE DI INIBITORI DELL'AROMATASI NELLE PAZIENTI AFFETTE DA CARCINOMA DELLA MAMMELLA ORMONOPOSITIVO* | Medical Oncology 1 | Alessandra Fabi | 47 |
| O | MULTICENTER, RANDOMIZED, PHASE II STUDY OF NEOADJUVANT CHEMOTHERAPY ASSOCIATED OR NOT WITH ZOLEDRONATE AND ATORVASTATIN IN TRIPLE NEGATIVE BREAST CANCERS - YAPPETIZER STUDY | Medical Oncology 1 | Alessandra Fabi | 3 |

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| O | *IL RUOLO DEL TDM-1 NELLA REAL WORLD EVIDENCE* | Medical Oncology 1 | Alessandra Fabi | 0 |
| O | ADJUVANT TREATMENT FOR HIGH-RISK TRIPLE NEGATIVE BREAST CANCER PATIENTS WITH THE ANTI-PD-L1 ANTIBODY AVELUMAB: A PHASE III RANDOMIZED TRIAL | Medical Oncology 1 | Francesco Cognetti | 2 |
| O | OBSERVATIONAL PROSPECTIVE STUDY WITH ERIBULIN FOR BREAST CANCER WITH BRAIN METASTASES | Medical Oncology 1 | Alessandra Fabi | 3 |
| O | *STUDIO RETROSPETTIVO OSSERVAZIONALE MULTICENTRICO SULLE SEQUENZE DELLA TERAPIA ORMONALE NEL TRATTAMENTO DEL TUMORE DELLA MAMMELLA METASTATICO ORMONODIPENDENTE* | Medical Oncology 1 | Alessandra Fabi | 40 |
| O | A MULTI-CENTRE, OPEN-LABEL, RANDOMIZED CLINICAL TRIAL COMPARING THE EFFICACY AND SAFETY OF THE ANTIBODY-DRUG CONJUGATE SYD985 TO PHYSICIAN'S CHOICE IN PATIENTS WITH HER2-POSITIVE UNRESECTABLE LOCALLY ADVANCED OR METASTATIC BREAST CANCER | Medical Oncology 1 | Francesco Cognetti | 1 |
| O | NAB-PACLITAXEL BEYOND CLINICAL TRIALS: RETROSPECTIVE COHORT STUDY IN METASTATIC BREAST CANCER PATIENTS. THE NORMA STUDY | Medical Oncology 1 | Alessandra Fabi | 29 |
| O | FULVESTRANT FOLLOWED BY EVEROLIMUS PLUS EXEMESTANE VS EXAMESTANE AND EVEROLIMUS FOLLOWED BY FULVESTRANT IN POSTMENOPAUSAL WOMEN WITH HR+ AND HER2- LOCALLY ADVANCED (LABC) OR METASTATIC BREAST CANCER (MBC) PREVIOUSLY TREATED WITH NSAI | Medical Oncology 1 | Francesco Cognetti | 1 |
| O | *STUDIO OSSERVAZIONALE PROSPETTICO SUL TRATTAMENTO DEL CARCINOMA MAMMARIO IN GRAVIDANZA E SUL FOLLOW UP DELLE DONNE CHE HANNO AVUTO UNA GRAVIDANZA DOPO DIAGNOSI E TRATTAMENTO DI UN CARCINOMA MAMMARIO: PREFER2 (PREGNACY AND FERTILITY)* | Medical Oncology 1 | Francesco Cognetti | 0 |
| O | *PREGNANCY AND FERTILITY - PREFER STUDIO OSSERVAZIONALE PROSPETTICO SULLA PRESERVAZIONE DELLA FERTILITÀ NELLE PAZIENTI GIOVANI CON PATOLOGIA ONCOLOGICA. PREFER (PREGNACY AND FERTILITY)* | Medical Oncology 1 | Francesco Cognetti | 0 |
| O | A PHASE III STUDY COMPARING THE CONCURRENT VERSUS THE SEQUENTIAL ADMINISTRATION OF CHEMOTHERAPY AND AROMATASE INHIBITORS, AS ADJUVANT TREATMENT OF POST-MENOPAUSAL PATIENTS WITH ENDOCRINE RESPONSIVE EARLY BREAST CANCER | Medical Oncology 1 | Francesco Cognetti | 7 |
| O | STUDIO DI FASE II, RANDOMIZZATO IN APERTO, MULTICENTRICO MIRATO A VALUTARE A RANDOMISED, MULTICENTRE, OPEN-LABEL PHASE II TRIAL INVESTIGATING ACTIVITY OF CHEMOTHERAPY AND LAPATINIB AND TRASTUZUMAB IN PATIENTS WITH HER2-POSITIVE METASTATIC BREAST CANC | Medical Oncology 1 | Francesco Cognetti | 2 |
| O | EVALUATION OF MEDICAL TREATMENTS (CHEMOTHERAPY, ORMONAL THERAPY AND BIOLOGICAL THERAPY) IN METASTATICA BREAST CANCER PATIENTS ACCORDING TO BIOLOGICA SUBTYPE AND LINE OF TREATMENT | Medical Oncology 1 | Francesco Cognetti | 39 |
| O | *STUDIO OSSERVAZIONALE PROSPETTICO SUI CAMBIAMENTI DELLE ABITUDINI ALIMENTARI DOPO LA DIAGNOSI DI CARCINOMA MAMMARIO (ECHO STUDY)* | Medical Oncology 1 | Alessandra Fabi | 116 |

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| O | *STUDIO BRIDE. DIAGNOSI E TRATTAMENTO DEL CARCINOMA MAMMARIO IN ITALIA: STUDIO OSSERVAZIONALE PROSPETTICO NAZIONALE DELLA FONDAZIONE AIOM* | Medical Oncology 1 | Alessandra Fabi | 31 |
| O | SECOND LINE ERIBULIN FOLLOWED BY CAPECITABINE OR THE REVERSE SEQUENCE IN HER2-NEGATIVE METASTATIC BREAST CANCER (MBC) PATIENTS: A RANDOMIZED PHASE II STUDY – ERICA TRIAL | Medical Oncology 1 | Alessandra Fabi | 1 |
| O | LIQUID BIOPSY: INTERCEPTING MUTATIONAL TRAJECTORIES OF HER2 BREAST CANCER IN PATIENTS UNDER T-DM1 TREATMENT | Medical Oncology 1 | Alessandra Fabi | 4 |
| O | ATEZOLIZUMAB, PERTUZUMAB AND TRASTUZUMAB WITH CHEMOTHERAPY AS NEOADJUVANT TREATMENT OF HER2 POSITIVE EARLY HIGH-RISK AND LOCALLY ADVANCED BREAST CANCER (APTNEO) | Medical Oncology 1 | Alessandra Fabi | 0 |
| O | ERIBULIN CONCOMITATN TO RADIOTHERAPY IN HER-2 NEGATIVE ADVANCED BREAST CANCER DISEASE WITH BONE METASTASES: MULTICENTER NON INTERVENTISTIC OBSERVATIONAL STUDY | Medical Oncology 1 | Alessandra Fabi | 0 |
| O | *STUDIO OSSERVAZIONALE RETROSPETTIVO PER LA VALUTAZIONE DELLA TOSSICITÀ CARDIACA DEL TRASTUZUMAB NEL TRATTAMENTO ADIUVANTE DELLE PAZIENTI AFFETTE DA CARCINOMA MAMMARIO HER2-POSITIVO CON ETÀ ≥70 ANNI* | Medical Oncology 1 | Alessandra Fabi | 0 |
| O | *ASSOCIAZIONE DI EVEROLIMUS ED EXEMESTANE: RUOLO NEL TRATTAMENTO DI I LINEA NELLA NEOPLASIA DELLA MAMMELLA LOCALMENTE AVANZATA O METASTATICA ORMONO-SENSIBILE. STUDIO OSSERVAZIONALE RETROSPETTIVO* | Medical Oncology 1 | Alessandra Fabi | 0 |
| O | NEW THERAPEUTIC APPROACHES IN HER2-DRIVEN BREAST CANCER: ROLE OF THE CHAPERONIN HSP90 IN RESPONSE TO PHARMACOLOGICAL TREATMENTS | Medical Oncology 1 | Gianluigi Ferretti | 0 |
| C | INTERNATIONAL, MULTICENTER, PHASE II, RANDOMIZED, PARALLEL-ARM TRIAL INVESTIGATING THE ROLE OF TWO DIFFERENT METRONOMIC CHEMOTHERAPY REGIMENS IN LOCALLY ADVANCED OR METASTATIC TRIPLE NEGATIVE BREAST CANCER PATIENTS (TNBC) AS MAINTENANCE THERAPY AFTER | Medical Oncology 2 | Patrizia Vici | 0 |
| C | *TERAPIA CON PERTUZUMAB IN PAZIENTI AFFETTE DA CARCINOMA MAMMARIO AVANZATO HER2 POSITIVO: STUDIO OSSERVAZIONALE RETROSPETTIVO MULTICENTRICO* | Medical Oncology 2 | Patrizia Vici | 2 |
| C | DISSECTING THE ROLE OF ANTI-ESTROGEN RECEPTOR ALPHA AUTOANTIBODIES IN BREAST CANCER | Medical Oncology 2 | Patrizia Vici | 2 |
| C | *VALUTAZIONE CLINIMETRICA E ASSESSMENT MULTIDIMENSIONALE PSICOLOGICO-CLINICO NELLA TERAPIA ORMONALE ADIUVANTE CON INIBITORI DELLE AROMATASI PER IL CARCINOMA DELLA MAMMELLA OPERATO* | Medical Oncology 2 | Patrizia Vici | 2 |
| C | *VALUTAZIONE DELL'EFFICACIA E DELLA TOLLERABILITA' DEL TRATTAMENTO CON PALBOCICLIB IN PAZIENTI AFFETTE DA CARCINOMA MAMMARIO AVANZATO ER+/HER2- NELLA PRATICA CLINICA. STUDIO OSSERVAZIONALE RETROSPETTIVO MULTICENTRICO – PALBOSS STUDY* | Medical Oncology 2 | Patrizia Vici | 8 |
| C | NAB-PACLITAXEL BEYOND CLINICAL TRIALS: RETROSPECTIVE COHORT STUDY IN METASTATIC BREAST CANCER PATIENTS | Medical Oncology 2 | Patrizia Vici | 4 |

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| C | MULTICENTER, INTERVENTIONAL. SINGLE-ARM, PHASE IV STUDY EVALUATING TOLERABILITY OF ERIBULIN AND ITS RELATIONSHIP WITH A SET OF POLYMORPHISMS IN AN UNSELECTED POPULATION OF FEMALE PATIENTS WITH METASTATIC BREAST CANCER | Medical Oncology 2 | Patrizia Vici | 0 |
| C | A PHASE IIIB, OPEN-LABEL, LOCAL, MULTICENTER STUDY OF THE MOLECULAR FEATURES OF POSTMENOPAUSAL WOMEN WITH HORMONE RECEPTOR-POSITIVE (HR+) HER2-NEGATIVE ADVANCED BREAST CANCER ON FIRST-LINE TREATMENT WITH RIBOCICLIB AND LETROZOLE (BIOITALEE) | Medical Oncology 2 | Patrizia Vici | 3 |
| C | A RANDOMISED, DOUBLE-BLIND, PARALLEL GROUP, EQUIVALENCE, MULTICENTRE PHASE III TRIAL TO COMPARE THE EFFICACY, SAFETY, AND PHARMACOKINETICS OF HD201 TO HERCEPTINÂ IN PATIENTS WITH HER2+ EARLY BREAST CANCER | Medical Oncology 2 | Patrizia Vici | 1 |
| C | A PHASE III, MULTICENTER, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF ATEZOLIZUMAB (ANTI-PD-L1 ANTIBODY) IN COMBINATION WITH PACLITAXEL COMPARED WITH PLACEBO WITH PACLITAXEL FOR PATIENTS WITH PREVIOUSLY UNTREATED INOPERABLE LOCALLY ADVANCED | Medical Oncology 2 | Patrizia Vici | 0 |
| O | *STUDIO OSSERVAZIONALE, RETROSPETTIVO, MULTICENTRICO ATTO A VALUTARE IL BENEFICIO DEL TRATTAMENTO ORMONALE ADIUVANTE NELLE PAZIENTI AFFETTE DA ERALY BREAST CANCER HER2 NEGATIVO CON ESPRESSIONE RECETTORIALE DI ER E/O PGR COMPRESA TRA 1 E 9% E =>10%* | Medical Oncology 2 | Patrizia Vici | 0 |
| O | A STUDY EVALUATING THE PREGNANCY OUTCOMES AND SAFETY OF INTERRUPTING ENDOCRINE THERAPY FOR YOUNG WOMEN WITH ENDOCRINE RESPONSIVE BREAST CANCER WHO DESIRE PREGNANCY | Medical Oncology 2 | Patrizia Vici | 0 |
| O | *VALUTAZIONE DELLE VARIAZIONI QUANTITATIVE E QUALITATIVE DEL DNA TUMORALE LIBERO CIRCOLANTE IN PAZIENTE AFFETTE DA CARCINOMA MAMMARIO AVANZATO IN TRATTAMENTO CON EVEROLIMUS E EXEMESTANE* | Medical Oncology 2 | Patrizia Vici | 3 |
| O | *TERAPIA CON T-DM1 IN PAZIENTI AFFETTE DA CARCINOMA MAMMARIO AVANZATO HER2 POSITIVO. STUDIO OSSERVAZIONALE RETROSPETTIVO MULTICENTRICO* | Medical Oncology 2 | Patrizia Vici | 17 |
| O | *VALIDAZIONE PROSPETTICA DEL TAZ-SCORE COME BIOMARKER DI RISPOSTA COMPLETA PATOLOGICA IN PAZIENTI AFFETTE DA CARCINOMA MAMMARIO LUMINAL B/HER2-POSITIVO TRATTATE CON TERAPIA NEOADIUVANTE A BASE DI TRASTUZUMAB - TRISKELE TRIAL* | Medical Oncology 2 | Patrizia Vici | 10 |
| O | *IDENTIFICAZIONE BIOMARCATORI PREDITTIVI/PROGNOSTICI NEL CARCINOMA MAMMARIO TRIPLO-NEGATIVO. NEOTAZ STUDY* | Medical Oncology 2 | Patrizia Vici | 16 |
| O | *STUDIO DI CORRELAZIONE FRA LE MODIFICAZIONI DEI MARKER DI RISERVA OVARICA E SVILUPPO DI INSUFFICIENZA OVARICA PRIMARIA IN PAZIENTI AFFETTE DA CARCINOMA MAMMARIO CHE NECESSITANO DI TRATTAMENTO POLICHEMIOTERAPICO CON FINALITÀ NEO-ADIUVANTE* | Medical Oncology 2 | Patrizia Vici | 0 |
| O | FULVESTRANT FOLLOWED BY EVEROLIMUS PLUS EXEMESTANE VS EXAMESTANE AND EVEROLIMUS FOLLOWED BY FULVESTRANT IN POSTMENOPAUSAL WOMEN WITH HR+ AND HER2- LOCALLY ADVANCED (LABC) OR METASTATIC BREAST CANCER (MBC) PREVIOUSLY TREATED WITH NSAI | Medical Oncology 2 | Patrizia Vici | 0 |

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| O | IMPACT OF HIPPO PATHWAY COMPONENT IN BREAST CANCER PATIENTS TREATED OR TO BE TREATED WITH NEOADJUVANT CHEMOTHERAPY | Medical Oncology 2 | Patrizia Vici | 16 |
| O | *EFFICACIA E TOLLERABILITÀ DELLA CHEMIOTERAPIA NEOADIUVANTE CONTENENTE CARBOPLATINO NELLE PAZIENTI AFFETTE DA CARCINOMA MAMMARIO TRIPLO NEGATIVO: STUDIO MULTICENTRICO OSSERVAZIONALE PROSPETTICO. NEOCARBO STUDY* | Medical Oncology 2 | Patrizia Vici | 6 |
| O | *STUDIO OSSERVAZIONALE RETROSPETTIVO SUL CARCINOMA LOBULARE MAMMARIO LOBULARE PRECOCE E AVANZATO* | Medical Oncology 2 | Patrizia Vici | 0 |
| O | *TAZ COME BIOMARCATORE PROGNOSTICO IN PAZIENTI AFFETTE DA CARCINOMA MAMMARIO IN FASE INIZIALE. PHOBOS TRIAL* | Medical Oncology 2 | Patrizia Vici | 0 |
| O | *STUDIO OSSERVAZIONALE PROSPETTICO SUI CAMBIAMENTI DELLE ABITUDINI ALIMENTARI DOPO LA DIAGNOSI DI CARCINOMA MAMMARIO - (ECHO STUDY)* | Medical Oncology 2 | Patrizia Vici | 21 |
| O | *STUDIO BRIDE. DIAGNOSI E TRATTAMENTO DEL CARCINOMA MAMMARIO IN ITALIA: STUDIO OSSERVAZIONALE PROSPETTICO NAZIONALE DELLA FONDAZIONE AIOM* | Medical Oncology 2 | Patrizia Vici | 5 |
| O | *STUDIO RETROSPETTIVO OSSERVAZIONALE MULTICENTRICO SULLE SEQUENZE DELLA TERAPIA ORMONALE NEL TRATTAMENTO DEL TUMORE DELLA MAMMELLA METASTATICO ORMONODIPENDENTE* | Medical Oncology 2 | Patrizia Vici | 16 |
| O | *STUDIO OSSERVAZIONALE RETROSPETTIVO PER LA VALUTAZIONE DELLA TOSSICITÀ CARDIACA DEL TRASTUZUMAB NEL TRATTAMENTO ADIUVANTE DELLE PAZIENTI AFFETTE DA CARCINOMA MAMMARIO HER2-POSITIVO CON ETÀ ≥70 ANNI* | Medical Oncology 2 | Patrizia Vici | 8 |
| O | *ASSOCIAZIONE DI EVEROLIMUS ED EXEMESTANE: RUOLO NEL TRATTAMENTO DI I LINEA NELLA NEOPLASIA DELLA MAMMELLA LOCALMENTE AVANZATA O METASTATICA ORMONO-SENSIBILE. STUDIO OSSERVAZIONALE RETROSPETTIVO* | Medical Oncology 2 | Patrizia Vici | 0 |
| O | *INFILTRATO LINFOCITARIO TUMORALE NEL CARCINOMA DELLA MAMMELLA TRIPLO NEGATIVO PT1 PN0* | Medical Oncology 2 | Patrizia Vici | 0 |
| O | *RADIOTERAPIA ACCELERATA IPOFRAZIONATA IN PAZIENTI OPERATE PER TUMORE DELLA MAMMELLA CON INDICAZIONE ANCHE ALL'IRRADIAZIONE DELLE STAZIONI LINFONODALI REGIONALI. STUDIO DI FATTIBILITÀ* | Radiotherapy | Giuseppe Sanguineti | 22 |
| C | *RUOLO DELLA 18F-FDG PET/CT DUAL-TIME PER LA DIAGNOSI DI METASTASI EPATICHE NEL TUMORE DELLA MAMMELLA* | Nuclear Medicine | Alessio Annovazzi | 151 |
| O | LIQBREASTRACK: TRACKING MUTATIONAL HOTSPOTS IN BREAST CANCER PATIENTS TREATED WITH T-DM1 BY LIQUID BIOPSY | Oncogenomics and Epigenetics | Matteo Allegretti | 10 |

## ENDOCRINE

| STATUS* | TITLE | DIVISION | Principal Investigator | Patients IRE 2018 |
|---|---|---|---|---|
| C | EFFICACYAND SAFETY OF LANREOTIDE ATG 120 MG IN COMBINATION WITH TEMOZOLOMIDE IN SUBJECTS WITH PROGRESSIVE WLL DIFFERENTIATED THORACIC NEUROENDOCRINE TUMORS | Medical Oncology 1 | Vanja Vaccaro | 0 |

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| C | *STUDIO DI CONFRONTO IN TERMINI DI COSTO-EFFICACIA DI TRE DIVERSI APPROCCI/STRATEGIE NELLA PREVENZIONE DELL'IPOCALCEMIA TRANSITORIA DOPO TIROIDECTOMIA* | Otolaryngology Head & Neck | Giuseppe Mercante | 102 |
| C | EFFICACY OF ADJUVANT MITOTANE TREATMENT IN PROLONGING RECURRANCE-FREE SURVIVAL IN PATIENTS WITH ADRENOCORTICAL CARCINOMA AT LOW-INTERMEDIATE RISK OF RECURRANCE | Endocrinology | Marialuisa Appetecchia | 0 |
| O | *PROGETTO DI PRESCRIZIONE DELL'INFORMAZIONE INFO RP* | Endocrinology | Marialuisa Appetecchia | 0 |
| O | *LIQUID BIOPSY PER LA VALUTAZIONE PROGNOSTICA DEL CARCINOMA MIDOLLARE DELLA TIROIDE* | Endocrinology | Marialuisa Appetecchia | 12 |

## GASTROINTESTINAL

| STATUS* | TITLE | DIVISION | Principal Investigator | Patients IRE 2018 |
|---|---|---|---|---|
| C | TOXINS PRODUCED BY INTESTINAL BACTERIA AND PREDISPOSING GENETIC VARIATIONS: A DANGEROUS LINK FOR COLORECTAL CANCER DEVELOPMENT? | Hepato-Biliary-Pancreatic Surgery | Andrea Oddi | 4 |
| O | *PREVALENZA DELLA MALNUTRIZIONE IN CHIRURGIA/PREVALENCE OF MALNUTRITION IN SURGERY* | Hepato-Biliary-Pancreatic Surgery | Pasquale Perri | 18 |
| O | *REGISTRO ITALIANO DI RESEZIONI EPATICHE MINI-INVASIVE* | Hepato-Biliary-Pancreatic Surgery | Gianluca Grazi | 15 |
| O | DISSECTING THE ADIPOSE TRIGLYCERIDE LIPASE (ATGL) FUNCTIONS IN THE PATHOGENESIS OF HEPATOCARCINOMA | Hepato-Biliary-Pancreatic Surgery | Gianluca Grazi | 0 |
| O | ISOLATION AND CHARACTERIZATION OF TUMOR STEM CELLS IN INTRA- AND EXTRA-HEPATIC CHOLANGIOCARCINOMA | Hepato-Biliary-Pancreatic Surgery | Gianluca Grazi | 0 |
| O | *IDENTIFICAZIONE DI NUOVI BERSAGLI IMMUNOTERAPEUTICI NELL'EPATOCARCINOMA ATTRAVERSO LO STUDIO DELLE CELLULE T REGOLATORIE E DEL SECRETOMA* | Hepato-Biliary-Pancreatic Surgery | Gianluca Grazi | 0 |
| C | A PHASE 1/2, MULTICENTER, OPEN-LABEL, DOSE FINDING STUDY TO ASSESS THE SAFETY, TOLERABILITY, AND PRELIMINARY EFFICACY OF CC-122 IN COMBINATION WITH NIVOLUMAB IN SUBJECTS WITH UNRESECTABLE HEPATOCELLULAR CARCINOMA (HCC) | Medical Oncology 1 | Michele Milella | 0 |
| C | DEFINING THE GENETIC BACKGROUND THAT MODULATES ANGIOGENIC POTENTIAL IN COLORECTAL CANCER MODELS | Medical Oncology 1 | Fabiana Conciatori | 184 |
| C | A MULTI-CENTRE RANDOMISED CLINICAL TRIAL OF BIOMARKER-DRIVEN MAINTENANCE TREATMENT FOR FIRST-LINE METASTATIC COLORECTAL CANCER (MODUL) | Medical Oncology 1 | Massimo Zeuli | 0 |
| C | A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER STUDY OF PEGYLATED RECOMBINANT HUMAN HYALURONIDASE (PEGPH20) IN COMBINATION WITH NAB-PACLITAXEL PLUS GEMCITABINE COMPARED WITH PLACEBO PLUS NAB-PACLITAXEL AND GEMCITABINE IN PARTICIPANTS WITH HYALURONAN-HIGH STAGE IV PREVIOUSLY UNTREATED PANCREATIC DUCTAL ADENOCARCINOMA | Medical Oncology 1 | Francesco Cognetti | 0 |

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| O | PHASE II RANDOMIZED STUDY OF MAINTENANCE REGORAFENIB VS PLACEBO IN NO PROGRESSION PATIENTS AFTER FIRST-LINE PLATINUM AND FLUOROPYRIMIDINES BASED CHEMOTHERAPY IN HER2 NEGATIVE LOCALLY ADVANCED/METASTATIC GASTRIC OR GASTROESOPHAGEL JUNCTION CANCER (A-MANTRA STUDY) | Medical Oncology 1 | Francesco Cognetti | 0 |
| O | A MULTICENTER, RANDOMIZED, OPEN-LABEL PHASE 3 STUDY OF ENCORAFENIB + CETUXIMAB +/-BINIMETINIB VS. IRINOTECAN + CETUXIMAB WITH A SAFETY LEAD-IN OF ENCORAFENIB + BINIMETINIB + CETUXIMAB IN PATIENTS WITH BRAF V600E-MUTANT METASTATIC COLORECTAL CANCER | Medical Oncology 1 | Fabiana Cecere | 0 |
| O | RANDOMIZED PHASE III STUDY OF TRIPLET MFOLFOXIRI PLUS PANITUMUMAB VERSUS MFOLFOX6 PLUS PANITUMUMAB AS INITIAL THERAPY FOR UNRESECTABLE RAS AND BRAF WILDTYPE METASTATIC COLORECTAL CANCER PATIENTS | Medical Oncology 1 | Francesco Cognetti | 0 |
| O | ERBITUX METASTATIC COLORECTAL CANCER STRATEGY STUDY: A PHASE III RANDOMIZED TWO ARM STUDY WITH FOLFIRI + CETUXIMAB UNTIL DISEASE PROGRESSION COMPARED TO FOLFIRI + CETUXIMAB FOR 8 CYCLES FOLLOWED BY CETUXIMAB ALONE UNTIL DISEASE PROGRESSION IN FIRST LINE TREATMENT OF PATIENTS WITH RAS AND BRAF WILD TYPE METASTATIC COLORECTAL CANCER | Medical Oncology 1 | Massimo Zeuli | 0 |
| O | INTERMITTENT OR CONTINUOUS PANITUMUMAB PLUS FOLFIRI FOR FIRST-LINE TREATMENT OF PATIENTS WITH RAS/B-RAF WILD-TYPE METASTATIC COLORECTAL CANCER: A RANDOMIZED PHASE 2 TRIAL | Medical Oncology 1 | Massimo Zeuli | 0 |
| O | A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER, TRIAL OF CRENOLANIB IN SUBJECTS WITH ADVANCED OR METASTATIC GASTROINTESTINAL STROMAL TUMORS WITH A D842V MUTATION IN THE PDGFRA GENE | Medical Oncology 1 | Virginia Ferraresi | 0 |
| O | GUIDELINE APPLICATION IN REAL WORLD: MULTI-INSTITUTIONAL BASED SURVEY OF ADJUVANT AND FIRST LINE PANCREATIC DUCTAL ADENOCARCINOMA TREATMENT IN ITALY | Medical Oncology 1 | Michele Milella | 11 |
| O | A PHASE III, RANDOMISED, DOUBLE BLIND, PLACEBO CONTROLLED, MULTICENTRE STUDY OF MAINTENANCE OLAPARIB MONOTHERAPY IN PATIENTS WITH GBRCA MUTATED METASTATIC PANCREATIC CANCER WHOSE DISEASE HAS NOT PROGRESSED ON FIRST LINE PLATINUM BASED CHEMOTHERAPY | Medical Oncology 1 | Vanja Vaccaro | 1 |
| O | PROSPECTIVE VALIDATION OF A DNA DAMAGE REPAIR-HIPPO PATHWAY SIGNATURE IN PATIENTS WITH ADVANCED GASTRIC CANCER | Medical Oncology 2 | Marcello Maugeri Saccà | 3 |
| O | *LA TERAPIA RADIOEMBOLIZZANTE DELLE LESIONI PRIMITIVE E SECONDARIE DEL FEGATO: GESTIONE DELLA FASE DIAGNOSTICA E POST TRATTAMENTO* | Radiology | Giuseppe Pizzi | 0 |
| O | *STUDIO INTERVENTISTICO SENZA MEDICINALE MULTICENTRICO IN PAZIENTI AFFETTI DA ADENOCARCINOMA LOCALMENTE AVANZATO DEL PANCREAS: RADIOTERAPIA STEREOTASSICA - IRENE-1* | Radiotherapy | Giuseppe Sanguineti | 0 |
| C | TOXINS PRODUCED BY INTESTINAL BACTERIA AND PREDISPOSING GENETIC VARIATIONS: A DANGEROUS LINK FOR COLORECTAL CANCER DEVELOPMENT? | Digestive Endoscopy | Vittoria Anna Maria Stigliano | 28 |
| C | CYTOKINESIS FAILURE, CHROMOSOMAL INSTABILITY AND TUMORIGENICITY: HIPK2 ROLE IN PANCREATIC CANCER | Immunology and Immunotherapy | Paola Nisticò | 0 |
| O | INNOVATIVE TOOLS FOR EARLY DIAGNOSIS AND RISK ASSESSMENT OF PANCREATIC CANCER | Immunology and Immunotherapy | Paola Nisticò | 12 |

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| O | *MKK3 COME TARGET TERAPEUTICO IN TUMORE AL COLON-RETTO* | Medical Physics | Lidia Strigari | 0 |
| O | ACCURATE DOSIMETRY AND BIOMARKERS IMPROVE SURVIVAL IN HCC PATIENTS TREATED WITH RESIN 90Y-MSPHERES: A RANDOMIZED TRIAL | Medical Physics | Lidia Strigari | 9 |
| O | *IMPATTO SULLA SOPRAVVIVENZA GLOBALE DI PIANO TERAPEUTICO PERSONALIZZATO CON DOSIMETRIA QUANTITATIVA 3D VERSUS PIANO TERAPEUTICO STANDARD NELLA RADIOEMBOLIZZAZIONE EPATICA CON 90Y NELL'EPATOCARCINOMA: TRIAL CLINICO RANDOMIZZATO* | Nuclear Medicine | Rosa Sciuto | 9 |
| O | HIPK2 AS A PROGNOSTIC BIOMARKER IN STAGE I AND STAGE II COLORECTAL CANCER: VALIDATION AND UNDERLYING MECHANISMS | Cellular Network and Therapeutic Targets | Silvia Soddu | 80 |
| C | ANALYSIS AND TARGETING OF ONCOGENIC SIGNALS GENERATED BY FGFR2 FUSION PROTEINS IN INTRAHEPATIC CHOLANGIOCARCINOMA | Oncogenomics and Epigenetics | Oreste Segatto | 0 |
| O | ULTRASENSITIVE PLASMONIC DEVICES FOR EARLY CANCER DIAGNOSIS | Oncogenomics and Epigenetics | Patrizio Giacomini | 3 |
| O | EXTRA-TELOMETRIC FUNCTIONS OF TRF2 IN MALIGNANT TRANSFORMATION | Oncogenomics and Epigenetics | Annamaria Biroccio | 0 |
| O | *ANALISI DIFFERENZIALE DEI PROFILI DI ESPRESSIONE DEI MICRORRNA IN COLANGIOCARCINOMA, EPATOCARCINOMA E METASTASI EPATICHE* | Oncogenomics and Epigenetics | Giovanni Blandino | 48 |
| O | THERAPEUTIC TARGETING OF FGR2 FUSIONS IN MODELS OF INTRAHEPATIC CHOLANGIOCARCINOMA | Oncogenomics and Epigenetics | Oreste Segatto | 2 |
| O | *VALIDAZIONE DELL'USO DEL TEST PIVKA-II SU SIERO NEL MONITORAGGIO DELLA PROGRESSIONE DELL'EPATOCARCINOMA NEI PAZIENTI CANDIDATI A TRAPIANTO DI FEGATO E NELLA STRATIFICAZIONE DEI PAZIENTI CON MAGGIOR RISCHIO DI RECIDIVA DI HCC DOPO TRAPIANTO DI FEGATO: STUDIO PROSPETTICO* | Clinical Pathology | Laura Conti | 9 |

## GYNECOLOGICAL

| STATUS* | TITLE | DIVISION | Principal Investigator | Patients IRE 2018 |
|---|---|---|---|---|
| O | MICROVESICLES' MICRORNA PROFILING IN BIOLOGICAL FLUID AND TISSUES OF OVARIAN CANCER PATIENTS | Pathology | Mariantonia Carosi | 0 |
| O | ATTACKING PROLIFERATION AND CHEMORESISTANCE IN OVARIAN CANCER: THERAPEUTIC POTENTIAL OF A NEW FUNCTIONAL LINK BETWEEN OCT4 AND THE RB PATHWAY | Pathology | Mariantonia Carosi | 0 |
| C | *PATOLOGIA ENDOMETRIALE TAMOXIFENE CORRELATA IN PAZIENTI CON PREGRESSO CARCINOMA MAMMARIO: ANALISI DI UNA CASISTICA RETROSPETTIVA MULTICENTRICA* | Ginecology | Enrico Vizza | 212 |
| C | *INIEZIONE ISTEROSCOPICA VS. CERVICALE DI TRACCIANTE PER IDENTIFICAZIONE DEL LINFONODO SENTINELLA NEL TUMORE DELL'ENDOMETRIO: STUDIO RANDOMIZZATO, MULTICENTRICO* | Ginecology | Enrico Vizza | 0 |
| O | ENDOMETRIAL CANCER CONSERVATIVE TREATMENT - A MULTICENTRE REGISTRY | Ginecology | Enrico Vizza | 0 |

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| O | MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL COMPARING TWO FOLLOW-UP REGIMEN AT DIFFERENT FREQUENCIES OF EXAMINATIONS IN PATIENTS TREATED FOR ENDOMETRIAL CANCER | Ginecology | Enrico Vizza | 0 |
| O | *IL DNA LIBERO CIRCOLANTE (CFDNA) COME BIOMARCATORE PROGNOSTICO NEL CANCRO DELL'ENDOMETRIO* | Ginecology | Enrico Vizza | 0 |
| O | MULTICENTER RETROSPECTIVE STUDY ON MINIMALLY INVASIVE INTERVAL DEBULKING SURGERY IN OVARIAN CANCER | Ginecology | Enrico Vizza | 0 |
| O | *REGOLAZIONE DELLA SINTESI DI MEDIATORI LIPIDICI PRO-INFIAMMATORI E PRO-RISOLVENTI DEL PROCESSO INFIAMMATORIO NEL TUMORE DELL'OVAIO* | Ginecology | Enrico Vizza | 28 |
| O | *TUMORI RARI IN GINECOLOGIA ONCOLOGICA* | Ginecology | Enrico Vizza | 0 |
| O | *STUDIO OSSERVAZIONALE RETROSPETTIVO SU ANDAMENTO CLINICO E TRATTAMENTO NELLE PAZIENTI AFFETTE DA SARCOMA UTERINO* | Ginecology | Enrico Vizza | 65 |
| C | A PHASE 2, RANDOMIZED STUDY OF MLN0128 (A DUAL TORC1/2 INHIBITOR), MLN0128+MLN1117 (A PI3KÎ± INHIBITOR), WEEKLY PACLITAXEL, OR THE COMBINATION OF WEEKLY PACLITAXEL AND MLN0128 IN WOMEN WITH ADVANCED, RECURRENT, OR PERSISTENT ENDOMETRIAL CANCER | Medical Oncology 1 | Antonella Savarese | 0 |
| C | PHASE III, MULTICENTER, RANDOMIZED STUDY OF ATEZOLIZUMAB VERSUS PLACEBO ADMINISTERED IN COMBINATION WITH PACLITAXEL, CARBOPLATIN, AND BEVACIZUMAB TO PATIENTS WITH NEWLYDIAGNOSED STAGE III OR STAGE IV OVARIAN, FALLOPIAN TUBE, OR PRIMARY PERITONEAL CANCER | Medical Oncology 1 | Antonella Savarese | 0 |
| C | A PHASE III, OPEN LABEL, RANDOMISED, CONTROLLED, MULTI-CENTRE STUDY TO ASSESS THE EFFICACY AND SAFETY OF OLAPARIB MONOTHERAPY VERSUS PHYSICIAN'S CHOICE SINGLE AGENT CHEMOTHERAPY IN THE TREATMENT OF PLATINUM SENSITIVE RELAPSED OVARIAN CANCER IN PATIENTS CARRYING GERMLINE BRCA1/2 MUTATIONS | Medical Oncology 1 | Francesco Cognetti | 0 |
| C | A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 STUDY TO ASSESS THE EFFICACY AND SAFETY OF FARLETUZUMAB (MORAB 003) IN COMBINATION WITH CARBOPLATIN PLUS PACLITAXEL OR CARBOPLATIN PLUS PEGYLATED LIPOSOMAL DOXORUBICIN (PLD) IN SUBJECTS WITH LOW CA125 PLATINUM-SENSITIVE OVARIAN CANCER | Medical Oncology 1 | Antonella Savarese | 0 |
| O | MAINTENANCE THERAPY WITH TRABECTEDIN AFTER COMBINATION THERAPY LIPOSOMAL DOXORUBICIN PLUS TRABECTEDIN VS LIPOSOMAL DOXORUBICIN PLUS TRABECTEDIN IN PATIENTS AFFECTED BY RELAPSED OVARIAN CANCER RECURRING BETWEEN 6 AND 12 MONTHS AFTER | Medical Oncology 1 | Antonella Savarese | 1 |
| O | A PHASE IIIB, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTRE STUDY OF OLAPARIB MAINTENANCE RETREATMENT IN PATIENTS WITH EPITHELIAL OVARIAN CANCER PREVIOUSLY TREATED WITH A PARPI AND RESPONDING TO REPEAT PLATINUM CHEMOTHERAPY (OREO) | Medical Oncology 1 | Francesco Cognetti | 0 |
| C | *STUDIO RETROSPETTIVO MULTICENTRICO: CORRELAZIONE TRA GENOTIPO, FENOTIPO E OUTCOME CLINICO NEI TUMORI OVARICI EREDITARI BRCA 1 E BRCA 2 MUTATI* | Medical Oncology 2 | Patrizia Vici | 0 |

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| C | RANDOMIZED PHASE III TRIAL ON TRABECTEDIN (ET-743) VS CLINICIAN'S CHOICE CHEMOTHERAPY IN RECURRENT OVARIAN, PRIMARY PERITONEAL OR FALLOPIAN TUBE CANCERS OF BRCA MUTATED OR BRCANESS PHENOTYPE PATIENTS | Medical Oncology 2 | Patrizia Vici | 0 |
| O | PHASE II TRIAL ON TRABECTEDIN IN THE TREATMENT OF ADVANCED UTERINE AND OVARIAN CARCINOSARCOMA | Medical Oncology 2 | Patrizia Vici | 0 |
| O | MAINTENANCE THERAPY WITH TRABECTEDIN AFTER COMBINATION THERAPY LIPOSOMAL DOXORUBICIN PLUS TRABECTEDIN VS LIPOSOMAL DOXORUBICIN PLUS TRABECTEDIN IN PATIENTS AFFECTED BY RELAPSED OVARIAN CANCER RECURRING BETWEEN 6 AND 12 MONTHS AFTER | Medical Oncology 2 | Patrizia Vici | 0 |
| O | PREDICTIVE ROLE OF A MICRORNA SIGNATURE IN RELAPSED, HIGH-GRADE SEROUS, OVARIAN CANCER PATIENTS RECHALLENGED WITH PLATINUM-BASED REGIMENS | Medical Oncology 2 | Patrizia Vici | 0 |
| O | *STUDIO OSSERVAZIONALE RETROSPETTIVO SU ANDAMENTO CLINICO E TRATTAMENTO NELLE PAZIENTI AFFETTE DA SARCOMA UTERINO* | Medical Oncology 2 | Patrizia Vici | 0 |

## HAEMATOLOGICAL

| STATUS* | TITLE | DIVISION | Principal Investigator | Patients IRE 2018 |
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| O | *ADERENZA, PERSISTENZA ED EFFICACIA DI DASATINIB E NILOTINIB NEL TRATTAMENTO DI PAZIENTI AFFETTI DA LEUCEMIA MIELOIDE CRONICA IN FASE CRONICA* | Pharmacy/Pharmacovigilance | Felice Musicco | 24 |
| O | RADIOTHERAPY IN THE INITIAL STAGES OF HODGKIN LYMPHOMA: EVALUATION OF THE IMPACT OF THE USE OF PET-TC PERFORMED IN CORRESPONDENCE OF THE TREATMENT SITE ON THE TARGET DELINEATION. OBSERVATIONAL STUDY | Radiotherapy | Maria Grazia Petrongari | 0 |
| C | PHASE II STUDY WITH GA101-DHAP AS INDUCTION THERAPY IN RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL) PATIENTS BEFORE HIGH-DOSE CHEMOTHERAPY BEAM WITH AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) | Haematology Oncology | Francesca Palombi | 0 |
| C | *STUDIO PROSPETTICO MULTICENTRICO SULLA DIAGNOSTICA INTEGRATA DEGLI INFILTRATI POLMONARI NEI PAZIENTI AFFETTI DA EMOPATIA MALIGNA TRAMITE BRONCOLAVAGGIO ALVEOLARE* | Haematology Oncology | Francesco Marchesi | 10 |
| C | A RETROSPECTIVE STUDY TO EVALUATE THE CLINICO-BIOLOGIC CHARACTERISTICS AND OUTCOME OF PATIENTS TREATED IN ITALY ACCORDING TO THE IBRUTINIB-NAMED PATIENT PROGRAM (NPP) FOR PATIENTS WITH RELAPSED OR REFRACTORY CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) | Haematology Oncology | Andrea Mengarelli | 0 |
| C | *STUDIO RETROSPETTIVO MULTICENTRICO SULLE COMPLICANZE INFETTIVE IN PAZIENTI CON PATOLOGIE LINFOPROLIFERATIVE IN TERAPIA CON FARMACI A BERSAGLIO* | Haematology Oncology | Antonio Spadea | 16 |
| C | AN OPEN-LABEL, MULTICENTER, PHASE IIIB STUDY TO ASSESS THE SAFETY AND EFFICACY OF MIDOSTAURIN (PKC412) IN PATIENTS 18 YEARS OF AGE OR OLDER WITH NEWLY-DIAGNOSED FLT3-MUTATED ACUTE MYELOID LEUKEMIA WHO ARE ELIGIBLE FOR 7+3 OR 5+2 CHEMOTHERAPY | Haematology Oncology | Andrea Mengarelli | 3 |

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| C | 10-DAY DECITABINE VERSUS CONVENTIONAL CHEMOTHERAPY ( 3+7 ) FOLLOWED BY ALLOGRAFTING IN AML PATIENTS>60 YEARS: A RANDOMIZED PHASE ILL STUDY OFTBE EORTC LEUKEMIA GROUP, CELG, GIMEMA AND GERMAN MDS STUDY GROUP | Haematology Oncology | Andrea Mengarelli | 2 |
| C | A RANDOMIZED, OPEN-LABEL, MULTICENTRE, TWO-ARM PHASE III COMPARATIVE STUDY ASSESSING THE ROLE OF INVOLVED MEDIASTINAL RADIOTHERAPY AFTER RITUXIMAB CONTAINING CHEMOTHERAPY REGIMENS TO PATIENTS WITH NEWLY DIAGNOSED PRIMARY MEDIASTINAL LARGE B-CELL LYMP | Haematology Oncology | Francesco Pisani | 0 |
| C | *STUDIO MIRO (MOLECULARLY IMMUNO-RADIO-THERAPY ORIENTED): STUDIO MULTICENTRICO DI FASE II PER IL TRATTAMENTO SU BASE MOLECOLARE DEI LINFOMI FOLLICOLARI STADIO I/II CON RADIOTERAPIA LOCALE CON/SENZA OFATUMUMAB* | Haematology Oncology | Francesca Palombi | 0 |
| C | PHASE II, OPEN-LABEL, NOT COMPARATIVE, MULTICENTER STUDY OF MULTIPLE DOSES OF NEPA (NETUPITANT+PALONOSETRON) IN PREVENTING CHEMOTHERAPY INDUCED NAUSEA AND VOMITING (CINV) IN PATIENT WITH NON HODGKIN'S LYMPHOMA RECEIVING SALVAGE CHEMOTHERAPY FOLLOWED BY HIGH DOSE CHEMOTHERAPY AND AUTOLOGOUS HEMATOPOIETIC STEM CELLS SUPPORT | Haematology Oncology | Andrea Mengarelli | 1 |
| O | A RANDOMISED PHASE III STUDY TO COMPARE ARSENIC TRIOXIDE (ATO) COMBINED TO ATRA VERSUS STANDARD ATRA AND ANTHRACYCLINE-BASED CHEMOTHERAPY (AIDA REGIMEN) FOR NEWLY DIAGNOSED, NON HIGH-RISK ACUTE PROMYELOCYTIC LEUKEMIA | Haematology Oncology | Andrea Mengarelli | 0 |
| O | ITALIAN REGISTRY ON THE PREVALENCE OF IDH1/IDH2 MUTATIONS IN PATIENTS WITH ACUTE MYELOID LEUKEMIA | Haematology Oncology | Andrea Mengarelli | 11 |
| O | LONG TERM QUALITY OF LYFE SYMPTON BURDEN IN ACUTE PROMYELOCYTIC LEUKEMIA (APL) PATIENTS TREATED WITH ARSENIC TRIOXIDE (ATO) OR STANDAR CHEMIOTHERAPY | Haematology Oncology | Atelda Romano | 1 |
| O | *REGISTRO EPIDEMIOLOGICO DELLA LEUCEMIA MIELOIDE CRONICA (LMC)* | Haematology Oncology | Atelda Romano | 0 |
| O | NEXT-GENERATION SEQUENCING FOR BCR-ABL KD MUTATION SCREENING IN PHILADELPHIA CHROMOSOME-POSITIVE LEUKEMIAS | Haematology Oncology | Andrea Mengarelli | 0 |
| O | PHASE-III RANDOMIZED STUDY TO OPTIMIZE TKIS MULTIPLE APPROACHES - (OPTKIMA) - AND QUALITY OF LIFE (QOL) IN ELDERLY PATIENTS ( >=60 0 YEARS) WITH PH+ CHRONIC MYELOID LEUKEMIA (CML) AND MR3.0 / MR4.0 STABLE MOLECULAR RESPONSE | Haematology Oncology | Atelda Romano | 1 |
| O | FRONT-LINE TREATMENT OF PHILADELPHIA POSITIVE (PH+)/BCR-ABL POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) WITH AP24534 (PONATINIB), A NEW POTENT TYROSINE KINASE INHIBITOR (TKI). A PHASE II EXPLORATORY MULTICENTRIC STUDY IN PATIENTS MORE THAN 60 YEARS OLD OR UNFIT FOR A PROGRAM OF INTENSIVE CHEMOTHERAPY AND STEM CELL TRANSPLANTATION | Haematology Oncology | Antonio Spadea | 0 |
| O | NATIONAL TREATMENT PROGRAM WITH SEQUENTIAL CHEMOTHERAPY AND BLINATUMOMAB TO IMPROVE MINIMAL RESIDUAL DISEASE RESPONSE AND SURVIVAL IN PHILADELPHIA CHROMOSOME-NEGATIVE B-CELL PRECURSOR ADULT ACUTE LYMPHOBLASTIC LEUKEMIA | Haematology Oncology | Antonio Spadea | 0 |
| O | HIGH-DOSE CHEMOTHERAPY AND AUTOLOGOUS STEM CELL TRANSPLANT OR CONSOLIDATING CONVENTIONAL CHEMOTHERAPY IN PRIMARY CNS LYMPHOMA - RANDOMIZED PHASE III TRIAL | Haematology Oncology | Francesco Pisani | 0 |
| O | LIQUID BIOPSY: CIRCULATING MICRORNAS AND TUMOR DNA(CTDNA) AS NOVEL NON-INVASIVE BIOMARKERS IN DIFFUSE LARGE B-CELL LYMPHOMA | Haematology Oncology | Francesco Marchesi | 2 |

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| O | AN INTERNATIONAL PHASE II TRIAL ASSESSING TOLERABILITY AND EFFICACY OF SEQUENTIAL METHOTREXATE-ARACYTIN-BASED COMBINATION AND R-ICE COMBINATION, FOLLOWED BY HIGH-DOSE CHEMOTHERAPY SUPPORTED BY AUTOLOGOUS STEM CELL TRANSPLANT, IN PATIENTS WITH SYSTEMI | Haematology Oncology | Francesca Palombi | 0 |
| O | *STUDIO PROSPETTICO OSSERVAZIONALE SULL'UTILIZZO E SUL MONITORAGGIO DELLA CARDIOTOSSICITÃ  DELLE ANTRACICLINE IN PAZIENTI CON LINFOMA DIFFUSO A GRANDI CELLULE B* | Haematology Oncology | Francesca Palombi | 0 |
| O | A RANDOMIZED PHASE III MULTICENTER TRIAL ASSESSING EFFICACY AND TOXICITY OF A COMBINATION OF RITUXIMAB AND LENALIDOMIDE (R2) VS RITUXIMAB ALONE AS MAINTENANCE AFTER CHEMOIMMUNOTHERAPY WITH RITUXIMAB-BENDAMUSTINE FOR RELAPSED/REFRACTORY FL PATIENTS NO | Haematology Oncology | Francesca Palombi | 0 |
| O | EFFICACY AND SAFETY OF BRENTUXIMAB VEDOTIN PLUS BENDAMUSTINA IN PATIENTS WITH RELAPSED/REFRACTORY HODGKIN'S LYMPHOMA: A RETROSPECTIVE ANALYSIS | Haematology Oncology | Francesca Palombi | 0 |
| O | ACCURACY OF ALTERNATIVE TP53 SOMATIC MUTATIONAL AND EXPRESSION ANALYSES FOR THE PROGNOSTICATION OF MYELODYSPLASTIC SYNDROME | Haematology Oncology | Atelda Romano | 0 |
| O | EFFICACY OF ELTROMBOPAG PLUS LENALIDOMIDE COMBINATION THERAPY IN PATIENTS WITH IPSS LOW AND INTERMEDIATE-RISK MYELODYSPLASTIC SYNDROME WITH ISOLATED DEL5Q: A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY | Haematology Oncology | Atelda Romano | 0 |
| O | ELTROMBOPAG FOR THE TREATMENT OF THROMBOCYTOPENIA DUE TO LOW- AND INTERMEDIATE RISK MYELODYSPLASTIC SYNDROMES. (EQOL-MDS) | Haematology Oncology | Atelda Romano | 0 |
| O | DETECTION OF POOR MOBILIZER (PM) IN MULTIPLE MYELOMA (MM) PATIENTS: PROSPECTIVE PRODUCT REGISTRY | Haematology Oncology | Andrea Mengarelli | 2 |
| O | CHANGES IN DISEASE APPROACH AND OUTCOME IN 2010 AND 2013 OF NEWLY DIAGNOSED AND 2ND LINE MULTIPLE MYELOMA PATIENTS TREATED IN HEMATOLOGY CENTERS IN LAZIO REGION (ITALY) | Haematology Oncology | Francesco Pisani | 0 |
| O | HEMATOLOGICAL MALIGNANCIES ASSOCIATED BLOODSTREAM INFECTIONS SURVEILLANCE | Haematology Oncology | Antonio Spadea | 18 |
| O | ROLE OF CHE-1 IN TRANSCRIPTIONAL ADDICTION OF MULTIPLE MYELOMA | SAFU | Maurizio Fanciulli | 41 |

## HEAD AND NECK

| STATUS* | TITLE | DIVISION | Principal Investigator | Patients IRE 2018 |
|---|---|---|---|---|
| C | *STUDIO OSSERVAZIONALE CON REATTIVI DIAGNOSTICI CE-IVD* | Pathology | Maria Benevolo | 160 |
| O | ELUCIDATING HOW HUMAN PAPILLOMAVIRUS MODULATES AUTOPHAGY IN OROPHARYNGEAL SQUAMOUS CELL CARCINOMA: IMPACT ON THE PROGNOSTIC AND THERAPEUTIC POTENTIAL OF AUTOPHAGY IN THE RESPONSE TO CISPLATIN-TREATMENT | Pathology | Francesca Rollo | 0 |

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| O | PHASE III STUDY ASSESSING THE BEST OF RADIOTHERAPY COMPARED TO THE BEST OF SURGERY (TRANS-ORAL SURGERY (TOS)) IN PATIENTS WITH T1-T2, N0 OROPHARYNGEAL CARCINOMA | Otolaryngology Head & Neck | Raul Pellini | 0 |
| O | APPLICATION OF ECT FOR THE LOCAL TREATMENT OF HEAD AND NECK CANCER. ANALYSIS OF THE EFFICACY OF THE PROCEDURE FOR TUMOR CONTROL AND SURVIVAL | Otolaryngology Head & Neck | Barbara Pichi | 8 |
| O | *RADIOTERAPIA STEREOTASSICA SU SINGOLA CORDA VOCALE PER CARCINOMA GLOTTICO IN STADIO INIZIALE (CTIS-1)* | Radiotherapy | Giuseppe Sanguineti | 8 |
| O | EARLY DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING CHANGES TO PREDICT TUMOR RESPONSE TO CHEMORADIOTHERAPY IN HN CANCER | Radiotherapy | Giuseppe Sanguineti | 25 |
| O | *TOSSICITÀ ED EVENTUALE SUA ASSOCIAZIONE CON LA RISPOSTA IMMUNITARIA DURANTE TERAPIA CON RADIO-CETUXIMAB NEI PAZIENTI AFFETTI DA CARCINOMA SQUAMOSO DEL DISTRETTO CERVICO-CEFALICO IN III E IV STADIO* | Radiotherapy | Giuseppe Sanguineti | 4 |
| O | OPEN LABEL STUDY OF IMMUNE MONITORING OF TEMOPORFIN MEDIATED PHOTODYNAMIC THERAPY (PDT-FOSCAN) FOR THE TREATMENT OF RECURRENT SUPERFICIAL MULTIPLE CARCINOMA OF THE HEAD AND NECK | Immunology and Immunotherapy | Paola Nisticò | 0 |
| C | *VALUTAZIONE DEI PARAMETRI DI DIFFUSIONE E PERFUSIONE RM IN PAZIENTI AFFETTI DA TUMORI DEL TESTA-COLLO: CONFRONTO TRA DIVERSE MODALITA' DI ANALISI QUANTITATIVA DELLE IMMAGINI* | Medical Physics | Simona Marzi | 22 |
| O | STUDY OF OF MYC AND YAP CONTRIBUTION TO MUTANT P53 TRANSCRIPTIONAL ACTIVITY IN HEAD AND NECK SQUAMOUS CELL CARCINOMAS | Oncogenomics and Epigenetics | Giovanni Blandino | 4 |
| O | STUDY OF THE CORRELATION BETWEEN THE EXPRESSION PROFILE OF MICRORNAS AND CLINICAL EVOLUTION IN PATIENTS WITH SQUAMOUS CARCINOMAS OF HEAD AND NECK | Oncogenomics and Epigenetics | Giovanni Blandino | 4 |

## LUNG

| STATUS* | TITLE | DIVISION | Principal Investigator | Patients IRE 2018 |
|---|---|---|---|---|
| C | *APPLICAZIONE DI METODICHE DI NEXT GENERATION SEQUENTING MEDIANTE PIATTAFORMA ION TORRENT SU BIOPSIE E PREPARATI CITOLOGICI CAMPIONATI DA PAZIENTI AFFETTI DA CARCINOMA DEL POLMONE NON A PICCOLE CELLULE (NSCLC) PER L'IDENTIFICAZIONE DI MUTAZIONI CLINICAMENTE RILEVANTI* | Pathology | Paolo Visca | 0 |
| O | *SORVEGLIANZA ATTIVA DELLE COMPLICANZE INFETTIVE POLMONARI POSTOPERATORIE DOPO INTERVENTI DI CHIRURGIA TORACICA: INSTITUZIONE DI UN DATABASE PER LA VALUTAZIONE DELL'APPROPRIATEZZA DELLA PROFILASSI ANTIBIOTICA* | Anaesthesiology, Critical Area and Intensive Care | Cecilia Coccia | 0 |
| O | DECURARIZATION AFTER THORACIC ANESTHESIA - A PROSPECTIVE MULTICENTER DOUBLE-BLIND RANDOMIZED TRIAL COMPARING SUGAMMADEX VS NEOSTIGMINE REVERSAL AFTER THORACIC ANESTHESIA | Anaesthesiology, Critical Area and Intensive Care | Cecilia Coccia | 0 |

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| O | *STUDIO DEI MECCANISMI DI IMMUNO-EVASIONE DELLE CELLULE STAMINALI TUMORALI (CSC) DI ADENOCARCINOMA DEL POLMONE* | Thoracic Surgery | Francesco Facciolo | 40 |
| O | A RANDOMIZED CONTROLLED NON-INFERIORITY STUDY TO EVALUATE THE EFFICACY AND SAFETY OF HEMOPATCH COMPARED TO TACHOSIL IN PREVENTING OR REDUCING POSTOPERATIVE AIR LEAKS AFTER PULMONARY RESECTION | Thoracic Surgery | Francesco Facciolo | 0 |
| C | A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 STUDY OF ROVALPITUZUMAB TESIRINE AS MAINTENANCE THERAPY FOLLOWING FIRST-LINE PLATINUM-BASED CHEMOTHERAPY IN SUBJECTS WITH EXTENSIVE STAGE SMALL CELL LUNG CANCER (MERU) | Medical Oncology 1 | Francesco Cognetti | 0 |
| C | BE-TEAM: ITALIAN OBSERVATIONAL STUDY ON SECOND-LINE TREATMENT APPROACHES FOR EGFR-MUTATED, PROGRESSING NSCLC PATIENTS IN REAL WORLD CLINICAL PRACTICE | Medical Oncology 1 | Fabiana Cecere | 4 |
| C | RAMES: A DOUBLE-BLIND, PLACEBO CONTROLLED, RANDOMIZED MULTICENTER PHASE II STUDY EVALUATING GEMCITABINE WITH OR WITHOUT RAMUCIRUMAB AS II LINE TREATMENT FOR ADVANCED MALIGNANT PLEURAL MESOTHELIOMA) | Medical Oncology 1 | Francesco Cognetti | 2 |
| C | STUDY COMPARING ROVALPITUZUMAB TESIRINE VERSUS TOPOTECAN IN SUBJECTS WITH ADVANCED OR METASTATIC SMALL CELL LUNG CANCER WITH HIGH LEVELS OF DELTA-LIKE PROTEIN 3 (DLL3) AND WHO HAVE FIRST DISEASE PROGRESSION DURING OR FOLLOWING FRONT-LINE PLATINUM-BAS | Medical Oncology 1 | Francesco Cognetti | 3 |
| C | A PHASE 3, RANDOMIZED, OPEN-LABEL STUDY OF LORLATINIB (PF-06463922) MONOTHERAPY VERSUS CRIZOTINIB MONOTHERAPY IN THE FIRST-LINE TREATMENT OF PATIENTS WITH ADVANCED ALK-POSITIVE NON-SMALL CELL LUNG CANCER | Medical Oncology 1 | Francesco Cognetti | 2 |
| C | A RANDOMIZED OPEN-LABEL PHASE 3 TRIAL COMPARING BEVACIZUMAB + ERLOTINIB VS ERLOTINIB ALONE AS FIRST LINE TREATMENT OF PATIENTS WITH EGFR MUTATED ADVANCED NON SQUAMOUS NON SMALL CELL LUNG CANCER | Medical Oncology 1 | Fabiana Cecere | 2 |
| O | A PHASE 2 STUDY OF POZIOTINIB IN PATIENTS WITH NON-SMALL CELL LUNG CANCER, LOCALLY ADVANCED OR METASTATIC, WITH EGFR OR HER2 EXON 20 INSERTION MUTATION (POZITIVE20-1) | Medical Oncology 1 | Fabiana Cecere | 0 |
| O | A PHASE II RANDOMIZED STUDY OF PEMBROLIZUMAB IN PATIENTS WITH ADVANCED MALIGNANT PLEURAL MESOTHELIOMA | Medical Oncology 1 | Fabiana Cecere | 6 |
| O | A STANDARD REGIMEN OF DEXAMETHASONE IN COMPARISON TO TWO DEX-SPARING REGIMENS IN ADDITION TO NEPA IN PREVENTING CINV IN NAAVE NSCLC PATIENTS TO BE TREATED WITH CISPLATIN BASED CHEMOTHERAPY: A THREE-ARM, OPEN-LABEL, RANDOMIZED STUDY | Medical Oncology 1 | Fabiana Cecere | 0 |
| O | VALIDATION OF THE ALLIANCE AGAINST CANCER LUNG PANEL IN PATIENTS WITH NON SMALL CELL LUNG CANCER. | Medical Oncology 1 | Fabiana Cecere | 18 |
| O | A PHASE III PROSPECTIVE DOUBLE BLIND PLACEBO CONTROLLED RANDOMIZED STUDY OF ADJUVANT MEDI4736 IN COMPLETELY RESECTED NON-SMALL CELL LUNG CAN | Medical Oncology 1 | Fabiana Cecere | 2 |
| O | PHASE II SINGLE ARM STUDY WITH CABOZANTINIB IN NON-SMALL CELL LUNG CANCER PATIENTS WITH MET DEREGULATION | Medical Oncology 1 | Fabiana Cecere | 0 |

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| C | *STUDIO MULTICENTRICO OSSERVAZIONALE SULL'UTILIZZO DELLA SIGARETTA ELETTRONICA IN ITALIA* | Pulmonary Phisiopathology | Maria Papale | 0 |
| O | *REGISTRO ASMA GRAVE - STUDIO OSSERVAZIONALE, TRASVERSALE E/O RETROSPETTIVO, NON INTERVENTISTICO, MULTICENTRICO, NAZIONALE* | Pulmonary Phisiopathology | Maria Papale | 9 |
| C | LINKING TUMOR STROMA TO NUCLEUS VIA CYTOSKELETON: HMENA ISOFORMS, SIGNAL CHECKPOINTS AND BIOMARKERS OF NSCLC RELAPSE | Immunology and Immunotherapy | Paola Nisticò | 28 |
| O | HMENA SPLICING IN THE DIALOGUE BETWEEN TUMOR, ECM, CAFS AND IMMUNE CELLS: ROLE IN NSCLC PROGRESSION AND DRUG RESISTAN | Immunology and Immunotherapy | Paola Nisticò | 88 |
| O | DEVELOPMENT OF AN IMMUNOSCORE TEST TO DEFINE IMMUNOLOGICAL PARAMETERS ASSOCIATED WITH THE RISK OF RECIRRENCE IN N0 NSCLC PATIENTS, WITHIN THE NATIONAL ONCOLOGY NETWORK ALLEANZA CONTRO IL CANCRO OF THE ITALIAN MINISTRY OF HEALTH | Immunology and Immunotherapy | Paola Nisticò | 0 |
| O | EXPLORATORY STUDY FOR THE IDENTIFICATION OF THE COMPONENTS OF AN IMMUNOLOGICAL SCORE BASED ON BIOMOLECULAR ANALYSIS AND ITS ASSOCIATION WITH THE RESPONSE TO ICBS IN PATIENTS WITH ADVANCED LUNG CANCER, WITHIN THE NATIONAL ONCOLOGY NETWORK ALLEANZA CONTRO IL CANCRO OF THE ITALIAN MINISTRY OF HEALTH | Immunology and Immunotherapy | Paola Nisticò | 0 |
| O | *ANALISI DEL RUOLO DELL'ESTRADIOLO E DEI SUOI METABOLITI NELLA PROGRESSIONE DELLA PATOLOGIA PLEURICA* | Preclinical Models and new Therapeutics | Rossella Galati | 21 |

## SARCOMA

| STATUS* | TITLE | DIVISION | Principal Investigator | Patients IRE 2018 |
|---|---|---|---|---|
| C | EXPRESSION OF THE ABCB1/P-GLYCOPROTEIN AS A FACTOR FOR THE BIOLOGICAL STRATIFICATION OF NON-METASTATIC OSTEOSARCOMA OF THE LIMBS: PROSPECTIVE STUDY | Medical Oncology 1 | Virginia Ferraresi | 0 |
| O | LOCALIZED HIGH-RISK SOFT TISSUE SARCOMAS OF THE EXTREMITIES AND TRUNK IN ADULTS: AN INTEGRATED APPROACH COMPRISING STANDARD VS HISTOTYPE-ORIENTED NEOADJUVANT CHEMOTHERAPY (ISG-STS 10-01) | Medical Oncology 1 | Virginia Ferraresi | 0 |
| O | PHASE III TRIAL ON THE EFFICACY OF DOSE INTENSIFICATION IN PATIENTS WITH NON-METASTATIC EWING SARCOMA | Medical Oncology 1 | Virginia Ferraresi | 1 |
| O | INTERNATIONAL RANDOMISED CONTROLLED TRIAL OF CHEMOTHERAPY FOR THE TREATMENT OF RECURRENT AND PRIMARY REFRACTORY EWING SARCOMA | Medical Oncology 1 | Virginia Ferraresi | 0 |
| O | THE METROPHOLYS STUDY. METRONOMIC CYCLOPHOSPHAMIDE VS DOXORUBICIN IN ELDERLY PATIENTS WITH ADVANCED SOFT TISSUE SARCOMAS RANDOMIZED, CONTROLLED OPEN LABEL CLINICAL TRIAL | Medical Oncology 1 | Virginia Ferraresi | 0 |
| O | *VALUTAZIONE RADIOLOGICA DELLA RISPOSTA IN PAZIENTI CON SARCOMI DEI TESSUTI MOLLI LOCALMENTE AVANZATI/METASTATICI TRATTATI CON TRABECTEDINA* | Radiology | Vincenzo Anelli | 0 |

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| O | *RISCHIO DI OSTEOPENIA/OSTEOPOROSI INDOTTE DA CHEMIOTERAPIA IN PAZIENTI CON SARCOMI OSSEI. STUDIO OSSERVAZIONALE PROSPETTICO* | Endocrinology | Marialuisa Appetecchia | 1 |
| C | *RUOLO DELLA 18F-FDG PET/CT NELLA DIAGNOSI DIFFERENZIALE TRA TUMORI BENIGNI E MALIGNI A MATRICE CARTILAGINEA E NELLA PREDITTIVITÃ  DEL GRADING ISTOLOGICO* | Nuclear Medicine | Alessio Annovazzi | 95 |
| O | TARGETING TELOMERE REPLICATION IN ALT TUMORS | Oncogenomics and Epigenetics | Erica Salvati | 12 |

## SKIN

| STATUS* | TITLE | DIVISION | Principal Investigator | Patients IRE 2018 |
|---|---|---|---|---|
| O | A MICRORNA-BASED APPROACH TO ADVANCED DIAGNOSIS AND THERAPY OF METASTATIC MELANOMA. | Scientific Directorate | Gennaro Ciliberto | 11 |
| O | *ANALISI DEI PROFILI DI ESPRESSIONE DEI MICRORNA E GENOTIPIZZAZIONE DEL PAPILLOMAVIRUS UMANO IN UNA CASISTICA RETROSPETTIVA DI MELANOMA VULVARE* | Pathology | Mariantonia Carosi | 10 |
| C | A RETROSPECTIVE CHART REVIEW STUDY OF DABRAFENIB AND TRAMETINIB COMBINATION THERAPY IN PATIENTS WITH ADVANCED OR METASTATIC BRAF V600 MUTATED MELANOMA TREATED IN ITALY WITHIN THE INDIVIDUAL PATIENT PROGRAM: THE DESCRIBE ITALY STUDY | Medical Oncology 1 | Virginia Ferraresi | 0 |
| C | A PHASE II, OPEN-LABEL, MULTICENTER TRIAL TO INVESTIGATE THE CLINICAL ACTIVITY AND SAFETY OF MSB0010718C IN SUBJECTS WITH MERKEL CELL CARCINOMA | Medical Oncology 1 | Gianluigi Ferretti | 1 |
| C | A PHASE III, DOUBLE-BLINDED, RANDOMIZED, PLACEBO-CONTROLLED STUDY OF ATEZOLIZUMAB PLUS COBIMETINIB AND VEMURAFENIB VERSUS PLACEBO PLUS COBIMETINIB AND VEMURAFENIB IN PREVIOUSLY UNTREATED BRAFV600 MUTATION–POSITIVE PATIENTS WITH UNRESECTABLE LOCALLY ADVANCED OR METASTATIC MELANOMA | Medical Oncology 1 | Francesco Cognetti | 2 |
| O | PATTERN OF RESPONSE/PROGRESSION TO FIRST LINE TREATMENT WITH DABRAFENIB AND TRAMETINIB IN PATIENTS WITH UNRESECTABLE OR METASTATIC BRAF MUTATION–POSITIVE CUTANEOUS MELANOMA: THE T-WIN STUDY | Medical Oncology 1 | Virginia Ferraresi | 1 |
| O | THREE ARMS PROSPECTIVE, RANDOMIZED PHASE II STUDY TO EVALUATE THE BEST SEQUENTIAL APPROACH WITH COMBO IMMUNOTHERAPY (IPILIMUMAB/NIVOLUMAB) AND COMBO TARGET THERAPY (LGX818/MEK162) IN PATIENTS WITH METASTATIC MELANOMA AND BRAF MUTATION | Medical Oncology 1 | Virginia Ferraresi | 3 |
| O | A PHASE III, OPEN-LABEL, MULTICENTER, TWO-ARM, RANDOMIZED STUDY TO INVESTIGATE THE EFFICACY AND SAFETY OF COBIMETINIB PLUS ATEZOLIZUMAB VERSUS PEMBROLIZUMAB IN PATIENTS WITH PREVIOUSLY UNTREATED ADVANCED BRAFV600 WILD-TYPE MELANOMA | Medical Oncology 1 | Francesco Cognetti | 2 |
| O | BEYOND TUMOR CELL TARGETING WITH PATHWAY INHIBITORS IN HUMAN MELANOMA: ROLE OF THE MICROENVIROMENT | Medical Oncology 1 | Ludovica Ciuffreda | 51 |
| O | A PHASE II TRIAL OF VEMURAFENIB PLUS COBIMETINIB IN PATIENTS TREATED WITH PRIOR FIRST-LINE SYSTEMIC IMMUNOTHERAPY FOR INOPERABLE LOCALLY ADVANCED OR METASTATIC MELANOMA | Medical Oncology 1 | Francesco Cognetti | 0 |

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| O | AN EVALUATION OF THE EFFICACY BEYOND PROGRESSION OF VEMURAFENIB COMBINED WITH COBIMETINIB ASSOCIATED WITH LOCAL TREATMENT COMPARED TO SECOND-LINE TREATMENT IN PATIENTS WITH BRAFV600 MUTATION-POSITIVE METASTATIC MELANOMA IN FOCAL PROGRESSION WITH FIRST-LINE COMBINED VEMURAFENIB AND COBIMETINIB | Medical Oncology 1 | Virginia Ferraresi | 0 |
| O | *VALIDAZIONE DI UN NUOVO PANNELLO DI NEXT GENERATION SEQUENCING PER L'ANALISI MUTAZIONALE DI CAMPIONI ISTOPATOLOGICI DI PAZIENTI CON MELANOMA METASTATICO TRATTATI CON INIBITORI DI BRAF E MEK O CON ANTICORPI ANTI-PD-1* | Medical Oncology 1 | Virginia Ferraresi | 7 |
| O | COMBI-APLUS: OPEN-LABEL, PHASE IIIB STUDY OF DABRAFENIB IN COMBINATION WITH TRAMETINIB IN THE ADJUVANT TREATMENT OF STAGE III BRAF V600 MUTATION-POSITIVE MELANOMA AFTER COMPLETE RESECTION TO EVALUATE THE IMPACT ON PYREXIA RELATED OUTCOMES OF AN ADAPTED PYREXIA AE-MANAGEMENT ALGORITHM (PLUS) | Medical Oncology 1 | Virginia Ferraresi | 2 |
| O | SPANNING BCL-2 FUNCTIONS IN MELANOMA MODELS: FROM MICROENVIRONMENT TO MICRORNA MODULATION | Preclinical Models and new Therapeutics | Donatella Del Bufalo | 0 |
| **THYMIC** | | | | |
| **STATUS*** | **TITLE** | **DIVISION** | **Principal Investigator** | **Patients IRE 2018** |
| O | *CONTRIBUTO ALLO STUDIO CLINICOPATOLOGICO E MOLECOLARE DEI TUMORI EPITELIALI TIMICI (TET) SULLA BASE DEL DATABASE INTERNAZIONALE ITMIG* | Pathology | Mirella Marino | 11 |
| **UROLOGICAL** | | | | |
| **STATUS*** | **TITLE** | **DIVISION** | **Principal Investigator** | **Patients IRE 2018** |
| O | *VARIAZIONI DI PRESSIONE TRANSPOLMONARE IN CONDIZIONI DI PNEUMOPERITONEO E STEEP TRENDELENBURG DURANTE CHIRURGIA VIDEOLAPAROSCOPICA ROBOT-ASSISTITA. STUDIO PILOTA PROSPETTICO OSSERVAZIONALE* | Anaesthesiology, Critical Area and Intensive Care | Ester Forastiere | 0 |
| C | TARGETED THERAPY WITH OR WITHOUT NEPHRECTOMY IN METASTATIC RENAL CELL CARCINOMA: LIQUID BIOPSY FOR BIOMARKERS DISCOVERY (TARIBO) | Medical Oncology 1 | Michele Milella | 0 |
| O | A RANDOMIZED PROSPECTIVE MULTICENTRE OPEN-LABEL PHASE II STUDY OF ANDROGEN DEPRIVATION THERAPY (ADT) PLUS RADIOTHERAPY WITH OR WITHOUT ABIRATERONE ACETATE AND PREDNISONE IN LOCALLY ADVANCED VERY HIGH-RISK PROSTATE CANCER | Medical Oncology 1 | Paolo Carlini | 0 |
| O | A PHASE III, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL OF PEMBROLIZUMAB (MK-3475) AS MONOTHERAPY IN THE ADJUVANT TREATMENT OF RENAL CELL CARCINOMA POST NEPHRECTOMY (KEYNOTE-564) | Medical Oncology 1 | Gianluigi Ferretti | 3 |
| O | AXITINIB IN ADVANCED / METASTATIC RENAL CELL CARCINOMA - A NON-INTERVENTIONAL STUDY OF REAL WORLD TREATMENT OUTCOMES IN PATIENTS RECEIVING 2ND LINE AXITINIB AFTER 1ST LINE SUNITINIB (ADONIS) | Medical Oncology 1 | Francesco Cognetti | 0 |

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| O | A PHASE 3 RANDOMIZED, DOUBLE-BLIND, MULTI-CENTER STUDY OF ADJUVANT NIVOLUMAB VERSUS PLACEBO IN SUBJECTS WITH HIGH RISK INVASIVE UROTHELIAL CARCINOMA | Medical Oncology 1 | Francesco Cognetti | 0 |
| O | PROGNOSTIC ROLE OF MULTIGENIC ANALYSIS IN RENAL CELL CARCINOMA WITH LOSS OF BAP1 EXPRESSION | Medical Oncology 1 | Michele Milella | 0 |
| O | *STUDIO PILOTA DI VALUTAZIONE DELL'UTILIZZO DELLA 64CU-PET/TC TOTAL BODY IN PAZIENTI CON RECIDIVA IN LOGGIA PROSTATICA VISIBILE IN RMMP* | Radiotherapy | Giuseppe Sanguineti | 26 |
| O | A RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED PHASE 3 STUDY OF JNJ-56021927 IN SUBJECTS WITH HIGH RISK, LOCALIZED OR LOCALLY ADVANCED PROSTATE CANCER RECIVED TREATMENT WIRH PRIMARY RADIATION THERAPY | Radiotherapy | Giuseppe Sanguineti | 2 |
| O | *VALIDAZIONE DI MODELLI PREDITTIVI DI TOSSICITÀ DOPO TRATTAMENTO RADIOTERAPICO PER TUMORE DELLA PROSTATA. DISFUNZIONE URINARIA ED ERETTILE - 02* | Radiotherapy | Giuseppe Sanguineti | 17 |
| O | *STUDIO DI FASE I-II SULLA FATTIBILITA' E ATTIVITA' DELLA RADIOTERAPIA STEREOTASSICA CON ACCELERATORE LINEARE IN 3 FRAZIONI PER CARCINOMA DELLA PROSTATA A RISCHIO BASSO/INTERMEDIO* | Radiotherapy | Giuseppe Sanguineti | 11 |
| O | *STUDIO OSSERVAZIONALE PROSPETTICO MULTICENTRICO DELLA TOSSICITA' INTESTINALE, EMATOLOGICA E URINARIA DA IRRADIAZIONE DELL'AREA LINFONODALE PELVICA (IHU WPRT TOX) NEL TUMORE DELLA PROSTATA* | Radiotherapy | Giuseppe Sanguineti | 16 |
| O | *STUDIO PILOTA DI RADIOTERAPIA STEREOTASSICA PRE-OPERATORIA PER CARCINOMA RENALE OPERABILE IN STADIO INIZIALE (CT1)* | Radiotherapy | Giuseppe Sanguineti | 0 |
| C | *VALUTAZIONE RETROSPETTIVA DEI RISULTATI INTRAOPERATORI, PERIOPERATORI E FUNZIONALI DELLA PROSTATECTOMIA SEMPLICE ROBOTICA CON NEAR INFRARED FLUORESCENCE IMAGING PER IL RISPARMIO FUNZIONALE DELL'URETRA E DELLA FUNZIONE EIACULATORIA* | Urology | Giuseppe Simone | 50 |
| C | *VALUTAZIONE RETROSPETTICA DEI RISULTATI INTRAOPERATORI, PERIOPERATORI E FUNZIONALI DELLA NEFRECTOMIA PARZIALE ROBOTICA CON NEAR INFRARED FLUORESCENCE IMAGING DOPO RILASCIO TRANSARTERIOSO SUPERSELETTIVO DI ICG-LIPIODOL* | Urology | Giuseppe Simone | 50 |
| C | *VALUTAZIONE RETROSPETTIVA DEI RISULTATI INTRAOPERATORI, PERIOPERATORI E FUNZIONALI DEL REIMPIANTO URETERO-NEOVESCICALE ROBOTICO CON RILASCIO TRANSNEFROSTOMICO DI ICG E NEAR INFRARED FLUORESCENCE IMAGING* | Urology | Giuseppe Simone | 20 |
| C | *VALUTAZIONE RETROSPETTIVA DEI RISULTATI PERIOPERATORI E FUNZIONALI DELLA SURRENALECTOMIA PARZIALE MININVASIVA NEI PAZIENTI AFFETTI DA IPERALDOSTERONISMO PRIMITIVO SECONDARIO AD ADENOMA SURRENALICO UNILATERALE/BILATERALE (SINDROME DI CONN)* | Urology | Giuseppe Simone | 10 |
| O | *CISTECTOMIA RADICALE OPEN VERSUS ROBOTICA CON DERIVAZIONE URINARIA TOTALMENTE INTRACORPOREA. STUDIO PROSPETTICO RANDOMIZZATO MONO-CENTRICO* | Urology | Giuseppe Simone | 37 |
| O | *CORRELAZIONE TRA DOSIMETRIA FISICA, EFFETTI BIOLOGICI E TOSSICITA' CLINICA NEL PAZIENTE CON CARCINOMA DELLA PROSTATA METASTATICO RESISTENTE ALLA CASTRAZIONE (MCRPC) TRATTATO CON RADIUM-223* | Medical Physics | Lidia Strigari | 5 |

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| O | *RUOLO DELLA PET CON 64CU-PSMA NEL CARCINOMA DELLA PROSTATA (PC): DIAGNOSI PRECOCE DI RECIDIVA BIOCHIMICA* | Nuclear Medicine | Rosa Sciuto | 70 |
| O | UTILIZZO DELL'IMAGING PET/CT CON 64CUCL2 NELLA SELEZIONE DEI PAZIENTI CON TUMORE DELLA PROSTATA IN RECIDIVA BIOCHIMICA DOPO PROSTATECTOMIA, DA TRATTARE CON SUCCESSO CON RADIOTERAPIA DI SALVATAGGIO SUL LETTO PROSTATICO | Nuclear Medicine | Rosa Sciuto | 2 |
| O | EVALUATION OF URINE MIRNAS AS NON-INVASIVE TOOL TO PREDICTE BACILLUS CALMETTE-GUÉRIN TREATMENT EFFICACY IN BLADDER CANCER | Oncogenomics and Epigenetics | Maria Giulia Rizzo | 15 |

## MISCELLANEA

| STATUS* | TITLE | DIVISION | Principal Investigator | Patients IRE 2018 |
|---|---|---|---|---|
| C | *APPLICAZIONE DELLA MEDICINA BASATA SULLA NARRAZIONE IN RADIOTERAPIA* | Epidemiology and tumor registry | Maria Cecilia Cercato | 20 |
| C | *I COSTI SOCIALI DEL CANCRO: VALUTAZIONE DI IMPATTO SOCIALE ED ECONOMICO SUI MALATI E SUI CAREGIVER* | Psychology | Patrizia Pugliese | 3 |
| O | *FACILITATORI E/O BARRIERE ALL'ACCESSO AL SUPPORTO PSICOLOGICO IN PAZIENTI ONCOLOGICI: UNO STUDIO MULTICENTRICO* | Psychology | Patrizia Pugliese | 0 |
| C | METAGENOMIC SEARCH FOR MICROBIOLOGICAL DETERMINANTS OF HUMAN TUMORS | Pathology | Edoardo Pescarmona | 0 |
| O | *LA MALATTIA DI CASTLEMAN MULTICENTRICA: UNA RIVISITAZIONE DELLO STATO DELL'ARTE* | Pathology | Mirella Marino | 1 |
| O | NON CODING RNA IN SOLID TUMORS | Pathology | Mariantonia Carosi | 30 |
| C | INTERNATIONAL OBSERVATIONAL STUDY TO UNDERSTAND THE IMPACT AND BEST PRACTICES OF AIRWAY MANAGEMENT OF CRITICALLY ILL PATIENTS | Anaesthesiology, Critical Area and Intensive Care | Lorella Pelagalli | 0 |
| O | *STUDIO OSSERVAZIONALE, MULTICENTRICO, PER LA VALUTAZIONE DELL'EFFICACIA DI UN INTERVENTO MULTIFATTORIALE PER MIGLIORARE LA COMUNICAZIONE VERSO I FAMILIARI DI PAZIENTI RICOVERATI IN TERAPIA INTENSIVA* | Anaesthesiology, Critical Area and Intensive Care | Lorella Pelagalli | 0 |
| C | MODIFICATION OF THE MICRORNA EXPRESSION PROFILE DURING CHEMO HYPERTHERMIA IN PATIENTS UNDERGOING PERITECTOMY FOR OVARIAN CARCINOSIS: PILOT STUDY | Digestive Surgery | Mario Valle | 0 |
| C | *STUDIO OSSERVAZIONALE RETROSPETTIVO SUI RISULTATI CLINICI DEL TRATTAMENTO DELLE LESIONI METASTATICHE VERTEBRALI IN PAZIENTI AFFETTI DA NEOPLASIE SOLIDE ED EMATOLOGICHE CON PROCEDURA DI CIFOPLASTICA A CIELO APERTO* | Neurosurgery | Stefano Telera | 50 |
| O | *STUDIO CLINICO SULL'UTILIZZO DI UN POLIMERO ELASTICO A BASE DI SILICONE (VK-100) PER L' "AUGMENTATION " VERTEBRALE (ELASTOPLASTICA), IN COMPARAZIONE (2:1) CON IL PMMA (CEMENTO), NELLE FRATTURE SOMATICHE DA INSUFFICIENZA CORRELATE CON PATOLOGIE METASTATICHE O LOCALIZZAZIONI DI MALATTIE EMOLINFOPROLIFERATIVE E VERTEBRE OSTEOPOROTICHE IN MALATTIE NEOPLASTICHE* | Neurosurgery | Stefano Telera | 2 |

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|---|---|---|---|---|
| C | A PHASE 1B OPEN-LABEL THREE-ARM MULTI-CENTER STUDY TO ASSESS THE SAFETY AND TOLERABILITY OF PF-05212384 (PI3K/MTOR INHIBITOR) IN COMBINATION WITH OTHER ANTI-TUMOR AGENTS | Medical Oncology 1 | Gianluigi Ferretti | 0 |
| O | *STUDIO NAZIONALE NICSO: PROGETTO DI MONITORAGGIO MEDICO-INFERMIERISTICO DEGLI EFFETTI COLLATERALI DA TERAPIE ONCOLOGICHE* | Medical Oncology 1 | Alessandra Fabi | 14 |
| O | VIP: VALIDATION OF THE ITALIAN VERSION OF THE PATIENT- REPORTED OUTCOMES - COMMON TERMINOLOGY CRITERIA FOR ADVERSE EVENTS (PRO-CTCAE): A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY ON DIFFERENT CANCER TYPES | Medical Oncology 1 | Antonella Savarese | 0 |
| O | ANALISI DEL VALORE PREDITTIVO DI EFFICACIA DELLE TERAPIE ANTI-NEOPLASTICHE BASATA SULLA VALUTAZIONE DI PATHWAYS MOLECOLARI CONNESSI ALLE CELLULE STAMINALI TUMORALI: STUDIO MULTI-SETTING E MULTI-TUMORE. HIERARCHY STUDY | Medical Oncology 2 | Patrizia Vici | 16 |
| O | VIP: VALIDATION OF THE ITALIAN VERSION OF THE PATIENT- REPORTED OUTCOMES - COMMON TERMINOLOGY CRITERIA FOR ADVERSE EVENTS (PRO-CTCAE): A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY ON DIFFERENT CANCER TYPES | Medical Oncology 2 | Patrizia Vici | 0 |
| O | A PHASE 1 DOSE ESCALATION AND COHORT EXPANSION STUDY OF TSR-042, AN ANTI-PD-1 MONOCLONAL ANTIBODY, IN PATIENTS WITH ADVANCED SOLID TUMORS | Medical Oncology 2 | Patrizia Vici | 0 |
| C | *STUDIO OSSERVAZIONALE RESTROSPETTIVO SUI RISULTATI CLINICI DEL TRATTAMENTO CON SISTEMA DI STABILIZZAZIONE ENDOMIDOLLARE ILLUMINOSS PER I PAZIENTI AFFETTI DA FRATTURA O DA OSTEOLISI A RISCHIO DI FRATTURA DELL'OMERO PER LESIONI RIPETITIVE O MIELOMA* | Orthopaedics | Carmine Zoccali | 10 |
| O | *STUDIO CLINICO SPONTANEO, MULTICENTRICO, OSSERVAZIONALE, PROSPETTICO, IN APERTO NON CONTROLLATO, PER LA VERIFICA DELL'EFFICACIA DEL KIT DAC® (DENFENSIVE ANTIBACTERIAL COATING) GEL NELLA PREVENZIONE DELLE COMPLICANZE SETTICHE NELLA CHIRURGIA MEGAPROTESICA IN PAZIENTI SOTTOPOSTI A RICOSTRUZIONE DOPO GRANDI RESEZIONI OSSEE* | Orthopaedics | Carmine Zoccali | 0 |
| O | SACRAL CHORDOMA: A RANDOMIZED & OBSERVATIONAL STUDY ON SURGERYVERSUS DEFINITIVE RADIATION THERAPY IN PRIMARY LOCALIZED DISEASE (SACRO) | Radiotherapy | Maria Grazia Petrongari | 4 |
| O | DEVELOPMENT AND VALIDATION OF A TOOL FOR PATIENT-REPORTED ASSESSMENT OF CANCERRELATED FINANCIAL TOXICITY | Biostatistic | Diana Giannarelli | 6 |
| O | KARYOTYPIC ABERRATIONS IN CANCER STEM CELLS AS A SOURCE OF IMMUNOGENS FOR ADOPTIVE T-CELL THERAPY: THE RIGHT ALLIES FOR THERAPEUTIC SUCCESS? | Immunology and Immunotherapy | Ilio Vitale | 8 |
| C | ENDOTHELIN AXIS/BETA-ARRESTIN-DRIVEN ACTIN REORGANIZATION: BRINGING THE RIGHT NETWORK OF PROTEINS TO DIRECT INVADOPODIA | Preclinical Models and new Therapeutics | Anna Bagnato | 0 |
| O | PHASE 1 DEVELOPMENT OF AN EORTC QOL CANCER SURVIVORSHIP QUESTIONNAIRE | Neurology | Andrea Pace | 1 |
| O | *LA BIOPSIA LIQUIDA: STUDIO DI FATTIBILITÀ E TRASFERIBILITÀ ALLA ROUTINE CLINICA* | Oncogenomics and Epigenetics | Patrizio Giacomini | 0 |

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| O | ANALYSIS OF THE TRANSCRIPTIONAL EXPRESSION PROFILE AND MICRORNAS IN BRAIN METASTASES FROM PRIMARY TUMORS OF VARIOUS ORIGIN | Oncogenomics and Epigenetics | Giovanni Blandino | 6 |
| O | MOLECULAR MECHANISM OF QUADRUPLEX-TARGETED DRUGS: TOWARDS CLINICAL CANDIDATE SELECTION | SAFU | Carlo Leonetti | 15 |
| O | *REVER3MAB: UN FARMACO BIOLOGICO INNOVATIVO PER REVERTIRE LA RESISTENZA A TERAPIE ONCOLOGICHE CONVENZIONALI* | SAFU | Maurizio Fanciulli | 3 |
| **MULTIPLE SCLEROSIS** | | | | |
| **STATUS*** | **TITLE** | **DIVISION** | **Principal Investigator** | **Patients IRE 2018** |
| O | COAGULATION/COMPLEMENT ACTIVATION AND CEREBRAL HYPOPERFUSION IN RELAPSING-REMITTING MULTIPLE SCLEROSIS | Neurology | Tatiana Koudriavtseva | 56 |

**Status***

O = Open

C= Close

# ISTITUTIONAL COURSES

# ISTITUTIONAL COURSES 2018

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| 1 | 03/05/2018 | 17/05/2018 | Le risorse elettroniche della biblioteca per la ricerca sperimentale e clinica | Dr.ssa Gaetana Cognetti |
| 1 | 06/06/2018 | 06/06/2018 | La medicina narrativa | Dr.ssa Gaetana Cognetti |
| 3 | 17/09/2018 | 27/09/2018 | Le risorse elettroniche della biblioteca per la ricerca sperimentale e clinica | Dr.ssa Gaetana Cognetti |
| 2 | 21/11/2018 | 21/11/2018 | La medicina narrativa | Dr.ssa Gaetana Cognetti |
| 1 | 10/04/2018 | 29/05/2018 | Ridait Seminars - I modulo | Dr. Aldo Venuti |
| 1 | 03/07/2018 | 02/10/2018 | Ridait Seminars - II modulo | Dr. Aldo Venuti |
| 1 | 04/07/2018 | 04/07/2018 | "Gestione e monitoraggio degli studi clinici . La piattaforma SMART" | Dr.ssa Federica Falcioni |
| 1 | 30/10/2018 | 18/12/2018 | Ridait Seminars - III modulo | Dr. Aldo Venuti |
| 1 | 04/12/2018 | 04/12/2018 | Gestione degli studi clinici Principali aspetti normativi-organizzativi e la piattaforma smart | Dr.ssa Federica Falcioni |

**DMT: Patients under our care**

| Edition | Date from | Date to | Title | Scientific Coordinator |
|---|---|---|---|---|
| 1 | 16/04/2018 | 30/04/2018 | DMT neoplasie gastro - intestinali ed epatobiliopancreatiche - I modulo | Prof. Alfredo Garofalo |
| 1 | 16/04/2018 | 25/06/2018 | DMT Neoplasie muscolo-scheletriche - sarcomi viscerali e GIST | Dr.ssa Virginia Ferraresi |
| 1 | 18/04/2018 | 27/06/2018 | Presentazione, analisi, discussione casi clinici complessi in oncologia medica. Concomitante analisi della più recente letteratura oncologica inerente i casi clinici presentati - I Modulo | Dr. Ferretti Gianluigi |
| 1 | 23/04/2018 | 11/06/2018 | DMT- Incontri multidisciplinari in ematologia | Dr. Andrea Mengarelli |
| 1 | 02/05/2018 | 30/05/2018 | DMT - Incontri multidisciplinari in | Dr. Enrico Vizza |

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| | | | ginecologia oncologica - I modulo | |
| 1 | 10/05/2018 | 24/05/2018 | DMT Carcinoma Tiroide | Dr.ssa Marialuisa Appetecchia |
| 1 | 07/06/2018 | 26/07/2018 | DMT Tumori della cute non melanoma- II modulo | Dr.ssa Laura Eibenschutz |
| 1 | 22/06/2018 | 20/07/2018 | Incontri multidisciplinari della Breast Unit: disease management team delle neoplasie della mammella - I modulo | Prof. Francesco Cognetti Prof. Roy De Vita |
| 1 | 12/09/2018 | 31.10.2018 | DMT - Incontri multidisciplinari in ginecologia oncologica - I modulo | Dr. Enrico Vizza |
| 1 | 01/10/2018 | 05/11/2018 | DMT- Incontri multidisciplinari in ematologia- III modulo | Dr. Mengarelli Andrea |
| 1 | 13/09/2018 | 27/09/2018 | Incontri multidisciplinari di endocrinologia oncologica: disease management team carcinoma tiroideo II modulo | Dr.ssa Marialuisa Appetecchia |
| 1 | 17/09/2018 | 05/11/2018 | DMT Neoplasie gastrointestinali ed epato-bilio-pancreatiche II Modulo | Prof. Alfredo Garofalo |
| 1 | 24/09/2018 | 17/12/2018 | Incontri multidisciplinari di ortopedia oncologica:disease management team delle neoplasie mesenchimali muscolo-scheletriche, sarcomi viscerali e GIST | Dr.ssa Virginia Ferraresi |
| 1 | 01/10/2018 | 26/10/2018 | Incontri multidisciplinari Breast Unit:disease management team delle neoplasie della mammella - II Modulo | Prof. Francesco Cognetti Prof. Roy De Vita |
| 1 | 22/10/2018 | 24/10/2018 | Incontri multidisciplinari Dose Team - I modulo | Dr.ssa Lidia Strigari |
| 1 | 30/10/2018 | 11/12/2018 | Incontri multidisciplinari DMT Melanoma | Dr Pasquale Frascione |
| 1 | 19/11/2018 | 21/11/2018 | Incontri multidisciplinari Dose Team - II modulo | Dr.ssa Lidia Strigari |
| 1 | 26/11/2018 | 17/12/2018 | DMT- Incontri multidisciplinari in ematologia- IV modulo | Dr. Andrea Mengarelli |
| 1 | 10/12/2018 | 21/12/2018 | Incontri multidisciplinari Breast Unit:disease | Prof. Francesco Cognetti Prof. Roy De Vita |

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| | | | management team delle neoplasie della mammella - II Modulo | |

**BLSD: Patient Safety and Treatment Safety**

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|---|---|---|---|---|
| 1 | 09/04/2018 | 09/04/2018 | Corso BLSD- Medici | Dr.ssa Francesca Principi |
| 1 | 18/04/2018 | 18/04/2018 | BLSD - Esecutore Cat. B Infermieri | Dr.ssa Francesca Principi |
| 6 | 04/05/2018 | 04/05/2018 | BLSD - Esecutore Cat. B Infermieri | Dr.ssa Francesca Principi |
| 2 | 09/05/2018 | 09/05/2018 | Corso BLSD- Medici | Dr.ssa Francesca Principi |
| 3 | 07/06/2018 | 07/06/2018 | Corso BLSD- Medici | Dr.ssa Francesca Principi |
| 3 | 20/06/2018 | 20/06/2018 | BLSD - Esecutore Cat. B Infermieri | Dr.ssa Francesca Principi |
| 4 | 01/10/2018 | 01/10/2018 | Corso BLSD- Medici | Dr.ssa Francesca Principi |
| 5 | 08/11/2018 | 08/11/2018 | Corso BLSD- Medici | Dr.ssa Francesca Principi |
| 4 | 15/10/2018 | 15/10/2018 | BLSD - Esecutore Cat. B Infermieri | Dr.ssa Francesca Principi |
| 5 | 21/11/2018 | 21/11/2018 | BLSD - Esecutore Cat. B Infermieri | Dr.ssa Francesca Principi |

**PSYCHO ONCOLOGY: Care and Assistance towards caregivers and families**

| Edition | Date from | Date to | Title | Scientific Coordinator |
|---|---|---|---|---|
| 1 | 22/01/2018 | 24/01/2018 | Dal benessere alla patologia. La persona e il suo contesto | Dr.ssa Anita Caruso |
| 1 | 05/02/2018 | 07/02/2018 | L'intervento clinico interdisciplinare | Dr.ssa Anita Caruso |
| 1 | 04/06/2018 | 06/06/2018 | Aspetti biologici e aspetti relazionali della malattia oncologica. Dal curare al prendersi cura | Dr.ssa Anita Caruso |
| 1 | 11/06/2018 | 11/06/2018 | Il contesto familiare e le dinamiche emotive degli operatori | Dr.ssa Anita Caruso |
| 1 | 17/09/2018 | 19/09/2018 | Il bambino, l'adolescente e la | Dr.ssa Anita Caruso |

| | | | | |
|---|---|---|---|---|
| | | | malattia oncologica | |
| 1 | 24/09/2018 | 26/09/2018 | La comunicazione in ambito oncologico | Dr.ssa Anita Caruso |
| 1 | 10/12/2018 | 12/12/2018 | Il Counselling genetico. La morte e il morire | Dr.ssa Anita Caruso |
| 1 | 03/12/2018 | 05/12/2018 | Prospettive in Oncologia | Dr.ssa Anita Caruso |

**PHASE I clinical trials**

| Edition | Date from | Date to | Title | Scientific Coordinator |
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| 1 | 16/04/2018 | 16/04/2018 | Workshop Good Clinical Practice | Dr. Milella Michele |
| 2 | 20/04/2018 | 20/04/2018 | Workshop Good Clinical Practice | Dr. Milella Michele |
| 1 | 23/04/2018 | 23/04/2018 | Introduzione alla metodologia della ricerca | Dr.ssa Iacorossi Laura |
| 3 | 23/04/2018 | 23/04/2018 | Workshop Good Clinical Practice | Dr. Milella Michele |
| 2 | 27/04/2018 | 27/04/2018 | Introduzione alla metodologia della ricerca | Dr.ssa Iacorossi Laura |
| 1 | 11/05/2018 | 11/05/2018 | Le buone pratiche cliniche nella documentazione scientifica | Dr.ssa Gaetana Cognetti |
| 4 | 30/05/2018 | 30/05/2018 | Workshop Good Clinical Practice | Dr. Milella Michele |
| 5 | 30/05/2018 | 30/05/2018 | Workshop Good Clinical Practice | Dr. Milella Michele |
| 1 | 28/11/2018 | 20/12/2018 | Farmaci sperimentali. Interazioni critiche. Interazioni farmaci-alimenti | Dr Ferretti Gianluigi |

**Training on health care procedures**

| Edition | Date from | Date to | Title | Scientific Coordinator |
|---|---|---|---|---|
| 1 | 11/10/2018 | 11/10/2018 | Corso teorico pratico nursing perioperatorio in chirurgia robotica | Dr Spano Alessandro |
| 1 | 10/10/2018 | 10/10/2018 | “La gestione delle terapie citotossiche nell'ambulatorio Urologia IRE” | Dr.ssa Silvia Lolli |

**Training offered by all Departments**

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| Edition | Date from | Date to | Title | Scientific Coordinator |
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| 1 | 12/04/2018 | 19/04/2018 | Comunicazione efficace: strategie per migliorare la relazione | Dr.ssa Anita Caruso |
| 1 | 13/04/2018 | 13/04/2018 | Corso Base Vie Aeree | Dr.ssa Cecilia Coccia<br>Dr.ssa Silvia Lolli<br>Dr.ssa Maria Sofra |
| 1 | 18/04/2018 | 12/12/2018 | Metodologie di governo clinico delle attività clinico-.assistenziali di medicina nucleare basate sulla collaborazione e valorizzazione delle varie professionalità | Dr.ssa Sciuto Rosa |
| 1 | 20/04/2018 | 20/04/2018 | Il rischio da sovraccarico biomeccanico per gli operatori sanitari: strumento di valutazione e prevenzione | Dr.ssa Silvia Lolli<br>Dr.Franco Lufrani<br>Dr.ssa Marcucci Marisa |
| 1 | 03/05/2018 | 03/05/2018 | La prevenzione del back pain: il mantenimento del benessere psico-fisico tramite lo stretching e l'arte del massaggio” | Dr.ssa Marisa Marcucci<br>Dr. Luciano Urbani |
| 1 | 10/05/2018 | 17/05/2018 | Lavorare in Team | Dr.ssa Anita Caruso |
| 2 | 14/06/2018 | 21/06/2018 | Lavorare in Team | Dr.ssa Anita Caruso |
| 1 | 14/05/2018 | 15/05/2018 | Gestione e semplificazione dei percorsi clinico-assistenziali presso IFO | Dr. Giuseppe Navanteri |
| 1 | 16/05/2018 | 16/05/2018 | “Corso teorico-pratico sulla gestione vie aeree: corso avanzato” | Dr.ssa Coccia Cecilia<br>Dr.ssa Silvia Lolli<br>Dr.ssa Lorella Pelagalli |
| 2 | 25/05/2018 | 25/05/2018 | Il rischio da sovraccarico biomeccanico per gli operatori sanitari: strumento di valutazione e prevenzione | Dr.ssa Silvia Lolli<br>Dr. Franco Lufrani<br>Dr.ssa Marcucci Marisa |
| 3 | 26/10/2018 | 26/10/0208 | Il rischio da sovraccarico biomeccanico per gli operatori sanitari: strumento di valutazione e prevenzione | Dr.ssa Silvia Lolli<br>Dr. Franco Lufrani<br>Dr.ssa Marcucci Marisa |
| 1 | 08/06/2018 | 08/06/2018 | La legge 24/2017. La responsabilità professionale degli esercenti la professione sanitaria. Aspetti normativi e assicurativi | Dr.ssa Allocca Eleonora<br>Dr.Burgio Massimo |
| 1 | 14/06/2018 | 14/06/2018 | Aggiornamenti in tema | Dr.ssa Marcucci Marisa |

| Edition | Date from | Date to | Title | Scientific Coordinator |
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| | | | rischio biologico in ambito ospedaliero | |
| 1 | 19/06/2018 | 19/06/2018 | Tabagismo e inquinamento ambientale | Dr.ssa Maria Papale |
| 2 | 05/07/2018 | 12/07/2018 | Comunicazione efficace: strategie per migliorare la relazione | Dr.ssa Anita Caruso |
| 1 | 13/09/2018 | 19/10/2018 | I Gruppi di tipo Balint | Dr.ssa Anita Caruso |
| 2 | 03/10/2018 | 03/10/2018 | La prevenzione del back pain: il mantenimento del benessere psico-fisico tramite lo stretching e l'arte del massaggio | Dr.ssa Marisa Marcucci<br>Dr. Luciano Urbani |
| 1 | 05/10/2018 | 05/10/2018 | Il paziente pneumologico e la gestione della patologia respiratoria nei pazienti oncologici | Dr.ssa Maria Papale |
| 1 | 08/10/2018 | 08/10/2018 | Ruolo e finalità dei Comitati Unici di Garanzia nella Sanità | Dr.ssa Appetecchia Marialuisa |
| 3 | 11/10/2018 | 18/10/2018 | Lavorare in Team | Dr.ssa Anita Caruso |
| 1 | 17/10/2018 | 17/10/2018 | Il sistema qualità e la gestione del rischio clinico | Dr.ssa De Luca Assunta<br>Dr.ssa Adriana Concetta Pignatelli |
| 1 | 18/10/2018 | 18/10/2018 | La prevenzione e la gestione delle infezioni | Dr Toma Luigi |
| 2 | 23/10/2018 | 23/10/2018 | Corso Base Vie Aeree | Dr.ssa Cecilia Coccia<br>Dr.ssa Silvia Lolli<br>Dr.ssa Maria Sofra |
| 2 | 09/11/2018 | 09/11/2018 | Aggiornamenti in tema rischio biologico in ambito ospedaliero | Dr.ssa Marcucci Marisa |
| 2 | 14/11/2018 | 14/11/2018 | "Corso teorico-pratico sulla gestione vie aeree: corso avanzato" | Dr.ssa Coccia Cecilia<br>Dr.ssa Silvia Lolli<br>Dr.ssa Lorella Pelagalli |
| 1 | 14/11/2018 | 14/11/2018 | La medicina di genere in oncologia | Dr.ssa Appetecchia Marialuisa |
| 1 | 22/11/2018 | 22/11/2018 | Le raccomandazioni ministeriali 7,11,17: pratiche sicure al servizio dei pazienti e degli operatori | Dr. ssa Vujovic Branka |
| 1 | 27/11/2018 | 27/11/2018 | Sistema qualità e rischio clinico: programma di audit su processi di cura e assistenza nei reparti e servizi degli IFO | Dr.ssa De Luca Assunta<br>Dr.ssa Adriana Concetta Pignatelli |

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| | 30/11/2018 | 30/11/2018 | Trattamento delle metastasi epatiche | Dr Grazi Gian Luca |
| 1 | 03/12/2018 | 03/12/2018 | La donazione degli organi e dei tessuti. Fare team in ambito oncologico | Dr.ssa Stigliano Carmela |
| 2 | 03/12/2018 | 03/12/2018 | Sistema qualità e rischio clinico: programma di audit su processi di cura e assistenza nei reparti e servizi degli IFO | Dr.ssa De Luca Assunta<br>Dr.ssa Adriana Concetta Pignatelli |
| 3 | 04/12/2018 | 04/12/2018 | Sistema qualità e rischio clinico: programma di audit su processi di cura e assistenza nei reparti e servizi degli IFO | Dr.ssa De Luca Assunta<br>Dr.ssa Adriana Concetta Pignatelli |
| 2 | 05/12/2018 | 05/12/2018 | Il sistema qualità e la gestione del rischio clinico | Dr.ssa De Luca Assunta<br>Dr.ssa Adriana Concetta Pignatelli |
| 3 | 06/12/2018 | 13/12/2018 | Comunicazione efficace: strategie per migliorare la relazione | Dr.ssa Anita Caruso |
| 1 | 06/12/2018 | 07/12/2018 | Metodologie di progettazione implementazione e verifica degli studi clinici con radiofarmaci | Dr.ssa Rosa Sciuto |
| 1 | 07/12/2018 | 17/12/2018 | Processi e metodi per organizzare al meglio le attività nei servizi di segreteria | Dr.ssa Lavalle Tiziana |
| 2 | 10/12/2018 | 10/12/2018 | Le raccomandazioni ministeriali 7,11,17: pratiche sicure al servizio dei pazienti e degli operatori | Dr. ssa Vujovic Branka |
| 3 | 12/12/2018 | 12/12/2018 | Il sistema qualità e la gestione del rischio clinico | Dr.ssa De Luca Assunta<br>Dr.ssa Adriana Concetta Pignatelli |
| 2 | 12/12/2018 | 12/12/2018 | La donazione degli organi e dei tessuti. Fare team in ambito oncologico | Dr.ssa Stigliano Carmela |
| 3 | 14/12/2018 | 14/12/2018 | Aggiornamenti in tema rischio biologico in ambito ospedaliero | Dr.ssa Marcucci Marisa |

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# ISTITUTO NAZIONALE TUMORI REGINA ELENA

Via Elio Chianesi, 53
00144 Roma
www.ifo.it

Scientific Direction
E-mail: dirscire@ifo.gov.it
Tel. +39 06 52662728 Fax +39 06 52665523