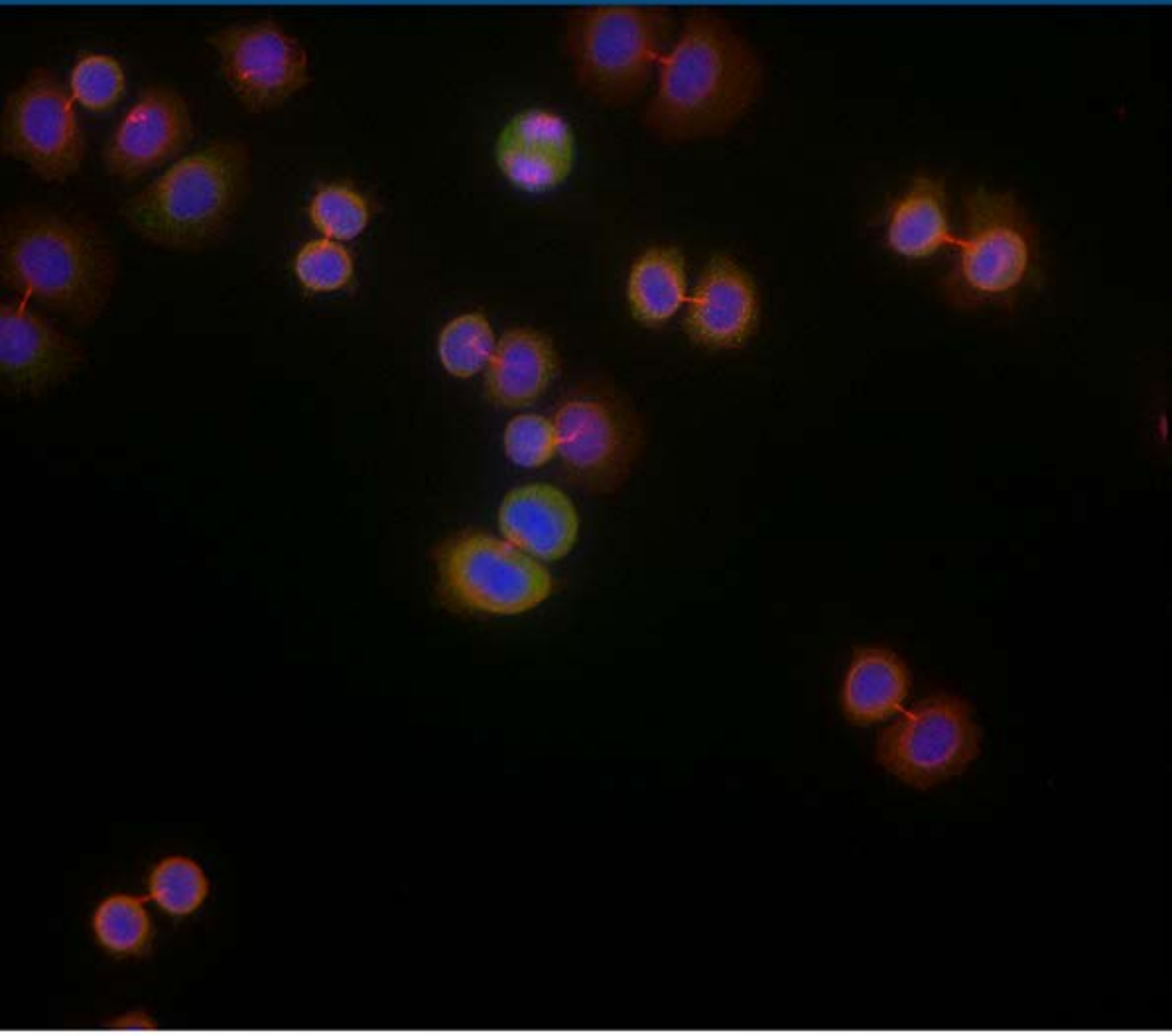
IRE

ISTITUTO NAZIONALE TUMORI

REGINA ELENA

ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO



Scientific Report 2017

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CEO MESSAGE

Dear Readers,

2017 was my first year as head of this general direction at IFO, which includes overseeing two Scientific Institutes of Hospitalization and Care (IRCCS), the Regina Elena National Cancer Institute and the San Gallicano Dermatological Institute. The 5-year term will allow me to plan and accomplish ambitious goals.

This year we have worked towards building a firm foundation for activities that will propel us towards a brighter future. Some significant dates and events in 2017 include: reconfirmation of our status as an IRCCS by the Ministry of Health allowing to obtain funding for research, and the approval of Lazio Region to an increase in expenditure compared to what had already been agreed on for the year. These two events brought with it the implementation of important scientific technology for research, diagnosis and treatment. In August 2017, we inaugurated the Cyberknife in the presence of the President of the Italian Republic Sergio Mattarella, and the President of the Lazio Region, Nicola Zingaretti. Immediately afterwards, we presented the project and related investments for the construction of the first public proton therapy unit in central Italy. Another goal included the definition of the 2018-2020 strategic plan, a demanding task carried out together with dynamic and constant exchanges with the strategic management team and the medical management. After carrying out a careful and thorough analysis and coming out better and stronger from these experiences, we are now more than ever ready to work towards making significant progress.

The strategic plan includes three lines of development focusing mainly on innovation that will aid us to face current and future challenges.

These include: research, then working on our position within the regional, national and international health system, as well as developing a productive service system. Along with these, there are two crucial aspects to consider, on the one hand is identity, which is made up of our Institute's history, professionalism, skills, traditions and values and on the other is economic sustainability aimed at generating and managing resources for growth.

The path to developing the strategic plan started with identifying the Institute's identity: two institutes traditionally referring centres for their respective specializations (oncology and dermatology) for the city, the territory and other national and international treatment centers. There are various synergies and possible integrations for the benefit of research and clinical settings. In fact, our Institute is the only center in Italy where 2 high-tech companies coexist. It is made up of the ISG, the only public dermatological center and referring centre for the research and training of all Italian dermatologists and the IRE, a referring centre for oncology, especially in the central-southern area of Italy. Our Institute does not only develop diagnostic and clinical strategies but also avant-garde management models (quality, data management, information systems, etc.).

The first line of development is Research: we aim to become increasingly competitive with international institutes, especially on topics related to omics, precision medicine and immunotherapies. We also strive to increase collaboration efforts and agreement contracts with universities and private industries in order to become of innovation. We aim to strengthen translational research, through the reorganization of the clinical trial center and the development of phase 1, as well as biobanks. The research work agenda is very rich and articulate and well-rounded.

The second line of development is Positioning: we seek to become a regional and national hub for low-prevalence and complex diseases. We promote to build networks for clinical collaborations all over the territory and on an international level in order to spread innovation and good clinical practices, as well as for "patient oriented" organizational models.

The third line of development concerns the consolidation of the integrated organizational model centered on taking care of the patient, in order to make IFO more efficient and innovative in its production status: which entails more research, more clinical assistance and an excellent economy scale.

Finally, we are committed to feedback and partnerships for future investments in the patient-centered technology.

SCIENTIFIC DIRECTOR MESSAGE

Dear Readers,

I am delighted to present you the 2017 Research report of the IRCCS Istituto Nazionale Tumori "Regina Elena" of Rome.

During the last year, the Istituti Fisioterapici Ospitalieri (IFO) have undergone significant changes following the settlement of a new Strategic Directorate. The unrelenting efforts by the Director General, Dr. Francesco Ripa di Meana, the Medical Officer, Dr Branka Vujovic and the Administrative Director, Dr Laura Figorilli, towards the financial consolidation of IFO, have recently led to the rapid exit from the efficiency plan, which is an extraordinary result. I would like to express my personal thanks for their priceless collaborative support to the Scientific Directorate of the Istituto Regina Elena in the many initiatives carried out in the last year.

In 2017 Regina Elena's scientific productivity has grown having published almost 300 papers in international scientific journals and having achieved a normalized impact factor of more than 1.400 points, the highest ever reached during its history. The Institute is also constantly very active in experimental clinical trials with approximately 150 active clinical studies and thousands of patients involved. We expect to further expand these activities in the future thanks to the recent establishment of a centralized Clinical Trials Center and the forthcoming activation of the IFO Early Phase Study Center where it will be possible to conduct Phase I Clinical Trials.

In June last year, a significant internal decree came into effect regarding the establishment of a centralized Tumor Biobank where a series of samples and data are collected for research purposes. The Biobank is currently coordinated by both the Pathology and Clinical Pathology Units. Thousands of tumor samples and body fluids (mainly blood, serum and plasma samples) are being collected and stored centrally, ready for use in experimental studies directed to identify and validate new biomarkers.

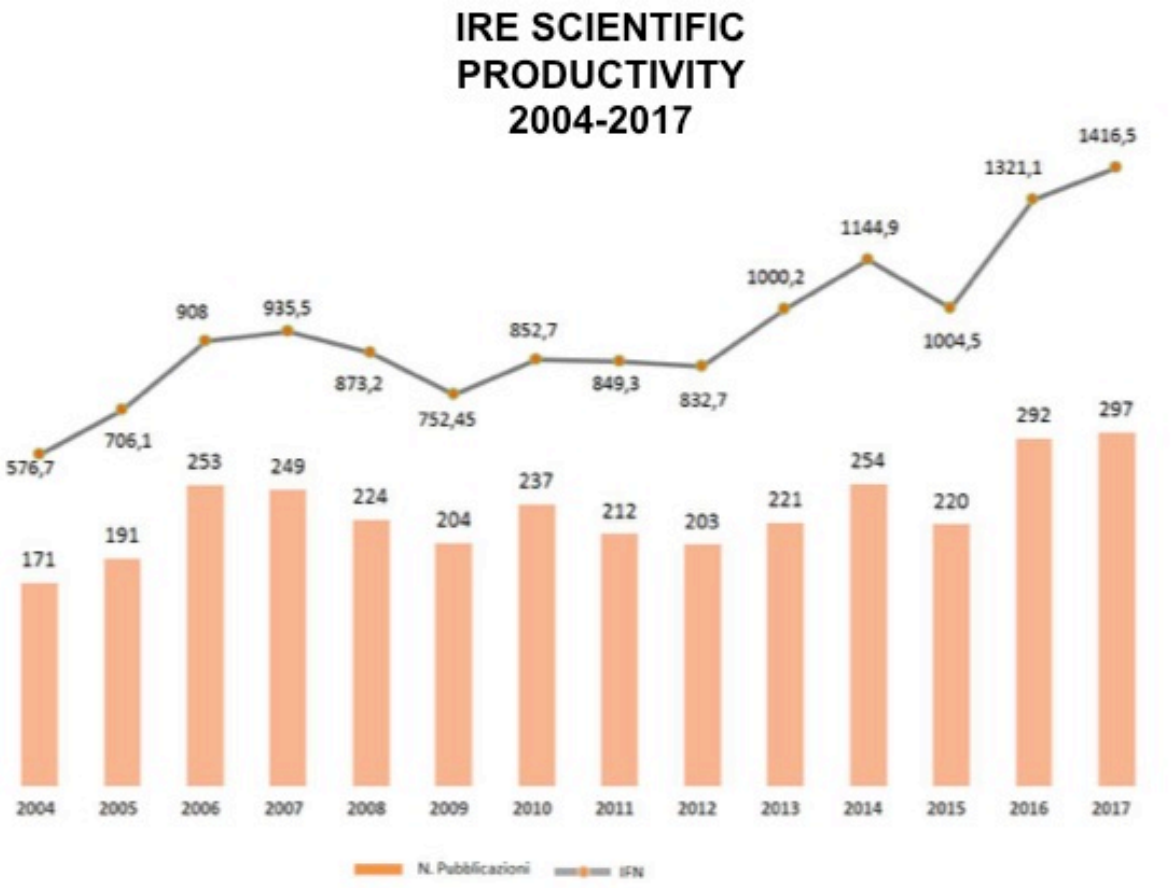
This is possible thanks to the active participation of our patients who donate their material as well as to several of our employees including, surgeons, radiologists, radiotherapists, medical oncologists and nurses.

The Institute maintains increasing action towards investing in technological resources. Last year, the robotic radio-surgery device called 'Cyberknife' was officially unveiled. This is the first machine of its kind in the center/southern Italy. In recognition of these accomplishments, the Presidente della Repubblica, Sergio Mattarella, and the Presidente of Lazio Region, Nicola Zingaretti visited IFO.

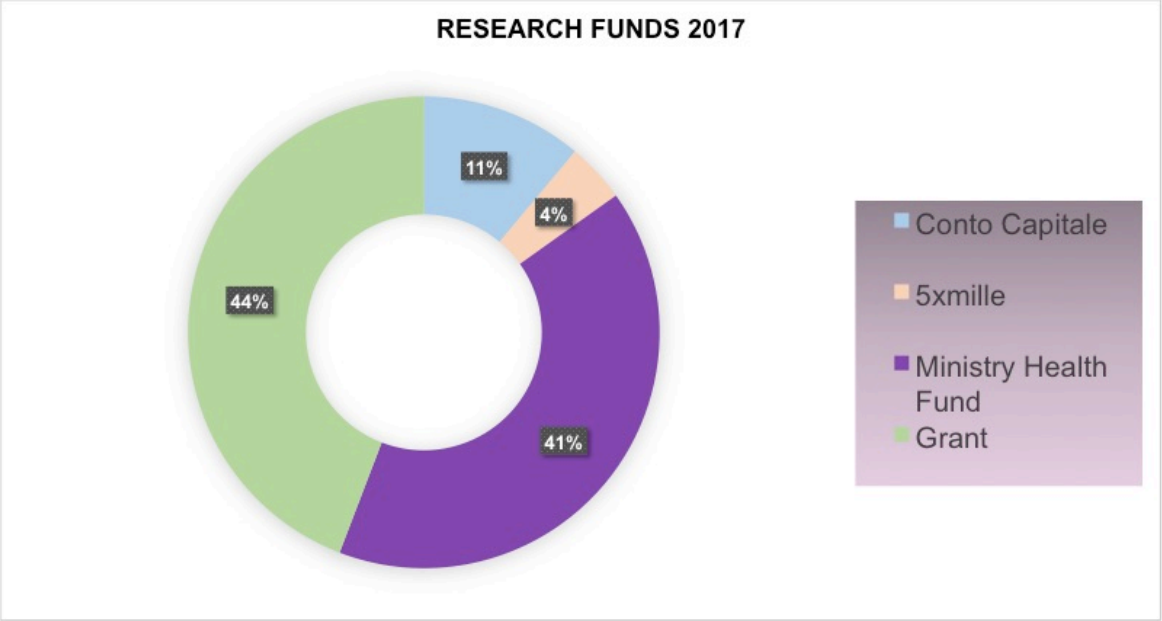
Moreover, thanks to the contribution in Conto Capitale by the Ministry of Health, the Institute was granted financial support in order to invest in a last generation cell sorter, of a single cell analyzer for image-based isolation of circulating cancer cells and their molecular analysis, of Confocal Laser Ultramicroscopy (pCLE) system. In addition, the Fondazione Roma also awarded us a grant which will allow the acquistion of a last generation last generation confocal microscope for the year 2018.

Last but not least, in 2017 the first translational research groups were created, i.e. multidisciplinary groups aiming to create synergies between basic researchers and clinicians on specific topics requiring focused efforts and leveraging our best skills and expertise. The translational groups that initiated their activities in 2017 include: the Genomics Group, the Rare Cancers Group and the Melanoma Group, a joint group with Istituto San Gallicano Dermatological Institute. These groups have been actively involved in the conception and practical implementation of new approaches for the personalized and precision treatment of cancer.

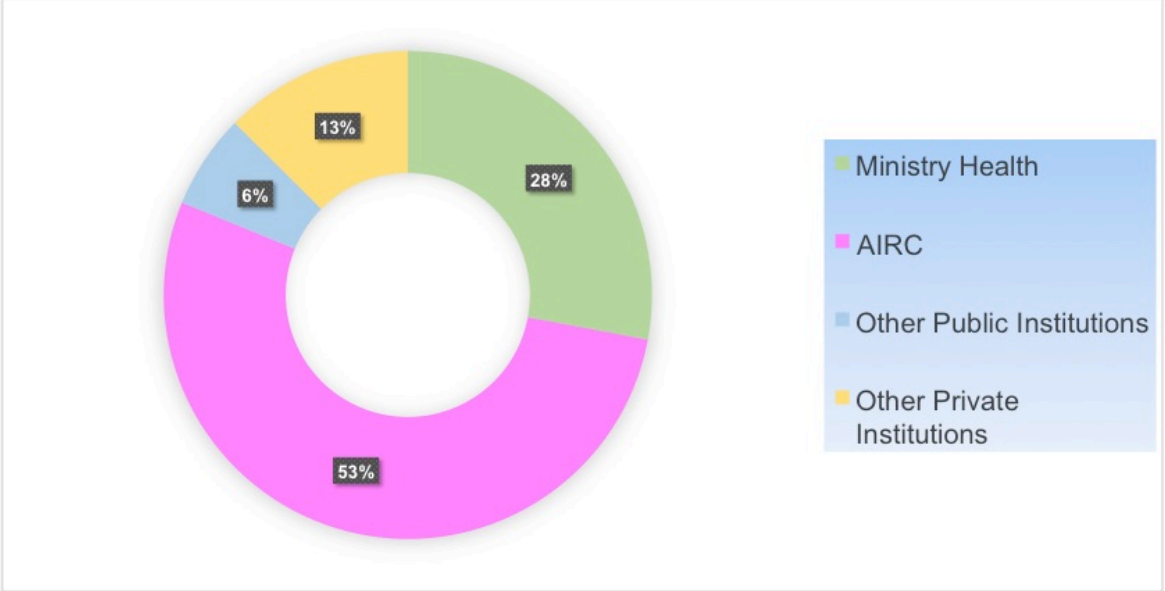
Finally but most importantly, I would like to close by thanking all the researchers for their daily contribution and commitment in making our Institute an outstanding example of translational research and innovation in cancer.



The figure shows the IF and number of scientific publications produced during 2004-2017. As shown in the graph, the total IF generated by IRE publications has constantly increased over the years, indicating IRE's continuous scientific improvement



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



Graph B - Details on grant source funding

CONTROL AND VERIFICATION BOARD

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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President

Prof. Paolo Marchetti

Members

Prof. Angela Santoni

Dr. Roberto Scrivo

Prof. Maria Rosaria Torrisi

PRESS OFFICE

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 2017	35
Agency launches 2017	147
Mass media presences 2017	1210
News items 2017	130
Facebook	710 post; 2.5 million views
Youtube	378.000 views; 1.081.000 minutes watched
Twitter	1086 tweet; 611 mentions; 2185 retweets
Instagram	opened on August 4th; 115 post; 25.000 views

HERE ARE SOME OF THE PUBLIC COMMUNICATION CAMPAIGNS, WEB PROJECTS OF 2017

- World Cancer Day campaign for promotion public awareness. *February 2017*
- 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 2017*
- Press conference presenting the surgical robot Cyberknife in the presence of the President of the Republic Sergio Mattarella. *July 2017*
- Campaign for the European Researchers' Night : to bring researchers closer to the general public and to increase awareness of research and innovation activities. *September 2017*
- OncoLine (Repubblica.it) blogs: Yoga & Pagaie" and "Insieme più belle".

Ethics Committee

As from December 2017

Chairman
Prof. Francesco D'Agostino
Expert in Bioethics

Vice Chairman
Prof. Agata Amato Mangiameli
Expert in Legal Matters

Secreterary
Anna D'Ambrosio

Technical-Scientific Secretariat
Diana Giannarelli
Barbara Matrascia

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 (ad interim): Dott.Mauro Picardo
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 Committee 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 2017 the Central Ethics Committee IRCCS Lazio examined and expressed its opinion on 152 studies including clinical trial protocols, observational studies and research projects, 153 substantial amendments, 19 therapeutic use.

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.

ADMINISTRATIVE DIRECTION

Head: Dr. Laura Figorilli

Staff

Nicoletta Avitabile

Paola Cocuzza

Mission

The Administration Office manages and coordinates the administrative activities within the Institute, as well as considering the functional independence of the departmental units (UOC). Furthermore, it has 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 Administration Officer works closely with the General Director in the administrative, financial and organizational management of the Institute and ensures that all necessary administrative interventions are in place to carry out the activities of all the structures within the Institute. It also has the responsibility to ensure that all administrative activities are run efficiently and are transparent. 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 is in charge of all the technical/ administrative activities supporting the health care services and the Scientific Directions as far as research is concerned.

The Administration Officer:

- as a member of the Strategic Management, it 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, 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 Office of Research Administration provides administrative support to the Scientific Directorates and researchers of the Regina Elena National Cancer Institute and the San Gallicano Dermatological 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 (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 2017 the Research Administration Office dealt with managing the administrative and economical aspects of public and privately research projects funded by the Regina Elena National Cancer Institute (IRE).

The Research Administration Office (SAR) handled the administrative and accounting procedures of all expenses concerning Ricerca Corrente 2017 funding (€3.534,201.08) for IRE and prepared the economic report for Ricerca Corrente 2016 funding (€ 1,074,518.11).

36 decrees were drawn to accept funding destined for research projects, where IFO is the leading partner. This Office handles all relations between both the lenders and the External Operating Units involved in these projects. In the case of the External Operating Units, 6 Memoranda of Understanding were signed between 4 different units.

The SAR Office managed 3 projects as an external Operating Unit.

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 2017 were prepared to concede the loans in the Conto Capitale 2014-2015, seeing the SAR Office assisting the Scientific Directorates with gathering the appropriate documentation to provide the Ministry of Health.

The SAR office also signed the provision of 23 onerous agreements (within the scope of approved projects) and 12 free of charge licence agreements. During 2017, the SAR Office continued to manage projects from previous years, handled more than 170 projects and supported 12 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.

The employment collaboration sector saw a major change in the recruitment legislative framework;

In fact, from the Jobs Act of 2017 Budget Law, numerous legislations profoundly innovated and modified the types of contracts given: D. Legislative Decree no. 81 (Jobs Act) of 15/06/2015 Art. 2 paragraph 4; D. Law no. 244 (Mille Proroghe) of 25/05/2017; D. Legislative Decree no. 75/2017 (Madia Law) in force since 22/06/2017 Art.5 and Art. 22 Paragraph 8; Law no. 205 of 27 December 2017, the State budget.

Having said this, activating and subsequently managing employment relationships was accomplished by:

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).

In summary: during the year 2017, the following decrees were activated: 201 decrees for Co.Co.Co contracts (76 with public calls, 113 extensions and 12 direct conferrals); 22 other types of work relationships; 23 scholarships; 16 withdrawals; 7 requests for maternity leave and return.

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 2017, 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 2017, the SAR office activated 77 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 68 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.

GENERAL IFO MEDICAL OFFICE

Dr. Branka Vujovic

I was appointed as IFO's Chief Medical Officer in March 2017 (Del.125 22/02/2017). I am a member of the the Governing Board along with the General Director Francesco Ripa di Meana, the Administrative Director Dr. Laura Figorill as well as the Scientific Directors of the IRE and the ISG, Prof. Gennaro Ciliberto and Dr. Aldo Morrone, respectively. I have gained experience as Chief Medical Officer in university and regional hospitals. In fact, one of the Governing Board's strategic directions is to work in synergy in order to face and explore the Efficiency Plan (Del 96 and 217/2017) on the one hand, and on the other to develop a strategic plan for the future.

The Regina Elena National Cancer Institute is a Comprehensive Cancer Centre based on an operating model that covers:

- global patient-centered care
- multi-professional and interdisciplinary approach
- integration between clinical area and basic research area

To achieve the above-mentioned purposes, the following objectives are to be reached:

Clinical pathways able to implement the management and temporal planning of all patient care interventions, coordinate and complement the chain of interventions (diagnostic, therapeutic, nutritional, educational, safety, security, discharge planning, pre-hospitalisation screening, counselling), in accordance with the national and regional guidelines. IFO is a member of the Lazio Oncological Net and actively participates in the definition of clinical pathways (PTDA).

Disease Management Team – DMT, allows to implement an integrated approach to care where different specialties come together with the aim to overcome fragmented patients care processes and the search for appropriateness of treatments, on the basis of the principles of Evidence Based Medicine.

Translational Research Interest Groups – TRIG, consists of clinicians, epidemiologists and basic researchers to support translational research across different disciplines (oncology, infectious diseases, dermatology) in order to develop efficient pathways for transferring bio-medical research results into clinical practice.

Reference Centre for Rare Tumours – The Regina Elena National Cancer Institute is part of the European project EURACAN, which deals with diagnosis, treatment and research on rare solid tumours of adults and rare diseases such as adenomatous polyposis.

The main IFO objective is to pursue the dictates of the Mission in compliance with the National Regional indications (National Health Plan), guaranteeing the efficiency in the use of resources through a process aimed at continuous improvement in terms of productivity levels for the resources employed and a level of research and assistance increasingly adequate, in terms of quality as well as in terms of appropriateness, trying to align production values with management costs.

At the managerial level, the institutes have as a constant point of reference the need to combine health and research objectives with the available resources in order to make the system sustainable, also from the economic point of view.

In 2017, the Company identified a set of areas of significant results with reference to its mission, dividing each of them into operational research and clinical objectives, assigned to the individual Centres of Responsibility through the budgeting process.

In line with this logical path, the planning of clinical and healthcare activities was based on a modulation of healthcare supply, in line with national and regional indications, which followed criteria of appropriateness and encouraged "virtuous" organizational models with regard to both personal care and the rationalization of resources.

Pharmacovigilance

Staff

Felice Musicco, Pharmacist (Responsible)

Elisabetta Umana, 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

Clinical Activities

• Number of ADR reports registered in RNF: 149

• Drug safety information to doctors: highlight and internal transmission of alerts published by regulatory agencies (EMA, AIFA)

• Hospital reports, guidelines, procedures:

- Report of suspected adverse drug reactions at "Istituti Fisioterapici Ospitalieri" in 2015-2016.
- Updated procedures to report ADR to drugs published on the hospital website
- Participation in OECI certification activities

Research Activities

• Number of ADR reports registered in RNF from observational studies: 14

• Hospital reports and guidelines:

- Draft of Internal Procedures to report adverse drug reactions in clinical trials.

Publications

Scala D, Parazza S, Di Tommaso R, Dusi G, Musicco F, Tarantino D. Attività di informazione scientifica per i professionisti della salute e di educazione sanitaria per i cittadini/pazienti Bollettino SIFO. 2016;62(3):138-144.

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; bibliographic 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. Generates the yearly report of research productivity (publications) to the Ministry of Health (Research Workflow)

Technology Transfer Office (TTO)

The Technology Transfer Office (TTO) operates within the Scientific Directorates and cooperates with the IFO Patent Commission established by resolution no. 725 of 01.08.2016.

The TTO brings together the researchers' inventive proposals, promotes their protection and technology transfer to businesses.

To this end, it assists and supports researchers in the management of intellectual property, from the start of the patenting process to the commercialisation of the patent.

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).

Clinical Trial Center - CTC

The Clinical Trial Center (CTC) is an organizational procedure that centralizes and unifies the coordination and monitoring of clinical trials, with the aim of providing management and methodological services to researchers, also promoting collaboration between them. In support of the activities of the CTC. CTC also provides an incentive for private investment, which favours those institutions within which a structure is active that can support, transversally to the internal operating units, the entire clinical trial process (phase I, II, III, IV studies).

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

Publication

Ascierto PA, Agarwala SS, Ciliberto G, Demaria S, Dummer R, Duong CPM, Ferrone S, Formenti SC, Garbe C, Halaban R, Khleif S, Luke JJ, Mir LM, Overwijk WW, Postow M, Puzanov I, Sondel P, Taube JM, Thor Straten P, Stroncek DF, Wargo JA, Zarour H, Thurin M. Future perspectives in melanoma research "melanoma bridge", Napoli, november 30th-3rd december 2016. J Transl Med 2017;15(1):236-017-1341-2. **IF 3.786**

Augustin LS, Libra M, Crispo A, Grimaldi M, De Laurentiis M, Rinaldo M, D'Aiuto M, Catalano F, Banna G, Ferrau' F, Rossello R, Serraino D, Bidoli E, Massarut S, Thomas G, Gatti D, Cavalcanti E, Pinto M, Riccardi G, Vidgen E, Kendall CW, Jenkins DJ, Ciliberto G, Montella M. Low glycemic index diet, exercise and vitamin D to reduce breast cancer recurrence (DEDiCa): Design of a clinical trial. BMC Cancer 2017;17(1):69 **IF 3.288.**

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LIBRARY

Staff

Gaetana Cognetti, Senior Staff Librarian – Digital Library Knowledge center "R.Maceratini"

Fabio D'Orsogna, Graduated Specialized Librarian (until june 2017)

Francesca Servoli, Graduated Specialized Librarian

Domenico Verbicaro, Administrative Staff

Virginia Scarinci, fellow (from november 2017)

Emanuela Dimiziani, Senior Staff Librarian

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 to institutional processes of computerisation 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 (health information literacy).
- The Library supports the institutional clinical staff offering: consultation of the main biomedical databases; document delivery through interlibrary exchange system, NILDE (in 2017 total borrowing 403, total lending 187); organisation of training courses; the librarian staff offers also support the bibliographic searches, systematic reviews and meta-analyses. The main activities of the library consist of management of monographs, periodicals following international standards and guidelines; updating of union catalogues; managing reference desk also through the personalized service Book a librarian, tailored courses on demand by the users (43 meetings in 2017). In 2017, thanks also to the Bibliosan Network, the Library subscribed electronic resources: thousands of on line journals, databases as Scopus, Web of Science, Journal Citation Reports, BMJ BestPractice, Cochrane Library, Faculty 1000, Cinahl, etc.
- 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. In 2017, 102 patients and family members asked for information (42 tailored search using Internet portals and websites and about 205 information booklets delivered).
- Inventory and accommodation of the library's paper heritage.

Research Activities – Digital Library

The Library is involved in various research and educational activities and participates in libraries networks. The Library collaborated to a project about health information literacy in old age population promoted by the Pescara AUSL. The results of the survey will be published in 2018. 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 (21,8 credits each course), the participants were about 100 (interactive teaching - maximum 25 participants each course), as well as being made available, through Bibliosan, 15 BMJ Online CME courses (75 credits).

The Library has organized also courses concerning Bibliosan's resources and for students (La Sapienza University/IFO Nursing School). The library staff is involved in the teaching and tutorship of the most courses organized on site and participated as lecturer in a distance-learning courses: Disease management in Sanità Digitale (CME) and Scientific documentation (CME).

In 2017 the Library coordinated the OECI Improvement Plan on patient involvement and empowerment, concerning humanization of the care, communication and information and produced a census and a leaflet of the activities and services for patients offered by associations and institutional units inside the Institute.

The Library collaborated also in 2017 with the narrative medicine project "Raccontami di te". 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 Catalogue of Periodicals (ACNP) for the cataloguing and management on the web of the periodicals;
4. Library Network of Biomedical Research Institutes (Bibliosan);

Pubblication

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JOURNAL OF EXPERIMENTAL & CLINICAL CANCER RESEARCH

Editor-in-Chief: Mauro Castelli, PhD

Staff

Gabriella D'Orazi, MD, PhD, Deputy Editor

Alice Castelli, PhD, Managing Editor

Journal of Experimental & Clinical Cancer Research (JECCR), the official scientific journal of the "Regina Elena" National Cancer Institute since 1986, has proceeded its editorial activity maintaining its partnership with the Publisher BioMed Central in London. Starting from 2008 the journal became "open access" (OA), meaning online rapid publication of the articles (instead of print version), that in this way receive higher visibility in the scientific community with consequent increase of the Citation Ranking. Actually JECCR is ranked 48/211 journals in subject category Oncology (ISI Web Os Science – WOS).

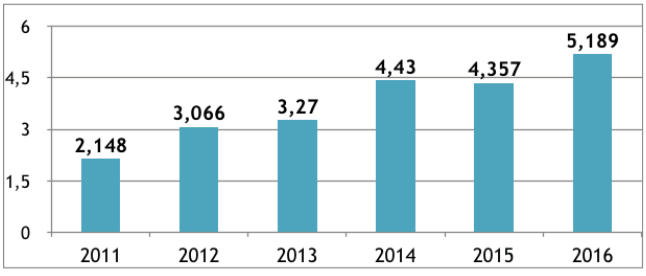
The journal publishes scientific studies on the experimental and clinical aspects of cancer research. Topics covered by the journal range from molecular oncology to tumor-microenvironment interaction and include new technologies (RNA-seq, oncogenomics, etc) for diagnostic and prognostic purpose.

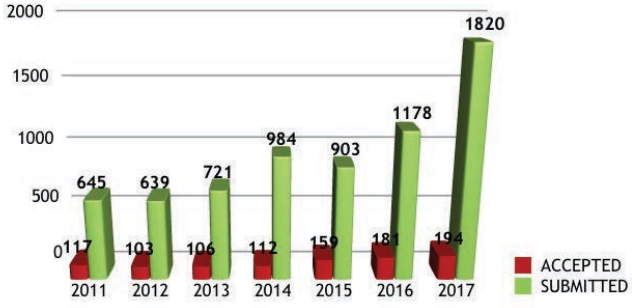
The main accomplishments achieved by JECCR in 2017 years are:

- Impact Factor: 5.189
- Ranking in the 1st quartile among International Oncology Journals
- Over 1800 articles submitted
- Over 190 articles published in 2017 (Research articles 174, Reviews 12)
- In 2017 JECCR started to publish Meeting Report and Commentary publications
- Over 100.000 article accesses (online) each month
- Articles submissions increased in the last 5 years of about 30%.

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/





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.

NETWORK

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 better space in which the flow of information between basic research and clinical observations is bi-directional.

NETWORK

OECI

The "Organisation of European Cancer Institutes" is a non-governmental, 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.

NETWORK

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.

EORTC

European Organization for Research and Treatment of Cancer

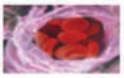
Is an independent, non-profit cancer research organisation, its mission is to coordinate and conduct international translational and clinical research to improve the standard of cancer treatment for patients.

Translational Group

BIOBANK - BBIRE

Tumor Tissue Biobank IRE

DEPARTMENT	PATHOLOGY	PATIENTS	SAMPLE PRESERVATION MODE					
			TUMOR TISSUE CRYOPRESERVATION	NOT TUMOR TISSUE CRYOPRESERVATION	TUMOR TISSUE OCT	NOT TUMOR TISSUE OCT	FFPE	TOTAL
ORTHOPEDIC SURGERY	Sarcoma	24	286	64	23	4	24	401
THORACIC SURGERY	Adenocarcinoma	72	586	411	50	30	72	1149
	Thymoma	14	114	33	5	5	13	170
	Pleural Effusion	31						
	Lymphoma	4	14	0	1	0	4	19
MEDICAL ONCOLOGY 2	Brest Cancer	30	198	94	17	9	30	348
MEDICAL ONCOLOGY 1/2	Melanoma	1	8	4	0	0	1	13
NEURONCOLOGY	Brain cancer	8	31	1	1	0	6	39
GYNECOLOGICAL SURGERY	Endometrial Carcinoma	21	140	21	11	1	17	190
	Ovary Carcinoma + Peritoneal washing	19	299	50	15	2	18	384
	Ovary Carcinoma	12	134	18	7	1	13	173
	Uterine Cervix Carcinoma	2	9	10	1	0	2	22
	Uterine Carcinoma	12	124	60	9	2	12	207
	Carcinosarcoma	5	68	4	10	1	5	88
	Peritoneal Washing	6						
UROLOGY SURGERY	Renal Cancer	41	332	134	26	10	41	543
	Bladder Cancer	24	232	78	15	8	22	355
	Retroperitoneal Sarcoma	1	50	0	1	0	1	52
HEPATOBILIARY SURGERY	Colon cancer	27	193	129	20	14	27	383
	Stomach cancer	5	22	18	2	3	5	50
	Liver cancer	2	14	14	0	0	2	30
	Pancreas cancer	12	79	27	9	2	12	129
	Gist	1	8	0	1	0	1	10
	Metastasis (Colon/ Ovary)	3	20	4	2	0	3	29
	Retroperitoneal Sarcoma	2	36	16	2	1	2	57
	Cholangiocarcinoma	1	4	10	0	0	1	15
	Biliary tract cancer	1	0	0	1	1	1	3
ORL	Parotid cancer	1	0	0	1	0	1	2
OTHERS	Metastasis (melanoma)	6	34	8	5	0	6	53

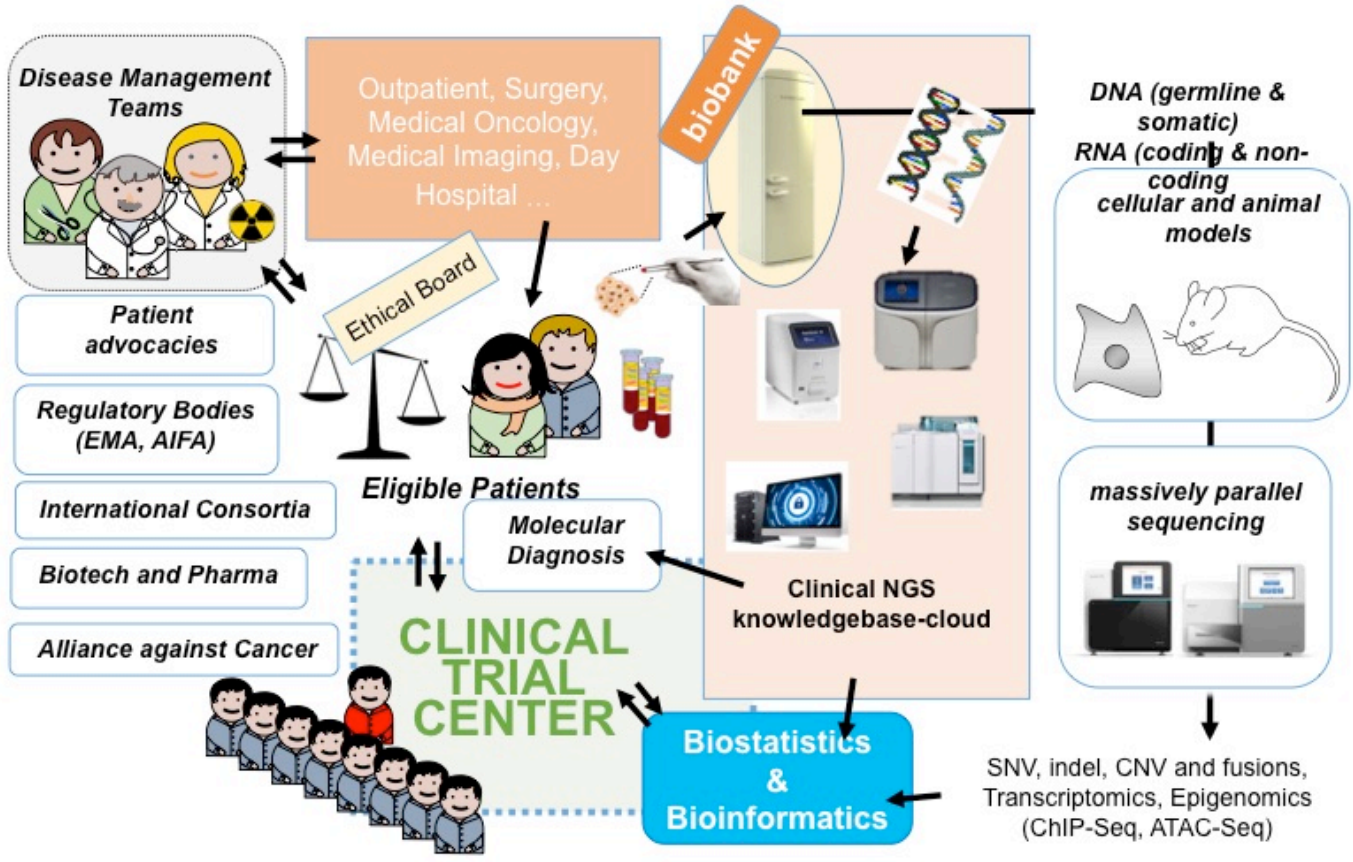


Body Fluids Biobank IRE

Sample Collection (March 2015 - September 2018)

Department	Pathology	Patients	Withdrawals	Sample Aliquot ~ 500µL				2mL*	1mL	Total
				Whole Blood	Plasma EDTA	Plasma Citrate	Serum	Plasma EDTA	PBMC	
Orthopedic Surgery	Sarcoma	389	920	1830	6090	987	3795	1090	-	13792
Thoracic Surgery	Lung cancer	138	138	276	757	-	534	266	-	1833
Thoracic Surgery	Thymoma	40	41	82	301	19	165	37	-	604
Medical Oncology 2	Breast cancer	65	67	133	334	186	448	10	3	1114
Medical Oncology 1/2	Melanoma	14	32	62	195	3	140	60	-	460
Radiotherapy	prostate/ oropharynx/ breast ca.	104	240	480	1765	-	1131	477	-	3853
BTO	Various	51	51	102	394	150	238	70	-	954
Medical Oncology 1	Lung cancer (ACC LUNG)	14	28	83	-	-	-	183	48	314
Neuroncology/ NCH surgery	Brain cancer	22 47	22 48	44 96	124 282	60	95 191	40 96	-	363 665
Endocrinology	Medullary thyroid ca.	16	16	32	4	-	-	30	-	66
Gastroenterology	Hereditary colon cancer	40	40	80	51	-	-	78	-	209

GENOMICS



This is a translational, inter-department, multidisciplinary, collaborative group that has been recently set up and endorsed under the authority of the IRE Scientific Direction. The Genomics Workgroup is meant to act as an incubator for ideas and technologies. Its aim is to expedite the systematic application of methods for nucleic acid analysis, including Next Generation Sequencing (NGS), Nanostring, and digital PCR (dPCR), to institutional programs with a strong clinical-translational impetus and practice-changing potential. The group embeds diverse areas of expertise, from routine molecular diagnosis to basic research.

It includes Surgeons, Pathologists and Clinical Pathologists, Medical Oncologists, Radiation Therapists, Medical Imaging experts, Geneticists, Molecular Biologists, Biotechnologists, Bioinformaticians and Biostatisticians. Staff Members from our BioBank (tissue and body fluids sections) provide input and criticism. The group meets monthly for update and discussion. Attention is paid to major Medline breakthroughs, theory advancements, and the biotech world altogether. Intramural programs and new ideas are extensively reviewed and collegially discussed.

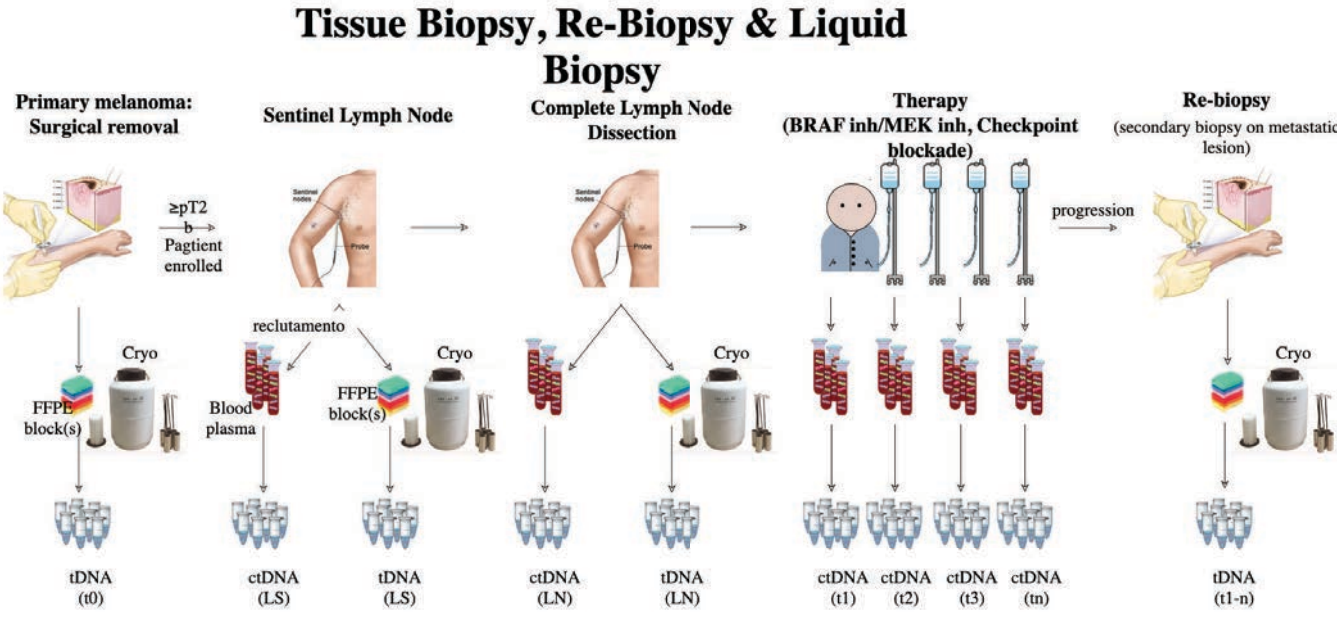
Leveraging on the power of clinical NGS, two important goals have been achieved in 2017. On the one hand we have filed 369 molecular diagnostic reports on germline DNA (heredofamilial cancer), and >1800 on tumor tissue DNA (somatic aberrations), providing our clinical departments with advanced, state-of-art options for cancer prevention, diagnosis, and therapy. On the other hand, we have considerably enhanced and streamlined our bioinformatic pipeline with the acquisition of an NGS-dedicated Cluster Biocomputing server. This provides computational power and seamless knowledgebase searching abilities, including the possibility to match actionable mutations with ongoing clinical trials. Semi-automatic reporting and intranet-accessible, anonymized cloud storage optimize molecular diagnosis and personnel labor, foster cross-cutting communication among the clinics and the labs, and rule out many potential sources of human error.

Moreover, for research purposes we have adopted targeted DNA and RNA sequencing, as well as Whole Exome Sequencing and other innovative genomic platforms to identify somatic or germline mutations (SNV), copy number variations (CNV), small insertions/deletions, and gene fusions.

The combination with other molecular markers and clinical data enables us to discover biomarkers which will ultimately improve prediction of survival and response to therapy. Transcriptomic and epigenomic approaches are routinely applied to investigate

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-biopises and blood samples (liquid biopsies) collected longitudinally from melanoma patients throughout their disease history, 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.



NON-CODING-RNA (NCR)

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) (Figure 1A).

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.

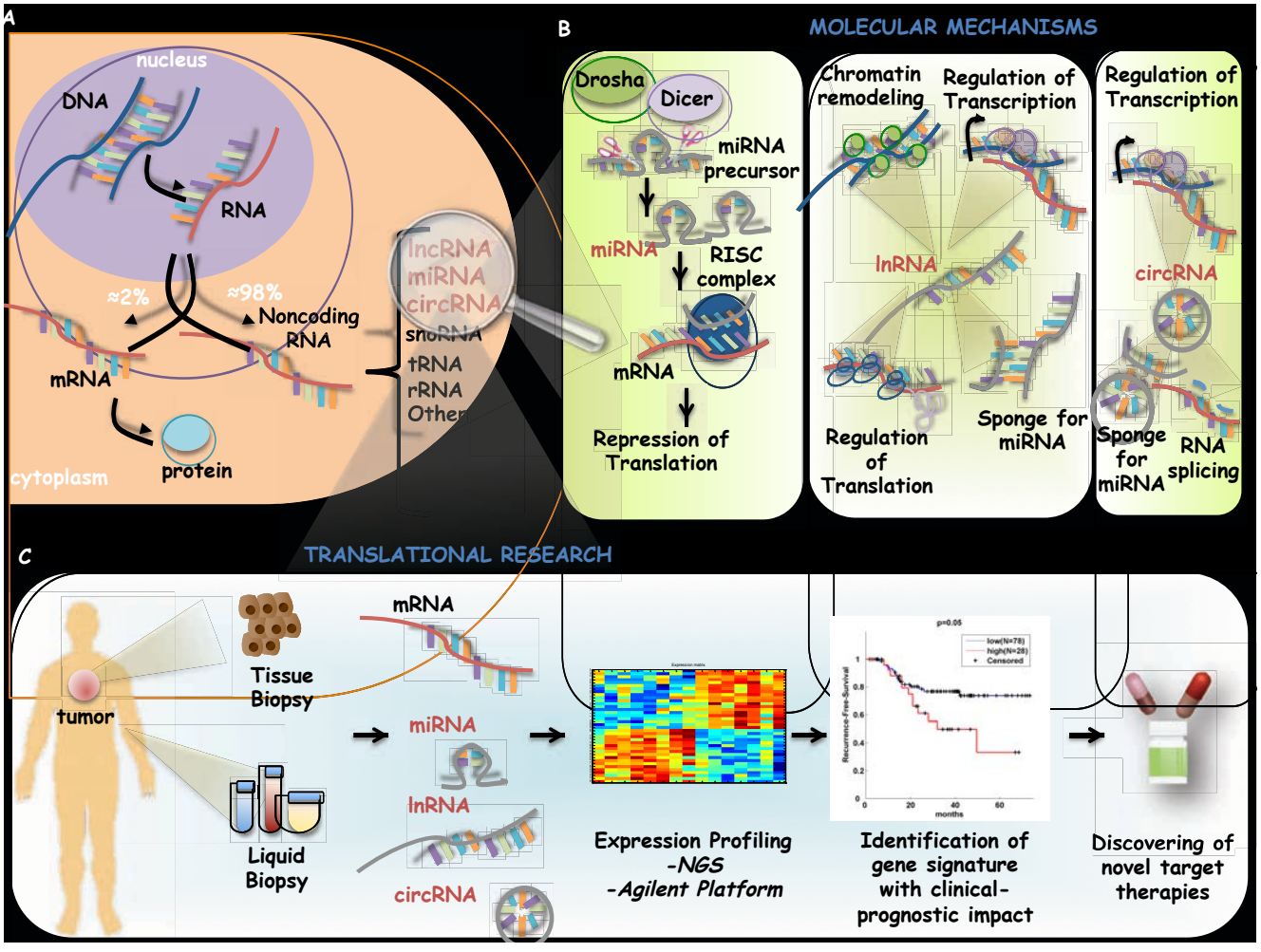
The NCR group is mainly focused on three classes of ncRNA: microRNAs (miRNAs) long-non-coding RNAs (lncRNAs) and circular RNAs (circRNAs) (Figure 1A).

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 (Figure 1B).

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 (Figure 1B).

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 (Figure 1B).

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 (Figure 1B); b) the other one is based on translational research approaches (Figure 1C) 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.



RARE TUMORS

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 National Cancer Institute represents one recognized center for the diagnosis and treatment of rare solid tumors.

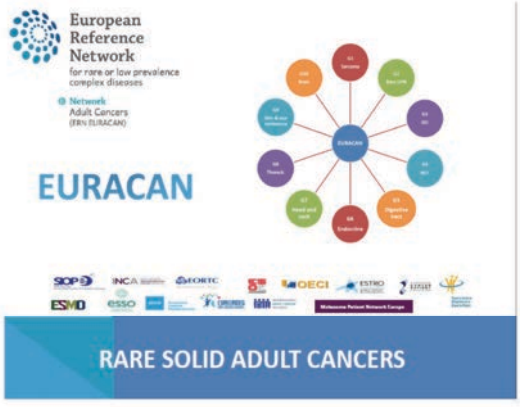
Over the past 10 years, IFO played an active role in the collaborative efforts of the national network on rare tumors (Rete Tumori Rari, RTR). Since 2016 IFO are involved in EURACAN (European network for Rare adult solid Cancer) and have become a European Referral Center for eight rare tumors (soft tissue, viscerae and bone sarcomas, rare neoplasm of the male genital organs, and of the urinary tract, neuroendocrine tumours, rare neoplasm of 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 centers 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 centers of the network.

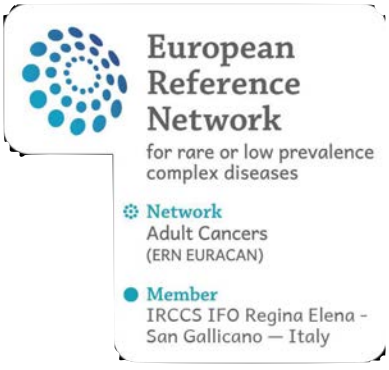
Our Institute is actively involved in International collaboration and revision of specific guidelines of various type of rare tumors and is engaged in national and international clinical trials.

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.

In the last months, 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.

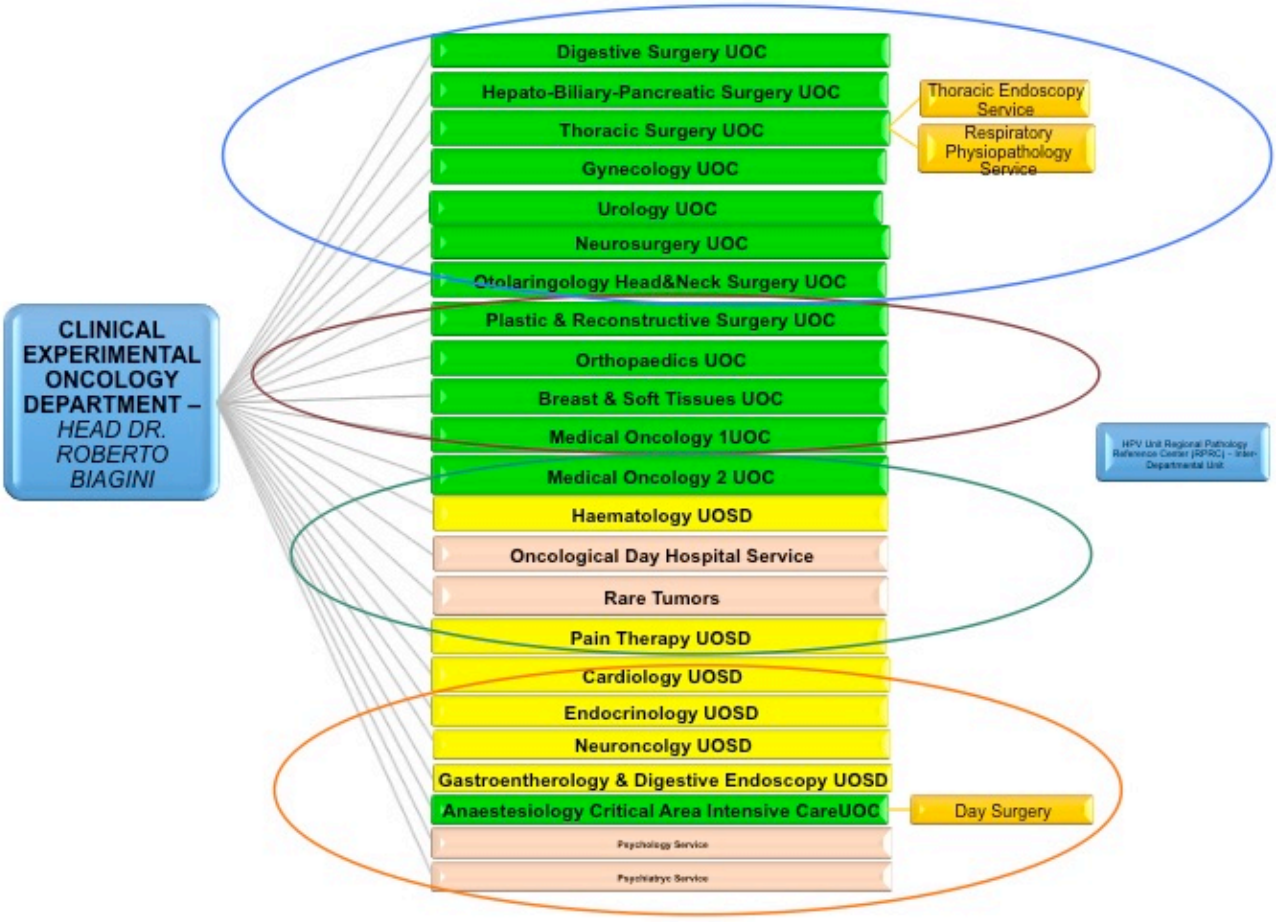
Increasing emphasis is moreover given to the collaboration with basic researchers to identify, as for more common cancers, molecular diagnostic, prognostic or predictive biomarkers and regular translational meetings, under the supervision of our Scientific Direction, are organized on bimonthly basis.





DEPARTMENT OF EXPERIMENTAL CLINICAL ONCOLOGY

Director: Dr. Roberto Biagini



DIGESTIVE SURGERY UNIT

Head: Alfredo Garofalo, MD

Staff

Fabio Carboni, MD
Orietta Federici, MD
Mario Valle, MD
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: 612

First visits: 123

Follow up visits: 489

Of the 123 patients undergoing the First Visit:

11 were Ca metastases and were initiated to front line chemotherapy

6 were anus carcinomas, sent to chemotherapy radiotherapy

4 were sent to exclusive endoscopic treatment.

The remaining 100 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

Canu V, Sacconi A, Lorenzon L, Biagioni F, Lo Sardo F, Diodoro MG, Muti P, Garofalo A, Strano S, D'Errico A, Grazi GL, Cioce M, Blandino G. MiR-204 down-regulation elicited perturbation of a gene target signature common to human cholangiocarcinoma and gastric cancer. Oncotarget 2017;8(18):29540-29557 **IF 5.168.**

Cavaliere D, Cirocchi R, Coccolini F, Fagotti A, Fambrini M, Federici O, Lorusso D, Vaira M, Ceresoli M, Delrio P, Garofalo A, Pignata S, Scollo P, Trojano V, Amadori A, Ansaloni L, Cariti G, De Cian F, De Iaco P, De Simone M, Deraco M, Donini A, Fiorentini G, Frigerio L, Greggi S, Macrì A, Pasqual EM, Roviello F, Sammartino P, Sassaroli C, Scambia G, Staudacher C, Vici P, Vizza E, Valle M. 1st evidence-based italian consensus conference on cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal carcinosis from ovarian cancer. Tumori 2017;103(6):525-536 **IF 1.233.**

Di Giorgio A, de Iaco P, de Simone M, Garofalo A, Scambia G, Pinna AD, Verdecchia GM, Ansaloni L, Macrì A, Cappellini P, Ceriani V, Giorda G, Biacchi D, Vaira M, Valle M, Sammartino P. Cytoreduction (peritonectomy procedures) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) in advanced ovarian cancer: Retrospective italian multicenter observational study of 511 cases. Ann Surg Oncol 2017;24(4):914-922 **IF 4.041.**

Hepato Biliary Pancreatic Surgery

Head: Gian Luca Grazi, MD, PhD

Staff

Maurizio Cosimelli, MD
Marco D'Annibale, MD
Fabiola Nazzicone, 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. 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. Laparoscopy and robotics are used when appropriate.

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.

Publications

Aldrighetti L, Ratti F, Cillo U, Ferrero A, Ettorre GM, Guglielmi A, Giuliante F, Calise F, Italian Group of Minimally Invasive Liver Surgery (I GO MILS). Diffusion, outcomes and implementation of minimally invasive liver surgery: A snapshot from the I go MILS (italian group of minimally invasive liver surgery) registry. Updates Surg 2017;69(3):271-283

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THORACIC SURGERY UNIT

***Head*: Francesco Facciolo, MD**

Staff

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Edoardo Mercadante, MD
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Enrico Melis, MD
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Claudia Ramacci, Case Manager
Valeria Simonetti, Nurse
Antonio Ricciuti, Nurse
Alessio Calabretta, Nurse
Emanuele Egidi, Nurse
Vincenzo Lodico, Nurse
Paola Giordano, Nurse
Chiara Spadavecchia, Nurse
Massimiliano De Vecchis, Nurse
Adriana Ciacci, Nurse
Raffaele Tomasone, 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

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GYNECOLOGIC ONCOLOGY UNIT AND REGIONAL BIO-BANK OF OVARIAN TISSUE

***Head*: Enrico Vizza, MD**

Staff

Giuseppe Cutillo, MD
Luciano Mariani, MD
Cristina Vincenzoni, MD
Giuseppe Vocaturo, MD
Ermelinda Baiocco, MD
Giacomo Corrado, MD
Anna Di Luca Sidozzi, MD
Emanuela Mancini, MD
Marcello Iacobelli, Biologist
Anna Maria Lobascio, Biologist
Arabella Bufalo, Data Manager
Ashanti Zampa, Data Entry
Ward Nurse
Fabiola Nazzicone, Head
Domenico Cafarello
Tatiana Chierichek
Fabiana Cipriani
Fabiana Egidi
Laura Filip
Valeria Fiumara
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Claudi Parrini
Catalina Partenie
Sabrina Santini
Mirko Benedini, Health worker
Monika Szoldra, Health worker Outpatient Clinic Nurse
Maria Fortunati, Head
Cristina Patone
Maria Piccolo
Enrica Ruffo
Maria Di Luccio, Health worker Francesco Malci, Health worker

Mission

To take care of women with suspect or histological confirmed diagnosis of tumors of the female reproductive tract and provide high-quality, patient-centered treatment including diagnosis, staging, surgical treatment and follow-up in a well-coordinated, multidisciplinary fashion so as to improve, enhance, and sustain quality of life. Fertility preservation in oncological young patients. Developing of minimally invasive procedures including robotic surgery and sentinel node mapping.

Clinical Activity

The Division has 16 in-patient beds (two of which are dedicated to day-surgery activities) and 3 full-day surgical rooms every week. During 2017 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 coordinated on a weekly basis meeting by a multidisciplinary team involving 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 young patients with several cancer types is available. The Division includes also an outpatient clinic mainly dedicated to the diagnosis and treatment of genital cancer precursor and a multidisciplinary HPV center.

Research Activity

The main fields of research include: 1) minimally invasive surgery (MIS) for the treatment of gynecological tumors, 2) ovarian tissue cryopreservation (bank of ovarian tissue), 3) bio-molecular characterization of endometrial cancer, 4) HPV vaccination and screening. 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. In this field our center have tested novel single-site instruments and accessories for the Da Vinci System showing the feasibility and the advantages of MIS also for more extensive procedures (surgical treatment of cervical and ovarian cancer) and in severely obese patients. Laparoscopic treatment of advanced ovarian cancer patients, in clinical response following neoadjuvant chemotherapy, has also been evaluated and validated by our group.

A prospective study on the feasibility and diagnostic accuracy of sentinel-node biopsy with indocyanine green in endometrial cancer 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. Bio-molecular characterization of endometrial cancer aimed to a better prognostic stratification of these patients is starting in our Division and will include prospective evaluation of L1-CAM, POL-E, MSI, beta-catenin and p53 expression in early stage endometrioid cancer. The main topics of research of HPV multidisciplinary unit are: 1) adult women, male and post-treatment vaccination, 2) new screening modalities in vaccinated girls, 3) HPV impact on the couple fertility.

Publications

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UROLOGY UNIT

Head: Michele Gallucci, MD

Staff

Ruggero Cantiani
Giuseppe Cusumano
Salvatore Guaglianone
Luciano Lamanna
Vincenzo Pompeo
Giuseppe Simone

Fellows

Mariaconsiglia Ferriero
Francesco Minisola

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 Urothelial Cancer.

Clinical Activity

The clinical activities of our Unit of Urology mainly concerns minimally invasive surgery: 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 Unit's main research objectives. Basic research on molecular biomarkers, genetic assessments and stem cells in urological malignancy are additional research activities that our Unit carries out in cooperation with the dedicated departments of the Regina Elena National Cancer Institute and other national and international Institutions.

The Unit of Urology has been National Site Coordinator of the observational study FE200486CS39, and is involved in multiple clinical trials on prostate cancer treatments, kidney cancer and urothelial cancer.

Publications

Cannistraci A, Federici G, Addario A, Di Pace AL, Grassi L, Muto G, Collura D, Signore M, De Salvo L, Sentinelli S, Simone G, Costantini M, Nanni S, Farsetti A, Coppola V, De Maria R, Bonci D. C-Met/miR-130b axis as novel mechanism and biomarker for castration resistance state acquisition. Oncogene 2017;36(26):3718-3728 **IF 7.519.**

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NEUROSURGERY UNIT

***Head*: Carmine Maria Carapella, MD**
since March 2018 Riccardo Boccaletti, MD

Staff

Carmine Maria Carapella, MD
Fabio Cattani - Associate Neurosurgeon
Piero Oppido - Associate Neurosurgeon
Laura Raus - Associate Neurosurgeon
Stefano Telera - Associate Neurosurgeon
Francesco Crispo – Assistant Neurosurgeon

Nurse:

Cinzia Mori - Nurse Coordinator & Case Manager
Abate Maria
Angelocola Anna
Balzano Silvana
Berrè Cinzia
Cacciarelli Daniele
De Martino Stefania
Iacobelli Cesarina
Lauro Gerarda
Ragnacci Luisa
Rinaldi Sabrina

Marzia Piccoli – Administrative Assistant

Mission

The activity of Neurosurgical Unit is mainly devoted to research, diagnosis and treatment of nervous system tumours, with a prevalent interest in malignant primary and secondary lesions. Our activity is deeply embedded in the multidisciplinary group of Neuro-Oncology, with the aim of defining more specific and active diagnostic and therapeutic strategies for the most relevant brain and spine tumours. 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 tumours of the nervous system. In this field we take active part to national and international cooperative groups, participating to relevant academic and sponsored clinical trials. In the field of secondary CNS lesions we are integrated with our Hematologic and Oncologic Units, offering important support into diagnostic and therapeutic process of systemic tumour disease.

Clinical Activity

In 2017 the Unit of Neurosurgery performed more than 150 surgical procedures, mainly operations for intracranial tumour removal (more than 90 primitive brain tumours - gliomas, meningiomas, pituitary adenomas, et al - and a quarter of metastatic brain lesions), but also procedures on spinal tumours (two thirds on metastatic spine lesions).

Following the experience of last years, our activity has been devoted to increase the efficacy of new therapeutic strategies (microsurgical resection fluorescence guided, with second surgical look and intratumoural antiblastic treatment, conformal radiotherapy, with eventual focal boost, adjuvant and/or concomitant chemotherapy) and allow in selected patients the indication to second surgery followed by new combined therapeutic strategies.

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. In

this field, the European Association of Neuro-Oncology (EANO) created a multidisciplinary Task Force (CMC is a member of this group) to draw evidence-based guidelines for patients with brain metastases from solid tumours, with the aim of defining a consensus review of evidence and recommendations for diagnosis by neuro-imaging and neuropathology, staging, prognostic factors, and different treatment options. Specifically, were addressed options such as 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 and breast and renal cancer), and supportive care. The final result of this group activity was recently published on Neuro-Oncology.

Furthermore, a relevant neuro-endoscopic surgical activity has been performed. In the case of pituitary region tumours a trans-nasal-sfenoidal endoscopy-guided approach has been realised; in other cases a pure endoscopic trans-ventricular procedure has been performed with bioptic tumour sampling, opening and drainage of cystic components, as well as third ventriculostomy.

In the field of spinal tumours different programs have been developed during last years: mainly considering the use of new technologies and approaches; during this year mainly patients affected by metastatic spinal tumours have been treated with augmentation procedures (vertebroplasty and/or kyphoplasty), associated in many cases with open decompression procedures.

Research Activity

Research activity is oriented either in translational neuro-oncological projects as well as on 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 activity of our multi-specialist translational group was aimed at identifying new molecular and imaging glioma biomarkers useful for diagnosis, prognosis and/or predictive of tumour therapeutic response; we are trying to correlate the data regarding tumour bio-molecular characteristics with clinical data of these patients; on these bases, we believe to eventually yield a significant improvement in the managements of these patients. To accomplish these aims we take advantage of an extensive database including retrospective as well as prospective case series collected at IRE. Presently, our database includes clinical and molecular information obtained from more than 800 patients affected with primary brain tumours (mainly malignant gliomas; more than 400 glioblastomas). An average of 60 patients are included every year.

On this basis we already analysed the value of the expression of MGMT as a relevant predictor of therapeutic response and good prognosis in GBM patients. Our study reinforces the importance of MGMT in the management of GBM patients; presently a large cooperative study with other Italian groups is in progress and the preliminary result will be presented at the next ASCO meeting. Utilizing the same data set, we are analysing 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 as potential predictive/prognostic factors in GBM long survivors. Recently a cooperative study, under the auspices of Alliance Against Cancer, has been designed on this setting of long survivors with the aim of deeply understand molecular characteristics as well as therapeutic strategies that allowed these relevant results.

A second aim has been the research of circulating biomarkers for detection and prognosis of primary brain tumours. We already reported our recent study on a serum microRNA signature in a cohort of malignant glioma patients, evaluating eleven circulating/serum microRNAs (miR-15b*, -23a, -99a, -125b, -133a, -150*, -197, -340, -497, -548b-5p and let-7c), previously associated with brain tumours, as potential non-invasive diagnostic biomarkers for glioma patients. Preliminary data of this relevant study have been published.

Another relevant aspect in this field is the potential contribute of cerebrospinal fluid flow cytometry analysis for early detection and characterization of tumour cells in the presence of leptomeningeal carcinomatosis, in the phases of first diagnosis as well as during treatment, with the aim of monitoring the extent of residual disease. As matter of fact it is well known the important increase of CNS involvement during the clinical evolution of malignant solid tumours, mainly lung, breast and melanoma (5-25%). Our pilot study, recently published, documents the expression of prognostic markers as well as putative stem cell markers in breast cancer leptomeningeal metastasis, through flow cytometric analyses of CSF samples.

A third relevant research activity is directed toward the evaluation of new surgical strategies in the treatment of brain and spinal and vertebral tumours.

In particular, fluorescence-guided resection represents an interesting tool for identifying tumour 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 (ALA). Our experience regarding more than 80 patients affected by malignant glioma (newly diagnosed as well as recurrent tumours) has been presented in several scientific meetings and a publication is in progress. In the present experience, more than 90% of patients showed intraoperative red fluorescence of core tumour tissue; mainly in recurrent GBM, when MRI documented heterogeneous lesions with enhancing areas mixed with non enhancing gliotic scars, fluorescence-guided surgery allowed a better definition of active tumour, with net margins from perilesional "healthy" brain. In the present experience the procedure did not determine any relevant additional neurological deficit. This experience supports the potential value of fluorescence-guided surgery, improving tumour detection and allowing extended resection of malignant glioma, without any relevant impact on neurological status, with a consistent effect on overall survival.

In addition, unconventional treatment modalities of malignant gliomas have been studied. In this field our group participated to a prospective, multicentre randomised trial of novoTTF-100a; very low-intensity, properly tuned, intermediate-frequency electric fields, termed tumour-treating fields (TTFields), selectively stunt the growth of tumour cells; this inhibitory effect was demonstrated in numerous proliferating cell types, while non-proliferating cells and tissues were unaffected. In this Phase III study novoTTF together with temozolomide has been compared to temozolomide alone in patients with newly diagnosed GBM (Novocure EF-14). This phase III randomised clinical trial has been concluded; final results have been published documenting a significant advantage on PFS and OS in the group treated with NovoTTF.

With regard to spinal tumours, vertebral pathological fractures represent one of the most challenging issues. Due to its minimal invasion and immediate pain relief ballon kyphoplasty has gained an increased popularity for the treatment of symptomatic tumour or osteoporotic vertebral fractures; 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 material VK100 (the study was approved by our EC, activated and presently more than 50 patients have been accrued), with the aim of investigating the results obtained with this new silicone in oncologic patients with vertebral compression fracture, in terms of safety of the procedure, pain reduction, functional capacity and quality of life.

Publications

Cordone I, Masi S, Summa V, Carosi M, Vidiri A, Fabi A, Pasquale A, Conti L, Rosito I, Carapella CM, Villani V, Pace A. Overexpression of syndecan-1, MUC-1, and putative stem cell markers in breast cancer leptomeningeal metastasis: A cerebrospinal fluid flow cytometry study. Breast Cancer Res 2017;19(1):46 **IF 6.345.**

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Soffietti R, Abacioglu U, Baumert B, Combs SE, Kinhult S, Kros JM, Marosi C, Metellus P, Radbruch A, Villa Freixa SS, Brada M, Carapella CM, Preusser M, Le Rhun E, Ruda R, Tonn JC, Weber DC, Weller M. Diagnosis and treatment of brain metastases from solid tumors: Guidelines from the european association of neuro-oncology (EANO). Neuro Oncol 2017;19(2):162-174 **IF 7.786.**

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OTOLARYNGOLOGY HEAD AND NECK SURGERY UNIT

***Head*: Giuseppe Spriano, MD**
since May 2018 Raul Pellini, MD

Staff

Giovanni Cristalli, MD
Valentina Manciocco, MD
Barbara Pichi, MD
Giuseppe Mercante, MD
Paolo Marchesi, MD

Francesco Bianco, Audiometrist
Sonia Gambardella , Audiometrist

Alessandra Masiello, Speech Therapist

Rossella Leonardi, Nurse Coordinator

Alba Ara Pina, Nurse
Bruna Boldrini, Nurse
Serena Cucchiella, Nurse
Anna Ferrante, Nurse
Fernando Golino, Nurse
Maria Teresa Imperi, Nurse
Marina Macis, Nurse
Iolanda Mantuano, Nurse
Francesco Mautone, Nurse
Attilio Santolamazza, Nurse

Debora Cacciato, Nurse Case Manager

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 Activity

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

- Human papillomavirus involvement in Head and Neck cancer
- Feasibility and efficacy of electrochemotherapy in Head Neck Cancer
- mRNA expression profiling in Head Neck Cancer

Publications

Donà MG, Pichi B, Rollo F, Gheit T, Laquintana V, Covello R, Pescarmona E, Spriano G, Pellini R, Giuliani M, Tommasino M, Benevolo M. Mucosal and cutaneous human papillomaviruses in head and neck squamous cell papillomas. Head Neck 2017;39(2): 254-259 IF 3.376.

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Spriano G, Mercante G, Cristalli G, Pellini R, Ferreli F. Lateral cervical approach for supracricoid partial laryngectomy. Am J Otolaryngol 2017;38(5):598-602 IF 1.033 .

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PLASTIC & RECONSTRUCTIVE SURGERY

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 an:cancer drugs in Oncology: Prevention, treatment and outcomes The incidence of extravasation of an: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 alterna:ve in the treatment of solid tumors, particularly breast cancer, local toxicity levels are higher in these drugs than those that preceded them.

Publications

De Vita R, Zoccali G, Buccheri EM. The balcony technique of breast augmentation and inverted-T mastopexy with an inferior dermoglandular flap. Aesthet Surg J 2017;37(10):1114-1123 IF 2.697.

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ORTHOPAEDICS UNIT

Head: Roberto Biagini, MD

Staff

Leonardo Favale, MD
Nicola Salducca, MD
Carmina Zoccali , MD
Wioletta Faltyn, Case Manager
Elisa Checcucci, Data Manager

Nurse
Grazia Amato
Paolo Asquini
Fabio Conti
Antonella Cutini
Rosario D'Angelo
Carolina Destito
Matteo Ferraro
Stefano Landi
Giovanni Meogrossi
Alessia Milotti,
Sabrina Ganzenua
J. Baldi, MD (Resident in Orthop and Trauma)

Mission

The 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 2017, the unit has perfected computer assisted navigated techniques and reconstruction with titanium 3D-printing prostheses after bone tumor removal.

Clinical Activity

The patients who have to undergo surgeries are hosted in the ward (12 regulars beds). In the ward is also present a pediatric room fully furnished with videogames and a video-school (available for long-term stay young patients), a room decorated for adolescent patients and other two decorated rooms.

The surgeries were performed every month in 8 operative theatre's days (2 par week).

During the week there are three outpatients clinics: on Monday an orthopedic outpatient clinic for benign and low-grade malignant tumor; on Wednesday a multidisciplinary clinic for high grade sarcomas and Friday a clinic for metastatic patients. One time par month there is also an outpatient clinic reserved for patients affected by multiple exostoses and cartilaginous tumors. One day a week there is an outpatients clinic for biopsies and one for wound care. Twice par week there is a Disease Management Team meeting for cases discussion. A Biobank stores biological samples from patients with musculoskeletal neoplasm, visceral sarcomas and muscular-skeletal metastasis.

Research Activities

SARCOMA TROBS Trabectedin in Soft Tissue Sarcomas a retrospective analysis.

- 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: closed at the moment jun-2016 2 19 ISG-OS-02 Multicentric, prospective, randomized clinical trial in patients with recurrence of osteosarcoma.

- 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 – IREStudio 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 ttivo mediante radioterapia, risposto alla sola radioterapia, in pazienti affetti da Sarcoma della parete dei tessuti molli degli arti e del tronco, localmente avanzato.

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BREAST AND SOFT TISSUE SURGERY UNIT

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Staff

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Maria Antonietta Di Ceglie, nurse
Fiorella Molinari, nurse
Maria Antonietta Picano, nurse
Viviana Ruspolini, nurse
Emanuela Vincenzi, 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 (in collaboration with the Division of Plastic and Reconstructive Surgery). In selected cases intraoperative radiotherapy (IORT) is performed.The intraoperaMve evaluation of sentinel lymph node is performed by means of One Step Nucleic Acid Amplification (OSNA).
- Locoregional treatment of primitiv and recurrent melanoma (wide excision, sentinel lymph node biopsy, radical regional lymphadenectomy, hyperthermic--antiblastic perfusion, electrochemotherapy).
- Locoregional treatment of primary and recurrent sarcoma (wide excision, compartmentctomy,radical regional lymphadenectomy when indicated, hyperthermic--antiblastic perfusion)

Research Activity

Main research lines:

- Identification of new imaging techniques in senology (CESM)
- Identification of signature responsiveness to innovative drugs

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

Efficacy 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 Effectiveness and Tolerability
- Analysis of the predictive value of efficacy of anti--neoplastic therapies based on the evaluation of molecular pathways associated with tumor stem cells: muti-setting and multitumor study. HIERARCHY Study
- Primary chemotherapy with Trastuzumab in combination with Docetaxel followed by Epirubicin + Cyclophosphamide in breast cancer with positive HER--2. DECT protocol
- 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

Barba M, Vici P, Pizzuti L, Di Lauro L, Sergi D, Di Benedetto A, Ercolani C, Sperati F, Terrenato I, Botti C, Mentuccia L, Iezzi L, Gamucci T, Natoli C, Vitale I, Mottolese M, De Maria R, Maugeri-Saccà M. Body mass index modifies the relationship between gamma-H2AX, a DNA damage biomarker, and pathological complete response in triple-negative breast cancer. BMC Cancer 2017;17(1):101 **IF 3.288.**

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MEDICAL ONCOLOGY 1 UNIT

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Antonella Gagliardo, Nurse
Anna Franca Speranza, Nurse
Anna Maria Biscu, Nurse
Teresa Borruso, Nurse
Anna Maria Barberini, Nurse
Eleonora Bertini, Secretariat
Francesca Sabbatini, Secretariat

Mission

The Division of Medical Oncology 1 has a long standing commitment in improving the 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 three 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 for administration of oral and intravenous antineoplastic drugs and supportive cares. 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 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 2017, 62 clinical studies were ongoing in different tumors , with the enrolment of about 300 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.

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MEDICAL ONCOLOGY 2 UNIT

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Mission

The Unit of Medical Oncology 2 seeks to gain insights that lead to improving diagnosis and treatment of adult cancer patients. Moreover, much time is dedicated to scientific research, mostly in breast and gynecological cancers, through the design and the coordination of many studies in collaboration with other Italian oncologic centres. The Unit is composed of specialists in Medical Oncology subdivided into small groups where each group is dedicated to a specific tumor, dedicating time to management of over 600 new cancer patients/year. Each group is responsible for both clinically managing patients and applying the scientific strategies in their pertinent field. Due to the complexity of neoplastic pathology, a close collaboration among various specialists is required, and therapeutic procedures used for each single patient are defined weekly during “Disease Management Team” (DMT) under different residency specialist areas. Moreover, a relevant percentage of patients are enrolled in clinical studies, both retrospective and prospective.

Clinical Activity

The clinical activities of the Unit are organized along the lines of an

inpatient hospital service and program outpatient clinics. Clinics: The outpatient clinics are organized mainly into tumor types through the first-time visit with the patient, routine controls and oncological screening activities. All the first-time visits for breast cancer/gynecological cancers take place in a dedicated clinic, as well as for patients enrolled/to be enrolled in clinical trials. The waiting time for first-time visits or oncological screenings does not exceed three days. Hospitalization: All hospitalized patients are admitted to a Medical Oncology 2 Ward Service. Activities: chemotherapy/supporting therapies, advice from other specialists, diagnostic examinations, psychological support. The waiting-time before being admitted to the Unit is of approximately four days. Day-Hospital: Activities: chemotherapy treatments/supporting therapies, advice from other specialists, examinations, psychological support. The waiting-time for a patients first-time visit/admission does not exceed four days.

Research Activity

During 2017, the clinical research activities focused on evaluating new treatment strategies, and identifying novel predictive/prognostic biomarkers for solid tumors, specifically regarding breast, , gynecological, and gastrointestinal cancers. Breast Cancer (19 publications): The Unit is the coordinating center in a variety of multicentric breast cancer trials in the neoadjuvant, adjuvant, and advanced setting, in collaboration with several cancer centers. Neoadjuvant Setting: The Triskele study, with biological evaluations on pretreatment biopsy is ongoing. Other studies, concerning metabolic determinants, anthropometric indicators, and Hippo pathway, were recently published. Two more studies, i.e., the Neocarbo and NeoTaz, are ongoing in triple-negative breast cancer patients. Adjuvant Setting: A study of early breast cancer patients was published, and other trials are ongoing, evaluating biomarkers on surgical specimen (PHOBOS), or fertility in young patients (MARIO, POSITIVE). Advanced Setting: Our Unit participated in three studies of HR+HER2-metastatic breast cancer, i.e., the COMPLEEMENT-1, PALBOSS, and in the IMPASSION 131 study (enrolling triple negative breast cancer patients). Adjunctive studies recently published were focused on the efficacy and toxicity of paclitaxel/bevacizumab in metastatic breast cancer patients, biomarkers related to DNA damage and DNA damage repair in male breast cancer. Two additional studies of T-DM1 and pertuzumab in HER2+metastatic breast cancer cases are ongoing, along with the inherent preclinical studies. Two more studies concerning eribulin (PAINTER) and nab-paclitaxel (NORMA) are ongoing. Additional manuscripts have been published in terms of reviews, i.e., expert opinions, and systematic reviews with meta-analyses. Other Tumors (9 publications): In specific regard to ovarian cancer, a further study is currently testing the predictive role of a miR signature in relapsed, high-grade serous ovarian cancer. Moreover, this Unit is involved in several MITO trials. Reviews concerning gynecologic cancer risk have been published. The Ovarian Translational Group (TG) pursued the set up and implementation of a data-base reporting on patients' data and metabolic determinants in ovarian cancer. Our Unit offers consultancy support for the ovarian-tissue preservation bank (BTO), and HPV-Unit. Moreover, we have implemented our research pipeline on predictive/prognostic biomarkers in gastrointestinal cancers, i.e., advanced gastric cancer and colorectal cancer. Congresses/events organization: "Breast cancer from bench to bedside" (15 Giu 2017), "Carcinoma mammario metastatico: stato dell'arte" (04 Lug 2017) .

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HAEMATOLOGY AND STEM CELL TRANSPLANTATION UNIT

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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 2016 five PDTA (percorsi diagnostici terapeutici assistenziali aziendali) were approved 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 will take place in 2018.

In 2017 RTN registered 216 Transplants (55 allogeneic and 161 autologous), 70 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.

The tables summarize the activity of our Unit for over the last five years inpatients as well outpatients.

Ordinary hospitalization

Diagnosis Related Group	2013	2014	2015	2016	2017
Discharged	209	246	207	184	219
Medium weight	4,755	4,526	5,02	5,78	6,11
Average hospitalization	18,86	16	17,24	19,47	17,15
First 5 DRG by discharged number					
481 stem cell transplant	46	53	47	53	68
473 acute leukemia > 17 years old	28	25	39	26	32
410 chemotherapy	51	70	29	31	31
404 lymphoma and leukemia without complications	21	29	17	22	32
403 lymphoma and leukemia with complications	9	18	22	10	11

DH

Diagnosis Related Group	2013	2014	2015	2016	2017
Accesses	510	315	198	199	202
Cycles	249	159	106	108	96
Medium weight	1,09	1,03	1,1	1,07	1,03
First 3 DRG by accesses number					
404 lymphoma and leukemia without complications	242	155	67	84	92
410 chemotherapy	128	85	70	79	64
492 chemotherapy associated with a diagnosis of acute leukemia	14	28	38	10	27

Outpatient

Activity	2013	2014	2015	2016	2017
PAC	95	212	130	133	155
Chemotherapy (code 99.25)	2123	2170	2251	2149	2738
All therapies (codes 99.25, 99.22, 99.23, 99.07.1, etc.)	6714	7108	7018	6184	6578
Bone marrow aspirates and biopsies (code 41.31)	237	356	451	375	489
Visits (code 89.01 e 89.7)	9572	10369	10380	10621	10996

Research Activity

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 submitted for publication 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.

• Hodgkin Lymphoma: Currently, up to 30 percent of newly diagnosed advanced-stage classical Hodgkin lymphoma patients will experience disease progression after treatment with the current standard of care ABVD, representing a significant need for improved treatment options for these often younger patients. The ECHELON-1 trial was a bold, five-year effort to redefine the frontline treatment of Stage III/IV classical Hodgkin lymphoma and provide patients with a more effective treatment regimen. In the ECHELON-1 study, Brentuximab Vedotin plus AVD (AAVD) was shown to have superior efficacy to ABVD. FDA approved AAVD in April 2018 for previously untreated Stage III or IV Hodgkin lymphoma patients. The FDA approval is based on positive results from a phase 3 trial called ECHELON-1 that were presented at the 59th American Society of Hematology (ASH) annual meeting in December 2017 with simultaneous publication in the New England Journal of Medicine. Our physicians participated in the ECHELON-1 trial which supported the FDA approval of this novel regimen.

• 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. In 2017 an our original study on cryotherapy prophylaxis to prevent oral mucositis in myeloma high-dose melphalan transplanted patients was published on Bone Marrow Transplantation.

• CMV update by ECIL: In September 2017 the 7th European Conference on Infections in Leukemia presented the CMV updated guide-lines, in which some studies from our Unit published in 2014 and 2015 were cited in the setting of autologous transplant.

• 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 in hematologic patients.

This study (SEIFEM BAL 2017), promoted and coordinated by our Unit, started on enrolling patients on January 2018.

• 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 160 patients were included with FL and 280 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 2017. 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 22 new patients, continued follow-up evaluation of all patients enrolled in the study (to date 58 patients), and administered a total of 220 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 2017, 33 clinical research protocols proposed by Hematology and Transplant Unit and approved by Regina Elena I.F.O. 48 new patients were enrolled. Ethics Committee have been open to recruitment and 257 patients have been enrolled.

Publications

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CARDIOLOGY UNIT

Head: Francesco Rulli, MD

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Armando Carpino, MD
Fabio Maramao, MD
Nicola Antonio Morace, MD
Giuseppe Canio Toglia MD
Rosella Graziani, Nurse in Chief
Laura Cervellione, Nurse
Gianni Chiarabini, Nurse
Gianni Pompei, Nurse
Antonella Perenzin, Nurse

Mission

The Cardiology Task Force 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 of Regina Elena National Cancer Institute and San Gallicano Dermatological 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 intraoperative 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
- The UO Cardiology is part of the most solid and accreditated reality 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.

ENDOCRINOLOGY UNIT

Head: Marialuisa Appetecchia, MD

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Endocrinologists:
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Agnese Barnabei
Rosa Lauretta

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Paolo Basili

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Maria Di Luccio

Attending Endocrinologists:
Agnese Persichetti

Traineers from Endocrinology Specialization Schools of Universities La Sapienza - PTV- S. Andrea

Mission

The UOSD of Endocrinology 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 of the endocrine-metabolic sequelae in cancer patients by using diagnostic and therapeutic pathways (PDTA) and using dedicated Disease Team Management (DMT) for discussing patients with thyroid cancer and / or neuroendocrine tumors.

It has collaborative relationships and participates in multicenter clinical trials with major Italian Universities and Research Institutes, including within Scientific Societies (SIE, SIOMMS) and is part of the European Network for Euracan Cancer for endocrine and neuroendocrine tumors.

The job setting is based on constant attention to the technical and professional quality and the continuous improvement and updating of the service delivery and management techniques, and to the preservation of the human aspect and the quality of the relationship with the Patient and with the Staff.

Clinical Activity

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 Endocrinology follows to date approximately 2000 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 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.

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 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 UOSD of Endocrinology follows to date approximately 200 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:

1. thyroid carcinoma
2. osteoporosis
   neuroendocrine tumors
3. pituitary tumors

Research Activity

The research efforts of the Endocrinology Unit involve evaluating and developing novel clinical and laboratory tools useful in the diagnosis and monitoring of human endocrine cancers.

The Endocrinology Unit has long-standing commitment and care in improving the detection and treatment of endocrine 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

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NEURONCOLOGY UNIT

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Andreina Rotondi, Social worker
Lara Guariglia, Psychologist
Sonia Ieraci, Psychologist
Cristiano Parisi, Physioterapist
Stefano Di Felice, Physioterapist
Margaux Lamaro, Physioterapist
Silvia Focarelli, Data Manager
Antonio Tanzilli, Neuro-psychologist
Andrea Maialetti, Neuro-psychologist
Alessia Zarabla, Neurophysiologist

Research collaborations with graduate and undergraduate students
Marzia Piccoli

Mission

Clinical and research activity of the Neuroncology Unit is mainly 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 neurological complication of cancer.

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 for brain tumor patients
- Neurophysiology lab (Electromyography, Electroencephalography, Evoked Potentials)
- Rehabilitation service specialized in cancer rehabilitation for in- and outpatients
- 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, carboplatin, regorafenib.
- 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 has been submitted for publication.
- 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, rehospitalization rate and the impact on Health System costs. The results of this project have been presented in national and international scientific meeting and published on Neuro-Oncology.
- 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 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.
- 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. The preliminary results was published in 2015 on Disease Markers. 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 study has been published.
- 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. Research activity of the Center of Tumor-related Epilepsy (CET) of the Regina Elena National Cancer Institute includes studies on new antiepileptic drugs (lacosamide, zonisamide, brivaracetam) and:

- Retrospective observational study in patients with Acute Lymphoid Leukemia treated with Citosina Arabinoside (ARA-C)
- Social cognition in adult with epilepsy
- Patterns of care of brain tumor-related epilepsy: a cohort study of italian epilepsy centers

Publications

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GASTROENTEROLOGY AND DIGESTIVE ENDOSCOPY UNIT

Head: Vittoria Stigliano , MD

Staff

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3 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 the 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).

Moreover, the Gastroenterology and Digestive Endoscopy Unit is a Centre of Excellence to which cancer patients from central and southern Italy are referred. The Unit is equipped with the latest advanced technologies in endoscopy.

Another important area of interest and development is the Nutritional support to cancer patients. The nutritional counselling is offered to patients at risk of malnutrition at the diagnosis and during the oncological treatment.

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)
- 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 , foreign bodies extraction
- Percutaneous Endoscopic Gastrostomy (PEG) for long term enteral nutrition
- Referral Centers And Counselling For Outpatients And Inpatients
- Since 2005, the Unit has been recognized Referral Centre of Lazio Region for Familial Adenomatous Polyposis (FAP) and

- since September 2017 Referral Centre of Lazio Region for Lynch syndrome. The Hereditary Colorectal cancer syndromes Clinics of the Unit guarantee an adequate management of these rare diseases.
- Since 2009 the Unit has been recognized Referral Center of Lazio Region for celiac disease.
- The nutritional counselling is offered to patients at risk of malnutrition at the diagnosis and during the oncological treatment. Artificial nutrition through nasogastric tube feeding or Percutaneous enteral gastroscopy is offered, where necessary, according to International Guidelines.
- A counseling 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 2017 we pursued the following Research Projects

- Progetto AIRC 2017: "Extracellular vesicles in colorectal cancer: diagnostic and therapeutic implications ". PI IRE: Dr. V. Stigliano.
- "Toxins produced by intestinal bacteria and predisposing genetic variations: a dangerous link for colorectal cancer development?" (Ricerca Finalizzata PE-2011-02347510) collaboration with ISS PI IRE: Dr. V. Stigliano.
- Progetto di Ricerca Corrente: New screening and follow-up molecular strategies in patients with suspected hereditary syndrome of colon-rectal carcinoma. PI: Dr. V. Stigliano.
- Progetto di Ricerca Corrente: The epigenetic contribution to Lynch syndrome. PI: Dr. V. Stigliano.
- Progetto di Ricerca Corrente: Hereditary colorectal cancer: molecular characterization of novel genetic variants to improve cancer screening and surveillance programs. PI: Dr. V. Stigliano.
- Progetto di Prevenzione per familiarità del tumore del colon-retto Campagna D'informazione 2016 -2017 Proponente AMOC Onlus (Associazione Onlus Malati Oncologici colon-retto).

Publications

Ricci MT, Miccoli S, Turchetti D, Bondavalli D, Viel A, Quaia M, Giacomini E, Gismondi V, Sanchez-Mete L, Stigliano V, Martayan A, Mazzei F, Bignami M, Bonelli L, Varesco L. Type and frequency of MUTYH variants in italian patients with suspected MAP: A retrospective multicenter study. J Hum Genet 2017;62(2): 309-315 IF 2.471.

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ANESTHESIA, INTENSIVE CARE UNIT AND PAIN THERAPY UNIT

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Staff

MD:

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Giampiero Pontrandolfi
Francesco Rendina
Carmela Stigliano
Lamberto Laurenzi

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.

Pain therapy clinic: positioning of vascular accesses, PICC and PORT, treatment of oncologic pain with invasive and non invasive procedures.

Research Activity

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 16th December 2016, 4th edition.

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.
- Ultra short acting beta – blocker in cardiovascular high risk patients in videolaparoscopic surgery.

Publications

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PSYCHOLOGY UNIT

Head: Patrizia Pugliese, Psychologist

Staff

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Giovanna D'Antonio, Psychologist
Chiara Falcicchio, Psychologist
Luana Fotia, Psychologist
Gabriella Maggi, Psychologist
Maria Perrone, Psychologist
Paola Torti, 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 Activity

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 2017. In accordance with project of humanization, the Psychology Unit has achieved levels of satisfaction in 98% of patients.

Research Activity

Quality of life study

"Miglioramento della qualità dell'assistenza nella pratica clinica quotidiana – percorsi psicologici diagnostico-terapeutici" aimed to enhance patient and relatives quality of care through experimentation of psychological paths in daily clinical practice.

In 2017 the project has been extended to patients with haematological malignancy. From January 2017 to December 2017, investigation of psychological distress evaluated with the Distress Thermometer (DT 0-10) was performed on almost six hundred patients. The results showed an incidence of high distress (Levels of distress> 4) in 83% of patients. Early psychological intervention in 51% of patients at risk showed an improvement of distress in almost 85% of patients.

The main needs of advanced patient relatives were psychological support and doctor-family communication.

The study "Modifiche delle abitudini alimentari in corso di terapie oncologiche" is aimed to evaluate the extent of the nutritional problem in different neoplasms and in different geographical areas in collaboration with FAVO, AIOM, SINPE.

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

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 increase the strength of the data.

Satisfaction with care and disease awareness

The results of study “Consapevolezza di malattia e soddisfazione per le cure ricevute nei pazienti italiani con tumori solidi: uno studio multicentrico” are ongoing.

Publications

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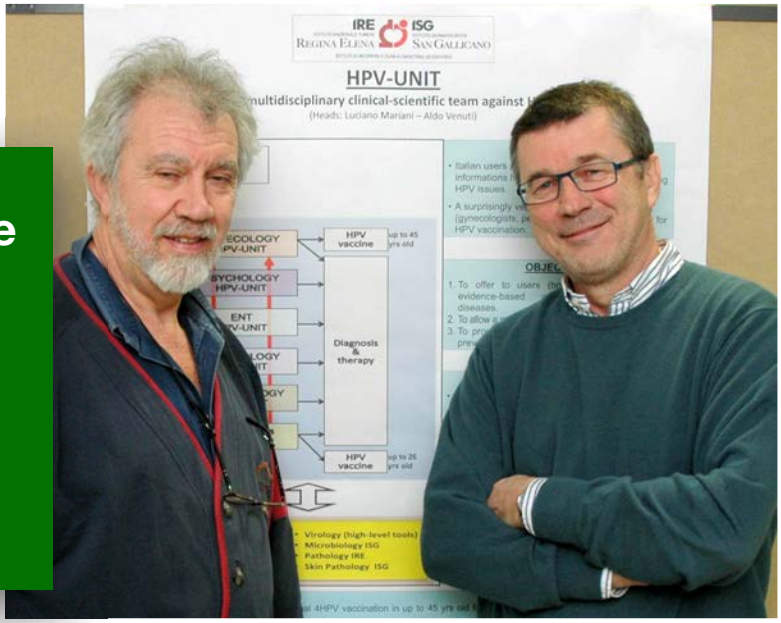
Regional Pathology Reference Center (RPRC) HPV Unit

Coordinators: Luciano Mariani MD and Aldo Venuti MD,



Staff

Qualified experts:

Regina Elena National Cancer Institute (IRE)

Gynecologic Oncology: Luciano Mariani, R. Sindico, Giuseppe Vocaturo, Cristina Vincenzoni, Enrico Vizza

UOSD Tumor immunology amd immunotherapy: Aldo Venuti, Federico De Marco, F Paolini

Proctology: Daniela Assisi, Cinzia Quondamcarlo

Otolaryngology: Giuseppe Spriano, Barbara Pichi, Raul Pellini

Medical Oncology B: Patrizia Vici, Marina della Giulia, Fiorentino Izzo.

Pathology and Cytopathology: Edoardo Pescarmona

Psychology: Patrizia Pugliese, Maria Perrone, Maria Condoleo, Chiara Falcicchio.

Epidemiology: Valerio Ramazzotti, Maria Cecilia Cercato

Clinical studies: Diana Giannarelli

San Gallicano Dermatological Institute (ISG)

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Lab. Pathology&Microbiology: Fabrizio Ensoli, Domenico Moretto, Amalia Giglio, Fulvia Pimpinelli

Sexually Transmitted Disease: Antonio Cristaudo, Alessandra Latini, Massimo Giuliani, Giampaolo Impara, Maria Gabriella Donà

Scientific Committee:

Amalia Allocca (Rome I), Xavier Bosch (Barcellona E), Jack Cuzick (London UK), Ruggero De Maria (Rome I), Aldo Di Carlo (Rome I), Ian Frazer (Brisbane AU), Sergio Pecorelli (Rome I), Silverio Tomao (Rome I), Enrico Vizza (Rome I), Barbara Suligoi (Rome I), Patrizia Vici (Rome I)

Mission

Formalizing an organizational model of a "unified and coordinated space" in which originate jointly initiatives related to the topic of HPV:

the clinical management (diagnosis and treatment guidelines, facilitated routes and more), and the scientific matching (creation of ad hoc database, sharing of researches and more). 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 Activity

The main purpose of HPV-UNIT is the multi-discipline involvement of IRE/ISG specialists. The primary activity is 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. In addition, HPV UNIT is actively engaged in second level diagnosis of virus-associated cancers, especially HPV and polyomavirus in skin, oral cavity, and genital/perianal areas.

Regarding HPV prevention, HPV vaccination, that is a program already started in 2014 for female, up to 45 years old, and later on extended to male, is fully operating with a constant rise in number of administrated doses (more than 150 globally for male and female). This program was implemented in 2017 by offering HPV vaccination to women as adjuvant prevention therapy after conization. An interim analysis of this patient seems to indicate that vaccination after conization is effective in reducing re-infection by HPVs that are included in vaccine formulation.

Research Activity

Scientific activities of HPV-UNIT were focused on developing strategies for permanent professional training and information addressed to the citizens. A meeting organized in Rome (03-25-2017) “10 Anni di Vaccinazione HPV” was really a success with the partnership of the Italian Society for Virology. In parallel, HPV-Unit is constantly carrying out a large activity of user’s information by upgrading the dedicated internet site (www.hpvunit.it), by telephone, and by email that are the preferred way of communication of users. In addition, HPV-Unit was involved in translational researches.

Molecular carcinogenesis. All available data were collected to highlight how HPV interacts with the ATM- and ATR-dependent DDR machinery during the viral life cycle to create an environment favourable to viral replication. In this activity the E5 protein of high risk HPV has a pivotal role.

Molecular epidemiology of HPV types. 1- Genital tumors. Benefits and potential issues of the nonavalent HPV vaccine were overviewed together with data on the implementation of cervical screening after vaccination. The assessment of vaccine effectiveness can be ascertained by the impact on genital warts: prevalence and incidence of this disease in Italian population were analyzed.

Finally, biomolecular follow-up of patients undertaken vaccination after conization continued 2- Extra-genital tumors. Presence and expression of HPV were demonstrated in pre-neoplastic lesions (i.e. actinic keratosis) of skin, suggesting that HPV might be involved in skin carcinogenesis. HPV was detected in Merkell carcinoma together with MCPyV. The co-existence of these oncogenic suggest a sort of co-carcinogenic process, opening new perspectives of immunotherapy.

New therapies of HPV-associated cancers. New therapeutic vaccines were produced, and tested in our mouse models demonstrating their high effectiveness in curing experimental tumors. Our genetic vaccine are able to induce not only cell-mediated but also humoral responses.

Publications

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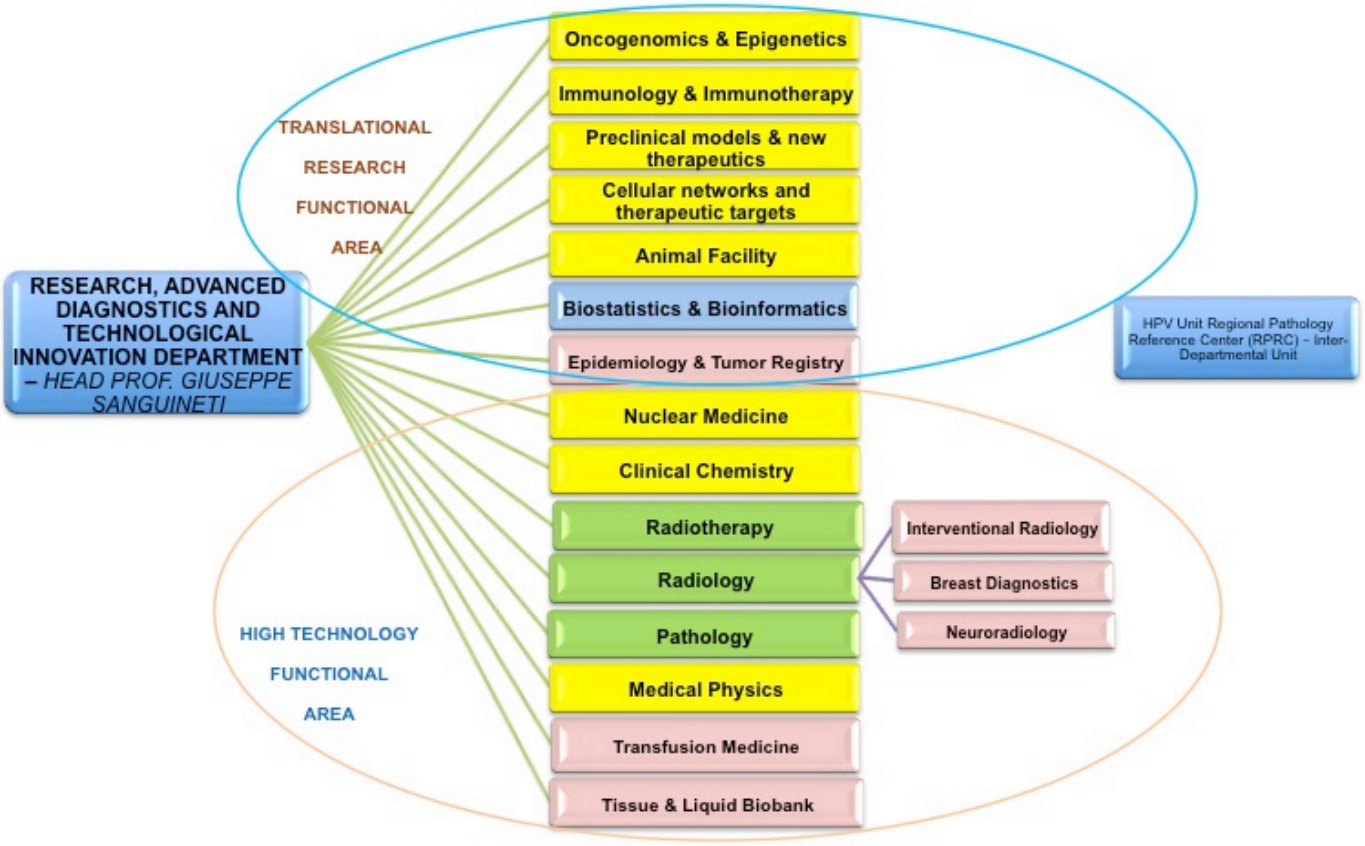
DEPARTMENT OF RESEARCH, ADVANCE DIAGNOSTICS AND TECHNOLOGICAL INNOVATION

Director: Prof. Giuseppe Sanguineti



ONCOGENOMICS & EPIGENETICS UNIT

Head: Giovanni Blandino, MD

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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

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IMMUNOLOGY & IMMUNOTHERAPY UNIT

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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. 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. We have investigated how the coordinated assembly of the cytoskeletal filaments is finely regulated by a variety of intra and extracellular signals and, in turn, modulates crucial signaling cascades. We found that the alteration of the ECM-integrin axis leads to cell–cell junction disruption and cell spreading resembling the EMT process. This process is regulated by the splicing program of hMENA, the actin cytoskeleton regulatory protein identified by this Unit. The alternative expression of the hMENA isoforms along with the expression of Fibronectin in the stroma identifies NSCLC patients with different prognosis. Cancer associated stromal cells, including CAFs, can promote remodeling of ECM and support tumor growth, and we have identified in pancreatic and NSCLC tumors a subgroup of CAFs related to hMENADv6 overexpression with a pro-invasive activity mediated by paracrine signaling.

We are characterizing the molecular bases that link immunogenic chemotherapy to the appearance of cancer stem cells and studying their immunogenicity for preventing tumor relapse through precision immunotherapeutic protocols.

In melanoma patients treated with chemo-immunotherapy we have identified an antigen-specific CD8+ T cell population with a peculiar phenotypic maturation profile, in terms of co-stimulatory or inhibitory molecules. The TCR repertoire has been analyzed in depth. Starting from the immunomonitoring of these patients we revealed a novel CD8+ subpopulation, CD28- PD-1+, which is polyfunctional although expressing the inhibitor molecule PD-1.

In Merkel carcinoma and in actinic keratosis we found the presence of HPV, suggesting its involvement in skin carcinogenesis. In a luminescent mouse tumor model, we found that E5 DNA vaccines induced specific immunological responses and tumor growth inhibition and that new therapeutic DNA vaccines based on HPV16 E7 fusion with a plant-derived signal sequence are able to cure experimental tumors.

The role of polyphenolic extracts of artichoke on crucial cancer-related pathways has been analyzed, suggesting that they may be employed for designing new combined therapies.

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PRECLINICAL MODELS AND NEW THERAPEUTIC AGENTS UNIT

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Mission

The effort of this Unit is to develop latest advances in cancer modeling, including patient-derived xenografts, and organoid/tumoroid technology (ovarian, lung, colon cancer, melanoma, sarcoma, 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 signaling) that become derailed to cause cancer, providing insight into pathways 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 mechanisms of resistance to cancer therapy, thereby helping to define strategies to overcome 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)

Emerging novel mechanistic aspects of endothelin-1 (ET-1) signaling in tumor development and progression to treatment resistance and metastasis steer the development of new treatment strategies. We explored how augmented levels and/or activity of

the ET-1receptor/β-arrestin-1 (βarr1) in ovarian, colorectal, and other cancers results in a transcriptional reprogramming that activates downstream transcription factors and promote pro-metastatic processes and chemoresistance. In recent research, we have identified ET-1 signaling as a critical upstream mediator of β-catenin transcriptional activity. Mechanistic understanding of this process has unveiled new opportunities for targeting ET-1R/βarr1 crosstalk in ovarian and colorectal cancer, a strategy that should be validated under clinical testing. These findings provide a mechanistic rationale to block ET-1/βarr1 signaling with newer antagonists to boost the effectiveness of anticancer chemotherapies.

(PI L. Rosanò)

In order to discover new determinants in ET-1R-driven invasive protrusions, invadopodia, we identify the right network of proteins, including members of the actin-cytoskeleton regulatory family, as novel interacting partners of β-arr1. The β-arr1-driven interactome triggered by ET-1 leads to enhanced invadopodial activity, and metastatic spread of serous ovarian cancer cells.

(PI D. Del Bufalo)

There has been an increased understanding of the critical molecular events and key signaling pathways that drive cancer, especially in the disease refractory setting where patients have progressed on standard treatment regimens. By using human melanoma and glioblastoma cell lines and their derivative BCL-XL overexpressing clones, we investigated the role of BCL-XL in aggressive features of these two tumor models. BCL-XL overexpression increased cell migration, invasion and the ability to form vasculogenic structures, as well as tumor spheres, supporting the concept that BCL-XL plays an essential role in the maintenance of cancer stem cell phenotype contributing to the aggressiveness of both melanoma and glioblastoma. All these BCL-XL-driven tumor progression-associated properties were completely inhibited by the exposure to a BCL-XL specific inhibitor. Finally, the markers of neoangiogenesis and vasculogenic mimicry were up-regulated in BCL-XL overexpressing xenografts. The relevance of BH4 domain in non-canonical roles of Bcl-2 and Bcl-xL proteins underlies the promising therapeutic potential of BH4 domain inhibitors and their future employment in novel anticancer strategy. This could lead to the development of novel combination regimens that have promising clinical activity.

(PI R. Galati)

An increasingly deep understanding of cancer biology is needed to guide the design of new regimens (e.g., rational combinations) that will address key unmet medical needs and to enrich clinical trials for those subsets of patients most likely to benefit from these regimens. To understand the role of estrogen in the pathogenesis of mesothelioma (MM), we quantified the levels and expression of estradiol (E2) and related metabolites in the plasma and tissues of MM patients, as potential predictive biomarkers. In MM cell lines, E2, after binding with GPR30, promotes MM cell proliferation via ERK and STAT3 phosphorylation. The treatment with an aromatase inhibitor, exemestane, by increasing the reactive oxygen species (ROS) and decreasing the E2, induce cellular death in MM cells and xenografts. Therefore agents like exemestane, with anti-aromatase effect and which increase ROS levels, may be useful in MM therapy.

Publications

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CELLULAR NETWORKS AND MOLECULAR THERAPEUTIC TARGETS UNIT

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Project Leaders:
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- **Gabriella D'Orazi, M.D., Ph.D.**
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- **Laura Monteonofrio, Ph.D.**

Administrative Collaborator:
- **Daniela Bona, Ph.D.**

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 the 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

Biobank of sarcoma's tissues and cells.

In collaboration with the Orthopedics Unit, Dr. Falcioni is 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.

ATM germline variants by p53-MCL 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 the rare variants with unknown, but predicted deleterious functions in breast cancer susceptibility gene such as ATM. We have developed and validated a functional test based on p53 mitotic centrosomal localization (p53-MCL) in peripheral blood mononuclear cells that diagnoses mutant ATM zygosity. Having demonstrated that p53-MCL contributes to the oncosuppressing activities of p53 (see below), we are employing the p53-MCL test to improve our ability to identify the BRCAness phenotypes.

Research Activity

Overcoming drug resistance in cancer. Both hypothesis-driven and computational drug repositioning have been undertaken toward targeted therapies. 1) Dr. Falcioni has studied the trabectedin-resistance in patients with liposarcoma and provided a rationale for combining NFkB inhibitors with trabectedin to overcome this drug-resistance. 2) Dr. Paggi focused his attention on the treatment of glioblastoma multiforme by repositioning old drugs and selecting novel SGK1 inhibitor, such as SI113. 3) Prof. D'Orazi has studied 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. 4) Dr. Cardone has repositioned FDA-approved drugs for the inhibition of the PI3K/AKT oncogenic pathway in breast cancer cells and with strong cytotoxic effects against metastatic and chemo-resistant cancer stem cells subpopulation in triple-negative breast cancer.

DNA damage response (DDR) and chromosomal instability (CIN). CIN is common in tumors developed in individuals carrying germline mutations in the DDR genes. Along with DNA caretaker functions, several DDR factors possess activities linked to mitosis-associated organelles, i.e., the ATM-mediated p53-MCL. Germline mutations in the ATM gene predispose to cancer and consistently impair p53-MCL (see above). We have now discovered that p53-MCL contributes to the "mitotic surveillance pathway" and chronic impairment of p53-MCL associates with CIN.

Publications

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SAFU

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Susanna Falcucci, Graduate Student
Umberto Brocco, 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.

Clinical Activity

On demand, remote (telefone and on-line) clinical counseling for non resident patients about HPV related diseases (HPV Unit).

Research Activity

G-quadruplex forming sequences have been described in crucial biological processes participating in tumor progression. In this context, Dr. Leonetti demonstrated that EMICORON bind to G4 structure present in gene promoters and introns of CD133 and VEGFR-2, thus reducing cell proliferation and tumor angiogenesis. These results indicate that EMICORON represents a good example of multimodal class of antitumoral drug, able to simultaneously affect multiple cancer targets.

Cancer cells frequently exhibit several epigenetic reprogramming suggesting that chromatin regulators are important for tumor development and growth. During this year, Dr. Fanciulli's group generated a mouse model (Vk*Che-1) in which the specific over-expression of Che-1 in plasma cells induces the development of multiple myeloma. When compared to plasma control cells, tumor cells from Vk*Che-1 mice showed increased chromatin opening and a global increase in gene transcription, and in particular of several genes involved in the transformation and progression of multiple myeloma. These findings are consistent with recent findings showing an opening of heterochromatin and numerous alterations of specific super enhancers in multiple myeloma.

Dr. De Marco has been working at the description of oxidative stress adducts, induced by the UV-B, UV-A, and short wave visible components of the solar radiation, on the proteome of keratinocytes, melanocytes and fibroblasts and their contribution to cancer initiation and progression. He is also involved in the study of the oxidative balance and antioxidant response in epithelial cells transformed by Human Papillomavirus oncogenes.

Dr. Gurtner studied the functional role of NF-Y and its associated protein complexes (lamin A, mutp53, Dicer, Ago2) focusing on transcriptional and posttrascriptional regulation mechanisms of deregulated miRNAs during epithelial mesenchymal transition of colon and pancreatic tumor cells.

Dr. Piaggio studied the role of the systemic macroenvironment before and during tumour development in order to identify early biomarkers of disease using genetically modified mouse models of breast and pancreatic cancer where the disease course can be tracked by bioimang. Moreover, her research deals with cancer patients sera characterization of new non-invasive diagnostic and/or prognostic biomarkers (such as the amount of cfDNA, the degradation index of cfDNA and/or the mitochondrial derived cfDNA). In this regard, she actively have collaborated with the Gynaecology Unit directed by Dr. Enrico Vizza for the analysis of these nucleic acids in the serum of patients with endometrial cancer.

Dr. Toietta focused his studies on regenerative medicine approaches aiming at restoring and maintaining normal function in diseased and injured tissues. He is assessing different strategies to enhance the chance of cell engraftment upon transplant.

Publications

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BIOSTATISTICS AND BIOINFORMATICS UNIT

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Staff

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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 Activity

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 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.

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.

Publications

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CLINICAL PATHOLOGY UNIT

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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 Activity

In 2017, 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.

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 are: identification of specific chromosome abnormalities, monitoring disease progression and the success of bone marrow transplantation.

Besides, we search for actionable genetic abnormalities to improve the prognosis of sarcoma patients

Research Activity

Diagnostic harmonization initiative on Multiple Myeloma for Gruppo Laziale Mieloma Multiplo.

PI Cordone I, Masi S, Merola R

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, Antenucci A

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, Cigliana G, Mandoj C

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".

Publications

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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 2017 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 2017 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 2017 cytological samples from about 8.400 patients have been studied, including FNAC, effusions, urine and cervico—vaginal cytology. In 2017 about 18.000 tests of diagnostic immunohistochemistry have been performed, including mainly tumour immunohistological typing and assessment of tumour prognostic and/or predictive factors. In 2017 about 700 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 2017 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 based on a panel of 22 different genes ('ONCOMINE'). Furthermore, in 2017 about 350 molecular tests for MGMT promoter gene mutational status and IDH1---IDH2 gene mutation in primary CNS tumours, and MSI evaluation, mainly in colorectal cancer, have been performed.

Research Activity

HPV related disease (head&neck and cervical cancer)

We have conducted epidemiological, clinical and molecular studies on HPV-related diseases on individuals affected by benign or malignant head & neck or cervical lesions, as well as on healthy high-risk populations. Regarding head & neck tumours, particularly those developed in the oropharynx, we collaborated with IARC, ISG, and a number of clinical and experimental Units of our Institute. Regarding cervical cancer prevention, we coordinated the NTCC2 study, a large Italian multicentric study aimed to investigate the cross-sectional and longitudinal value of the HPV mRNA and the p16/Ki67 tests as triage test for HPV DNA positivity in cervical screening.

miRNA studies (thymic epithelial tumours, prostate and gastric cancer)

- Identification of a 69-gene signature of miR-145-5p putative target mRNAs as further development of the multicentric study on mature MicroRNA profiling of thymic epithelial tumours.
- Investigation of c-Met/miR-130b axis as a new prognostic marker for prostate cancer risk assessment and as indicator of therapy resistance.
- Identification of a novel miR-204 gene target signature perturbed in gastric cancer and in cholangiocarcinoma.

Immunohistochemical (IHC) studies (breast and gastric cancer)

- IHC analysis of MST1/2 and LATS1/2 expression in neoadjuvant treated (NAT) breast cancer (BC) evidenced that the Hippo kinases localization differently impacts therapy efficacy, being protective when expressed in the tumour cell cytoplasm and in tumour-infiltrating lymphocytes and, conversely, inducing chemoresistance when present in the nucleus as a consequence of their cooperation with the DNA damage response (DDR). Moreover, we evidenced a relationship between DDR biomarkers (namely-H2AX and pChk1) and response to NAT according to Body Mass Index status.
- A multicentric study conducted on a series of advanced gastric cancer treated with first-line chemotherapy showed that the oncogenic YAP/TAZ-Wnt crosstalk may be active in this neoplasia, and confers chemoresistant traits that translate into adverse survival outcomes.

Molecular studies (breast,lung, colorectal, ovarian, and endometrial cancer)

- Logistic regression models have indicated that the cut-off of 2150 copies detected by One-Step Nucleic acid amplification (OSNA) discriminates with great accuracy BC patients with negative or positive lymph nodes in comparison with the conventional OSNA cut-off of 5000 copies, contributing to better identify patients who really need an axillary node dissection.
- We have evaluated HER2 status in a series of BC, defined as low amplified or equivocal by in situ hybridization (ISH), using a more objective molecular assay (MLPA), which resulted a reliable and objective supporting test in identifying HER2 positive BC patients.
- The recent introduction of Next Generation Sequencing (NGS) for routine molecular diagnosis mainly of Non Small Cell Lung Cancer and Colorectal Carcinoma allowed us to detect clinically actionable genomic alterations quickly and reliably. The diagnostic output generated by the Oncomine Knowledge Reporter (OKR) software provided clinical oncologists with continuously updated and readily accessible information in accordance with approved guidelines for patients' clinical management, and ongoing clinical trials for the potential enrollment of eligible patients.
- We have investigated the association between the expression of the glucose transporter GLUT1 in a series of FIGO high grade/stage serous ovarian carcinomas. The evidence that strong GLUT1 staining was inversely associated with circulating levels of fasting glucose may help to clarify the potential of biomarkers related to energy metabolism, in terms of prognosis definition and treatment assignment.

- We have contributed to evaluate the prognostic role of NF-Ya splicing isoform and Laminin A status in low grade endometrial cancer with high risk of progression.

Main International Collaborations (thymic epithelial tumours, male and female breast cancer, colon and ovarian cancer)

In the framework of international studies we have participated in the International Collaboration on Cancer Reporting (ICCR) initiative for the development of a dataset for TET reporting. Moreover, we have contributed to the new TNM staging of TET and of Lung cancer, by collaborating with UICC in the Staging and Prognostic Factors Committee (SPFC)

We have participated to a multicenter study (University of Leeds, UK) aimed to analyze the survival impact of 14 biomarkers (ERα, ERβ1, ERβ2, ERβ5, PR, AR, Bcl-2, HER2, p53, E-cadherin, Ki67, survivin, prolactin, FOXA1) in a large series of male breast cancer on tissue microarrays.

FOXA1 and AR were both positively prognostic for survival, remaining upon multivariate analysis.

We have been involved in a study aimed to investigate the prognostic role of a class of small RNAs generated during the maturation process of tRNA tRNA-derived small RNAs (tsRNA) known to be deregulated during carcinogenesis, in colon, breast and ovarian cancer (The Ohio State University Comprehensive Cancer Center, USA).discipline

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MEDICAL PHYSICS AND EXPERT SYSTEMS LABORATORY

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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 mission aims at reducing the in-debit dose to patients and environment trough specific procedures fulfilling the national and international legislation. In particular, the Lab provides daily assistance in 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 the

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 Activity

The Lab implements quality assurance protocols to perform efficiently and safely diagnosis and therapies. In particular it daily develops the 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 Imaging Departments 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) 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 also ISO 9001 certified.

Research Activity

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 "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

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NUCLEAR MEDICINE UNIT

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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 2017 over 16.000 therapeutic and diagnostic procedures were performed with approximately 330 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.

1. 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 900 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

2.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 131I SPET/CT and 18F-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.

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RADIOTHERAPY UNIT

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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

- 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.

- 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.

- 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.

- 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.

- 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.

- 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.

- 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.

- 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.

- 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)

- 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.

- 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.

- 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).

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Mission

The Department of Radiology offers comprehensive state-of-the-art equipment diagnostic radiology and image-guided interventional services such as MRIs (1.5 Tesla and 3 Tesla), TC (2 128-Layer Equipment), Ultrasounds, Senology and traditional X-rays for the diagnosis, staging and treatment of cancers as well as subsequent post-treatment follow ups. It specializes particularly in cervical-facial disorders, pleural mesothelioma, integrated breast diagnostics through ultrasounds and mammographies, mammotome and MRIs, multiparametric prostate MRI, imaging in neurooncology, soft tissue tumours and all interventional procedures that involve vascular and extravascular approaches. In addition, neoplasms of the female pelvic, lung, colon rectum and onco-hematologic diseases are also assessed by using various techniques. The Department is involved in all diagnostic and therapeutic pathways (PDTA) and actively participates in all Disease Management Team meetings (DMT).

Clinical Activity

The clinical activities carried out include: a reduction in the number of internal patients and a rise in the number of outpatients. Establish an agenda based on the PDTA in accordance with the General Director's Office (which is still ongoing). An increase in the use of the 3 Tesla examinations for outpatients. A rise in the use of CTs for outpatients after recruiting two new Radiologists with funding from the Balduzzi grant. An increase in the demand for exams in the Unit of Angiography with loco-regional treatment of liver tumors and liver embolization with Ittrio 90. The following health care services were carried out mainly on inpatients, these include: percutaneous ablative procedures, preoperative embolization of neoplastic osteo-muscular origin and percutaneous ablation of osteoid osteomas. An increase in the number of offering iPAC, Day Service and Day Surgery services instead of pre-hospitalization.

On Mondays to Fridays the following services are offered in the rooms below:

- 9 rooms (9-10 Radiologists on duty) (1 Traditional X-ray room, 1 Angiography room, 2 Mammography rooms)
- 1 Ultrasound room, 2 CT rooms, 2 MRI rooms). (On Wednesdays 1 CT room reserved for ISG; On Wednesdays the Mammotome room is open within the Breast Unit.)
- In the Afternoons 3-4 rooms are open with 2 physicians on duty to carry out CTs, MRIs or Ultrasounds, Traditional X-rays

On Saturdays the following services are available:

- In the Mornings 3 rooms are dedicated to carrying out CTs, MRIs, Traditional X-rays) with 2 Radiologists on duty.

Research Activity

Studies were conducted on the use of 1.5 MRI and 3 Tesla diffusion spectroscopy and tractography perfusion for distinguishing neoplasias or recurrences from inflammatory tissues or post-surgical or post-radiotherapeutic fibrosis tissues. Distinguishing between chemo and radiotherapy treated lymph node residues that are not evident on morphological imaging. Thanks to diffusion, we were able to hypothesize the nature of lymph node residues and to distinguish those that are metabolically active to fibrotic ones by correlating data with metabolic imaging such as PET-CT. Diffusion sequences allow the use of multiple B values (IVIM technique) that obtain information on the degree of perfusion and cellularity of tissues without the use of contrast media as well as permit monitoring the response to treatments both during and immediately after combined treatments.

One other goal that we achieved is linked to definition through the variation of perfusion fractions and the variation of apparent diffusion coefficient (ADC) or pure diffusion of patient responders from all non-responders. Once having completed the AIRC study protocol regarding the use of 3T MRI on rectal tumors with weighted diffusion and perfusion sequences, the results will be published. Studies on identifying MRI morpho-functional multiparameters of prostate cancer before and after therapy, in particular of morphofunctional alterations after radiotherapy compared with PET scan were carried out. MRI evaluation of morpho-functional characteristics of renal carcinoma before and after localized surgery and/or radiotherapy.

Ongoing functional studies allow to define neoangiogenesis using dynamic contrast-enhanced DCE providing information on perfusion and cellularity through brain tumor diffusion. Through an accurate determination of K, we were able to assess the degree of aggression on lesions. We evaluated neo-adjuvant treatments using 3T MRI adapting functional techniques on soft tissue sarcomas, osteosarcoma and Ewing sarcoma and evaluated patient response of sarcomas treated with Trabectin and Paz. Assessed the use of "Liquid Biopsies" in Ewing sarcoma treatments. Still carrying out an ongoing study on the use of iodinated contrast media in association with mammography (CESM) and digital mammography. The evaluation of this new technique between mammography as a second-level examination and an MRI mammogram have obvious implications on technical appropriateness and down steam care and costs of MRI activities.

Publications

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TRANSFUSION MEDICINE UNIT

Head: Maria Laura Foddai, MD

Staff

Mafalda de Rienzo, MD
Eleonora Fiorelli, MD
Alessandra De Masi, MD

Technicians:
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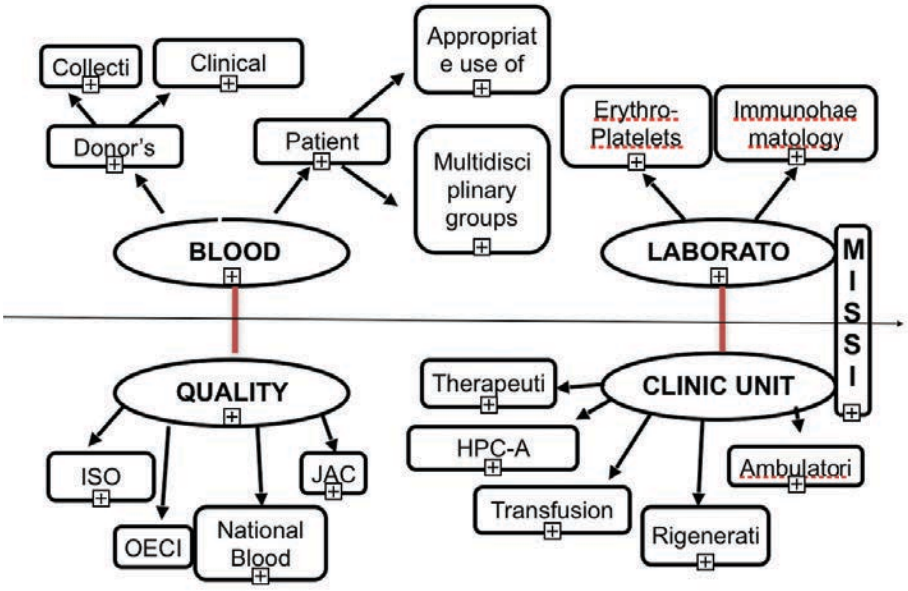
Tonino Federico
Nadia Coculo
Patrizio Ceccacci
Daniela Mozzetti
Emanuele Fazi
Silvia Paluzzi
Maria Piedimonte

Pina Chichierchia, Biologist
Maria Rosa Piras, Nurse
Patrizia Comuzzi, Nurse
Flavia Avellino, Administrative Collaborator



Clinical Activity

The Immunohaematology and Transfusion 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.

Publications

Cameli N, Mariano M, Cordone I, Abril E, Masi S, Foddai ML. Autologous pure platelet-rich plasma dermal injections for facial skin rejuvenation: Clinical, instrumental, and flow cytometry assessment. Dermatol Surg 2017;43(6):826-835 IF 2.351.

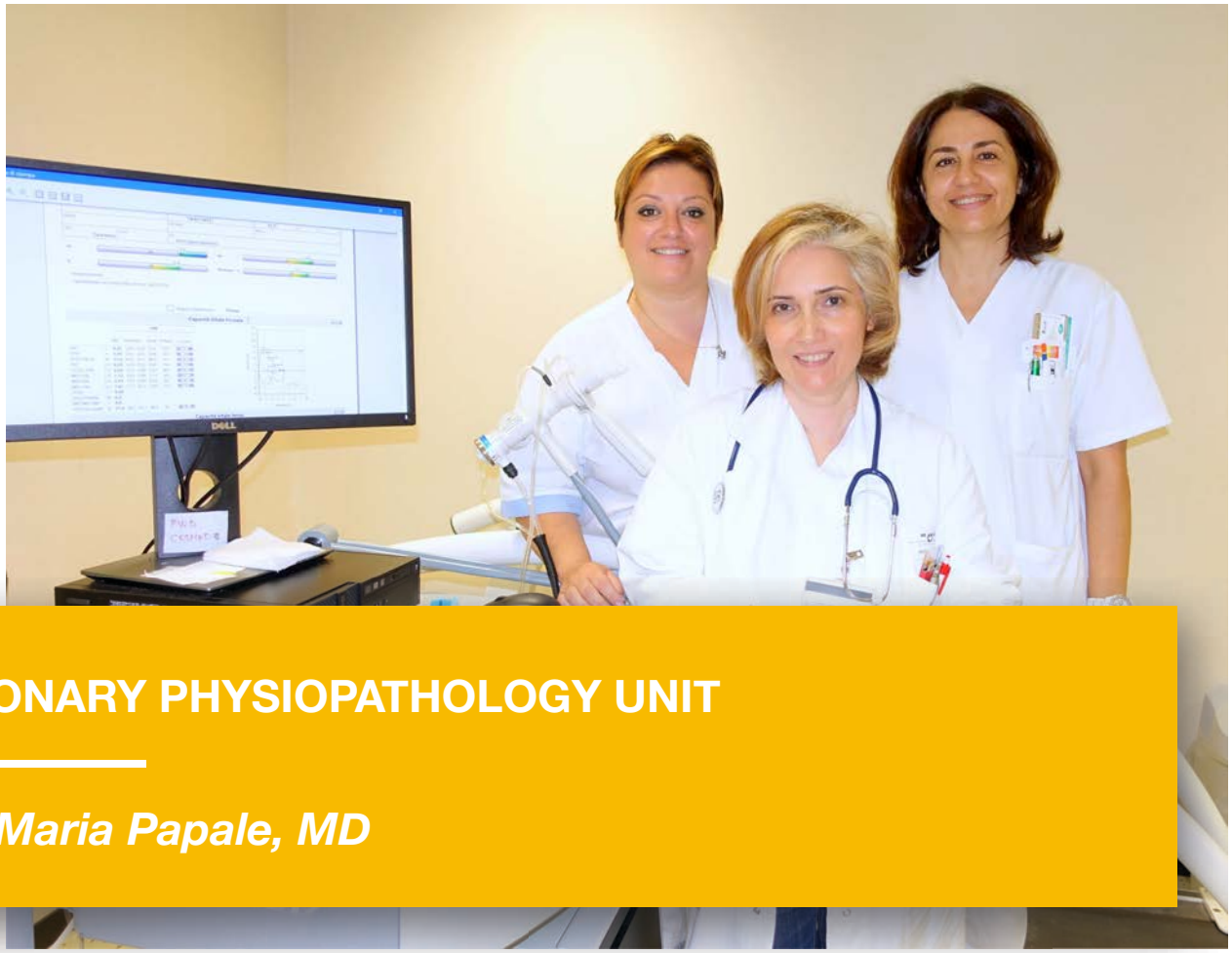
Research Activity

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.



PULMONARY PHYSIOPATHOLOGY UNIT

Head: Maria Papale, MD

Staff

Eliuccia Mastropasqua – MD
Giorgio Piperno – MD
Vincenzo Cilenti - MD
Antonio Scappaticci - Administrative collaborator
Sabrina Fraternali – Nurse
Maria Cassino - Nurse
Annalisa Carolina Damiani – Student

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 (above all concerning addiction to smoking and didactic intervention for young people in schools) 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 decided to implement respiratory rehabilitation activities with the aim to improve both the quality of life and increase our knowledge of an area of respiratory rehabilitation which requires further study in particular investigating quality of life and the recovery of respiratory functionality through suitable tests. The Unit commenced an internal Outpatient Clinic for the Interstitial lung disease and IPF (Idiopathic pulmonary fibrosis) rare diseases but frequently verified in our Istitute as outcomes of administered therapies. In addition to early diagnosis and therapy of the IPF, itcontributes 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 didactic intervention even in schools.

Clinical Activity

During 2017 about 17.086 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 15.238 services conducted for outpatients who came either for pulmonary oncology and other diseases or for to quit smoking or to run respiratory rehabilitation.

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 2017, about 4343 services of respiratory rehabilitation have been performed on internal patients and 3039 on external patients. In addition, about 90 patients were visited in the internal outpatient clinic of interstitial lung diseases and IPF.

Research Activity

- The “Hospital free of smoke” project goes on with didactic initiative and monitoring activities.
- The Unit has taken part along with “Istituto Mario Negri” e AIPO (Associazione Italiana Pneumologi Ospedalieri) in: “Studio has participated 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 developed PDTA about Interstitial lung disease and IPF and a PDTA about “Respiratory rehabilitation”.

Publications

Melani AS, Bonavia M, Mastropasqua E, Zanforlin A, Lodi M, Martucci P, Scichilone N, Aliani M, Neri M, Sestini P, Gruppo Educazionale Associazione Italiana Pneumologi Ospedalieri (AIPO). Time required to rectify inhaler errors among experienced subjects with faulty technique. Respir Care 2017;62(4):409-414 IF 4.352.

- The “Hospital free of smoke” project goes on with didactic initiative and monitoring activies.
- The Unit has also taken part in the international study: CQVA149A3401 (A prospective, multicenter, 12-week, randomized open label study to evaluate the efficacy and safety of glycopyrronium (50 micrograms o.d.) or indacaterol maleate and glycopyrronium bromide fixed-dose combination (110/50 micrograms o.d.) regarding symptoms and health status in patients with moderate chronic obstructive pulmonary disease (COPD) switching from treatment with any standard COPD regimen.
- The Unit has taken part along with “Istituto Mario Negri” e AIPO (Associazione Italiana Pneumologi Ospedalieri) in: “Studio multicentrico osservazionale sull’utilizzo della sigaretta elettronica in Italia” and has participated 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 started the realization with a specific multidisciplinary team of PDTA about Interstitial lung disease and IPF and a PDTA about “Respiatory rehabilitation”.

EPIDEMIOLOGY AND CANCER REGISTRY UNIT

Staff

Valerio Ramazzotti, MD
Maria Cecilia Cercato, MD
Marco Caperle, MD
Oreste Aronadio, MD

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.

Activity

Cancer Registration

Since 2015, in accordance to a regional law establishing the Population Based Cancer Registry of the Lazio region, 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 results of the preliminary activity were presented at workshop "Registro tumori del Lazio: stato dell'arte e prospettive" – 16 November 2017. Regione Lazio. Rome

The hospital-based cancer registry 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. A first internal report on cases from patients of the "Breast and soft tissue surgery unit" was released in November 2017.

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 demand 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" at the National Regina Elena National Cancer Institute.

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 designing and implementing an institutional database able to collect data from the rare solid cancer patients who are diagnosed and treated at the Institute.

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 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 pilot study). The Unit organized the conference "Progetto di Medicina Narrativa - Raccontami di te" (the 2nd meeting). "La narrazione alla base della conoscenza: applicazione nella pratica clinica in Oncologia". IFO, 31 May 2017.

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Fonte: JCR 2016

BRAIN

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
C	Weekly carboplatin in the treatment of recurring high-grade gliomas: observational study	Medical Oncology 1	Fabi	4
C	A Randomized, Placebo Controlled Phase 2b/3 Study of ABT-414 With Concurrent Chemoradiation and Adjuvant Temozolomide in Subjects With Newly Diagnosed Glioblastoma (GBM) With Epidermal Growth Factor Receptor (EGFR) Amplification (Intellance 1)	Neurology	Pace	0
C	Difference between neurocognitive impact with chemotherapy and radiation therapy hypofractionated temozolomide as single agent in elderly patients (<= 70 years) with newly diagnosed glioblastoma: a multicenter study	Neurology	Pace	0
C	Regorafenib in relapsed glioblastoma. REGOMA study. Randomized, controlled open-label phase II clinical study	Neurology	Pace	0
C	A noninterventional study of Vimpat® (Lacosamide) as adjunctive antiepileptic drug therapy in patients with Brain tumor-related EpilepSy (VIBES)	Neurology	Maschio	1
O	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	Maschio	8
C	The use of the F-FDOPA in the evaluation of gliomas: observational study	Neurology	Pace	10
C	Trabectedin for Recurrent Grade II or III Meningioma: a Randomized Phase II Study of the EORTC Brain Tumor Group	Neurology	Pace	1
O	Il processo decisionale relativo al trattamento nei pazienti neuronocologici	Neurology	Pace/Tanzilli	10
O	Andamento delle cefalee primarie in pazienti con glioma ad alto grado, uno studio osservazionale multicentrico.	Neurology	Pace/Villani	6
C	Studio osservazionale retrospettivo in pazienti con epilessia secondaria a neoplasia cerebrale trattati con perampanel in add-on	Neurology	Maschio	6
O	Spinal fluid microrna as new diagnostic and prognostic biomarkers in CNS	Pathology	Carosi	0

Breast

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
C	A multicenter, open-label, single-arm safety study of Herceptin SC in combination with Perjeta and Docetaxel in treatment of patients with HER2-positive advanced breast cancer (metastatic or locally recurrente)	Medical Oncology 1	Cognetti	3
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	Cognetti	0
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 receptor positive breast cancer subjects with bone metastases	Medical Oncology 1	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	Cognetti	6
O	A randomised, multicentre, open-label Phase II trial investigating activity of chemotherapy and lapatinib and trastuzumab in patients with HER2-positive metastatic breast cancer (MBC) refractory to anti HER2 therapies	Medical Oncology 1	Cognetti	4
O	A Randomized, Open-Label, Phase 3 Study of Abemaciclib Combined with Standard Adjuvant Endocrine Therapy versus Standard Adjuvant Endocrine Therapy Alone in Patients withHigh Risk, Node Positive, Early Stage, Hormone Receptor Positive, Human Epidermal Receptor 2 Negative, BreastCancer	Medical Oncology 1	Cognetti	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	Cognetti	0
C	COMPLEEMENT-1: An open-label, multicenter, Phase IIIb study to assess the safety and efficacy of ribociclib (LEE011) in combination with letrozole for the treatment of men and postmenopausal women with hormone receptorpositive (HR+) HER2-negative (HER2-) advanced breast cancer (aBC) with no prior hormonal therapy for advanced disease	Medical Oncology 1	Fabi	10
C	COMPLEEMENT-1: An open-label, multicenter, Phase IIIb study to assess the safety and efficacy of ribociclib (LEE011) in combination with letrozole for the treatment of men and postmenopausal women with hormone receptorpositive (HR+) HER2-negative (HER2-) advanced breast cancer (aBC) with no prior hormonal therapy for advanced disease	Medical Oncology 2	Vici	11

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	Cognetti	108
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	Cognetti	3
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	Vici	1
O	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	Fabi	0
O	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	Vici	1
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	Fabi	0
O	Nab-Paclitaxel beyOnd clinical tRials: retrospective cohort study in Metastatic breast cAncer patients. The NORMA Study	Medical Oncology 1	Fabi	0
O	Nab-Paclitaxel beyOnd clinical tRials: retrospective cohort study in Metastatic breast cAncer patients. The NORMA Study	Medical Oncology 2	Vici	0
O	Observational Prospective Study with Eribulin for Breast Cancer with Brain Metastases	Medical Oncology 1	Fabi	4
O	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	Cognetti	0
C	Phase I-II study of weekly nab (nanoparticle albumin-bound)-paclitaxel (nab-paclitaxel) in combination with liposomal encapsulated doxorubicin (LDox) in patients with HER2 negative metastatic breast cancer	Medical Oncology 1	Fabi	5
O	Randomized study of fulvestrant as maintenance therapy after first-line chemotherapy in HER2 negative postmenopausal metastatic breast cancer patients	Medical Oncology 1	Fabi	2
O	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	Fabi/Iacorossi	4

C	Indagine osservazionale sull'utilizzo del test Oncotype dx nella pratica clinica corrente	Medical Oncology 1	Cognetti	34
C	Indagine osservazionale sull'utilizzo del test Oncotype dx nella pratica clinica corrente	Medical Oncology 2	Vici	52
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	Cognetti	2
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	Fabi	46
O	Studio retrospettivo osservazionale multicentrico sulle sequenze della terapia ormonale nel trattamento del tumore della mammella metastatico ormonodipendente	Medical Oncology 1	Fabi	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	Cognetti	0
O	Studio Osservazionale Longitudinale di Coorte sulle scelte terapeutiche del carcinoma mammario metastatico HER2-negativo nella pratica clinica Italiana	Medical Oncology 1	Cognetti	0
O	Il ruolo del TDM-1 nella real world evidence	Medical Oncology 1	Fabi	33
O	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 or metastatic triple negative breast cancer	Medical Oncology 2	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	Vici	2
O	Dissecting the role of anti-estrogen receptor alpha autoantibodies in breast cancer	Medical Oncology 2	Vici	6
O	Impact of Hippo Pathway Component in Breast Cancer Patients Treated or to be Treated with Neoadjuvant Chemotherapy	Medical Oncology 2	Vici	22
O	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 first line treatment	Medical Oncology 2	Vici	0
O	Neoadjuvant chemotherapy in mammary carcinoma patients: retrospective evaluation of efficacy and tolerability	Medical Oncology 2	Vici	22
O	TAZ come biomarcatore prognostico in pazienti affette da carcinoma mammario in fase iniziale. PHOBOS Trial	Medical Oncology 2	Vici	0

C	Studio osservazionale, retrospettivo di valutazione dell'impiego di chemioterapia metronomica in pazienti con carcinoma mammario avanzato HER2-negativo	Medical Oncology 2	Vici	3
O	Valutazione Clinimetrica e Assessment Multidimensionale Psicologico-Clinico nella terapia ormonale adiuvante con Inibitori delle Aromatasi per il carcinoma della mammella operato	Medical Oncology 2	Vici	4
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	Vici	7
O	Terapia con Pertuzumab in pazienti affette da carcinoma mammario avanzato HER2 positivo: studio osservazionale retrospettivo multicentrico	Medical Oncology 2	Vici	21
C	Studio pilota osservazionale per la valutazione della qualità di vita nei pazienti trattati con Vinorelbina orale ed endovena per carcinoma mammario metastatico	Medical Oncology 2	Vici	1
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	Vici	12
O	Studio osservazionale retrospettivo sul carcinoma lobulare mammario lobulare precoce e avanzato	Medical Oncology 2	Vici	50
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	Vici	5
O	Terapia con T-DM1 in pazienti affette da carcinoma mammario avanzato HER2 positivo. Studio osservazionale retrospettivo multicentrico	Medical Oncology 2	Vici	1
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	Vici	1
O	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	Vici	8
C	Studio osservazionale, multicentrico, retrospettivo, per la caratterizzazione clinico-patologica di pazienti con carcinoma della mammella in fase avanzata, trattate in prima linea con Trastuzumab in associazione a chemioterapia, con sopravvivenza libera da progressione > a 3 anni	Medical Oncology 2	Vici	0
O	Identificazione biomarcatori predittivi/prognostici nel carcinoma mammario triplo-negativo. NeoTAZ study	Medical Oncology 2	Vici	12

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	Vici	114
C	Terapia con nab-paclitaxel in pazienti affette da carcinoma mammario avanzato. Studio osservazionale multicentrico	Medical Oncology 2	Vici	0
O	A dangerous RNA:DNA affair: Unraveling R-loop management in breast cancer genome integrity and chromatid cohesion	Pathology	Buglioni/Mottolese	0
O	A pilot prospective single blind study to evaluate by sonography the resorption rate of fat graft used as refinements in bilateral implant based breast reconstruction from two different harvesting site	Plastic & Reconstructive Surgery	De Vita/Solivetti	2
C	Phase IV, Multicenter, Open Label, Non Randomized Comparative Group Study to Assess the Safety and Performance of the OrbiSymm in Subjects Referred to Contra Lateral Breast Symmetrisation Involving a Breast Reduction following Breast Reconstruction Post Mastectomy	Plastic & Reconstructive Surgery	De Vita	1
C	Diagnostic Accuracy of Contrast-Enhanced, Spectral Mammography (CESM) and 3 Tesla Magnetic Resonance Compared with Full Field Digital Mammography plus Ultrasound in breast lesion detection and characterization: results from a (pilot), open-label, single-centre prospective study	Radiology	Ferranti	48
O	Radioterapia accelerata ipofrazionata in pazienti operate per tumore della mammella con indicazione anche all'irradiazione delle stazioni linfonodali regionali. Studio di fattibilità	Radiotherapy	Sanguineti	13
O	LiqBreasTrack: tracking mutational hotspots in breast cancer patients treated with T-DM1 by liquid biopsy	Translational Research Functional Area	Allegretti/Giacomini	7

ENDOCRINE

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
O	Liquid biopsy per la valutazione prognostica del carcinoma midollare della tiroide	Endocrinology	Appetecchia	0
O	Efficacyand safety of Lanreotide ATG 120 mg in combination with Temozolomide in subjects with progressive wll differentiated thoracic neuroendocrine tumors	Medical Oncology 1	Milella	1
O	Studio di confronto in termini di costo-efficacia di tre diversi approcci/strategie nella prevenzione dell'ipocalcemia transitoria dopo tiroidectomia	Otolaryngology Head & Neck	Mercante	67

GASTROINTESTINAL

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
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	Conti	12
O	Toxins produced by intestinal bacteria and predisposing genetic variations: a dangerous link for colorectal cancer development?	Digestive Endoscopy	Stigliano/Oddi	110
O	Toxins produced by intestinal bacteria and predisposing genetic variations: a dangerous link for colorectal cancer development?	Hepato-Biliary-Pancreatic Surgery	Oddi/Stigliano	9
O	Dissecting the Adipose Triglyceride Lipase (ATGL) functions in the pathogenesis of hepatocarcinoma	Hepato-Biliary-Pancreatic Surgery	Grazi	30
O	Isolation and characterization of tumor stem cells in intra- and extra-hepatic cholangiocarcinoma	Hepato-Biliary-Pancreatic Surgery	Grazi	15
O	Registro italiano di resezioni epatiche mini-invasive	Hepato-Biliary-Pancreatic Surgery	Grazi	10
O	A Multicenter, Randomized, Open-label, 3-Arm Phase 3 Study of Encorafenib + Cetuximab Plus or Minus Binimetinib vs. Irinotecan/Cetuximab or Infusional 5-Fluorouracil (5-FU)/Folinic Acid (FA) /Irinotecan (FOLFIRI)/Cetuximab with a Safety Lead-in of Encorafenib + Binimetinib + Cetuximab in Patients with BRAF V600E mutant Metastatic Colorectal Cancer	Medical Oncology 1	Cecere	0
O	A Multi-centre Randomised Clinical Trial of Biomarker-driven Maintenance Treatment for First-line Metastatic Colorectal Cancer (MODUL)	Medical Oncology 1	Zeuli	0
O	Prevalence of Malnutrition in Surgery	Hepato-Biliary-Pancreatic Surgery	Perri	2
C	CORRELATE - Safety and Efficacy of Regorafenib in Routine Clinical Practice Setting	Medical Oncology 1	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	Zeuli	0
O	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	Milella	0
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	Cognetti	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	Ferraresi	0
O	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	Milella	1
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	Milella	1
O	Valutazione dell'applicazione delle Linee Guida nella pratica medica in Italia. Studio osservazionale multicentrico per il trattamento adiuvante e di prima linea di pazienti con adenocarcinoma duttale del pancreas	Medical Oncology 1	Milella	0
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	Sciuto	0
C	Studio caso-controllo sull'aderenza del paziente alla preparazione alla colonscopia	Nursing Direction	Iacorossi	15
C	Evaluation of 3 Tesla MRI in primary and secondary hepatic tumors undergoing selective hepatic 90Y radioembolization. Correlation of morphologic MRI and clinical outcome	Radiology	Vallati	2
O	Extra-telometric functions of TRF2 in malignant transformation	Translational Research Functional Area	Biroccio	7
O	Survey on the UnMet Needs of Patients Living with mCRC	Translational Research Functional Area	altro	37
O	ULTRAsensitive PLAsmonic devices for early CAncer Diagnosis	Translational Research Functional Area	Giacomini	19
O	Analysis and targeting of oncogenic signals generated by FGFR2 fusion proteins in intrahepatic cholangiocarcinoma	Translational Research Functional Area	Segatto	0
O	Cytokinesis failure, chromosomal instability and tumorigenicity: HIPK2 role in pancreatic cancer	Translational Research Functional Area	Nisticò/Rinaldo	0
O	Innovative tools for early diagnosis and risk assessment of pancreatic cancer	Translational Research Functional Area	Nisticò	48
O	Analisi differenziale dei profili di espressione dei microrRNA in colangiocarcinoma, epatocarcinoma e metastasi epatiche	Translational Research Functional Area	Blandino/Grazi	26

GYNECOLOGICAL

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
O	Endometrial Cancer Conservative treatment - A multicentre registry	Ginecology	Vizza	0
O	Multicenter, randomized, controlled clinical trial comparing two follow-up regimen at different frequencies of examinations in patients treated for endometrial cancer	Ginecology	Vizza	0
O	Iniezione isteroscopica vs. cervicale di tracciante per identificazione del linfonodo sentinella nel tumore dell'endometrio: studio randomizzato, multicentrico	Ginecology	Vizza	0
C	Patologia endometriale tamoxifene correlata in pazienti con pregresso carcinoma mammario: analisi di una casistica retrospettiva multicentrica	Ginecology	Vizza	0
O	Il DNA libero circolante (cfDNA) come biomarcatore prognostico nel cancro dell'endometrio	Ginecology	Vizza/Piaggio	0
O	Multicenter retrospective study on Minimally Invasive Interval debulking Surgery In Ovarian Cancer	Ginecology	Vizza	0
O	Regolazione della sintesi di mediatori lipidici pro-infiammatori e pro-risolventi del processo infiammatorio nel tumore dell'ovaio	Ginecology	Vizza	0
O	Tumori rari in ginecologia oncologica	Ginecology	Vizza	0
C	Studio clinico randomizzato multicentrico sulle deiscenze vaginali dopo isterectomia totale laparoscopica: sutura della cupola per via endoscopica vs. vaginale	Ginecology	Vizza	18
O	A Phase 2, Randomized Study of MLN0128 (a Dual TORC1/2 Inhibitor), MLN0128+MLN1117 (a PI3Ka Inhibitor), Weekly Paclitaxel, or the Combination of Weekly Paclitaxel and MLN0128 in Women With Advanced, Recurrent, or Persistent Endometrial Cancer	Medical Oncology 1	Savarese	0
O	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	Cognetti	1
C	A Randomized, Double-Blind, Placebo-Controlled Phase II Trial of Neoadjuvant Carboplatin and Paclitaxel, With or Without Debio 1143 in Patients With Newly Diagnosed Advanced Epithelial Ovarian Cancer	Medical Oncology 1	Savarese	0
O	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	Savarese	2

O	Randomized, Double-Blind, Phase III Trial of Olaparib vs. Placebo in Patients with Advanced FIGO Stage IIIB - IV High Grade Serous or Endometrioid Ovarian, Fallopian Tube, or Peritoneal Cancer treated with standard First-Line Treatment, Combining Platinum-Taxane Chemotherapy and Bevacizumab Concurrent with Chemotherapy and in Maintenance	Medical Oncology 1	Savarese	0
O	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	Savarese	0
O	EWOC-1 (Elderly Women Ovarian Cancer) Trial: Multicenter, randomized trial of carboplatin +/- paclitaxel in vulnerable elderly patients with stage III-IV advanced ovarian cancer	Medical Oncology 2	Vici	0
O	Phase II trial on trabectedin in the treatment of advanced uterine and ovarian carcinosarcoma	Medical Oncology 2	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	Vici	27
O	Studio retrospettivo multicentrico: correlazione tra genotipo, fenotipo e outcome clinico nei tumori ovarici ereditari BRCA 1 e BRCA 2 mutati	Medical Oncology 2	Vici	0
O	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	Vici	0
C	Valutazione del test Xpert® HPV nella determinazione dell'infezione da Papillomavirus (HPV) in campioni tissutali di carcinoma dell'orofaringe fissati in formalina e inclusi in paraffina	Pathology	Benevolo	159
O	Attacking proliferation and chemoresistance in ovarian cancer: therapeutic potential of a new functional link between oct4 and the rb pathway	Pathology	Carosi	10
O	Microvesicles' microrna profiling in biological fluid and tissues of ovarian cancer patients	Pathology	Carosi	15

HAEMATOLOGICAL

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
O	Studio prospettico multicentrico sulla diagnostica integrata degli infiltrati polmonari nei pazienti affetti da emopatia maligna tramite broncolavaggio alveolare (BAL)	Haematology Oncology	Spadea/Marchesi	3
O	Hematological Malignancies Associated Bloodstream Infections Surveillance	Haematology Oncology	Spadea	23
O	Observational study for the monitoring of chronic, Ph negative myelodisplastic syndromes (SMPC-Ph neg) in adults	Haematology Oncology	Spadea	0

C	Survey of Nasal microbial Interaction with Fungi	Haematology Oncology	Spadea	4
C	"Geriatric Assessment Adapted" Therapy for Ph- ALL Elderly Patients	Haematology Oncology	Spadea	0
C	Studio multicentrico di validazione di un questionario self-report sulla percezione dell'isolamento protettivo in pazienti onco-ematologici sottoposti a trapianto di midollo osseo o di cellule staminali ematopoietiche	Nursing Direction	Pignatelli	10
O	10-day decitabine versus conventional chemotherapy ("3+7") followed by allografting in AML patients>- 60 years: a randomized phase III study oftbe EORTC Leukemia Group, CELG, GIMEMA and German MDS Study Group	Haematology Oncology	Mengarelli	3
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	Mengarelli	0
O	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	Mengarelli	0
C	Front-line treatment of BCR-ABL+ CHRONIC MYELOID LEUKEMIA (CML) with dasatinib. an observational multicentric study	Haematology Oncology	Romano	0
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	Spadea	0
O	Italian Registry on the prevalence of IDH1/IDH2 mutations in Patients with Acute Myeloid Leukemia	Haematology Oncology	Romano	0
O	Long Term Quality of Lyfe Sympton Burden in Acute Promyelocytic Leukemia (APL) Patients Treated with Arsenic Trioxide (ATO) or standar chemiotherapy	Haematology Oncology	Romano	0
O	Multicenter, prospective, non-interventional registry for the monitoring of therapy-related, acute leukemias/myelodisplastic syndromes. Molecular characterization and evaluation of individual susceptibility	Haematology Oncology	Spadea	0
O	Next-generation sequencing for BCR-ABL KD mutation screening in philadelphia chromosome-positive leukemias	Haematology Oncology	Mengarelli	0
O	Phase-III Randomized Study to Optimize TKIs Multiple Approaches - (OPTkIMA) - and Quality of Life (QoL) in Elderly Patients (=60 Years) With Ph+ Chronic Myeloid Leukemia (CML) and MR3.0 / MR4.0 Stable Molecular Response	Haematology Oncology	Romano	2

O	Retrospective study of bendamustine-rituximab and chlorambucil-rituximab as first-line treatment in elderly (>65 years) patients affected by chronic lymphocytic leukemia	Haematology Oncology	Mengarelli	0
O	Registro epidemiologico della leucemia mieloide cronica (LMC)	Haematology Oncology	Romano	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 not eligible for autologous transplantation (ASCT)	Haematology Oncology	Palombi	0
O	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 lymphoma (PMLBCL)	Haematology Oncology	Pisani	0
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 systemic B-cell lymphoma with central nervous system involvement at diagnosis or relapse (MARIETTA regimen)	Haematology Oncology	Palombi	0
O	High-dose chemotherapy and autologous stem cell transplant or consolidating conventional chemotherapy in primary CNS lymphoma - randomized phase III trial	Haematology Oncology	Pisani	0
O	Phase II multicentric study to evaluate the efficacy and the safety of Bendamustine in adjunct to Etoposide, Aracytabin and Melphalan (BeEAM) as a preparative regimen for autologous stem cell transplantation in refractory/relapsed aggressive B-cell non-Hodgkin lymphoma patients	Haematology Oncology	Mengarelli	0
O	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	Palombi	0
O	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	Mengarelli	1
O	Pospective collection of data of possible prognostic relevance in patients with indolent non-follicular b-cell lymphomas	Haematology Oncology	Palombi	0
O	Studio prospettico osservazionale sull'utilizzo e sul monitoraggio della cardiotossicità delle antracicline in pazienti con linfoma diffuso a grandi cellule B	Haematology Oncology	Palombi	0
O	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	Palombi	2

O	Accuracy of alternative TP53 somatic mutational and expression analyses for the prognostication of myelodysplastic syndrome	Haematology Oncology	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	Romano	0
O	Eltrombopag for the treatment of thrombocytopenia due to low- and intermediate risk myelodysplastic syndromes. (Eqol-MDS)	Haematology Oncology	Romano	1
O	Detection of Poor Mobilizer (PM) in Multiple Myeloma (MM) patients: prospective product registry	Haematology Oncology	Mengarelli	9
C	Multicenter, randomized, open label phase II study of CARFILZOMIB, CYCLOPHOSPHAMIDE and DEXAMETHASONE (CCyd) as pre transplant INDUCTION and post transplant consolidation or CARFILZOMIB, LENALIDOMIDE AND DEXAMETHASONE (CRd) as pre transplant INDUCTION and post transplant consolidation or continuous treatment with CARFILZOMIB, LENALIDOMIDE AND DEXAMETHASONE (12 cycles) without transplant, all followed by MAINTENANCE with LENALIDOMIDE (R) versus LENALIDOMIDE AND CARFILZOMIB (CR) in newly diagnosed multiple myeloma (mm) patients elegible for autologous transplant	Haematology Oncology	Pisani	0
C	Prevenzione della neurotossicità con nutraceutico e EMDR in pazienti affetti da mieloma	Neurology	Maschio/Mengarelli	9
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	Petrongari	0
O	MicroRNA coinvolti nella "MYB dependence" di cellule di leucemia Ph +	Translational Research Functional Area	Rizzo	2
O	Liquid biopsy: circulating micrornaS and tumor DNA(ctDNA) as novel non-invasive biomarkers in diffuse large B-cell lymphoma	Translational Research Functional Area	Rizzo/Marchesi	20
O	Role of Che-1 in multiple myeloma cell growth and progression	Translational Research Functional Area	Fanciulli	0

HEAD AND NECK

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
O	Global Treatment Patterns, Health Care Resource Utilization, and Survival Outcomes among Patients with Recurrent and/or Metastatic Squamous Cell Carcinoma of the Head and Neck	Medical Oncology 1	Cognetti	0
C	Study of MEDI4736 monotherapy and in combination with Tremelimumab versus Standard of Care Therapy in patients with head and neck cancer	Medical Oncology 1	Cognetti	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	Spriano	5
O	Observational study on the use of photodynamic therapy with temoporfin (Foscan®) for the palliative treatmnet of recurring head and neck tumors in patients not susceptible to other standard treatments	Otolaryngology Head & Neck	Spriano	2
C	Phase II study of preoperative TPF chemotherapy in locally advanced resectable oral cavity squamous cell cancer in order to improve the rate of pathological complete response	Otolaryngology Head & Neck	Spriano	0
C	Determinazione della presenza del DNA di Papillomavirus (HPV) in agoaspirati linfonodali laterocervicali	Pathology	Benevolo	63
O	Early Diffusion Weighted magnetic Resonance imaging changes to predict tumor response to chemoradiotherapy in HN cancer	Radiotherapy	Sanguineti	29
O	Radioterapia stereotassica su singola corda vocale per carcinoma glottico in stadio iniziale (cTis-1)	Radiotherapy	Sanguineti/Spriano	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	Translational Research Functional Area	Nisticò/Silipo	1
O	Study of the correlation between the expression profile of microRNAs and clinical evolution in patients with squamous carcinomas of head and neck	Translational Research Functional Area	Blandino	9

LUNG

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
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 andIntensive Care	Coccia/Pelagalli	5
O	Decurarization After Thoracic Anesthesia - A Prospective Multicenter Double-blind Randomized Trial Comparing Sugammadex vs Neostigmine Reversal After Thoracic Anesthesia	Anaesthesiology, Critical Area andIntensive Care	Coccia/Pierconti	0
O	Ventilazione protettiva versus ventilazione convenzionale durante ventilazione monopolmonare in pazienti sottoposti ad interventi di chirurgia toracica	Anaesthesiology, Critical Area andIntensive Care	Coccia	15
O	A Phase II Randomized Study of Pembrolizumab in Patients With Advanced Malignant Pleural Mesothelioma	Medical Oncology 1	Cecere	4

C	A randomized, double-blind, placebo-controlled study of the safety and efficacy of aAmatuximab in combination with pemetrexed and cisplatin in subjects with unresectable malignant mesothelioma	Medical Oncology 1	Cognetti	0
O	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	Cognetti	1
C	A Pase III, open-label, randomized study of Atezolizumab (MPDL3280A, anti-PD-l1 antibody) in combination with Carboplatin or Cisplatin+Pemetrexed compared with Carboplatin or Cisplatin+Pemetrexed in patients who are chemotherapy-naive and have stage IV non-squamous non-small cell lung cancer	Medical Oncology 1	Cognetti	2
O	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	Cognetti	0
C	A Phase III open-label, multicenter trial of MSB0010718C versus docetaxel in subjects with PD-L1 positive non-small cell lung cancer that has progressed after a platinum-containing doublet	Medical Oncology 1	Milella	2
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	Cecere	1
C	A Phase III, Randomized, Open-Label, Multi-Center, Safety and Efficacy Study to Evaluate Nab-Paclitaxel (Abraxane®) as Maintenance Treatment After Induction With Nab-Paclitaxel Plus Carboplatin in Subjects With Squamous Cell Non-Small Cell Lung Cancer (NSCLC)	Medical Oncology 1	Milella	0
O	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	Ceribelli	0
C	A Randomized, Double-Blind, Phase III Study of Platinum+ Pemetrexed Chemotherapy With or Without Pembrolizumab (MK-3475) in First Line Metastatic Non-squamous Non-small Cell Lung Cancer Subjects (KEYNOTE-189)	Medical Oncology 1	Cognetti	3
O	A standard regimen of dexamethasone in comparison to two dex-sparing regimens in addition to NEPA in preventing CINV in naïve nsclc patients to be treated with cisplatin based chemotherapy: a three-arm, open-label, randomized study	Medical Oncology 1	Cecere	0
O	An Open-Label, Trial of Nivolumab and Nivolumab Plus Ipilimumab Versus Platinum Doublet Chemotherapy in Subjects With Stage IV Non-Small Cell Lung Cancer (NSCLC)	Medical Oncology 1	Cognetti	2
O	Be-TeaM: Italian observational study on second-line treatment approaches for EGFR-mutated, progressing NSCLC patients in real world clinical practice	Medical Oncology 1	Cecere	2

O	Validation of the Alliance Against Cancer lung panel in patients with Non Small Cell Lung Cancer	Medical Oncology 1	Milella	0
O	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	Cognetti	0
O	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-based Chemotherapy	Medical Oncology 1	Cognetti	0
C	A study on the contribution of caregiver and patient dyads to self-care in COPD	Nursing Direction	Iacorossi	30
O	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	Visca	0
O	Studio multicentrico osservazionale sull'utilizzo della sigaretta elettronica in Italia	Pulmonary Phisiopathology	Papale	17
C	A phase II prospective, single blinded, randomized trial of Hemopatch compared to standard techniques to achieve air leak control after complex thoracic surgical procedures on high risk population for prolonged air leak (> 5 days - PAL)	Thoracic Surgery	Facciolo	17
O	Sperimentazione e validazione dell'estradiolo come nuovo marcatore per identificare individui esposti ad amianto a rischio di mesotelioma. Possibili applicazioni nella prevenzione	Translational Research Functional Area	Galati	0
C	Linking tumor stroma to nucleus via cytoskeleton: hMENA isoforms, signal checkpoints and biomarkers of NSCLC relapse	Translational Research Functional Area	Nisticò	72

SARCOMA

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
O	Rischio di osteopenia/osteoporosi indotte da chemioterapia in pazienti con sarcomi ossei. Studio osservazionale prospettico	Endocrinology	Appetecchia/ Ferraresi	0
O	Studio osservazionale retrospettivo su andamento clinico e trattamento nelle pazienti affette da sarcoma uterino	Ginecology	Vizza	0
O	Studio osservazionale retrospettivo su andamento clinico e trattamento nelle pazienti affette da sarcoma uterino	Medical Oncology 2	Vici	0
O	Sacral Chordoma: a Randomized & Observational study on surgeryversus definitive radiation therapy in primary localized disease (SACRO)	Radiotherapy	Petrongari	0

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	Ferraresi	0
O	Multicentric prospective, randomized, clinical trial for the treatment of patient with relapsed Osteosarcoma (OS)	Medical Oncology 1	Ferraresi	0
O	International randomised controlled trial of chemotherapy for the treatment of recurrent and primary refractory Ewing sarcoma	Medical Oncology 1	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	Ferraresi	0
O	Phase III trial on the efficacy of dose intensification in patients with non-metastatic Ewing sarcoma	Medical Oncology 1	Ferraresi	0
C	Trabectedina nei sarcomi dei tessuti molli. Un'analisi retrospettiva	Medical Oncology 1	Ferraresi	36
O	Valutazione radiologica della risposta in pazienti con sarcomi dei tessuti molli localmente avanzati/ metastatici trattati con trabectedina	Radiology	Anelli/Ferraresi	0
O	A multicenter, randomized open-label phase II/III study, to compare the efficacy of NBTXR3, implanted as intratumoral injection and activated by radiotherapy, versus radiotherapy alone in patients with locally advanced soft tissue sarcoma of the extremity and trunl wall	Radiotherapy	Sanguineti	0
O	Targeting telomere replication in ALT tumors	Translational Research Functional Area	Salvati/Biroccio	5

SKIN

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
O	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	Milella	0
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	Ferraresi	1
O	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	Cognetti	1
O	Beyond tumor cell targeting with pathway inhibitors in human melanoma: role of the microenvironment	Medical Oncology 1	Milella	0

C	Clinical Trial of Nivolumab (BMS-936558) Combined with Ipilimumab Followed by Nivolumab Monotherapy as First-Line Therapy of Subjects with Histologically Confirmed Stage III (Unresectable) or Stage IV Melanoma	Medical Oncology 1	Cognetti	3
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	Ferraresi	0
O	Spanning bcl-2 functions in melanoma models: from microenvironment to microRNA modulation	Translational Research Functional Area	Del Bufalo	0

UROLOGICAL

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
C	Treatment of Acute and Chronic Pain in the Minimally Invasive Partial Nephrectomy: Transversus Abdominis Plane Block vs Intravenous Patient Controlled Analgesia. Prospective Randomized Trial	Anaesthesiology, Critical Area andIntensive Care	Forastiere	0
O	Efficacy of adjuvant Mitotane treatment in prolonging recurrance-free survival in patients with adrenocortical carcinoma at low-intermediate risk of recurrance	Endocrinology	Appetecchia	0
O	A multinational, randomised, double-blind, placebo-controlled, phase III efficacy and safety study of ODM-201 in men with high-risk non-metastatic castration-resistant prostate cancer	Medical Oncology 1	Carlini	1
O	A prospective observational study of patients with metastatic castration resistant prostate cancer progressing after stanDard hormonal therapy suitable for abiraterone acetate trEatment - ABItude	Medical Oncology 1	Carlini	5
O	A prospective observational study of patients with metastatic castration resistant prostate cancer progressing after standard hormonal therapy suitable for abiraterone acetate treatment - ABItude	Urology	Gallucci	2
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	Carlini	0
C	Radium-223 Alpha Emitter Agent in Safety Study in mCRPC popUlation for long teRm Evaluation	Medical Oncology 1	Carlini	0
O	Studio Osservazionale, multicentrico, per la ricerca di fattori clinici predittivi di risposta e di sopravvivenza a Cabazitaxel (Jevtana®) in pazienti con cancro della prostata castrazione-resistente in fase metastatica (mCPRC)	Medical Oncology 1	Carlini	0
C	A phase 3, randomized, controlled, multi-Center, Open-lable study to compare Tivozanib Hydrochloride to Sorafenib in subjects with refrectory advanced renal cell carcinoma	Medical Oncology 1	Milella	2

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	Milella	0
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	Cognetti	0
O	Outcome-related factors in patients with metastatic renal cell carcinoma treated with Everolimus after failure of a first-line treatmentewith VEGF inhibitor.	Medical Oncology 1	Milella	0
O	Targeted Therapy With or Without Nephrectomy in Metastatic Renal Cell Carcinoma: Liquid Biopsy for Biomarkers Discovery (TARIBO)	Medical Oncology 1	Milella	0
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	Cognetti	1
C	Technical and diagnostic performances of PET/CT with 64Cu(II)Cl2 in localization of metastases from prostate carcinoma, in patients undergoing restaging for disease progression during ADT	Nuclear Medicine	Sciuto	24
O	Ruolo della PET con 64Cu-PSMA nel carcinoma della prostata (PC): diagnosi precoce di recidiva biochimica	Nuclear Medicine	Sciuto	35
O	A randomized, double-blind, placebo controlled phase 3 study of JNJ-56021927 in subjects qith high risk, localized or locally advanced prostate cancer recived treatment wirh primary radiation therapy	Radiotherapy	Sanguineti	1
O	Studio Pilota di valutazione dell'utilizzo della 64Cu-PET/TC total body in pazienti con recidiva in loggia prostatica visibile in RMmp	Radiotherapy	Sanguineti	10
O	Studio osservazionale prospettico multicentrico della tossicità intestinale, ematologica e urinaria da irradiazione dell'area linfonodale pelvica (IHU WPRT TOX) nel tumore della prostata	Radiotherapy	Sanguineti	19
O	Studio di fase I-II sulla fattibilità e attività della Radioterapia Stereotassica con Acceleratore Lineare in 3 frazioni per Carcinoma della Prostata a rischio basso/intermedio	Radiotherapy	Sanguineti	13
O	Validazione di modelli predittivi di tossicità dopo trattamento radioterapico per tumore della prostata	Radiotherapy	Sanguineti	1
O	Studio pilota di radioterapia stereotassica pre-operatoria per carcinoma renale operabile in stadio iniziale (Ct1)	Radiotherapy	Sanguineti/Gallucci	0
O	Valutazione di microRNA urinari come strumento non invasivo per predire la risposta alla terapia con BCG nei carcinomi della vescica	Translational Research Functional Area	Costantini/Rizzo	91
O	Effetto di un integratore a base di pomodoro e acqua di vegetazione delle olive (Lycoprozen®) sui marker dell'ossidazione lipidica e dell'infiammazione in pazienti con Ipertrofia Prostatica Benigna (BPH)	Urology	Gallucci	4

C	Valutazione dell'associazione tra obesità, sindrome metabolica e tumore della prostata nei pazienti sottoposti a biopsia prostatica e prostatectomia radicale	Urology	Simone	105
O	Lymphadenectomy in urothelial carcinoma in the renal pelvis and ureter. A randomized international clinical trial on lymphadenectomy in urothelial carcinoma in the renal pelvis and ureter	Urology	Simone	0
C	Observational prospective study to assess time efficiency of intracorporeal orthotopic diversion with robotic staplers after robot assisted radical cystectomy	Urology	Simone	5
O	Cistectomia radicale open versus robotica con derivazione urinaria totalmente intracorporea. Studio prospettico randomizzato mono-centrico	Urology	Simone	0

MISCELLANEA

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
C	DeterminAnts of Antimicrobial use aNd de-scalAtion in critica care	Anaesthesiology, Critical Area and Intensive Care	Pelagalli	10
O	Modification of the gene and microRNA expression profile in vivo during chemo hyperthermia in patients undergoing peritectomy for carcinosis of any origin except mesothelioma: pilot study	Digestive Surgery	Valle	4
O	Applicazione della Medicina basata sulla Narrazione nel trattamento chemioterapico di pazienti oncologici	Epidemiology & Tumor Registry	Cercato	26
C	A prospective, observational study measuring sodium improvement and outcomes in cancer patients treated for moderate to severe hyponatremia secondary to SIADH	Medical Oncology 1	Cognetti	1
O	Prospective Observational Trial to Assess the Impact of Mucositis in Patients Treated with Targeted Therapy in Oncology. (PRO-IMPacT)	Medical Oncology 1	Fabi	0
O	Studio osservazionale di coorte per l'analisi dell'incidenza, grado e management dell'ipertensione arteriosa in pazienti con neoplasia in fase metastatica in trattamento di prima linea con inibitori tirosin-chinasici di VEGFR (sunitinib, sorafenib, pazopanib)	Medical Oncology 1	Fabi	4
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	Vici	92
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	Vici	0
C	A panel of biomarkers as novel tool for early detection of radiation exposure	Medical Physics	Strigari	42
O	Percorso riabilitativo integrato per pazienti affetti da Epilessia Tumorale: la ri-partenza	Neurology	Maschio	1

C	Studio Osservazionale Restrospettivo sui risultati clinici del trattamento delle fratture vertebrali in pazienti affetti da neoplasie solide ed ematologiche, con procedura di elastoplastica con Silicone purificato VK100	Neurosurgery	Telera	46
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	Telera	7
C	Contesto di lavoro e Caring: studio correlazionale multicentrico in ambito assistenziale	Nursing Direction	Iacorossi	303
C	Studio prospettico randomizzato sui pazienti oncologici portatori di PICC e sui caregiver: medicazione ambulatoriale vs/medicazione domiciliare di catetere venoso centrale ad inserimento periferico (PICC)	Nursing Direction	Basili	40
O	La malattia di Casteman multicentrica: una rivisitazione dello "stato dell'arte"	Pathology	Marino	1
O	Metagenomic search for microbiological determinants of human tumors	Pathology	Pescarmona	0
O	Non coding RNA in solid tumors	Pathology	Carosi	30
C	Modifiche delle abitudini alimentari in corso di terapie oncologiche	Psychology	Pugliese	28
O	I costi sociali del cancro: valutazione di impatto sociale ed economico sui malati e sui caregiver	Psychology	Pugliese	97
O	Valutazione neuro-cognitiva in pazienti oncologici affetti da 1 a 3 metastasi cerebrali trattati con radioterapia: radioterapia stereotassica e radioterapia pan encefalica con risparmio dell'ippocampo	Radiotherapy	Marucci	0
O	Endothelin axis/ß-arrestin-driven actin reorganization: bringing the right network of proteins to direct invadopodia	Translational Research Functional Area	Rosanò/Bagnato	0
O	Molecular mechanism of quadruplex-targeted drugs: towards clinical candidate selection	Translational Research Functional Area	Leonetti	14
O	La Biopsia Liquida: studio di fattibilità e trasferibilità alla routine clinica	Translational Research Functional Area	Giacomini	1
O	Analysis of the transcriptional expression profile and microRNAs in brain metastases from primary tumors of various origin	Translational Research Functional Area	Blandino/Telera	11
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	Milella	0

THYMIC

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
O	Contributo allo studio clinicopatologico e molecolare dei Tumori epiteliali timici (TET) sulla base del Database internazionale ITMIG	Pathology	Marino	2

O	Biomarcatori di rilevanza proliferativa/prognostica / immunitaria e distribuzione di molecole di classe II di istocompatibilità nei tumori epiteliali timici e nella controparte normale (timo peritumorale): uno studio retrospettivo clinicopatologico e immunoistochimico	Pathology	Marino	0

MULTIPLE SCLEROSIS

STATUS	TITLE	DIVISION	Principal Investigator	Patients IRE 2017
O	Coagulation/complement activation and cerebral hypoperfusion in relapsing-remitting multiple sclerosis	Neurology	Koudriavtseva	1

Istitutional Courses 2017

Title	Dates from	to	Scientific Coordinator
La riabilitazione polmonare nei pazienti sottoposti a chirurgia polmonare	04-04-2017	04-04-2017	Dr.ssa M. Papale
RIDAIT Seminar-II Modulo	04-04-2017	27-06-2017	Dr. A. Venuti
La comunicazione efficace	13-04-2017	20-04-2017	Dr.ssa A. Caruso
Lavorare in team	04-05-2017	11-05-2017	Dr.ssa A. Caruso
Incontri multidisciplinari di ginecologia oncologia	10-05-2017	28-06-2017	Dr. E. Vizza
Cardio-oncologia patologie cardiache alla radioterapia e protocolli radiologici diagnostico-terapeutici nel contesto multidisciplinare	11-05-2017	11-05-2017	Dr. F. Maramao
I sistemi ibridi per l'acquisizione di immagini di medicina nucleare: siemens "symbia intevo"	18-05-2017	19-05-2017	Dr. R. De Leo
Pubblicare in ambito scientifico	24-05-2017	25-05-2017	Dr.ssa G. Cognetti

Tabagismo e principali patologie fumo-correlate	25-05-2017	25-05-2017	Dr.ssa M. Papale
Aspetti biologici e aspetti relazionali dal curare al prendersi cura	05-06-2017	07-06-2017	Dr.ssa A. Caruso
Pubblicare in ambito scientifico	07-06-2017	08-06-2017	Dr.ssa G. Cognetti
Gestione del paziente radioattivo in ambito sanitario: informazioni necessarie per lavorare insicurezza e miti da sfatare	14-06-2017	16-06-2017	Dr.ssa R. Sciuto
Pubmed metodologia della ricerca e dell'informazione	05-07-2017	06-07-2017	Dr.ssa G. Cognetti
Public Speaking: l'arte di parlare in pubblico in ambito sanitario	21-09-2017	28-09-2017	Dr.ssa A. Caruso
La comunicazione in ambito oncologico	25-09-2017	27-09-2017	Dr.ssa A. Caruso
Pubmed metodologia della ricerca e dell'informazione, II Ed	26-09-2017	27-09-2017	Dr.ssa G. Cognetti
RIDAIT seminars-III modulo	10-10-2017	12-12-2017	Dr. A. Venuti

Incontri multidisciplinari di ginecologia oncologica - II modulo	25-10-2017	20-12-2017	Dr. E. Vizza
Eventi oncosoppressione nello sviluppo dei tumori	26-10-2017	28-10-2017	Dr. G. Blandino
Cura di sé cura dell'altro	06-11-2017	08-11-2017	Dr.ssa G. Cognetti Dr.ssa S. Lolli
Gestione del paziente radioattivo in ambito sanitario: informazioni necessarie per lavorare insicurezza e miti da sfatare, II Ed	08-11-2017	10-11-2017	Dr.ssa R. Sciuto
L'iter diagnostico dei tumori mammari nel contesto di una diagnostica senologica dedicata ed integrata	16-11-2017	16-11-2017	Dr.ssa F. Ferranti Dr.ssa F. Fodde
Cura di sé cura dell'altro, II Ed	22-11-2017	24-11-2017	Dr.ssa G. Cognetti Dr.ssa S. Lolli
Incontri multidisciplinari di ortopedia oncologica. Disease Management Team delle neoplasie mesenchimali muscolo-scheletriche, sarcomi viscerali e GIST	27-11-2017	18-12-2017	Dr.ssa V. Ferraresi
La malattia oncologica nella famiglia	30-11-2017	04-12-2017	Dr.ssa A. Caruso
Incontri multidisciplinari di endocrinologia oncologica	07-12-2017	21-12-2017	Dr.ssa M. Appetecchia

La segnalazione delle reazioni avverse a farmaci in oncologia e dermatologia come ponte tra pratica clinica e la ricerca	15-12-2017	15-12-2017	Dr. Y. Ferrara

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