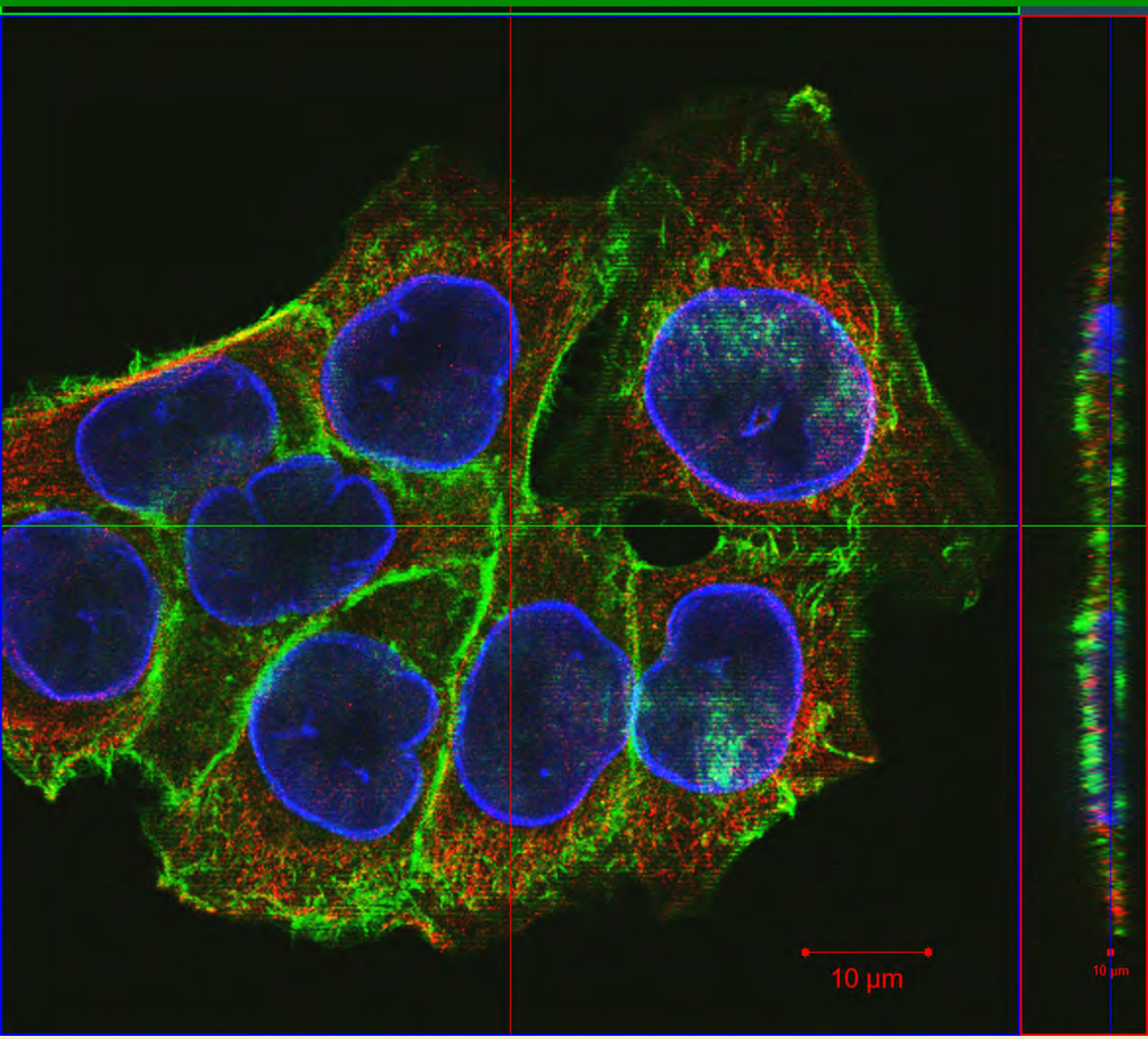
IRE

ISTITUTO NAZIONALE TUMORI

REGINA ELENA

ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO



Scientific Report 2016

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Scientific Report 2016

ISTITUTO NAZIONALE TUMORI REGINA ELENA

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Scientific Direction
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In copertina:
Confocal image of colon cancer cells acquired with a Zeiss LSM 510 Meta laser scanner. Green and red cytoplasmic proteins (phalloidin and beta-tubulin); blue nuclear protein (LaminB1). Magnification 63X. Courtesy of E. Salvati

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SCIENTIFIC REPORT 2016

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Francesca Servoli
Fabio D'Orsogna

with collaboration of:
Barbara Matrascia
Tania Merlino

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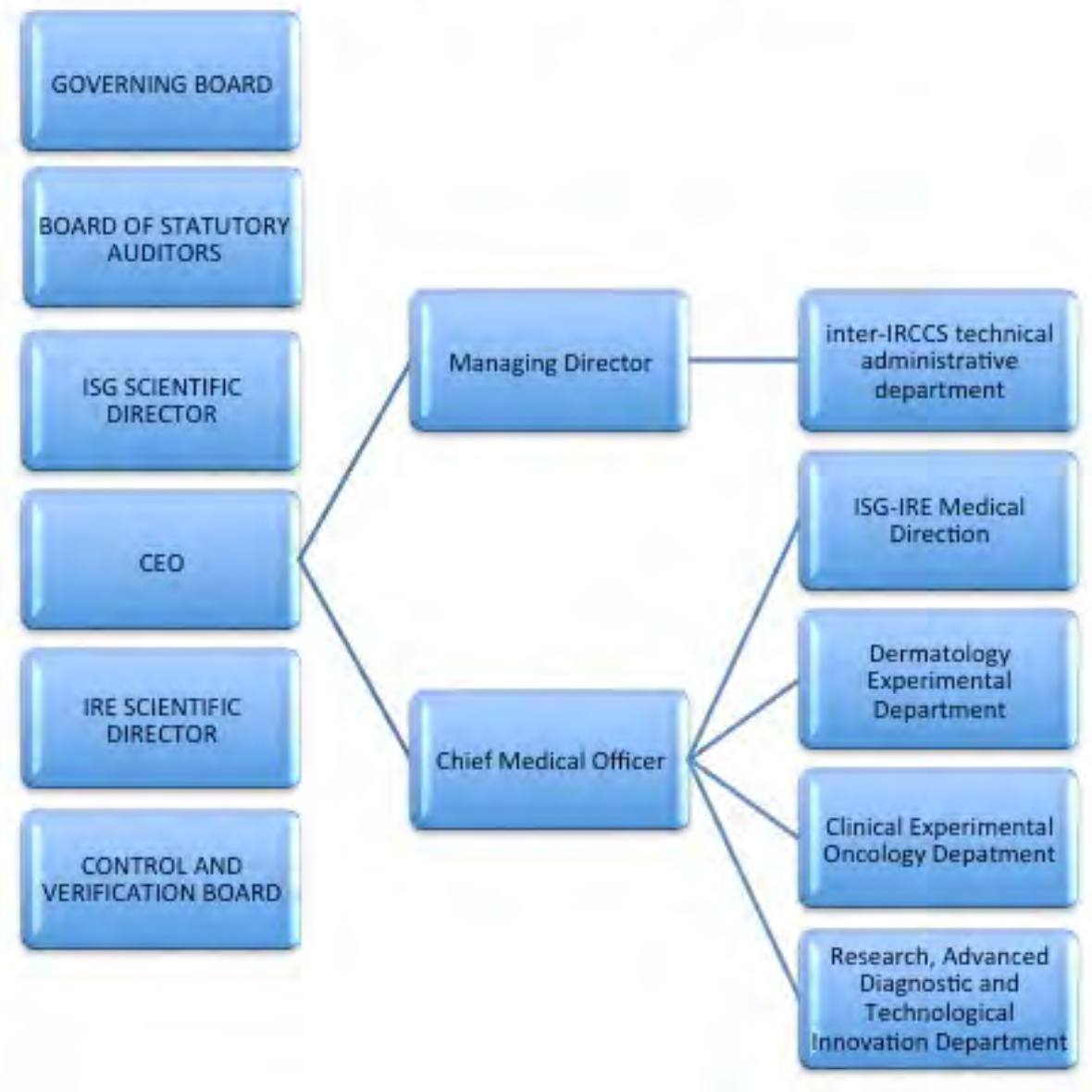
IFO ORGANIZATION CHART



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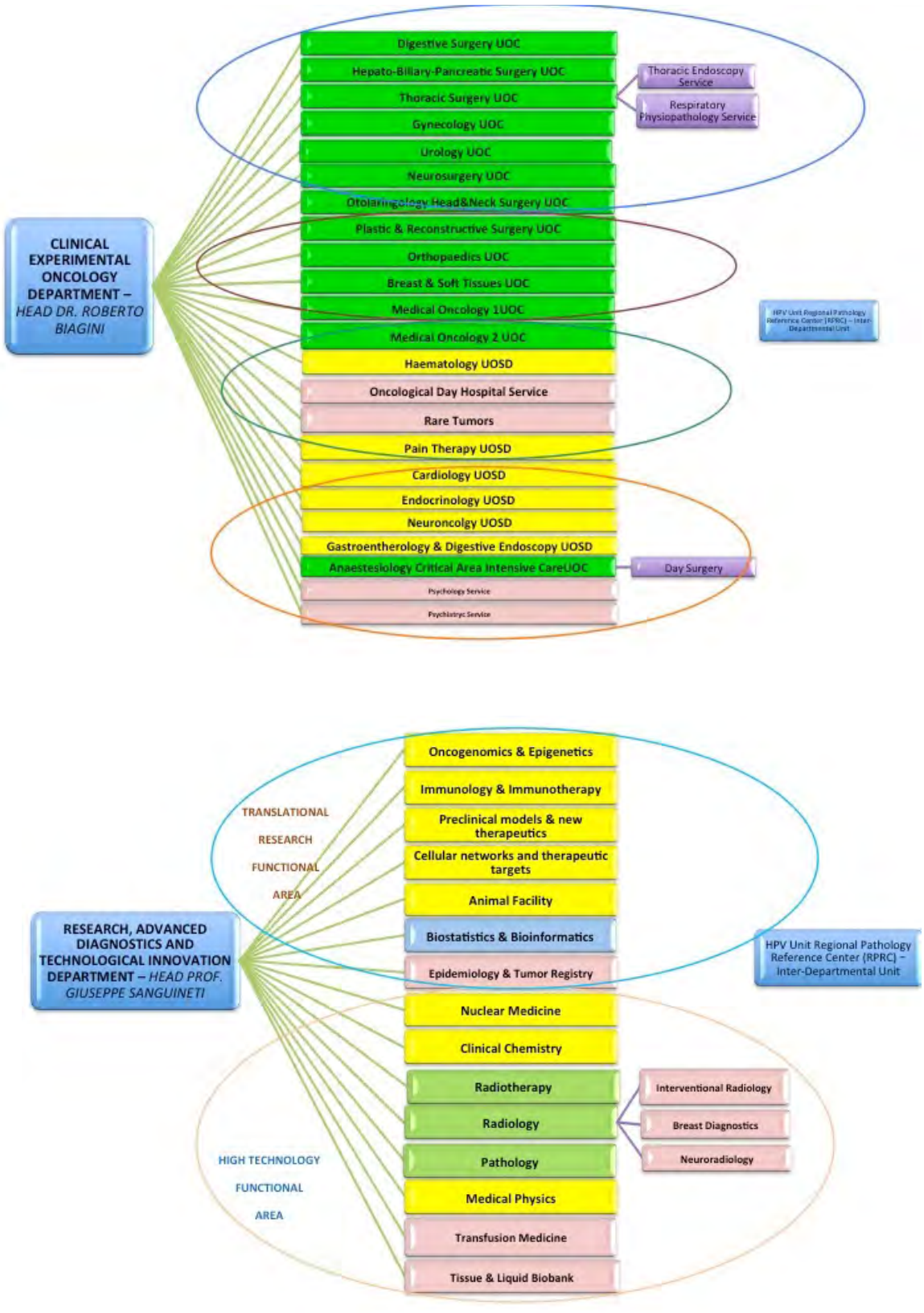

From General Manager

Francesco Ripa Di Meana

Dear Readers,
I've had the honor of being appointed as IFO's General Manager in December 2016. IFO includes both the Regina Elena National Cancer Institute (IRE) and San Gallicano Dermatological Institute (ISG). IFO have faced a long period of provisional management under Special Commissioners with frequent changes in leadership, including the General Director. Thankfully, the Institutes are now going through an era of managerial stability, seeing the entire Strategic Directorate currently in charge and composed by myself, Dr Branka Vujovic as Corporate Health Manager, Dr. Laura Figorilli as Administrative Director, the Scientific Directors of IRE and ISG respectively, working in synergy and seeking common goals for the forthcoming five years.

We are already appreciating the first signs of this change in management with the approval by Regione Lazio of our new "Efficiency Plan" which was presented in February this year (Del. 96) and further refined on March 21st (Del. 217). Furthermore, both IRE and ISG got reconfirmed their IRCCS status on April 2017 by the Italian Ministry of Health, which allowed unlocking the supply of necessary research funding for our translational research activities. Most importantly the Institutes are proceeding to the implementation of major technological investments such as for example the Cyberknife facility which officially opened in July 2017 with the visit of the President of the Republic, Mr. Sergio Mattarella and of the President of Regione Lazio, Mr Nicola Zingaretti. Finally the Institutes recently obtained the accreditation certificate ISO 9001/2008 as first Hospital in Regione Lazio.
I am a strong advocate of innovation, which I believe is the way forward for future medicine and am fully committed to make IRE become the reference Oncology Center in Regione Lazio. I encourage IRE professionals to accept the challenges of modern medicine and be projected into the future. This certainty of being bearers of a future is based on our familiarity with research and discovery, and should motivate us to do always better in our daily activities. On this context, among my goals for the next years is also the potentiation of the Clinical Trials Center, the opening of the Phase I platform, and a series of structural investments among which the contribution to creation of the first public Proton Therapy Unit in Central Italy.
I am confident that working together towards common goals of productivity, efficiency and excellence will increase our reputation nationally and internationally and improve quality of life for our patients.

From the Scientific Director

Gennaro Ciliberto

Dear Readers,
It has been a great honor and privilege for me to have been appointed Scientific Director of the Regina Elena National Cancer Institute in November last year. The Regina Elena Institute was founded in 1934 and is a prestigious Center of Excellence for cancer research, prevention and treatment. It has been recognized by the Ministry of Health as one of the first ever IRCCS "Research Institute of Hospitalization and Care" (Istituti di Ricovero e Cura a Carattere Scientifico) in Italy since 1939 and has recently been certified as a Comprehensive Research Cancer Center by the European Organization of Cancer Institutes (OECI).
Over the last few years, Regina Elena has been marked by several milestones in the area of scientific research, which is reflected by the numerous articles that have been published in first-class international scientific Journals, as well as for having built and established an undisputed reputation for delivering high quality clinical care assistance. These results have been implemented with the unlimited support of our highly esteemed and dedicated experimental and clinical researchers. One of our most important achievements was accomplished back in 2014 where, after several decades, the scientific laboratories and the clinical departments physically merged on the main campus located in Mostacciano, with the opening of first-class open laboratory spaces. This will undoubtedly help us facilitate and realize our mission of translational research in oncology in the coming years. Nevertheless, there is still a further need to bridge the gap between basic research and clinical activities. Yet, in order to reach the full potential of our translational research the laboratory area needs to be completed with a world-class animal facility for our pre-clinical research. Likewise, for our Clinical Research to become more competitive, our Clinical Trials Center needs to be further strengthened and consolidated and the Phase I platform needs to be set up and running. Only thanks to the full support from our Strategic Direction, from the Verification Review Committee (CIV) and the synergistic interaction with our sister IRCCS, San Gallicano Institute, can our goals be achieved. During my five year mandate, I plan to place constant attention on increasing our scientific

productivity, also, through the establishment of strategic collaborations with other Scientific Institutions in the Lazio Region. I aim to foster the capability of attracting financial resources through the activities of the Grant office, potentiate the institutional tissue and liquid tumor bank (BBIRE), facilitate the development of translational efforts directed towards the genomic and epigenomic characterization of cancers and to the routine implementation of liquid biopsies for precision medicine, integrate data analysis with bioinformatics, enhance the discovery of predictive biomarkers for immunotherapy, and exploit the full potential of several technological investments for research purposes of the Institute in robotic surgery, radiotherapy and medical physics. Furthermore, Translational Groups will be created and will be responsible for implementing daily interventions in integrating clinical and experimental research activities.

Finally, it is worth mentioning that the Regina Elena Institute is also a member of a number of national and international scientific consortia such as “Union International Contre le Cancer” (UICC); European Organization of Cancer Institutes (OECI); European Organization for Research and Treatment of Cancer (EORTC - Early Clinical Trial Group); Alliance Against Cancer (ACC); European Advanced Translational Research Infrastructure in Medicine (EATRIS); Italian Advanced Translational Research Infrastructure in Medicine Association (A-IATRIS). The Regina Elena Institute is also a referral center of the World Health Organization (WHO). Active participation in these consortia is fundamental in promoting collaborative research and clinical practices.

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 & Public Relation

Chief Press Officer & Public Relation IFO and L. Spallanzani

Lorella Salce

website editing manager, corporate identity manager, social media manager &strategist

Staff

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

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);
- Digital press review

Annual activities report

Press releases 2016: **41**
Agency launches 2016: **212**
Mass media presences 2016: **1163**
News items 2016: **200**
Facebook: **769 post; 4.45 million views**
Youtube: **220.000 views; 650.000 minutes watched**
Twitter: **1600 tweet; 460 mentions; 1770 retweets**

Crisis Communications, Public Communication, Campaigns, Web Projects

- Crisis communication management for Spallanzani: the first and second cases of ebola in Italy; Zika virus cases in Italy; Bacterial Meningitis C in Tuscany Disease Outbreak
- World Cancer Day campaign for promotion public awareness
- 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)
- Start of oncoLine (Repubblica.it) blogs: Yoga & Pagaie" and "Insieme più belle"

Ethics Committee

As from December 2016

Chairman
Prof. Francesco D'Agostino
Expert in Bioethics

Vice Chairman
Prof. Agata Amato Mangiameli
Expert in Legal Matters

Secreterary
Anna D'Ambrosio

Technical-Scientific Secretriat
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:
Prof. Aldo Di Carlo
IFO Chief Medical Officer (ad interim):
Dr. Ester Forastiere
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

Scientific Directorate

Staff:

Secretariat
CarmelaMatrascia,
Pina Gioffrè
Manuscript editing
Tania Merlino
Grant Office
Maria Guttinger,
Barbara Matrascia
Clinical Trial Monitoring
Federica Falcioni
Technology Transfer Office
Letizia Ciancio
IT
Marco Canfora

Digital Library Knowledge Center R. Maceratini (BDCC-IRE) and Patient Library (BP-IRE)

Staff

Senior Staff Librarian
Gaetana Cognetti

Professional staff with grant
Fabio D'Orsogna, Graduated Specialized Librarian
Francesca Servoli, Graduated Specialized Librarian
Administrative Staff
Domenico Verbicaro, Administrative Staff
Volunteers (National Civil Service)
Virginia Scarinci
Marinella Cisternino
Dario Paoletti

Mission

The Library offers its services to both the medical staff and the patients and their relatives. The Library supports research activities by offering scientific information, documentation and education (health information literacy). The 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. The Library is easy to find, being situated near the main entrance of the Institute and offers a multimedia room with 15 computers. The Patient Library is located, since 2005, in a special room providing quality information through professional staff and civil service volunteers using booklets for patients, scientific databases and trusted health portals.

Clinical Activity

The Library supports the institutional clinical staff offering: consultation of the main biomedical databases; document delivery through interlibrary exchange system, NILDE; organisation of training courses; 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 and databases 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 (32 meetings in 2016). The Library has about 8.000 monographs and approximately 100 titles of periodicals on print. In 2016, 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, 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 2016, 105 patients and family members asked for information (30 bibliographic research and about 350 information booklets delivered).

Research Activities

The Library is involved in various research, educational activity and library networks. In 2016 the Library coordinated the 1th survey on open access within the 60 Italian Research Institutes of the National Health System. The results were presented at the EAHIL Conference in Sevilla (June 6-11, 2016). The Library began also to collaborate with a project about health information literacy in old age population promoted by the Pescara AUSL. The results of the survey will be published in 2017. 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: 6 ECM courses on scientific documentation (20,4 ECM credits each course), the partecipants were about 150 (interactive teaching - maximum 25 participants each course), as well as being made available, through Bibliosan, 15 BMJ Online ECM courses (75 ECM credits). The Library has organized also no ECM courses concerning Bibliosan's resources and two more for the students (*La Sapienza University/IFO* Nursing School - High School "Francesco Vivona"). The library staff is involved in the teaching and tutorship of the most courses organized. In 2016 the Library coordinated the OECI Improvement Plan on patient involvement and empowerment, concerning humanization of the care, communication and information.

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

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, in 2016 total borrowing 403, total lending 187;
3. **National Union Catalog of Periodicals (ACNP)** for the cataloguing and management on the web of the periodicals;
4. **Library Network of Biomedical Research Institutes (Bibliosan).**

Publications

Cercato M, Servoli F, Scarinci V, Colella E, Fabi A, Bertazzi I, Sperduti I, Cognetti F, Cognetti G. Narrative medicine: A multidisciplinary study on knowledge and application in oncology. *Annals of Oncology*. 2016;27(Suppl 4):110. **IF 9.269**

Cognetti G. All'italia serve una biblioteca elettronica nazionale per la salute, ecco perché. *Forum Pubblica Amministrazione*. 2016;(18 Mar).

Cognetti G. Il diritto del paziente ad essere informato: Buone pratiche internazionali. *Forum Pubblica Amministrazione*. 2016;(22 Feb).

Cognetti G. s.t. In: Cosentino G, ed. *Osservatorio competenze digitali in sanità 2016.* AICA; 2016:38-44.

Cognetti G, Paoletti D. Non solo fertility day: Il piano nazionale combatte le lacune informative. *Forum della Pubblica Amministrazione*. 2016;(25 Jul).

Cognetti G, Poltronieri E. Come superare il gap informativo in sanità: Il progetto HelthDoc. *Forum della Pubblica Amministrazione*. 2016;(30 May).

Cognetti G, Poltronieri E. Come valutare l' appropriatezza degli interventi sanitari, per la sostenibilità. *Forum Pubblica Amministrazione*. 2016;(27 Jun).

Cognetti G, Poltronieri E. Accesso aperto alle conoscenze scientifiche in sanità: Una questione "vitale". *Forum Pubblica Amministrazione*. 2016; (17 Apr).

Cognetti G, Poltronieri E, De Castro P. Open access to research results within the italian national health service institutions: Still or troubled waters? *15° Eahil Conference, Siviglia*. 6-11 giugno 2016.

Cognetti G, Scarinci V. Perché è importante la narrazione sul web di pazienti e professionisti della salute. *Forum Pubblica Amministrazione*. 2016;(25 Jul).

Cosentino G, Cognetti G. Medicina, il web è cruciale per l'informazione: Anche per pazienti. *CORCOM Quotidiano online dell'economia digitale e dell'innovazione*. 2016;(1 Jul).

Regazzo G, Terrenato I, Spagnuolo M, Carosi M, Cognetti G, Cicchillitti L, Sperati F, Villani V, Carapella C, Piaggio G, Pelosi A, Rizzo MG. A restricted signature of serum miRNAs distinguishes glioblastoma from lower grade gliomas. *J Exp Clin Cancer Res*. 2016;35(1):124. **IF 4.347**

Journal of Experimental & Clinical Cancer Research

Mauro Castelli, PhD
Editor in Chief

The Journal of Experimental & Clinical Cancer Research (JECCR) is an online peer-reviewed journal that provides a high-quality forum for all aspects of basic, clinical and translational work in oncology. The journal publishes scientific studies on the immunological, pathological, biological and clinical aspects of oncology. Topics covered by the journal range from molecular genetics, oncogenomics proteomics, metabolomics, tumor theraputics and targets, etc.

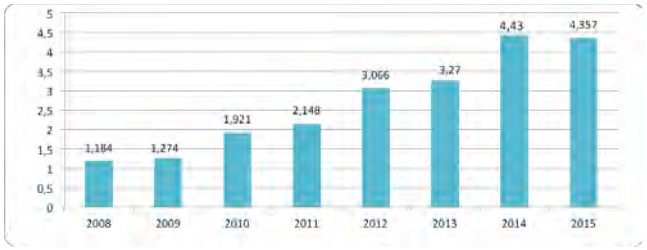
JECCR, the official scientific journal of the "Regina Elena" National Cancer Institute since 1986, has proceeded its editorial activity maintaining its partnership with the Publisher BioMed Central in London. Starting from 2008 the journal became "open access" (OA), meaning online rapid publication of 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 50/211 journals in subject category Oncology (ISI Web Os Science – WOS).

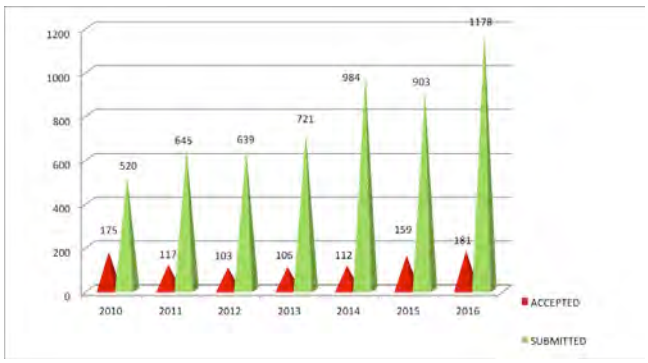
The main accomplishments achieved by *JECCR* in 2016 years are:

- Impact Factor: 4.357
- Ranking in the 1st quartile among International Oncology Journals
- Over 1000 articles submitted
- Over 180 articles published in 2016
- Over 100.000 article accesses (online) each month
- Articles submissions increased in the last 5 years of about 30%.

Most of submitted and published articles in the last years come from International Oncology Institutes and Universities worldwide.
In conclusion, the on-line open access procedure ensured a wider visibility for the Journal of Experimental and Clinical Cancer Research and therefore for "Regina Elena" National Cancer Institute of Rome.

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





General IFO Medical Office

Branka Vujovic, MD

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. Mauro Picardo, respectively. I have gained experience as Chief Medical Officer in university and regional hospitals, however this is my first time in a Research Institute of Hospitalization and Care (IRCCS). It is my duty as Chief Medical Officer to commit to performing my task, with an eye towards the future. 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.

Based on population health knowledge, the strategic mission of the Institute is to:

- pursue research, clinical and translational goals, both in the bio-medical field as well as in the organization and management of services;
- constantly implement technology to ensure excellence in patient care;
- provide an adequate response to the population's health care needs;
- harmoniously cooperate in an active relationship with the Lazio Region, the Ministry of Health and public research bodies, with a view to complement roles and facilitate and guarantee continuity of care.

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.

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.

A-IATRIS / EATRIS

A-IATRIS, Associazione Italian Advanced Translational Research Infrastructure, è una rete di istituzioni di eccellenza nel panorama nazionale in grado di dare contributi specifici e complementari nell'area della medicina traslazionale.
L'A-IATRIS rappresenta il nodo italiano di EATRIS (European Advanced Translational Research Infrastructure in Medicine).
L'EATRIS è concepita per colmare i divari e i deficit riscontrabili nel panorama della medicina traslazionale europea. I suoi obiettivi di EATRIS sono:

- favorire il processo di traduzione dei risultati della ricerca in strategie innovative volte alla prevenzione, la diagnosi e il trattamento delle malattie di particolare rilevanza sia sanitaria che economica per gli stati membri europei;
- costruire uno spazio migliore in cui il flusso delle informazioni tra la ricerca di base e le osservazioni cliniche sia bidirezionale.

OECI

The Organization of European Cancer Institutes (OECI) is a non-governmental, non-profit organization which was founded in Vienna back in 1979. It has currently more than 70 members Institutes in Europe, including the IRCCS Regina Elena National Cancer Institute.
The OECI aims to create and promote better collaboration between the European Cancer Institutes in order to:

- Create a critical mass of knowledge and transfer of skills that can identify and share new better cancer care models
- Improve the quality of care for cancer patients as well as translational research
- Improve the quality of life of cancer patients
- Provide a clear framework that facilitates and supports continuous improvement in standardizing the care of cancer patients with the standards and quality care levels across Europe.
- Promote the development of multicenter European research projects and use of EU-funding towards research.On 10 September 2015, OECI certified IRCCS Regina Elena National Cancer Institute as an OECI accredited member as it had met the quality standards for cancer care and research, thus qualifying it as a Comprehensive Cancer Centre or an oncologic IRCCS specializing in translational research, multidisciplinary approaches, continuous improvement of care, production of guidelines and diagnostic-therapeutic patient care pathways, as well as continuous education and training programmed at the same time placing the patient always first.

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.

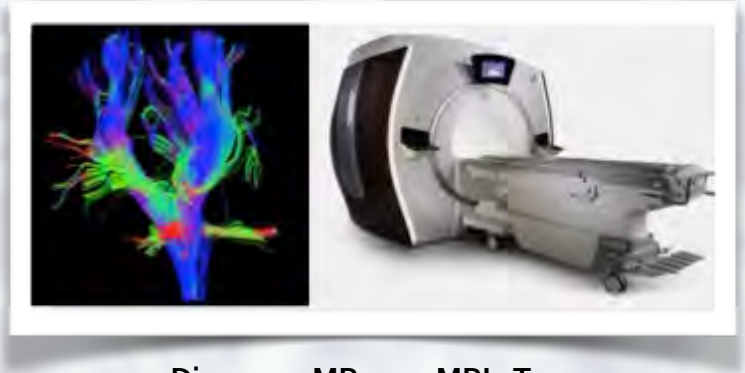
EXCELLENCE

EXCELLENCE

Advanced Clinical Technology

Da Vinci Surgical Robot

Radiology



Discovery MR750w MRI 3T

The Department of Radiology uses 3 modern Magnetic Resonance Imaging techniques including the RM 3 Tesla.

Nuclear Medicine

The Department is equipped with two SPET multihead tomographs and one ultramodern SPET / TC tomograph for diagnoses using conventional scintigrams as well as a unit dedicated to carrying out PET exams with 2 fast high-resolution tomographs.

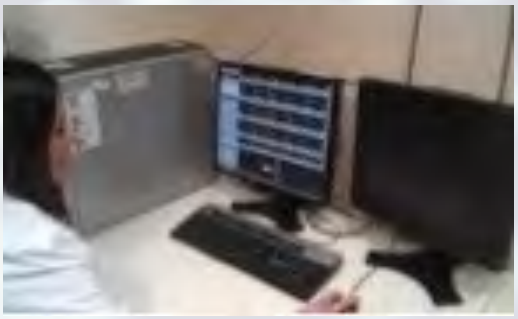
PET/CT scanners

Forthcoming SPECT CT

Radiotherapy

The Department of Radiotherapy of the Regina Elena Institute is one of the most modern in Europe. It is equipped with 3 Linear Radiation Radiation Accelerators, an Intraoperative Radiation Therapy Accelerator, a dedicated CT virtual simulation for patients and various Treatment Planning System solutions that facilitate the development and implementation of high-precision irradiation techniques.

True Beam Linear Accelerator Flattening



4 Dimensional CT for gated radiotherapy

Cyberknife

CyberKnife è il sistema robotico per la radiochirurgia, unico per potenzialità e precisione del trattamento dei tumori ed appena installato (luglio 2017) presso la Radioterapia dell'Istituto Nazionale Tumori Regina Elena.

EXCELLENCE

Postgenomics at IRE

Cancer genomes are sources of valuable diagnostic information, provide clues to target therapy and immunotherapy, and underpin mechanistic models of cancer evolution. The Regina Elena Cancer Institute empowers state of the art NGS and digital PCR (dPCR) to explore germline and somatic cancer aberrations, and accelerate clinical translation. Molecular diagnosis of hereditary Colorectal, Breast and Ovary cancers by customized NGS panels has resulted in 762 diagnostic reports over the past 5 years. During the last year, a CE-IVD 22-gene-panel has been used to diagnose 865 patients (Colorectal, Lung, Thyroid carcinomas, and Melanoma), 648 of whom displayed at least one somatic aberration. Of these, 390 were targetable or potentially targetable. In an effort to expand the clinical benefits of NGS, ongoing research projects include the design of dedicated NGS targeted panels to identify mutation patterns and signatures predictive of response to treatment (and lack thereof) in triple negative Breast Carcinoma, Lung, Colorectal and Gastric cancers as well as Glioblastoma, and to study germline mutations affecting DNA repair genes in Pancreatic tumors. Equipment and appropriate technical/bioinformatic expertise is available to analyze epigenomes, full transcriptomes, and exomes. Among epigenomic studies, we managed to profile chromatin accessibility with ATAC-seq in Multiple Myeloma patients. Recently, we have started offering CE-IVD liquid biopsy (LB) for lung cancer, and have implemented novel NGS/dPCR schemes to evaluate highly customized, ultrasensitive LB approaches in the context of diagnostic clinical trials (Colorectal and ERBB2 Breast cancers, Ewing Sarcoma).

EXCELLENCE

BioBank at IRE

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. 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.

The BBIRE belongs to the National Network of Oncology Biobanks called "RIBBO", to the European Biobank Network and also to biomolecular resources known as "BBMRI-IT (Crux of the Italian Research Infrastructure European Biobanking and Biomolecular Resources Research

EXCELLENCE

Clinical Trials at IRE

The Institute is aware that clinical trials are the most efficient way of offering the newest drugs to patients as soon as possible, so it has a lot of facilities to speed up approval and implementation of clinical trials.

Clinical studies ranges from phase I to phase IV when regarding drugs in development, from observational studies both retrospective and prospective to translational projects which are very frequent in our Institute due to the presence of several research laboratories. Ongoing clinical studies also include diagnostic trials, and quality of life trials.

A team supports the activation of each study in order to facilitate processes. Industry sponsored studies are also supported through a structures of experienced Data Managers and Study Coordinators which follows studies from the beginning to the end of the last follow-up, ensuring high quality conduct according to Good Clinical Practice. They work in strict connection with Investigators and Sponsor Monitors.

Another aspect is that of investigators initiated trials, also on this side the Institute supports researchers in studies design definition, protocol writing and Case Report Form development. When a multicenter study is planned principal investigator is supported by a team in order to contact regulatory authorities, participating centers and their Ethics Committees and to prepare documentation and center specific material. Informed consent is written according to guidelines of the Ethics Committee.

At the end of the study a group of biostatisticians analyze clinical data with the most updated software and help researchers in the interpretation of the results. They give support in slides presentation and paper writing.

During the year 2016 Ethics Committee received documentation related to 117 clinical studies and research projects in which structures and staffs of the Institute are involved.

The OECI certification process as a Comprehensive Cancer Center helps IRE in organizing and prioritizing all activities related to clinical trials to assure high quality

EXCELLENCE

Immunotherapy at IRE

Immunotherapy represents an advancing area of clinical oncology, and the introduction of immune-checkpoint inhibitors for the treatment of different types of cancer has given a unique opportunity to also effectively treat previously incurable malignancies. Hence, the need to understand how the immune system of each patient interacts with their cancer, both before and during treatments, to design new combined therapies favoring the patients anti-tumor host immune response, represent the new frontier in clinical oncology.

The great advances toward understanding and delivering precision immunotherapy has generated an urgent need for predictive biomarkers to identify patients likely to benefit from the novel immunotherapeutic treatments.

The main goal is to tailor treatment to the patient's immunological profile of both tumor and immune cells. To this aim the team of Tumor Immunology and Immunotherapy is working hard, in close cooperation with pathologists and bioinformatics, to explore the tumor immune contexture in a dynamic setting, defining new criteria for an "integrated-immune score" to identify criteria to stratify patients who may benefit or not from immune-mediated therapies.

The team of Tumor Immunology and Immunotherapy Unit is leader in patient Immune monitoring and has in depth studied the functional role of T lymphocyte response and identified specific subpopulations and T-cell clonality of antigen-specific CD8+ T cells able to protect the patients from cancer recurrence and progression. Multiple platforms have been developed for 'immune monitoring', and the research Laboratories are fully equipped and experienced to monitor immune response in patients.

Recently, a task force to identify predictive biomarkers of response to immune-checkpoint blockade treatments in Non-small cell lung cancer (NSCLC) patients, has been established, taking advantage of excellent thoracic surgeons, dedicated pathologists, oncologists, bioinformatics, biostatisticians and specialized team in genomic and transcriptomic analysis.

DEPARTMENT
OF EXPERIMENTAL CLINICAL ONCOLOGY

DIRECTOR: DR. ROBERTO BIAGINI

Department of experimental clinical oncology

DIGESTIVE SURGERY UNIT

Head: Alfredo Garofalo, MD

Staff

Fabio Carboni, MD
Orietta Federici, MD
Mario Valle, MD
Settimio Zazza, MD
Manuel Giofrè, MD fellow
Ilaria Ciangola, MD Trainees

Clinical and Research activities

- *Gastric Cancer*: the Interdisciplinary Working Group has standardized a general strategy for the integrated treatment of gastric cancer. The Traslational Oncogenomics Group, headed by Dr. Giovanni Blandino, conducts studies in translational research and has produced the following results: A Retrospective study using Microarray RNAs: gastric cancer samples deriving from patients who have undergone surgery at our Institute in the last four years compared to gastric gland samples deriving from patients under care at a different Institute in another region: two different series of molecular typing methods give overlapping bitmaps images. 4 MiRNAs were found regulated or upregulated against healthy tissues, in particular, miRNA 204. A prospective
study is still ongoing where patient recruitment is still in progress. Heads of Surgery: Dr Orietta Federici; Dr. Fabio Carboni. Two papers were published on Cancer Research and Investigation and on Oncotarget Advance Publications
- *Peritoneal Carcinosis:* The Department has become one of the two main Referring Centers for this type of tumour in Italy. It is currently collaborating with the SICO Peritoneal Carcinosis Oncoteam to establish a National Registry sponsored by the Italian Society of Surgical Oncology. It is also currently conducting a national survey on ovarian cancer carcinomas. The following studies are currently in progress at the Institute: a pilot study investigating the association between expression and heterogeneity of DNA markers and clinical outcomes in peritonectomy and hipec patients for peritoneal carcinosis of ovarian cancer. Scientific Investigator: Dr Mario Valle; Contractor: Dr. Manuel Giofrè
- *Minimally Invasive Techniques in Surgical Oncology:* experts worldwide are very familiar with the work published by our Group on Laparoscopic Staging of Peritoneal Carcinoma and Hyperthermic Abdominal Hyperthermic Peripheral Peritonitis in Intractable Neoplastic Cancer with Original Technique and Minimally Invasive Access (Cancer Journal 2009, EJSO 2009). Our Group has over 15 years of experience in minimally invasive advanced surgery including also colon and rectal resections, wedge resections of the stomach and small intestines, distal pancreatectomy, splenectomy for hematologic diseases, adrenalectomy. Scientific Investigators of the research line: Dr. Mario Valle and Dr. Orietta Federici
- *Rectal Cancer:* Early screening and early diagnosis for rectal cancer using cytology and high resolution anoscopy (HRA). This Pilot Study involves a close collaboration between this

- Department and the Department of Infectious Diseases of the Skin of the San Gallicano Institute. Scientific Investigators: Dr Settimio Zazza; Dr Manuel Giofrè.
- *Colorectal Tumors and Rare tumors of the Colon:* patient recruitment is now in progress in order to assess the new ULTRAPLACAD device within the framework of the European project (funds 15/07 / R / 33) Giacomini (Oncogenomics Laboratory), (ULTRAsensitive PLAsmonic devices for early CAncer Diagnosis). Very promising findings have been observed from the preliminary results on circulating neoplastic DNA which could be of great use in the early diagnosis of primary tumors and recurrences after treatment and indication for lines of chemotherapy. Scientific Investigators: Dr Fabio Carboni; Dr Settimio Zazza; Dr.ssa Ilaria Ciangola.

Publications

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Mori F, Canu V, Lorenzon L, Garofalo A, Blandino G, Strano S. Cancer gastric chemoprevention: Isolation of gastric tumor-initiating cells. Methods Mol Biol. 2016;1379:129-137.

Department of experimental clinical oncology

HEPATO BILIARY PANCREATIC SURGERY UNIT

Head: Gian Luca Grazi, MD

Staff
Maurizio Cosimelli, MD
Marco D'Annibale, 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 colo-rectal neoplastic diseases. A multimodal approach for rectal cancers is usually offered to the patients. Laparoscopy and robotics are used when appropriate.

Publications

de Latouliere L, Manni I, Iacobini C, Pugliese G, Grazi GL, Perri P, Cappello P, Novelli F, Menini S, Piaggio G. A bioluminescent mouse model of proliferation to highlight early stages of pancreatic cancer: A suitable tool for preclinical studies. *Ann Anat*. 2016;207:2-8. **IF 1.308**

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Department of experimental clinical oncology

THORACIC SURGERY UNIT

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.

Head: Francesco Facciolo MD

Staff

Sandro Carlini, MD
Edoardo Mercadante, MD
Gabriele Alessandrini, MD
Virna Cerasoli, MD
Felicita Corzani, MD
Daniele Forcella, MD
Enrico Melis, MD
Nicoletta De Bello, Nurse
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

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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Department of experimental clinical oncology

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 Chierichetti
Fabiana Cipriani
Fabiana Egidi
Laura Filip
Valeria Fiumara
Rachele Morani
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 2016, more than 740 surgical operations were performed: 276 in day-surgery setting and 465 (63%) 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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Department of experimental clinical oncology

UROLOGY UNIT

Head: Michele Gallucci, MD

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Francesco Minisola, Fellow

Mission

Development and standardization of complex surgical procedures in uro-oncology; 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 introcorporeal reconstruction of orthotopic and etherotopic urinary diversions, robot-assisted radical nephrectomy with inferior vena cava tumor trombectomy 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

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Department of experimental clinical oncology

NEUROSURGERY UNIT

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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 2016 the Unit of Neurosurgery performed about 240 surgical procedures, considering 140 operations for intracranial tumour removal (more than 90 primitive brain tumours - gliomas, meningiomas, pituitary adenomas, et al - and a quarter of metastatic brain lesions), and more than 60 procedures on spinal tumours (two thirds of metastatic spine lesions).
In the last years, several protocols for combined treatment of malignant gliomas have been defined, including new modalities of drug delivery. New therapeutic protocols have been activated, considering after surgical procedures (biopsy and/or microsurgical removal), radiation treatment and chemotherapy with different therapeutic schedules, both as first line (mainly

Temozolomide), and as second one (mainly with Fotemustine). In addition, the increasing 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) allowed in selected patients the indication to second and, in selected cases, third line chemotherapy.
Furthermore, clinical benefit of bevacizumab, as antiangiogenetic treatment alone or in combination with antiblastic drugs in the treatment of recurrent glioma has been evaluated; clinical benefit has been measured as reduction of steroid dosage and improvement of at least 20 point in the Karnofsky Performance Status. Data of recurrent glioma patients treated with bevacizumab alone or in combination were collected and the majority of recurrent glioma treated with bevacizumab reported a clinical benefit, even in those showing progression at MRI imaging. Preliminary results have been presented in national and international scientific meetings.
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 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 neuroimaging 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 (CMC is a member of this group) is in publication on Neuro-Oncology.
In the field of spinal tumours different programs have been developed during last years: mainly considering the use of new technologies and approaches; furthermore in 2016 more than 60 metastatic spinal tumours patients have been treated with augmentation procedures (vertebroplasty and/or kyphoplasty), or with one stage vertebrectomy with reconstruction and stabilization.

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 (TG group Coordinator CMC) has been aimed at identifying new molecular and imaging glioma biomarkers useful for diagnosis, prognosis and/or predictive of tumour therapeutic response; on these bases, we believe to eventually yield a significant improvement in the managements of these patients. Presently we are trying to correlate the data regarding tumour bio-molecular characteristics with clinical data of these patients. As a matter of fact, in this field the definition of predictive markers of potential efficacy of different therapeutic approaches assumes prominent interest, and a more adequate clinical, radiological, histological, and bio-molecular knowledge could contribute to define more selective and efficient diagnostic-therapeutic strategies, also allowing a more clear cut stratification of patients accrued in new clinical trials. In the literature different Authors (and our group too) described a series of prognostic markers, as expression of p53, amplification and over expression of EGFR, 10q LOH (loss of heterozygosis) in astrocytic gliomas, 1p and 19q LOH in oligodendrogliomas, and the well known methylation of O6-methylguanine-DNA-methyltransferase (MGMT), deeply involved in chemo-resistance to methylating and alkylating agents. 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 600 patients affected with primary brain tumours (mainly malignant gliomas; more than 300 glioblastoma). An average of 45-50 patients/months 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. We tried to define the cut-off value

correlated with good favourable prognostic outcomes. The best possible criteria for pyrosequencing-detected percentage of MGMT methylation that predicted progression-free survival (PFS) and overall survival (OS) were 19% and 13%, respectively. Patients with ≤19% of pyrosequencing-detected MGMT had a shorter PFS (HR: 0.24, $p < 0.01$); those ones with ≤13% had a shorter OS (HR: 0.33, $p < 0.05$). Our study reinforces the importance of MGMT in the management of GBM patients; presently a cooperative study with other Italian groups is in progress. 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.

A second aim has been the research of circulating biomarkers for detection and prognosis of primary brain tumours. Up today few data are available for circulating as well as resident biomarkers used for diagnosis, response to therapy, and/or early detection. However, a global serum microRNA signature in a large cohort of malignant glioma patients has been recently reported. In particular, in the present study eleven circulating/serum microRNAs (miR-15b*, -23a, -99a, -125b, -133a, -150*, -197, -340, -497, -548b-5p and let-7c), previously associated with brain tumours, were evaluated as potential non-invasive diagnostic biomarkers for glioma patients. We found that in high grade glioma patients (HGG) the expression levels of the serum miR-125b and -497 were significantly decreased, in respect to low grade gliomas (LGG). Moreover, receiver operating characteristic (ROC) curve analysis revealed that serum miR-125b and miR-497 expression levels show high sensitivity and specificity in discriminating patients with HGG from LGG. Thus, the serum level of miR-125b and -497 could mirror the miRNA expression in tumour tissue and could be useful to obtain real-time information on the biology of glioma. Interestingly, these identified serum miRNAs also exhibited a global decrease in tumour tissues relative to normal tissues and were markedly elevated after operation. Altogether, these data strongly suggest a promising role of serum miR-125b and -497 for differential diagnosis of high grade respect to low grade gliomas. Preliminary data of this relevant study have been published.

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

In particular, the role of extensive surgical resection of malignant glioma has been supported in the literature in the last years; recent data in the literature suggests that radical removal is associated with better survival. On this basis, 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 is related to more than 60 patients affected by malignant glioma (newly diagnosed as well as recurrent tumours). All patients selected for fluorescence-guided resection underwent preoperative and early postoperative MRI, showing contrast enhancing lesions. Microsurgical resection was performed by an operating microscope enabled to visualize fluorescence. 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. Early postoperative MRI confirmed gross total resection without contrast enhancement in 80 % of patients. In the present experience the procedure did not determine any relevant additional neurological deficit. Considering overall survival of recurrent patients we obtained a median extension of at least 9.0 months (4 – 16+ months). 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 2016 our group presented the data regarding the impact of 5-ALA on outcomes in elderly GBM. The prognosis of patients aged 65 years or older with GBM is universally poor: their median survival ranges from 4 to 9 months. The main reason is that older patients are often treated more conservatively than younger; this is a result of

reluctance to offer aggressive treatment for fear of postoperative complications. Our experience is related to 36 patients with range of age from 65 to 79 years (32 newly diagnosed and 4 recurrent GBM). Co-morbidities (CM) were identified with CIRS scale. All the patients have been submitted to radiotherapy and/or chemotherapy; second and in some cases third line treatments were utilized in recurrent cases. Follow-up ranged from 1 year to 2 years. The median OS was 18 months with a rate of survival at 2 years of 35%. In this experience 5-ALA fluorescence-guided surgery improves tumour detection and allows extended resection of GBM in elderly. Postoperatively, there is no impact on neurological status, with a consistent effect on overall survival. In our experience the evaluation of co-morbidities should drive the therapeutic decisions in elderly patients affected with GBM.

In addition, unconventional treatment modalities of malignant gliomas have been studied. In this field our group participated to a prospective, multi-center 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. At the cellular level, the TTFields effect was shown to be due to arrest of proliferation and selective destruction of dividing cells. The damage caused by the fields to the replicating cells was dependent on the orientation of the mitotic spindle in relation to the field vectors. 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 was approved by our EC, activated and presently closed; 8 patients have been registered and included into the study; 2 patients are still alive, under follow-up and clinical observation. The study has been concluded; final results have been presented and are in publication: significant results have been obtained documenting a relevant 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 issue. 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 study is in progress 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 48 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 (post-operative thorax and spine CT scan are planned for all patients to rule out cement leaks and embolism), pain reduction (evaluated with VAS scale), functional capacity (evaluated with Oswestry Disability index, ODI) and quality of life (evaluated with EuroQoL-5D). PMMA cement is considered the gold standard material for such procedures; although success rate is high, PMMA has also limitations and safety concerns: exothermic reaction, short working time (5 minutes), rapid solidification, it is not adhesive to bone, leakages are dangerous. VK100 is a mixture of dimethyl methylvinyl siloxane, barium sulphate, platinum catalyst, and methylhydrogensiloxane cross linker. Polymerisation occurs after mixture. Surgical procedure is the standard kyphoplasty. VK100 adheres to bone, has no exothermic reaction, leaves up to 15 minutes before definitive solidification, is more elastic. Accrual to the study began in April 2015. Follow-up controls are planned at 1, 3, 6 and 12 months and are currently in progress.

Last relevant research project involving our Neurosurgical Unit regards neuro-imaging; as matter of fact the improvement of MR imaging modalities could provide useful information about size, metabolic and physiological aspects of tumour tissues; in this field a relevant experience has been developed on Perfusion MRI, that is a non-invasive quantitative method of investigating microvascular structure and function by tracking the pharmacokinetics of injected low-molecular weight contrast agents as they pass through the tumour vasculature.

Response evaluation after antiangiogenic treatment has been studied with Perfusion MRI to define if early perfusion changes during treatment

may be predictive of response to antiangiogenic therapy in high grade gliomas. Results: Perfusion changes resulted in agreement with follow-up morphological MR imaging, anticipating, in the majority of cases, the post-gadolinium T1-weigthed and FLAIR volume modifications. Preliminary results have been presented in scientific meetings and recently published on *Neuroradiology*.

Furthermore, the diagnostic role of PET F-DOPA in low grade glioma has been evaluated in a prospective study. All patients affected by low grade glioma underwent F-DOPA PET and MRI examination for the evaluation of anaplastic progression or assessment of response during chemotherapy. The PET images were interpreted as positive when the lesion definitely presents increased F-DOPA accumulation taking into consideration the background and the controlateral site. We enrolled 56 (35 males and 21 females) patients affected by LGG. Quantitative measurement of metabolic activity of the tracer showed that a SUV max greater than 1.65 was the only independent predictor of disease progression (HR=4.59, 95% CIs from 0.99 to 21.31, p=0.054). This implies that a patient with a SUV max higher than 1.65 had an almost 5-fold increased risk of disease progression, regardless of its clinical and MRI characteristics. The study has been recently published on *Nuclear Medicine Biol* and *Anticancer Research*. Longitudinal analysis of data is ongoing.

Publications

Cordone I, Masi S, Carosi M, Vidiri A, Marchesi F, Marino M, Telera S, Pasquale A, Mengarelli A, Conti L, Pescarmona E, Pace A, Carapella CM. Brain stereotactic biopsy flow cytometry for central nervous system lymphoma characterization: Advantages and pitfalls. *J Exp Clin Cancer Res*. 2016;35(1):128. **IF 4.357**

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Telera S, Caroli F, Raus L, Pompili A, Carosi MA, Di Santo M, Sperduti I, Carapella CM, Fabi A. Spine surgery in patients with metastatic breast cancer: A retrospective analysis. *World Neurosurg*. 2016;90:133-146. **IF 2.685**

Department of experimental clinical oncology

OTOLARYNGOLOGY HEAD & NECK SURGERY UNIT

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Mission

- **Our mission is to deliver the highest possible clinical care for patients with cancer of the head and neck. Using an interdisciplinary approach, experts from across disciplines come together in the Head and Neck Center to provide state-of-the-art care for patients with all types and stages of head and neck cancer.**
- **Our team of specialists treats patients with tumors of the thyroid and parathyroid glands, salivary glands, oral cavity, larynx, pharynx, paranasal sinus, and skull base; melanomas; non melanoma skin cancers; sarcomas of the soft tissue and bone.**
- **In the department, a highly qualified staff with special expertise in head and neck surgery, endocrine surgery, oral oncology, and speech pathology offers patients with these tumors the latest and most effective treatment options.**

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 all the decisions regarding clinical cases are 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.

Research Activity

- Elettrochemotherapy as palliative treatment in advanced head and neck cancer
- miRNA profiling in head and neck squamous cell carcinoma
- Supracricoid Partial Laryngectomy vs Radiotherapy in the Management of T3 Laryngeal Cancer: oncological and functional result

Publications

Cristalli G, Costa M, Anelli A, Mercante G, Ferreli F, Spriani G. Il trattamento del collo nel carcinoma adenoidocistico delle ghiandole salivari. In: *Quaderni monografici di aggiornamento AOOI.* Roma: AOOI; 2016.

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Spriano G. Partial pharyngectomy. In: Myers EN, Feris RL, eds. *Head and neck surgery.* Wolters Kluwer; 2016:Volume 1, Section 5, Chapter 31.

Villani V, Zucchella C, Cristalli G, Galiè E, Bianco F, Giannarelli D, Carpano S, Spriano G, Pace A. Vitamin E neuroprotection against cisplatin ototoxicity: Preliminary results from a randomized, placebo-controlled trial. *Head Neck*. 2016;38:E2118-E2121. **IF 2.760**

Department of experimental clinical oncology

PLASTIC RECONSTRUCTIVE SURGERY

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

Publications

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Department of experimental clinical oncology

ORTHOPAEDICS UNIT

Head: Roberto Biagini, MD

Staff

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Paolo Asquini, Nurse
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Matteo Ferraro, Nurse
Stefano Landi, Nurse
Giovanni Meogrossi, Nurse
Alessia Milotti, Nurse
Sabrina Ganzenua, Nurse
J. Baldi MD (Resident in Orthop and Trauma)
D. Nano 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 any kind of orthopedic oncological operation for primitive and metastatic muscular-skeletal tumors in adults and pediatric patients.**
- **During 2016, the unit has perfected the computer assisted navigated techniques, becoming one of the centers with greater experience in using the new applications of titanium 3D-printing in complex reconstructions after bone tumor removal.**

Clinical Activity

- The patients who have to undergo surgeries are hosted in the ward (12 regulars beds). In the ward there is also a pediatric room fully furnished with videogames and a video-school (available for long-term stay young patients) and a room decorated for adolescent patients.
- Surgery is performed 12 months/year in 8 operative theatre's days (2 par week);
- During the week, there are three outpatients clinics: on Mondays an orthopedic outpatient clinic for benign and low-grade malignant tumor; on Wednesdays a multidisciplinary clinic for high grade sarcomas and on Fridays a clinic for metastatic patients. Once a monthmonth there is also an outpatient clinic reserved for patients affected by multiple exostoses. One day a week there is an outpatient clinic for biopsies and one for wound care. Twice a week there is a

Disease Management Team meeting for case discussion. A Biobank stores biological samples from patients with musculoskeletal neoplasm and visceral sarcomas.

Research Activity

- 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 recurrent 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.

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Department of experimental clinical oncology

BREAST AND SOFT TISSUE SURGERY UNIT

Head: Franco Di Filippo, MD

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Nadia D'Antoni, nurse
Daniele Deplano, nurse
Maria Antonietta Di Ceglie, nurse
Fiorella Molinari, nurse
Maria Antonietta Picano, nurse
Viviana Ruspolini, nurse
Emanuela Vincenzi, nurse

Mission

Taking care of patients with breast cancer, melanoma and sarcoma through a human approach that looks at the person and his illness in a multidisciplinary and comprehensive way. The UOC's activity is designed to provide high standards of therapy and assistance, to collaborate in basic and clinical research and to implement innovative therapeutic strategies in order to modify the natural history of neoplastic disease and the quality of life of cancer patients in a positive way interacting with both the hospital's other operating units and with other healthcare facilities in the area.

Clinical Activity

The activity of the General Surgery Unit A is divided into: multidisciplinary 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 oncoplastic surgery (volume displacement techniques, volume replacement and propeller flaps) and immediate reconstructive surgery in cases of mastectomy and preservative 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 intraoperative evaluation of sentinel lymph node is performed by means of One Step Nucleic Acid Amplification (OSNA).
- Locoregional treatment of primitive 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:

- Development of predictive nomograms of axillary lymph node status after intraoperative evaluation by OSNA method of sentinel node
- 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 Observational Study. NeoCarbo study
- Predictive / Prognostic Biomarkers Identification 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: multi-setting and multi-tumor 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

Department of experimental clinical oncology

MEDICAL ONCOLOGY 1 UNIT

Head: Francesco Cognetti, MD

Staff

Paolo Carlini, MD Assistants
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Gianluigi Ferretti, MD Assistants
Carlo Garufi, MD Assistants
Michele Milella, MD Assistants
Cecilia Nisticò, MD Assistants
Paola Papaldo, MD Assistants
Antonella Savarese, MD Assistants
Massimo Zeuli, MD Assistants
Carmen Nuzzo, MD Senior Fellows
Angela Torsello, MD Senior Fellows
Vanja Vaccaro, MD Senior Fellows
Paola Malaguti, MD Fellows
Domenica Pellegrini, MD Fellows
Sabrina Vari, MD Fellows:

Clinical Activity

The Division of Medical Oncology 1 has a long standing commitment in improving the detection and treatment of solid cancers. In 2016, approximately 3000 new patients with solid cancers visited our Division, which has one of the largest referral programs for this disease. The Division's clinical activity guarantees the treatment and assistance for cancer patients requiring drug administration and clinical follow up. In particular, the Division is developing clinical research and new treatment strategies on solid tumors, especially gastrointestinal, lung, breast, gynaecologic tumors and melanomas, using either biological response modulators or drugs, molecularly aimed at specific biologic targets for different tumors, in addition to the classic antineoplastic drugs. The Division adopts regimens with optimal efficacy and with a low toxicity profile, such as the continuous infusion regimens which produce a lower burden of individual toxicity, offering patients an acceptable quality of life. Other fields of interest include the treatment of cancers which require a wide experience in medical oncology (e.g. gonadal or extragonadal germinal cell tumors and soft tissue and bone sarcomas).

Clinical activity is supported by an interdisciplinary Disease Management Team (DMT). Currently, DMT are operational for patients with tumors of the breast, lung, pancreas, biliary tract, gastrointestinal, liver, central nervous system, genito-urinary, head and neck, and sarcoma. In each DMT, a group of Physicians is dedicated to the treatment and follow up of patients according to guidelines or to approved experimental protocols. 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.

The Division of Medical Oncology A consists of an in-patient unit including one with a total of 22 beds, an Ambulatory Service equipped with 14

visiting rooms for outpatient activities and a Day Hospital for delivering selected anticancer therapies. Approximately 20.000 visits and 15.000 medical antineoplastic treatments are performed every year.

The main research topic of the Division is the study of new drugs, their combinations and/or sequence and new strategies of integrated treatments.

The Division is committed to conducting clinical trials in collaboration with the pharmaceutical industry, and to designing. and carrying out investigator-driven clinical trials. Special emphasis is given to new drug developments and various collaborations with laboratory researchers to identify molecular prognostic or predictive biomarkers.

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Department of experimental clinical oncology

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, a noticeable amount of 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) meetings under different residency specialist areas. Moreover, a relevant percentage of patients are enrolled in retrospective and prospective clinical studies.

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 patient's first-time visit/admission does not exceed four days.

Research Activity

During 2016, the clinical research activities focused on evaluating new treatment strategies/ identification of novel predictive/prognostic biomarkers for solid tumors, specifically regarding breast/gynecological cancers.

- *Breast Cancer* - The Unit is the coordinator center in a variety of multicentric breast cancer trials in neoadjuvant, adjuvant, advanced setting, in collaboration with many other cancer centers.
  - Neoadjuvant: A prospective trial on trastuzumab/chemotherapy in Her2+ breast cancer (DECT) has been published. Another one, (Triskele) with biological evaluations on pretreatment biopsy, is ongoing. Other studies, concerning metabolic determinants/anthropometric indicators, Hippo pathway , have been

recently published. Two more studies are ongoing (triple-negative).

- Adjuvant: A study on "triple positive" early breast cancer has been published, and other studies, evaluating biomarkers on surgical specimens (PHOBOS) or fertility in young patients (MARIO), are ongoing.
- Advanced: The Unit participated in HERLAPAC, HERBA, PRO-HERBA studies in Her2+ patients. Another study, evaluating paclitaxel/bevacizumab, has been published, as studies concerning male breast cancer, while two studies on T-DM1 and pertuzumab are ongoing. Trials concerning everolimus (BALLET), BKM120 (BELLE3), fulvestrant (Fulfive), everolimus/exemestane metabolic determinants (EVEREXT) have been closed or published. Three more studies concerning eribulin (ESEMPIO, PAINTER, QoL), and nab-paclitaxel (ABROS), are ongoing. Moreover, some reviews have been published. Congress/events organization: "*Meet the professor: controversie nel carcinoma della mammella*" (25 Nov 2016); "*Antiangiogenetici nel carcinoma della mammella*" (23 Nov 2016).

- *Other Tumors:* Two translational studies on cervical cancer have been published concerning a) biological parameters in neoadjuvant chemotherapy b) HER-family expression/modulation during neoplastic progression. Another study is testing the predictive role of a miR signature in relapsed, high-grade serous ovarian cancer. Moreover, the Unit is involved in various MITO trials. Reviews concerning therapeutic vaccines in cervical lesions, bevacizumab in ovarian/endometrial cancer, gynecologic cancer risk, robotic surgery, have been published. The *Ovarian Translational Group (TG)* focused on the institution of a data-base reporting all ovarian cancer patients data, and metabolic determinants have been collected and published. The Unit works as a consultant for ovarian-tissue preservation bank (BTO), and for the HPV-Unit.

Publications

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Department of experimental clinical oncology

HAEMATOLOGY AND STEM CELL TRANSPLANTATION UNIT

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Mission

Hematology and Transplant Unit is fully devoted to the provision of care services and assistance of patients with hematologic malignancies, according to the policy and mission of Regina Elena National Cancer Institute. In this framework, through scientific research, development of medical knowledge, and collaboration with other organizations at national and international level, the Unit became 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

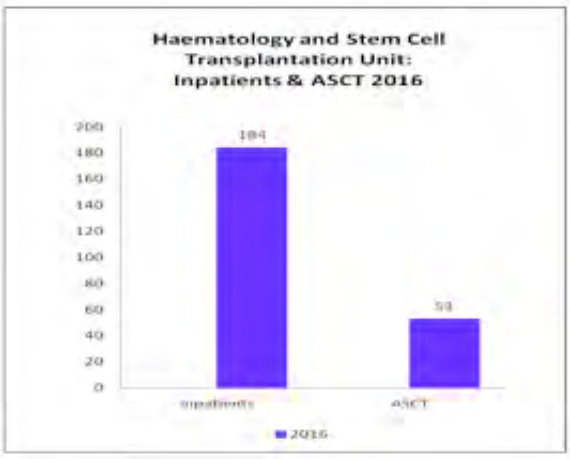
outside clinical trials, in 2016 five PDTA (percorsi diagnostici terapeutici assistenziali aziendali) were approved by the Institute for the following malignancies: acute myeloid leukemia, chronic myeloid leukemia, follicular lymphoma, diffuse large B cell lymphoma and multiple myeloma.

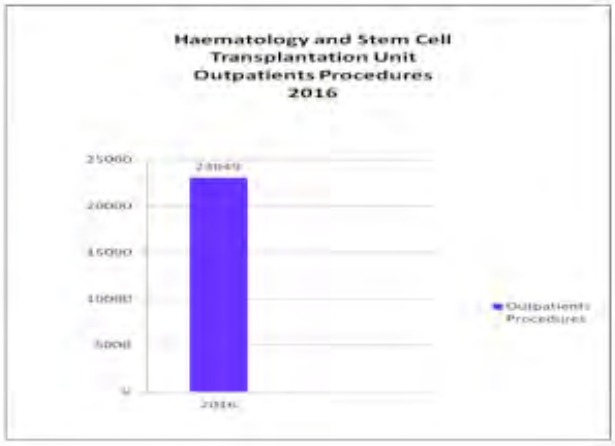
Stem cell transplantation often is indicated for the treatment of hematologic malignancies. U.O.S.D. Ematologia e Trapianti is one of the 6 Institutions located in Rome that belong to Rome Transplant Network (RTN), a Metropolitan Hematopoietic Stem Cell Transplant Program for adult patients established 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.

In 2016 RTN registered 200 Transplants (53 allogeneic and 147 autologous), 53 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 in 2016 for inpatients as well outpatients.





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).**

- *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 results suggest that the serum miR-22, as well as

miR-99a/let-7c/miR-125b miRna cluster, are of potential interest as non-invasive biomarkers to predict therapeutic response in DLBCL patients.

- *Invasive Pulmonary Aspergillosis (IPA)* - Evaluation of the role of Aspergillus PCR detection on bronchoalveolar lavage fluid (BAL) for IPA diagnosis: prospective study on hematologic patients. Out of 769 patients admitted in our ward between April 2013 and October 2016, 85 had LI and 47 of them underwent BAL (total procedures: 51). A causal agent of LI was detected in 33 cases (65%) allowing to modify the ongoing anti-microbial treatment in 25 of them(76%). Twelve cases of probable IPA, according to EORTC/MSG criteria, were diagnosed. In addition, we found 7 cases of LI with radiologic criteria suggestive for IPA but negative by serological tests and galactomannan on BAL, in which, however, the positive results gathered by Aspergillus PCR determination were followed by the administration of voriconazole, thus considering such a result as an "indirect" mycological criterion: all these 7 cases obtained a satisfactory clinical outcome with complete LI resolution. One life-threatening post-procedure complication was observed. These data strongly support the idea to include Aspergillus PCR detection on BAL among the "indirect" mycological tests of probable IPA and to consider BAL as an indispensable and safe diagnostic approach to LI also in "problematic" hematologic patients. This study was accepted for publication in Leukemia and Lymphoma in 2017.
- *Oral mucositis in melphalan-treated patients:* The Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology guidelines only suggest the use of oral cryotherapy to prevent oral mucositis in patients receiving high-dose melphalan as conditioning regimen for autologous stem cell transplantation (ASCT). Therefore, we performed a prospective randomized study to establish if cryotherapy prophylaxis is able to prevent grade 3-4 oral mucositis in myeloma patients who underwent ASCT after a chemo-free induction treatment and if cryotherapy prophylaxis is able to reduce the incidence of febrile episodes and documented infections in this setting of patients. The preliminary results of this study on 65 consecutive adult myeloma patients who underwent ASCT from October 2013 to September 2015, showing either a reduction of grade 3-4 oral mucositis or a lower risk of treatment with intravenous antibiotics for suspected or documented infections during the engraftment phase, have been presented at the 2016 Annual Meeting of the European Society for Blood and Marrow Transplantation and eventually published (Bone Marrow Transplant. 2016 Aug 15. doi: 10.1038/bmt.2016.207).
- Finally, during 2016, several original studies of our Unit in different issues (*reactivation of CMV after auto-transplant, biosimilar filgrastim in mobilization of stem cells, role of flow cytometry in diagnosis and monitoring of minimal residual disease in lymphoma and myeloma patients*) were published, and two original studies (one of which prospective) were initiated in collaboration with the neurologists.
- 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 the transfer of the clinical data of about a thousand 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 from patients who died, lost or those who left the follow-up. A computer file was then created in which 637 patients are included. The Unit chose to start with two diseases: Follicular Lymphoma (LF) and Diffuse Large Cell Lymphoma (DLBCL). To date, 140 patients with LF and 240 patients with DLBCL were included. In

September 2016, data-entry started with patients with multiple myeloma (actually more than 80 records). The activity of the Secretariat and Data Manager also provides the database update of DMT and satisfaction questionnaires.

- Patients enrollment in the project *"Psychological Functioning and quality of life after autologous stem cell transplantation in patients with onco-hematological disease"* continued in 2016. 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 2016 we enrolled 27 new patients, continued follow-up evaluation of all patients enrolled in the study, and administered a total of 125 questionnaires for measuring the quality of life, the perceived social support, psychological distress , resilience and self-efficacy. Furthermore, in-patients and outpatients with moderate to high levels of psychological distress, were referred to structured support intervention and 44 of them underwent psychotherapy.
- As for clinical trials, during the 2016, 33 clinical research protocols proposed by Hematology and Transplant Unit and approved by the Regina Elena I.F.O. Ethics Committee have been open for recruitment and 334 patients have been enrolled.

Publications

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Department of experimental clinical oncology

CARDIOLOGY UNIT

Head: Francesco Rulli, MD

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

Research Activity
The Cardiology operating Unit substantially has three aspects:

- Support to surgery in terms of preoperative cardiovascular function evaluation in the intraoperatorive emergency and in any patient's appreciation as a results of complications.
- The state of cardiological evaluation of the patient to be subjected to chemotherapy or radiotherapy, pre or post-surgery, given the already documented cardiotoxicity of

some therapeutic lines and in particular of some specific groups of drugs. To this is added the periodic monitoring, clinical and instrumental, the treated patient, and in accordance with research protocols defined and shared with colleagues oncologists conforming with the guidelines defined by available.

- The UO Cardiology is part of the most solid and accreditated reality 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.

Department of experimental clinical oncology

ENDOCRINOLOGY UNIT

Head: Marialuisa Appetecchia, MD

Staff

Roberto Baldelli MD,
Agnese Barnabei MD
Maria Fortunati Nurse,
Aurora De Leo Nurse,
Francesco Malci Nurse

Francesca Rota Attending Endocrinologists
Paola Di Giacinto Attending Endocrinologists
Claudia Annoscia Attending Endocrinologists
Agnese Persichetti Attending Endocrinologists

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

Mission

The Endocrinology Unit operates in three areas: clinical, research and training. Its mission is to achieve excellence in prevention, diagnosis and treatment of endocrine tumors and endocrine-metabolic sequelae in cancer patients by using diagnostic and therapeutic pathways (PDTA) and using a dedicated Disease Team Management (DMT) for discussing cases of 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 on one hand to the technical and professional quality and on the continuous improvement and updating of the service delivery and management techniques, on the other 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)*: The optimal frequency of follow-up assessments are personalized, in accordance with the stage of the patient's illness.The Endocrinology Unit follows to date approximately 2000 patients with Thyroid tumors (Differentiated and Medullary).

- *Hereditary endocrine tumours* Currently, the Endocrinology Unit follows:
- 100 patients with medullary thyroid cancer and their families
- Approximately 14 families with multiple endocrine neoplasia type I or type II (MEN 1 and 2),
- Approximately 10 families with Familiar Medullary Thyroid Cancer (FMTC),
- Approximately 50 families with Familiar Differentiated Thyroid Cancer (FDTC)
- 30 patients with pheochromocytoma syndrome or pheochromocytoma / paraganglioma and their families
- 81 patients with familial polyposis and endocrine diseases.

  A dedicated **outpatient clinic** has been activated for genetic counseling and prevention of hereditary oncological diseases. The incidence of these types of cancers is estimated to be approximately 5-10% of all cancers. Molecular analyses include the following markers: RET, MEN-1, VHL, SDHB, SDHD, SDHC. Patients with familial endocrine neoplasia are followed right from the first clinical suspicion of the disease up to molecular diagnosis, studying family history to organize 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.

- *Secondary osteoporosis and bone metabolism disorders in cancer patients* – Oncological patients often develop , as a result of therapeutic treatments, experience menopause at early times 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 more critical than in non-cancer patients, not only for the overall improvement of their compliance, but also for 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. Treatment of these patients needs to be based on indicators other than those usually employed for non-oncological patients with osteoporosis. A dedicated **outpatient clinic** has been activated.
- *Familial adenomatous polyposis (FAP)* - Patients with FAP have a higher risk of developing thyroid cancer; therefore a follow-up visit that includes annual ultrasound thyroid examination is needed. The Unit of Gastroenterology and Digestive Endoscopy is a Reference Center in the Lazio Region for FAP,a rare disease for which patients should be ensured to receive comprehensive clinical management, with dedicated paths, providing diagnostic evaluations and follow-ups of target organs, including 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 the 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 (INDIVIDUALS? Correct?) to gastrointestinal localization, 0.05 / 100,000 associated with Multiple Endocrine Neoplasia MEN-1 and / pancreatic 100,000. Sporadic forms have the highest incidence between 50-60 years, while familiar forms are diagnosed earlier. Their incidence is still rising, but nevertheless these 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 including: Adrenal Tumors, Fertility disorders in cancer patients, Endocrine side-effects of anti-cancer therapies, Pituitary Tumors and Adults Growth Hormone Deficiency (GHD).
- Endocrinology Unit is a Regional referral center for adult GHD (from 2003) and an AIFA accredited center (2012) Lazio Region to: thyroid carcinoma, osteoporosis, neuroendocrine tumors, 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. Ongoing projects include topics regarding osteoporosis and bone metabolism disorders in cancer patients.

Publications

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Department of experimental clinical oncology

NEURONCOLOGY UNIT

Head: Andrea Pace, MD

Staff

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Roberta Rafaelli, Nurse
Giuliana Graziano, Technician
Gianluca Petreri, Technician
Alessia Zizzari, Physioterapist
Andrea Minnetti, Physiotherapist
Luciano Urbani, Physiotherapist
Innorta Giacomo, Physiotherapist
Miccoli Raffaella, Physiotherapist
Rossi Marco, Physiotherapist
Veronica Villani, Neurologist
Dario Benincasa, Neurologist
Simona Scicchitano, Neurologist
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
Alessia Zarabla, Neurophysiologist
Dott. Andrea Maialetti, Neuro-psychologist

Research collaborations with graduate and undergraduate students: Marzia Piccoli

Clinical Activity

The clinical activities of Neuroncology Unit include:

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

- *Ongoing Clinical Trials (2016)* -
  - Observational study evaluating efficacy and safety of a weekly schedule of Carboplatin (AUC2) in recurrent glioblastoma. An Italian mulicentric study coordinated by Regina Elena Cancer Institute. Ongoing.
  - Multicenter, randomized, non-comparative, open-label phase II trial on the efficacy of Ortataxel and Fotemustine in recurrent glioblastoma. The enrollement has been recently closed. An interim analysis is ongoing.
  - TAMIGA trial: A double-blind, placebo-controlled, randomized, Phase IIIb trial evaluating the efficacy and safety of standard of care (SOC) +/-continuous bevacizumab treatment following progression of disease (PD) in patients with glioblastoma (GBM) after first (1st)-line treatment with radiotherapy, temozolomide and bevacizumab. The enrollement has been recently closed and the patients' follow-up is ongoing.
  - EORTC – BTG – 1320 Trabectedin For Recurrent Grade Ii Or Iii Meningioma: A Randomized Phase Ii Study Of The Eortc Brain Tumor Group. Ongoing
  - REGOMA study: Regorafenib in relapsed glioblastoma. Randomized, controlled open-label phase II clinical trial. The enrollement has been recently closed and the patients' follow-up is ongoing.
  - 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. Ongoing
  - EldCog: neurocognitive impact of hypofractionated radiotherapy associated with chemotherapy versus temozolomide chemotherapy alone in elderly patients (≥ 70 years) with newly diagnosed glioblastoma. A Multicenter study. Ongoing

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 including: temozolomide, fotemustine, bevacizumab, carboplatin, ortataxel, regorafenib.
- *Clinical Benefit of antiangiogenic treatment* - The aim of this study was to evaluate the clinical benefit (CB) of bevacizumab (BV) therapy alone or in combination in the treatment of recurrent glioma (RG).
- *Response evaluation to antiangiogenic treatment* - Response evaluation after antiangiogenetic treatment has been evaluated with Perfusion MRI to evaluate if early perfusion changes during treatment may be predictive of response to antiangiogenic therapy in high grade gliomas.
- *Temozolomide chemotherapy with extended schedule in low grade gliomas* - The activity of a low dose of temozolomide (50 mg/sq m) given for 1 week on and 1 week off for the treatment of newly diagnosed low grade glioma (LGG) requiring treatment for the presence of negative prognostic factors, such as residual tumors after surgery or biopsy, age higher than 40, neurological deficits or uncontrolled epilepsy has been evaluated in a phase II trial.
- *Role of PET f-dopa in low-grade glioma management* - The diagnostic role of PET FDOPA in LGG have been evaluated in a prospective study.
- *Cognitive impairment assessment and rehabilitation* - The role of cognitive rehabilitation programs has been investigated in different setting of care (inpatients, outpatients, home care setting).
- *Home-care for brain tumor patients* - A pilot program of comprehensive palliative care for brain tumour patients was started in the Regina Elena National Cancer Institute of Rome in October 2000, supported by the Lazio Regional Health System.
- *Palliative neuro oncology and telemedicine* - The lack of adequate continuity of care

for patients affected by BTs in the last stage of disease results in frequent hospital readmission with increased health expenditures and compromised quality of care. Information-Communication Technology (ICT) resources, applied to innovative models of health care (e-Care), are considered a powerful instrument of facilitation of clinical management and of health and social services delivery.

- *We developed a health WEB site portal applied to Neuro-Oncology* supportive and palliative care issues (www.portaleneuroncologia.it). The Web site is a tool for the promotion and diffusion of guidelines and treatment recommendations. 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 network includes European experts on palliative care in neuroncology . The guidelines produced by the palliative care task force have been recently submitted and accepted for publication in 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.
- *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:* Recent studies in cancer patients have shown that comorbidities should be considered a contraindication to aggressive approach, as they can influence the treatment compliance and/or patients' survival. Co-morbidities are often underestimated in GBM patients. This study evaluated the impact of comorbidities on outcomes in elderly GBM patients.
- *The prognostic value of pyrosequencing-detected MGMT-promoter hypermethylation in newly diagnosed patients with glioblastoma* - The MGMT gene is epigenetically silenced by promoter hypermethylation in gliomas, and this modification has emerged as a relevant predictor of therapeutic response and of better prognosis in glioblastoma patients.
- *Headache as a presenting symptom of glioma:* a cross-sectional study in 7 cases (1% of the overall sample). The manuscript has been submitted for publication.
- *Tumor related Epilepsy* - The *Center for tumor-related epilepsy* was formally approved by the Institute in January 2005. 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:

  - Evaluation of seizure control and quality of life in patients with brain tumor related epilepsy treated with Lacosamide as add-on therapy: a prospective explorative study with a historical control group
  - Evaluation of seizure control, quality of life and effect on EEG background activity in patients with brain tumor related epilepsy treated with Zonisamide as add-on therapy: a pilot study
  - Retrospective observational study in patients with Acute Lymphoid Leukemia treated with Citosina Arabinoside (ARA-C)

  Multicentric Studies on tumor related epilepsy:

  - Antiepileptic and antineoplastic effects on glioblastoma human cells of lacosamide and brivaracetam: preliminary experimental study
  - A non-interventional study of Vimpat® (Lacosamide) as adjunctive antiepileptic drug therapy in patients with Brain tumor-related EpilepSy (VIBES)
  - 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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Department of experimental clinical oncology

GASTROENTEROLOGY AND DIGESTIVE ENDOSCOPY UNIT

Head: Marcello Anti MD (2016); Vittoria Stigliano MD (2017)

Staff

Guglielmo Irti , Lead Nurse
Laura Argento, Nurse
Daniela Cannone, Nurse
Paola Capra, Nurse
Giuseppe Guastamacchia, Nurse
Alessandra Cinti , Nurse
Giuliana Panico, Nurse
Susanna Pampinella, Nurse
Marina Santamaria, Nurse
Cinzia Toresi, Health Worker
Mario Di Stefano, Health Worker
Daniela Assisi, MD
Rocco Lapenta, MD
Cinzia Quondamcarlo, MD
Lupe Sanchez Mete, MD
2 MD students of "La Sapienza" University of Rome

Mission

The 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 in several fields as in the diagnosis of pancreatic cancer, rectal cancer staging through the use of Endoscopic ultrasound (EUS); the diagnosis and palli ative treatment of biliary tree cancer by the use of endoscopic retrograde cholangiopancreatography (ERCP).
Moreover, recently, we introduced the combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer.
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

- Diagnosis of "early" cancerous lesions by using advanced technologies "Narrow Binding Imaging"
- Diagnosis and follow up of celiac disease
- Endoscopic treatment of neoplastic lesions (polipectomy, Mucosectomy, Argon Plasma Coagulation),
- Diagnosis and endoscopic treatment of neoplastic lesions in Hereditary colorectal cancer syndromes affected individuals
- Diagnostic and operative Endoscopic retrograde cholangiopancreatography
- Palliation of advanced cancer of gastrointestinal and hepato-biliary tract ("stenting" and dilation)
- Diagnostic and operative Endoscopic ultrasound
- "Wireless Endoscopy" (videocapsule endoscopy for small bowel)
- Upper and lower single balloon enteroscopy
- Emergency endoscopy for acute gastrointestinal bleeding , foreign bodies extraction
- Percutaneous Endoscopic Gastrostomy (PEG) for long term enteral nutrition

Referral Centres and Counselling for outpatients and inpatients

- Since 2005, the Unit has been recognized Referral Centre of Lazio Region for Familial Adenomatous Polyposis (FAP) and the Hereditary Colorectal cancer syndromes Clinics of the Unit guarantee an adequate management of these rare diseases.
- Since 2007, the Unit has been recognized Referral Centre 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 counselling is offered for all the gastroenterological and hepato-bilio-pancreatic diseases.

Research Activity

The major research interest of our Unit is in the field of colorectal cancer, in particular of familial and hereditary colorectal cancer.
Further fields of interest are EUS and biliary stent.
During 2016 we pursued the following Research Projects:

- Toxins produced by intestinal bacteria and predisposing genetic variations: a dangerous link for colorectal cancer development? (PE-2011-02347510) in cooperation with ISS
- Principal Investigator: Dr Vittoria Stigliano

- Use of a multitarget, stool DNA test to detect Advanced Adenoma and Colorectal Cancers compared with colonoscopy. A case-control study on Cologuard, an FDA-approved test based on the detection of DNA in the stool.
- Principal Investigator: Prof Marcello Anti

- New screening and follow-up molecular strategies in patients with suspected hereditary syndrome of colon-rectal carcinoma.
    - Principal Investigator: Dr. Vittoria Stigliano

- The epigenetic contribution to Lynch syndrome.
    - Principal Investigator: Dr. Vittoria Stigliano

- Hereditary colorectal cancer: molecular characterization of novel genetic variants to improve cancer screening and surveillance programs.
    - Principal Investigator: Dr. Vittoria Stigliano
- Studio multicentrico di confronto tra Enteroscopia Balloon assisted e videocapsula endoscopica in pazienti affetti da Poliposi Adenomatosa Familiare. In Cooperation with Università degli Studi La Cattolica, Policlinico Gemelli.
    - Principal Investigator: Dr. Vittoria Stigliano

Publications

Carboni F, Valle M, Federici O, Levi Sandri GB, Camperchioli I, Lapenta R, Assisi D, Garofalo A. Esophagojejunal anastomosis leakage after total gastrectomy for esophagogastric junction adenocarcinoma: Options of treatment. *J Gastrointest Oncol*. 2016;7(4):515-522.

Department of experimental clinical oncology

ANAESTHESIOLOGY, CRITICAL AREA AND INTENSIVE CARE UNIT

Head: Ester Forastiere, MD

Staff

Maria Sofra MD,
Piera Di Angelo MD,
Francesca Principi MD,
Maddalena Giovanetti MD,
Paolo Moricca MD,
Luana Fabrizi MD,
Luca Colantonio MD,
Maria Elena Marcelli MD,
Cecilia Coccia MD,
Federico Pierconti MD,
Alessandra Costantino MD,
Ilaria Monteferrante MD,
Claudia Frigieri MD,
Francesca Romano
Giordano MD,
Giulia Torregiani MD,
Emanuela Venti MD,
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Antonio Calamaro MD,
Gianfranco Fusco MD,
Giampiero Pontrandolfi MD,
Francesco Rendina MD,
Carmela Stigliano MD,
Lamberto Laurenzi MD

Mission

Perioperative evaluation of surgical patients. Management of intraoperative anesthesiology. Perioperative assistance to patients undergoing surgery. Intensive care of 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 to the Disease Management Teams of the various surgical teams.
- Intensive care of surgical, oncologic and hematologic patients.
- NORA sedation of patients in invasive procedures: interventional radiology, bronchoscopy, gastrocolonoscopy, CPRE.
- Pain therapy clinic: positioning of vascular accesses, PICC and PORT-CATH, treatment of oncologic pain with invasive and non-invasive procedures.

Research Activity

- *Treatment of acute and chronic pain in partial nephrectomy with tap-block technique vs intravenous analgesia. Randomized prospectic study.*
- Abdominal Sepsis Study - AbSeS: aetiologic epidemiology and outcome
- Decurarization After Thoracic Anesthesia: randomized multicentric study to evaluate neuromuscular blockage reversal induced by sugammadex and neostigmin after thoracic surgery.
- Surveillance of lung infections after thoracic surgery: creation of a database for the evaluation of appropriate antibiotic prophylaxis.
- Protective ventilation vs conventional ventilation in monopulmonary ventilation during thoracic surgery.
- Translational clinical research protocols, approved by the Ethics Committee with a retrospective, prospective, observational, randomized prospective structure.
- Collaboration with multi center studies, with the University of Udine, and the Cattolica del Sacro Cuore Rome.
- Scientific events on subjects closely associated with Anesthesiology: Hot Topics in Thoracic Anesthesia 16th December 2016, 4th edition.

Publications

Claroni C, Marcelli ME, Sofra MC, Covotta M, Torregiani G, Giannarelli D, Forastiere E. Preperitoneal continuous infusion of local anesthetics: What is the impact on surgical wound infections in humans? *Pain Med*. 2016;17(3): 582-589. **IF 2.324**

Claroni C, Torregiani G, Covotta M, Sofra M, Scotto Di Uccio A, Marcelli ME, Naccarato A, Forastiere E. Protective effect of sevoflurane preconditioning on ischemia-reperfusion injury in patients undergoing reconstructive plastic surgery with microsurgical flap, a randomized controlled trial. *BMC Anesthesiol*. 2016;16(1). **IF 1.320**

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Department of experimental clinical oncology

PSYCHOLOGY

Head: Patrizia Pugliese, MD

Staff

Maria Perrone, Psychologist
Gabriella Maggi, Psychologist
Maria Franca Condoleo, Psychologist
Giovanna D'Antonio, Psychologist
Anita Caruso, Psychologist
Paola Torti, Psychologist
Chiara Falcicchio, Psychologist
Alessandro Bonucci, Psychologist

Mission

The activities of the Psychology Unit mainly focus on the prevention, treatment and rehabilitation of psychological distress and mental health related to quality of life in clinical and research activity.

Clinical Activity

The main clinical approach adopted to achieve these objectives is the integration of psychological care within the medical care in DMT groups and in the Oncology and Dermatology departments, which aim to decrease both psychological stress together with the direct and indirect costs. The psychologists adopt individual, group, couple and family psychotherapy sessions, as well as telephone service support. Clinical activity involves also psychologists to take on the role of mediator in the doctor-patient relationship as well as in patient therapeutic pathways. Other activity include integrating psychologists together with other health professionals in the patient care setting (nurses and volunteers) as well as creating **network** of psychologists working in various hospitals and local structures in the Region of Lazio in appropriately referring patients.
This Unit's productivity is well in line with the 2016 budget. In accordance with the humanization project, the Psychology Unit has reached 99% patient satisfaction.

Research Activity

- *Quality of life study*
  "Miglioramento della qualità dell'assistenza nella pratica clinica quotidiana – percorsi psicologici diagnostico-terapeutici" aimed to enhance patient and family members quality of care through experimenting psychological paths in daily clinical practice.
  The 56% of patients showed levels of distress above the cut-off rate. 58% of these risk patients began psychological treatment with an improvement of distress levels in 85% of cases.
  The main needs of advanced patient family members were psychological support and doctor-family communication.
- *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 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.
80 women were enrolled the study. At baseline, 14.2% of women showed moderate levels of depression, 51.9% high anxiety, 34.4% a post-traumatic stress disorder, 50% a positive coping strategy and 78% instrumental support by partner; after chemotherapy, increased depression levels, decreased levels of anxiety and post-traumatic stress disorders, stable positive coping strategies and instrumental support. After 6 months from surgery increased levels of cortisolo, throughout the day suggested a state of chronic stress. After six months of chemotherapy, we observed an increased level of the chemokine MIP-1b LFA-IV, an increment of G-CSF and decreased levels of the pro-inflammatory cytokine IL-17 in breast cancer patients.

- *Patient Satisfaction with health care service received and disease awareness*
  The study "Consapevolezza di malattia e soddisfazione per le cure ricevute nei pazienti italiani con tumori solidi: uno studio multicentrico" aimed to evaluate the patient satisfaction with health care service recieved and related factors.

Publications

Pace A, Villani V, Parisi C, Di Felice S, Lamaro M, Falcicchio C, Bonucci A, Pugliese P, di Napoli A, Di Lallo D. Rehabilitation pathways in adult brain tumor patients in the first 12 months of disease. A retrospective analysis of services utilization in 719 patients. Supportive Care Cancer. 2016;24(11): 4801-4806. **IF 2.535**

Regional Pathology Reference Center (RPRC)

HPV UNIT

Coordinators: Luciano Mariani,MD
Aldo Venuti, MD

Staff

Qualified experts:

Regina Elena National Cancer Institute (IRE)

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

Virology: Aldo Venuti, Federico De Marco, Francesca 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

Psicology: Patrizia Pugliese, Marias Perrone, Maria Condoleo, Chiara Falcicchio.

Epidemiology: Valerio Ramazzotti, Maria Cecilia Cercato

Clinical studies: Diana Giannarelli

San Gallicano Dermatologic Institute (ISG)

Dermatology and istopathology: Vitaliano Silipo, Paola De Simone, A Carbone, Carlo Cota, Pietro Donati, Luca Muscardin

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. The consultation for gynaecological HPV-related diseases increases each year, by almost 35%. The adult female vaccination program, up to 45 years old, has been activated in 2014 and is still active (particularly as adjuvant prevention therapy after conisations, 100 patients enrolled). Male vaccination is fully operating with a constant increase from 2014 to 2016 (100 doses last year). HPV UNIT is actively engaged in the second level diagnosis of virus-associated cancers, especially HPV and polyomavirus. More than 200 samples from skin, oral cavity, and genital/perianal areas were analysed.

Research activity

Scientific activities of HPV-UNIT were focused on translational researches of virus–associated cancers and on the development of permanent professional training facilities and information addressed to the citizens

The training activity was scheduled with courses for HCWs while the activity of user's information was carried out by telephone, by email and through the continuous up-grading the dedicated internet site (www.hpvunit.it).

- *Molecular carcinogenesis* - A new activity of HPV 16 E2 protein was discovered, affecting the expression of ErbB receptor family with a clear inhibition of the ErbB 3 that could play a role during transformation in association with viral integration.
- *Molecular epidemiology of HPV types.*

  1- Genital tumors. Patients after cone biopsy were enrolled in a program to define recurrence risk associated to specific HPV genotypes. Preliminary results seem to indicate a different risk associated to different HPV types.

  2- Extra-genital tumors. Presence and expression of HPV in tonsil tumor and in contralateral healthy tonsil were detected to better define the carcinogenesis of these viruses in this localization. The oncogenic role of cutaneous HPV in skin cancer is still a controversial issue, therefore studies were undertaken to demonstrate presence and expression of HPV in pre-neoplastic lesions (i.e. actinic keratosis).
- *New therapies of HPV-associated cancers* - Therapeutic vaccines were produced, tested in new mouse models and patented (pending), in order to have: 1- low-cost 2nd-generation prophylactic vaccines against high immunogenic cross-reacting HPV antigens; 2- DNA therapeutic vaccines against HPV oncogenes able to overcome local immunosuppression and to generate acute inflammation at the tumor site. Finally, total new therapy was developed through the administration of intracellular antibodies (intrabodies) to alter the function of the specific targets E6-E7 of HPV16, representing a powerful alternative to methods of gene inactivation.

Publications

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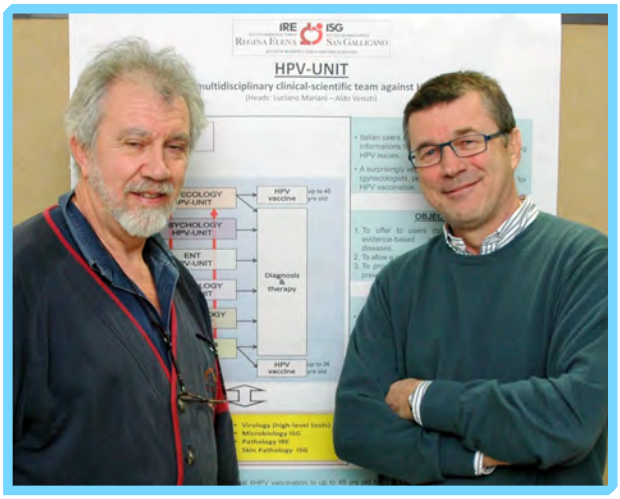

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Department of Research, Advanced Diagnostics and Technological Innovation

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Department of Research, Advanced Diagnostics and Technological Innovation

ONCOGENOMICS & EPIGENETICS

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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 Activities

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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Department of Research, Advanced Diagnostics and Technological Innovation

IMMUNOLOGY & IMMUNOTHERAPY CLINICAL PATHOLOGY UNIT

Head: Paola Nisticò, MD

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 rationale for designing novel treatments to be used in combination with immunotherapy, able to overcome therapy resistance. The mission is to develop and standardize methodologies for measuring the immune response to immunotherapies and establish surrogate biological markers for clinical response, forwarding cooperation with the clinical department for the benefit of the patients of the institute.

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Research activity

The lineage identity of tumors derives from the co-evolution of the 'cell of origin' and its tumor microenvironment, a major contributor to tumor progression and drug-resistance. Perturbation of epithelial cell integrity alters homeostatic balance between tumor cells and stroma, initiating a program enabling cancer cells to invade and metastasize. The tumor microenvironment exerts immunogenic or immunosuppressive effects depending on many factors, favoring or blocking the T lymphocyte recruitment in the tumors. Cancer associated fibroblasts (CAFs) have multiple

functions in the tumor microenvironment and, due to their ability to remodel extracellular matrix (ECM) and produce soluble factors, exert immunomodulatory functions. Epithelial to mesenchymal transition in tumors is a leading process regulating immune escape and resistance to therapy. The alternative splicing of the actin regulator hMENA is a crucial node in the signaling pathways related to this process and has been proposed as diagnostic, prognostic potential a theranostic marker in different tumors.

Our research activity aims to:

- Identify immune cell populations responsible for good/poor prognosis and of resistance/ sensitivity to immune checkpoint blockade inhibitors in NSCLC patients.
- Study of the mechanisms of Type-I-IFN-mediated induction of cancer stem cells during immunogenic chemotherapy and characterization of the immunogenicity of cancer stem cells.
- Design DNA vaccines, validated in pre-clinical models to develop new immunotherapies against HPV-associated cancers.
- Define new molecular functions of HPV16 E2 viral protein to improve diagnostic procedures for cervical cancer.
- Study the protein -protein interaction between HPV16 E7 and actin binding proteins.
- Validate the diagnostic, prognostic and theranostic potential of the pattern of hMENA isoforms in NSCLC and pancreatic cancer and identify signalling pathways related to hMENA splicing program.
- Characterize cancer associated fibroblast subtypes in NSCLC and pancreatic cancer to define their role in immune evasion and therapy resistance.
- Contribute in the identification of novel druggable pathways to develop new combined effective anti-tumor immunotherapy also using artichoke polyphenolic extracts,given their effects on cancer-related pathways.
- Set-up an immune-monitoring platform to be integrated with an immunoscore in NSCLC tumors in cooperation with the department of pathology.

Publications

Amici C, Visintin M, Verachi F, Paolini F, Percario Z, Di Bonito P, Mandarino A, Affabris E, Venuti A, Accardi L. A novel intracellular antibody against the E6 oncoprotein impairs growth of human papillomavirus 16-positive tumor cells in mouse models. *Oncotarget*. 2016;7(13):15539-15553. **IF 5.008**

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Department of Research, Advanced Diagnostics and Technological Innovation

PRECLINICAL MODELS AND NEW THERAPEUTIC AGENTS UNIT

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Mission

The aim of the Unit is to develop patient-derived models that will set the scene for target identification and for efficacious combination therapy in oncology. Results from preclinical studies conducted in these models are expected to identify new targeted approaches, able to hamper the malfunctioning signaling network. In particular, the resistance to targeted therapy highlights the need to discover drivers of an early non-mutational drug-tolerance state, before resistance occurs, providing an opportunity for more effective theranostic approaches.

The research topic concerns:

1 The role of growth factor and receptors (i.e. endothelin (ET-1), estrogen) or anti-apoptotic proteins (i.e. bcl-2) in invasion, metastasis, and response to anti-cancer therapy

2 The mechanism of tumor angiogenesis and lymphangiogenesis under hypoxia. Special attention is given to the relation with the microenvironment.

3 The membrane protrusions in cell migration and invasiveness

4 Preclinical models to evaluate new combinatorial therapies

The development of preclinical models "patient-derived" (PD), including primary cultures, tumoroids, circulating tumor cells, PD-xenografts, represents an important platform for the evaluation of new therapeutic agents and for the identification of new biomarkers. This platform (ovarian, lung, colon cancer, melanoma, sarcoma) can represent an opportunity of integration among inter-and intra-department that can reliably disclose the prospective results of clinical practice based on a strong pre-clinical rationale.

Research Activities

- *Endothelin and ET-1 receptors: signaling & functions in cancer* (PI A. Bagnato)
  The elucidation of the functional role and molecular mechanisms through which ET-1 controls invasiveness and drug response prompted us to the development of innovative diagnostic and therapeutic approaches. ET-1, acting on its GPCR (ETBR and ETAR), play functional roles in different cell populations, due to distinctive β-arrestin-dependent receptor complexes. We developed innovative combinatorial approaches based on the use of macitentan, a dual ET-1 receptor antagonist that regulates cancer cells and stromal cells in concomitant manner in the tumor microenvironment. In our studies, we provide evidence that ET-1R/β-arr1 links different signaling pathways (including Wnt/β-catenin, HIF-1α, RhoA GTPase, etc) to sustain resistant features and invadopodia formation, also through the amplification of ET-1 autocrine loop, further demonstrating that tumor progression is frequently associated with dysregulation of a signaling network, rather than of a single pathway. Moreover, ETAR are regulated by different miRNA (miR30a and miR200 family members) controlling angiogenesis, cell invasiveness, and metastatic progression.
- *Bcl-2 and related proteins: signaling & functions in cancer* (PI D. Del Bufalo)
  In order to decipher the functional role and the network through which bcl-2 controls the invasiveness of tumor cells and the formation of metastasis as well as angiogenesis, we characterized bcl-2 interactome by mass spectrometry, and identified SLIRP (SRA stem-loop interacting RNA-binding protein), a mitochondrial protein with a relevant role in regulating mitochondrial messenger RNA homeostasis. We showed that bcl-2 binds and stabilizes SLIRP protein and regulates

mitochondrial mRNA levels, through its BH4 domain. By using several human melanoma cell lines and their bcl-2 stably overexpressing derivatives, we demonstrated bcl-2 ability to modulate the expression of both miR-211 and miR-204 through a mechanism that involves the activity of MITF. Moreover, we provide evidence in lung cancer stem-like cells (LCSC) that inhibition of Histone acetyltransferase (HAT) confers a strong preferential inhibitory effect on undifferentiated LCSC lines when compared to their differentiated progeny, inhibits the growth of LCSC-derived xenografts by reducing cancer stem cell content.

- *Estradiol and its receptor: signaling & functions in cancer* (PI R. Galati)
  Continuing studies to understand the role of estrogen in the pathogenesis of malignant mesothelioma (MM), we focused mainly to examine the clinical and biological significance of estradiol (E2). We reported that the median survival in patients with absent E2 expression was longer than in those with high E2 expression. MM produces E2, interacts with GPR30, promoting tumor growth. In MM xenografts, the treatment with exemestane, an aromatase inhibitor (AI), induced a significant reduction of tumor growth, suggesting E2 as marker of MM development and AI as therapeutic and preventive agent.

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Department of Research, Advanced Diagnostics and Technological Innovation

CELLULAR NETWORKS AND MOLECULAR THERAPEUTIC TARGETS UNIT

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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 may assist other.

Clinical Activity

- *ATM germline variants by p53-MCL test* - Variant ATM heterozygotes have an increased risk of developing cancer, cardiovascular diseases, and diabetes. ATM gene variant complexity makes large-scale population screenings exceedingly time and money consuming. We have developed and validated a straightforward, rapid, and inexpensive test based on p53 mitotic centrosomal localization (p53-MCL) in peripheral blood mononuclear cells (PBMCs) that diagnoses mutant ATM zygosity and recognizes tumor-associated ATM polymorphisms. We have confirmed ATM as breast cancer susceptibility gene in BRCA1/2-negative patients with early-onset breast cancer and highlighted a possible association with breast/thyroid cancers. Our results open the possibility of cost-effective, large-scale screenings for ATM heterozygotes.
- *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.

Research Activity

- *DNA damage response factors preserve ploidy by organelle-specific functions* - Dysfunction of centrosomes and midbody, two mitosis and cytokinesis-associated organelles can cause mitotic spindle abnormalities and/or cytokinesis failure, conditions that can generate chromosomal instability. We discovered that DNA damage response factors, such as ATM, p53, HIPK2, and extra-chromosomal histone H2B, localize at the centrosomes (ATM and p53) and midbody (HIPK2 and H2B). Now, we show that, in addition to their DNA caretaker activities, p53, HIPK2 and H2B contribute to ploidy preservation by their organelle-specific, non-nuclear functions.
- *Overcoming drug resistance in cancer* - Both hypothesis-driven and computational drug repositioning have been undertaken toward targeted therapies. Dr. Falcioni overcomes HER3-dependent drug-resistance of colon-cancers by a dual targeting of HER3 and MEK pathways; Dr. Cardone identified inhibitor of PI3K/AKT oncogenic pathway among FDA-approved anthelmintic drugs; Dr. D'Orazi overcomes the hyperglycemia-induced resistance to adriamycin by $ZnCl_2$-mediated sustain of the HIPK2-p53 pathway; Dr. Paggi potentiates glioblasoma cell response to radiotherapy by SI113, a novel and selective inhibitor of SGK1; Dr. Vitale targets tetraploid cancer cells by abrogation of the spindle assembly checkpoint; finally, Dr. Campanella studies mitophagy and the therapeutic clearance of damaged mitochondria.

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Mission

The mission of the SAFU UOSD focuses on the establishment of innovative mouse models of human cancers, 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 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 (telephone and on-line) clinical counseling for non-resident patients about HPV related diseases (HPV Unit).

Research activity

- The G-quadruplex ligand EMICORON has a marked therapeutic efficacy against advanced models of human colon cancer. Interestingly, Dr. Leonetti demonstrated that EMICORON increases both in vitro and in vivo the efficacy of chemotherapy in colon cancer harbouring RAS mutation. These results suggest that the

- integration of EMICORON in standard regimens in this disease setting represent a promising strategy to improve the outcome of colon cancer.
- Cancer cells frequently exhibit several epigenetic reprogramming suggesting that chromatin regulators are important for tumor development and growth. Recently, Dr. Fanciulli has demonstrated by using several "next generation sequencing" approaches that the protein Che-1 affects global chromatin structure and general transcription in multiple myeloma, producing growth arrest and apoptosis. These results identify Che-1 as a specific target for cancer cells, whose inhibition may provide a beneficial therapeutic index even in absence of combining it with standard cytotoxic therapies.
- Dr. De Marco has focused its efforts on the Characterization of oxidative stress adducts, induced by UV-A, UV-B and the visible component of the solar radiation, on the proteome of keratinocytes, melanocytes and fibroblasts from human epithelial tissues and analysis of their role in epithelial tissues cancer initiation and progression. In addition, he investigated the modulation of the oxidative balance and antioxidant response in epithelial cells transformed by the whole genome of Human Papillomavirus or by single ORFs.
- Dr. Gurtner focused her efforts on new gain of function mechanisms by which mutant p53 interferes with miRNA biogenesis processes leading to miRNA deregulation observed in colon and breast cancer.
- Dr Piaggio studied the molecular mechanisms regulating proliferation in normal and transformed cells. Using a mouse model engineered to express luciferase gene in cells undergoing proliferation she images tumor evolution in living animals.
- 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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Department of Research, Advanced Diagnostics and Technological Innovation

BIOSTATISTICS AND BIOINFORMATICS UNIT

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Mission

The Biostatistical and Bioinformatic Unit gives statistical advice for the protocol design related to observational and e xperimental 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 informatics 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 a manuscript, we perform the analysis and discuss the interpretation of results.

The informatics section develops with Visual Studio 2012.NET4 software web based platforms to manage clinical data related to patients enrolled in research projects. It is also involved in the design and implementation of web sites with the software Joomla.

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Department of Research, Advanced Diagnostics and Technological Innovation

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 at the following main objectives:

- **achieve professional excellence in both nuclear diagnostics and nuclear therapy, according national and international standards**
- **develop 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**

Clinical Activity

The activities of the Nuclear Medicine Unit focus on clinical research directed towards **therapy and diagnostics in main oncology fields**. In 2016, over 16.000 therapeutic and diagnostic procedures were performed, with approximately 400 cancer radionuclide treatments.

1. **Therapy,** as the main field of clinical activities, includes the radionuclide treatment of thyroid carcinoma, liver tumors and bone metastases using both beta- and alfa-emitters. The Centre is leader in Italy and Europe in the field of selective internal radiation therapy of liver tumors
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

3. 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.

- 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

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 64Cu-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
- 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.

Department of Research, Advanced Diagnostics and Technological Innovation

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

Clinical Activity

In 2016, more than 1,000,000 examinations were carried out.

- *Onco-haematology* - Innovative activities include the Primary Central Nervous System Lymphoma diagnosis by 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 using a single-tube six-colors assay based on intra-cytoplasmic immunoglobulin (cy-Ig) light chains *ratio* evaluated on patient-specific plasma cells immune profile.
- *Cancer biomarkers validation* - Serum levels of soluble Calreticulin predict for time to first treatment in Early Chronic Lymphocytic Leukaemia: Calreticulin can play a role in the disease progression of patients with early CLL. The interaction of Calreticulin with different TNF-ligand family members can contribute to the perturbation of immunity associated with progression of early CCL .
- *Molecular Diagnostics*

  - Liquid biopsy - Comparing the mutation status in ctDNA to that in patients' tissues (with advanced NSCLC) to determine the specific subgroups of patients who may be the best candidates for EGFR mutation analyses.

  - 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).

  Thrombophilia and PICC related DVT

  Symptomatic PICC related deep venous Thrombosis (DVT) is frequent in cancer patients receiving chemotherapy. We evaluate the prevalence of hereditary Thrombophilia in patients with solid tumours that correlate with a significantly higher risk of PICC related DVT.

  - 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

- *Pilot Study of interference in vivo of biological antineoplastic drugs by electrophoretic methods used in the diagnosis of plasma cell dyscrasias*

  PI Cigliana G

  Biological drugs can cause interference on serum agarose gel/capillary electrophoresis and agarose gel immunofixation. In order to overcome this issue, it is important to be informed about the therapeutic treatment and be aware to avoid clinical misinterpretation.
- *Case Control Stool Sample Collection Study to Support Device Adoption in Italy*

  PI Antenucci A, Martayan A

  Conventional screening for CRC includes both invasive and non-invasive options. Cologuard, is a U.S. FDA approved next-generation stool-based test that detects complementary DNA biomarkers known to be associated with CRC and its precursor lesions as well as fecal hemoglobin.
- *Pilot Study for the design and validation of an innovative single-tube eight-color flow-cytometry assay for Multiple Myeloma Diagnosis and Minimal Residual Disease monitoring.*

  PI Cordone I

  Consensus on minimal residual disease monitoring in Multiple Myeloma has not reached yet. On the path of our clinical results, a new antibodies combination in a single-tube eight-color assay is in progress for the standardization, repeatability and reproducibility of Multiple Myeloma diagnosis and monitoring.
- *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.

- *Implementing a Biobank of Biological Fluid at IRE supported by Scientific Advisory Board PI Conti L, Cigliana G, Mandoj C*

Clinical Pathology is currently engaged in establishing and developing a centralized Biobank whose essential function is to collect biological samples in accordance with standardized criteria and cryopreserve them in order to provide biological materials for selected scientific projects and research programs. During 2016, the number of samples collected to date is 4182. The IRE Biobank has become part of a network of biobanks Regione Lazio within the regional project "Network of Lazio for Translational Medicine and Development of Cancer Biotherapy", coordinated by the National Health Institute.

Publications

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Department of Research, Advanced Diagnostics and Technological Innovation

RADIOTHERAPY UNIT

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Mission

The Radiotherapy Unit is characterized by experience and technology that allow the realization of high-precision irradiation techniques, such as Intensity Modulated Radiotherapy (IMRT) and Rapid Arc (RA), Radiotherapy Volumetric (VMAT), Stereotactic Radiotherapy Surgery (SRS) of both brain and body (SBRT), Image-Guided Radiation Therapy (IGRT). Also of the respiratory movements control techniques are available to reduce the confounding effect of the position of the target to be irradiated, and 'tracking' of the target through the placement of radiopaque landmarks. A constant collaboration with the Radiology and Nuclear Medicine allows access to sophisticated examinations and is essential for the correct identification of the disease location prior to treatment planning, such as MRI and CT PET.

Clinical Activity

All those correlated to treatment of tumors with external beam radiotherapy including Intensity Modulated Radiotherapy (IMRT) and Rapid Arc (RA), Stereotactic Radiotherapy Surgery (SRS) of both brain and extracranic lesions, intraoperative radiotherapy (IORT) of breast, head and neck tumors as well sarcomas. Research Activities

- Early Diffusion Weighted Magnetic Resonance Imaging Changes to Predict Tumor Response to Chemo-radiotherapy in H&N 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 evaluate feasibility and 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 with 1-3 brain metastases treated with stereotactic Radiotherapy or Ippocampal sparing whole brain radiotherapy: Observation study to evaluate 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 endpoint 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.

Publications

Buglioni S, Vici P, Sergi D, Pizzuti L, Di Lauro L, Antoniani B, Sperati F, Terrenato I, Carosi M, Gamucci T, Vincenzoni C, Mariani L, Vizza E, Venuti A, Sanguineti G, Gadducci A, Barba M, Natoli C, Vitale I, Mottolese M, De Maria R, Maugeri-Sacca M. Analysis of the hippo transducers TAZ and YAP in cervical cancer and its microenvironment. *Oncoimmunology*. 2016;5(6):1-7. **IF 7.644**

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I, Barba M, De Maria R, Mottolese M, Maugeri-Sacca M. DNA damage and repair biomarkers in cervical cancer patients treated with neoadjuvant chemotherapy: An exploratory analysis. *PLoS One*. 2016;11(3):1-11. **IF 3.057**

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Department of Research, Advanced Diagnostics and Technological Innovation

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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, mammotoms 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 Mammotom 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 Activities

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.

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Department of Research, Advanced Diagnostics and Technological Innovation

PATHOLOGY UNIT

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Livia Ronchetti, Biologist
Simona Baselice, Biologist
Tommaso Salvitti, Statician
Barbara Antoniani, Technician
Claudia Bonomo, Technician
Laura De Salvo, Technician

Mission

The Pathology Unit, as a discipline that bridges the basic and clinical studies, has the following three main objectives:

- **Oversee clinical testing and reporting to ensure the highest quality clinical services.**
- **Promote the delivery of clinical diagnostic services in a comprehensive, coordinated and cost-effective manner.**
- **Provide a unique intersection for clinical practice and research programs ranging from basic to translational research.**

We continuously innovate and implement our work to set up novel diagnostic technologies aimed at facilitating their rapid use into the diagnosis and care of cancer patients. During the present year, a great effort has been made to set up Next Generation Sequencing technologies focusing on the molecular characterization of tumors to provide useful information that guides patient treatment and tailors it to ensure the best response.

Finally, we organized with great accuracy our frozen tumor tissue biobank, with the aim to increase both national and international scientific collaborations.

Clinical Activity

In 2016 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, gene mutational status analysis (by NGS and/or real time PCR analysis), and molecular evaluation (OSNA) of sentinel lymph node in breast cancer patients were also routinely performed. In 2016 surgical or biopsy samples from about 11.300 patients have been studied, encompassing the whole spectrum of the main human tumours (in particular urogenital, lung, breast 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 cytological samples from about 8.600 patients have been studied, including FNAC, effusion, urine and cervico-vaginal cytology. In 2016 about 18.000-20.000 tests of diagnostic immunohistochemistry have been performed, including mainly tumour immunohistological typing and assessment of prognostic and/or predictive factors. In 2016 about 500 FISH/SISH, about 450 HPV molecular detection a/o genotyping, and about 100 OSNA tests have been performed. FISH/SISH analysis was performed mainly in cases of breast and gastric carcinoma (HER2), in cases of lung adenocarcinoma (ALK, ROS1), and in selected cases of 'aggressive' B-cell lymphomas (Bcl2, Bcl6, c-MYC) and of primary CNS tumours. EGFr, K-RAS, N-RAS, B-RAF, c-KIT and PDGF-alpha gene mutational status analysis were routinely performed in lung adenocarcinoma (EGFr, K-RAS), in colorectal adenocarcinoma (K-RAS, N-RAS, B-RAF), in metastatic melanoma (B-RAF), and Gastro-intestinal Stromal Tumours/GIST (c-KIT, PDGF-alpha) by real time PCR analysis in about 500 patients. From June 2016 about 500 patients with lung adenocarcinomas, colorectal adenocarcinomas, metastatic melanoma, and 'undefined' (THY 3B) thyroird lesions have been studied by a NGS procedure based on a panel of 22 different genes ('ONCOMINE'). Furthermore, about 250 molecular tests for MGMT promoter gene mutilation status and IDH1-IDH2 gene mutation in primary CNS tumours, and MSI evaluation in colorectal cancer have been performed in 2016.

Research Activities

*HPV-related diseases (head&neck, cervical, and anal cancer):*_We conducted epidemiological, clinical and molecular studies on HPV-related diseases on individuals affected by anal, Head-Neck (HNSCC), or cervical cancer (CC), collaborating with IARC and ISS. We participated to the international study on the HPV distribution in HNSCC and to the Consensus Conference for the cervical screening program in HPV vaccinated women, and in the preparation of Regione Lazio screening protocol. We coordinated an Italian multicentric study (NTCC2) to investigate the role of the HPV mRNA and the p16/Ki67 tests as triage test for HPV DNA positivity.

*miRNA studies (thymic epithelial tumours, and ovarian, colorectal, and prostate cancer):*_a number of collaborative studies on miRNAs were performed: in thymic epithelial tumors (TET) circulating miR-21-5p and miR-148a-3p are emerging as non-invasive biomarkers. An inverse correlation among microsatellite length and worse prognosis was observed in TET. In ovarian cancer a risk scoring model, termed MiROvaR, has been developed in a multicentric clinical trial by the use of a 35 miRNA signature and in gliomas serum miR-497 and -125b are promising diagnostic markers. In the context of an AIRC project, we studied the expression levels of miR-206, miR219, miR-192, miR-194 and miR-132 regulating clock-genes and three functional polymorphisms (rs11133373 C/G, rs1801260 T/C, rs11133391 T/C) in metastatic colorectal cancer (CRC) demonstrating their significant association to longer overall survival (OS) in women when compared to men.

In prostate cancer, concomitant loss of miR-15/miR-16 and gain of miR-21 aberrantly activate TGF-β and Hedgehog signaling, that mediate local invasion, distant bone marrow colonization and osteolysis.

*Immunohistochemical (IHC) studies (breast and colorectal cancer):*_a multicentric european study on a large series of male breast cancer (MBC) showed that the expression of the Hippo transducers TAZ/YAP and their target CTGF identify patients (pts) with significant shorter OS as well as

in MBC presenting TAZ/CTGF/AXL and YAP/CTGF/AXL phenotype.
HMG-CoAR a central enzyme of the mevalonate pathway, regulates the oncogenic Hippo transducers TAZ/YAP and in MBC is positively associated with the expression of hormone receptors. OS was longer in MBC with positive HMG-CoAR, suggesting a connection between the mevalonate pathway, the hormonal milieu and Hippo pathway.
The combined expression of YAP in tumor cells and in the surrounding stroma appears associated with a decreased pathological complete response (pCR) in triple negative female BC treated with neoadjuvant therapy (NA-CT).
The association between TAZ expression and reduced pCR rate was also demonstrated in CC pts whereas the expression of the Hippo transducers in TILs may predict increased treatment efficacy.
hMENA, an actin regulatory protein of the ENA/VASP family, cooperates with ErbB receptor family signaling in BC. The isoform hMENA(11a) can be proposed as a marker of HER3 activation and resistance to PI3K inhibition therapy.
In CC pts treated with NA-CT high levels of pWee1, a key G2/M checkpoint kinase and γ-H2AX, a marker of DNA double-strand breaks, is significantly associated with a reduced pCR.
HPV16 E7 expression level is directly related with CC cells migration and invasion capabilities. These HPV16 E7-related features are associated with Epithelial to Mesenchymal Transition processes due to the physical interaction of HPV16 E7 with Gelsolin.
In CRC patients, SIRT6 and TRF2 IHC expression is inversely correlated, as demonstrated in experimental model.
Main international collaborations: we participated to the multicentric international Cancer Genome Atlas study of TET (TCGA-THYM). We aso contributed to the new TNM staging system (8th edition) of Thoracic Tumors (TET, LC and Mesothelioma).

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Department of Research, Advanced Diagnostics and Technological Innovation

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 through 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 seeks quality assurance protocols to efficiently and safely perform 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 improve tumor control and sparing normal tissues. The Lab monitors devices, perform patient-specific dosimetry, guarantee the accuracy of image fusion from multimodality devices and develop 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, caregivers and population) and environment from physical agents. Main aim of this activity is reducing the clinical risk maintaining the level of safety at the standard request by technical regulation. Moreover, the Lab provides educational programs. Since 2009, the Lab is also ISO 9001 certified.

Research Activities

Main ongoing research projects of the Lab are: dosimetry in diagnostics and treatments, medical imaging applications, mathematical modeling of biological systems.

The Lab participates to clinical trials and performs data analysis of clinical and dosimetric results, such as:

- implementation of strategies for dose tracking/ adaptive/-omics for assessment of dosimetric predictors in oncological patients undergoing various therapies;
- investigation of toxicity after hypofractionated treatments in prostate and breast cancer patients;
- acquisition protocol optimization of advanced magnetic resonance imaging (MRI) techniques and the subsequent quantitative image analysis, by developing dedicated home-made software. This allows the quantification of biophysical parameters derived from multi-modal images, which are potentially useful for tumor characterization and staging, and for detection of residual disease after treatment (chemotherapy or RT);
- evaluation of the relationship between the perfusion parameters measured by IVIM DWI and the perfusion measured by conventional perfusion MRI techniques in soft tissue tumors.
- studying the impact of molecular markers (prognostic gene/miRNA) and/or radiobiological modeling to predict patient' outcome;
- exploring MAP2K3 targeting as novel anti-cancer therapeutical strategy;
- studying of the wtp53 roles in RT induced abscopal effects;
- plan comparison, robustness and quality in multicentric setting;
- Monte Carlo simulations;
- development of specific tools for predicting effects of ablative microwaves in liver disease;
- implementation of tool for studying the normal tissues effects using neurological imaging

Dr. A. Soriani is the PI of a project funded by Minister of Health: "Development and optimization of a dedicated self-shielded system to perform accelerated partial breast irradiation in prone position after breast conserving surgery". Dr. Strigari is Co-Director of a research project focusing on identification of innovative panel of biomarkers as novel tool for early detection of IR exposure, granted by NATO within the "Science for Peace" programme, together with ENEA and Alexandria University (Egypt). The results of this project will also improve the patients' treatment, by the knowledge of the individual radio-sensitivity. Dr. Strigari is member of Dosimetry Committee of EANM developing European guidelines on NM dosimetry.

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Department of Research, Advanced Diagnostics and Technological Innovation

TRASFUSION MEDICINE UNIT

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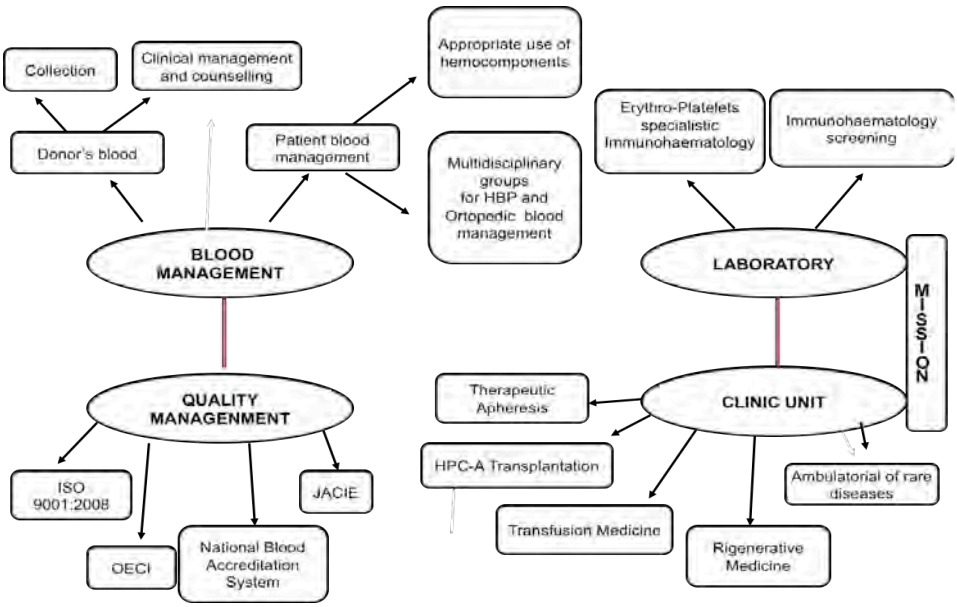
Clinical Activity

The Immunohaematology and Trasfusion Medicine Service is an articulated structure that complies with specific tasks provided by the Italian Legislation in the field of transfusion and supports with diagnostics and therapeutic activities the clinical departments for the treatment of haematological, dermatological, oncological, internal and surgical diseases. The activities are mainly directed to:

- Ensure the constant availability of blood and hemocomponents for the departments' needs;
- Verify the appropriateness of blood and hemocomponents clinical use;
- Manage cryopreserved pheripheral blood stem cells
- Control the quality and safety requirements of the hemocomponents.

In the Unit, there are the following areas of excellence which are intended to be implemented: Therapeutic Apheresis, Regenerative Medicine and Erytro-Platelets Immunohaematology.



The unit of Therapeutic Apheresis relies on the latest generation cell separators that allow to perform plasma exchange and photopheresis procedures in autoimmune and dysimmune diseases, in particularly in dermatological patients affected by Pemphigus Vulgaris, Atopic Dermatitis, Mycosis Fungoid, Psoriasis, etc.
The Regenerative Medicine is a new therapeutic approach aimed at the biological regeneration of tissues instead of replacing them, and finds its most relevant applications in orthopedics, dermatology and corrective medicine.
The Immunohaematological diagnostic is important in oncologic and polytransfused patients to prevent alloimmunization and consist in typing of rare erythrocyte groups, research of anti-erythrocyte and anti-platelets antibodies and identification of auto and allo-antibodies.

Research Activity

Blood derivatives ameliorate myogenic progenitor cells proliferation and differentiation:
In collaboration with Dr. Cesare Gargioli, researcher at the Department of Biology of Rome University Tor Vergata, we are developing a project regarding the effect of human blood derived serum and/or growth factor on human derived perivascular myogenic progenitor/stem cell, namely pericytes. So, the project purpose is to test human blood derivatives in order to supersede problems related to animal medium supplement and cell therapy for clinical application; moreover, working with human derived stem cells, we are analyzing the effect of human serum and growth factors on the myogenic capabilities of human skeletal muscle derived pericytes.
Bcl-2 promotes recruitment and differentiation of macrophages towards a M2-like phenotype:
In collaboration Dr. Donatella del Bufalo , preclinical models and new therapeutic agents unit – proposal AIRC investigator grant – Spanning bcl-2 functions in melanoma models from micro environment to microRNA modulation.

Pubications

De Matteis S, Fiorelli E, De Rienzo M, Chichierchia G, Tedesco M, Latini A, De Vita R, Foddai ML. Studio randomizzato in tre bracci per il trattamento del lichen sclerosus genitale (LSG) con frazione stromale da tessuto adiposo (FS) e plasma ricco di piastrine (PRP). *Blood Transfusion*. 2016;14(3):s322-23. **IF 1.042**
Fiorelli E, De Matteis S, De Rienzo M, Piras MR, Comuzzi P, Scarabello A, Cavuto C, Foddai ML. Il plasmaexchange nel trattamento d'attacco di un caso di pemfigo volgare severo e refrattario alle terapie convenzionali. *Blood Transfusion*. 2016;14(3):s248. **IF 1.042**

Department of Research, Advanced Diagnostics and Technological Innovation

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

TheThe 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 2016 about 16.404 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 16.614- 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 or suffer from COPD. In 2016 , about 3980 services of respiratory rehabilitation have been performed on internal patients and 3610 on external patients. In addition, about 70 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 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”.

Publications

1. Rocca GD, Vetrugno L, Coccia C, Pierconti F, Badagliacca R, Vizza CD, Papale M, Melis E, Facciolo F. Preoperative evaluation of patients undergoing lung resection surgery: Defining the role of the anesthesiologist on a multidisciplinary team. *J Cardiothorac Vasc Anesth*. 2016;30(2):530-538. **IF 1.519**

Department of Research, Advanced Diagnostics and Technological Innovation

EPIDEMIOLOGY AND CANCER REGISTRY SERVICE

Staff

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

Mission

The Unit of 'Epidemiology and Cancer Registry', a branch of the public health in the framework of the oncological discipline, aims at the monitoring, control and prevention of cancer. The unit is mainly involved in: descriptive epidemiology based on the 'cancer registration'; evaluative epidemiology based on the 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 Information and Communication Technology system of the Institute, aiming at providing easy access and analysis of clinical and research data.

Activity

- *Cancer Registration* - The Unit is a collaborative center with the Population based Cancer Registry of the Latina Province and the Italian Network of Cancer Registries (AIRTUM) with the purpose of estimating the distribution of cancer in the areas covered by the member registries including incidence, prevalence, survival, and mortality. Since 2015, in accordance to a regional law which established 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 hospital-based cancer registry of the 'Regina Elena' National Cancer Institute 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 recruitable patients for the clinical trials by specific neoplastic features.
- *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.

- *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 an ERN member with expertise on more than one rare malignancies. The Unit made a major contribution during the application process.
- *Patient Empowerment Network* - The Unit has been involved in the project development of a network for the patient empowerment and involvement. The following has been conducted: a) establishment of a permanent Working Group on Patient Empowerment; b) identification of the ongoing services, processes and resources, aiming at supporting, educating, and empowering cancer patients and their families; c) promotion of application of humanistic and narrative medicine. The whole process will be regularly checked for quality.
- *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.

Publications

AIRTUM working group., Ramazzotti V, Cercato M. I numeri del cancro in italia 2016. Il Pensiero Scientifico Editore; 2016:268.

AIRTUM Working Group, Busco S, Buzzoni C, Mallone S, Trama A, Castaing M, Bella F, Amodio R, Bizzoco S, Cassetti T, Cirilli C, Cusimano R, De Angelis R, Fusco M, Gatta G, Gennaro V, Giacomin A, Giorgi Rossi P, Mangone L, Mannino S, Rossi S, Pierannunzio D, Tavilla A, Tognazzo S, Tumino R, Vicentini M, Vitale MF, Crocetti E, Dal Maso L. Italian cancer figures--report 2015: The burden of rare cancers in italy. Epidemiol Prev. 2016;40(1 Suppl 2):1-120. **IF 0.924**

Cercato M, Servoli F, Scarinci V, Colella E, Fabi A, Bertazzi I, Sperduti I, Cognetti F, Cognetti G. Narrative medicine: A multidisciplinary study on knowledge and application in oncology. Annals of Oncology. 2016;27(Suppl 4):110. **IF 9.269**

Ramazzotti V, Cercato M. Contributo dei registri tumori alla letteratura scientifica internazionale. 2016.

Istitutional Courses 2016

Title	Dates	Credits	PI
Incontri multidisciplinari in ginecologia oncologica - I modulo	10/03 al 28/04 2016	12	E. Vizza
Educazione terapeutica del paziente	15/03 - 16/03 2016	25	G. Cognetti
Corso base. La gestione del rischio clinico (Ed. 1)	16/03/2016	17	V. Puro
Corso base. La gestione del rischio clinico (Ed. 2)	30/03/2016	12	V. Puro
Banche dati e Sistemi per l'informazione e la valutazione della ricerca	6-7/04/2016	20	G. Cognetti
Corso base. La gestione del rischio clinico (Ed. 3)	14/04/2016	22	V. Puro
La prevenzione e la gestione della caduta del paziente nelle strutture sanitarie. Alert report 2015	21/04/2016	14	S. Lolli
Biobanche tissutali, biobanche dati e registro tumori in oncologia: problemi etici, organizzativi e infrastrutturali	27/04/2016	25	Marino Mirella
Corso base. La gestione del rischio clinico (ed.4)	28/04/2016	10	V. Puro

Title	Dates	Credits	PI
Incontri multidisciplinari di ginecologia oncologica - II modulo	12 al 30/06/2016	11	E Vizza
Corso base. La gestione del rischio clinico (ed.5)	12/05/2016	11	V Puro
Corso base. La gestione del rischio clinico (ed.6)	26/05/2016	13	V Puro
Il percorso procedurale del campione istologico (ed. 1)	27/05/2016	13	M. Zucchiatti
Corso base. La gestione del rischio clinico(ed.7)	9/06/2016	19	V Puro
Elementi di lean management (ed 1)	10/06/2016	11	M Zucchiatti
Il contesto familiare e le dinamiche emotive degli operatori	13-15/06/2016	8	A. Caruso
I segreti di pubmed. Metodologia della ricerca dell'informazione (ed 1)	14-15/06/2016	12	G Cognetti
Il percorso procedurale del campione istologico (ed. 2)	15/06/2016	12	M Zucchiatti
La personalizzazione delle cure nei modelli organizzativi	16-17/06/2016	11	S Lolli
Le polmoniti iatrogene	21/06/2016	14	M Papale

Title	Dates	Credits	PI
Sicurezza del paziente. Procedure relative alle raccomandazioni ministeriali n 4-5-8-9-10-13-14	21/06/2016	40	V Puro
Corso BLSD (ed 1)	27/06/2016	5	F Principi
Elementi di lean management (ed 2)	27/06/2016	14	M Zucchiatti
Cancer genome atlas (TGCA)	1/07/2016	3	M Mirella
I segreti di pubmed. Metodologia della ricerca dell'informazione (ed 2)	5-6/07/2016	14	G Cognetti
Incontri multidisciplinari di ginecologia oncologica - III modulo	15/09 al 27/10 2016	16	E Vizza
Elementi di lean management (ed 3)	16/09/2016	12	M Zucchiatti
Il bambino, l'adolescente e la malattia oncologica	19/09/2016	18	A Caruso
Comunicazione efficace: strategie per migliorare la relazione	22-29/2016	19	A Caruso
Il ruolo del TSRM nel PDT del paziente SIRT	22/09/2016	20	R De Leo
Il percorso procedurale del campione istologico (ed. 3)	23/09/2016	10	M Zucchiatti

Title	Dates	Credits	PI
Come produrre documentazione e pubblicare in ambito scientifico (ed 1)	4-5/10/2016	22	G Cognetti
Ridait Seminars - I ciclo	4/10 al 20/12 2016	26	A Venuti
La personalizzazione delle cure nei modelli organizzativi (ed.2)	5-6/10/2016	9	S Lolli
Corso BLSD (Ed.2)	6/10/2016	8	F Francesca
Innovazioni normative gestionali e contrattuali nel management delle professioni sanitarie (ed.1)	11/10/2016	7	S Lolli
Corso teorico pratico sulla gestione vie aeree: corso base (ed.1)	12/10/2016	15	C Coccia
Approccio multiprofessionale, attualita' prospettive in radiologia interventistica oncologica (ed.1)	14-15/10/2016	16	G Sodero
Come produrre documentazione e pubblicare in ambito scientifico (Ed.2)	25-26/10/2016	21	G Cognetti
Corso BLSD (ed.3)	9/11/2016	7	F Principi
Innovazioni normative gestionali e contrattuali nel management delle professioni sanitarie	17/11/2016	24	S Lolli

Title	Dates	Credits	PI
Approccio multiprofessionale, attualita' prospettive in radiologia interventistica oncologica (ed.2)	18-19/11/2016	17	G Sodero
Corso teorico pratico sulla gestione vie aeree: corso base	25/11/2016	13	C Coccia
La salute dell'osso nel malato oncologico. Stato dell'arte e prospettive	26/11/2016	21	M.L. Appetecchia
Gestione del paziente radioattivo in ambiente sanitario: informazioni necessarie per lavorare in sicurezza e miti da sfatare	28/11 al 2/12 2016	19	R Sciuto
Corso BLSD (ed 4)	1/12/2016	6	F Principi
Corso teorico pratico sulla gestione vie aeree: corso base (ed. 3)	5/12/2016	19	C Coccia
Dipartimento di Ricerca.Diagnostica avanzata e Innovazione tecnologica.Stato dell'arte e aspettative del personale sanitario	8/11/2016	45	M Burgio

Title	Dates	Credits	PI
Gestione del paziente radioattivo in ambiente sanitario: informazioni necessarie per lavorare in sicurezza e miti da sfatare (ed 2)	5-7/12/2016	23	R Sciuto

Clinical Trials active in 2016

BRAIN				
Status	**TITLE**	**DIVISION**	**Principal Investigator**	**Patients (total IRE)**
O	A non interventional study of Vimpat® (Lacosamide) as adjunctive antiepileptic drug therapy in patients with Brain tumor-related EpilepSy (VIBES) VECCHIO titolo: A noninterventional study of Vimpat® (Lacosamide) added to one baseline antiepileptic drug therapy in patients with brain tumor-related epilepsy (VIBES)	Neurology	Maschio	5
O	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	*Analisi economica dei costi sociali e sanitari dell'epilessia secondaria a neoplasia cerebrale*	Neurology	Maschio	82
O	Eflornithine for the treatment of patients with recurrent anaplastic astrocytomas (AA) who have progressed following irradiation and an adjuvant temozolomide regimen	Neurosurgery	Carapella	
C	Evaluation of seizure control and quality of life in patients with brain tumor related epilepsy treated with Lacosamide as add-on therapy: a prospective explorative study with a historical control group	Neurology	Maschio	25
O	Observational study for the evaluation of the cognitive impairment in patients with brain tumors	Neurology	Pace	557
C	Perfusion imaging with 3 Tesla MR in the early evaluation of the response to antiangiogenic treatment in patients with recurrring, high-grade malignant glioma	Radiology	Vidiri	26
O	Regorafenib in relapsed glioblastoma. REGOMA study. Randomized, controlled open-label phase II clinical study	Neurology	Pace	5
O	Spinal fluid microrna as new diagnostic and prognostic biomarkers in cns	Pathology	Carosi	2
O	The use of the F-FDOPA in the evaluation of gliomas: observational study	Neurology	Pace	92
C	Tissue characterization of glial tumors with 3 Tesla diffusion, perfusion and spectroscopy MR. Correlation with morphologic MR and histopatholgic findings	Radiology	Vidiri	40
O	Trabectedin for Recurrent Grade II or III Meningioma: a Randomized Phase II Study of the EORTC Brain Tumor Group	Neurology	Pace	0

O	Weekly carboplatin in the treatment of recurring high-grade gliomas: observational study	Medical Oncology 1	Fabi	24
BREAST				
O	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	7
O	A Phase 2/3, Multi-Center, Open-Label, Randomized Study of Weekly Nab®-Paclitaxel in Combination With Gemcitabine or Carboplatin, Compared to Gemcitabine/Carboplatin, as First Line Treatment in Subjects With ER, PgR, and HER2 Negative (Triple Negative) Metastatic Breast Cancer	Medical Oncology 1	Cognetti	4
O	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 II Single Arm Trial Evaluating the Efficacy and Safety of Eribulin in Combination With Bevacizumab for Second-Line Treatment of Human Epidermal Growth Factor Receptor 2–Negative Metastatic Breast Cancer Progressing after First-Line Therapy With Bevacizumab and Paclitaxel	Medical Oncology 1	Cognetti	3
O	A phase II, randomized, non-comparative, pre-surgical study of atorvastatin or observation in Ki-67 positive, TAZ-expressing early breast cancer patients (TRINACRIA Trial)	Medical Oncology 2	Vici	0
O	A phase III randomized, double blind placebo controlled study of BKM120 with fulvestrant, in postmenopausal women with hormone receptor-positive HER2-negative locally advanced or metastatic breast cancer which progressed on or after aromatase inhibitor treatment	Medical Oncology 1	Cognetti	3
O	A Phase III Randomized, Double Blind, Placebo Controlled Study of BKM120 With Fulvestrant, in Postmenopausal Women With Hormone Receptor-positive HER2-negative AI Treated, Locally Advanced or Metastatic Breast Cancer Who Progressed on or After mTOR Inhibitor Based Treatment	Medical Oncology 2	Vici	3
O	A phase III randomized, double blind, placebo controlled study of BKM120 with fulvestrant, in postmenopausal women with hormone receptor-positive HER2-negative AI treated, locally advanced or metastatic breast cancer who progressed on or after mTOR inhibitor based treatment	Medical Oncology 1	Cognetti	4
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	15

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 III Study of Single Agent Pembrolizumab versus Single Agent Chemotherapy per Physician's Choice for Metastatic Triple Negative Breast Cancer (mTNBC) – (KEYNOTE-119)	Medical Oncology 1	Fabi	5
C	A Randomized, Double-Blind Study Of PF-05280014 Plus Taxotere® And Carboplatin Versus Herceptin® Plus Taxotere® And Carboplatin For The Neoadjuvant Treatment Of Patients With Operable HER2 Positive Breast Cancer	Medical Oncology 2	Vici	5
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	1
O	A study of Neratinib plus Capecitabine versus Lapatinib plus Capecitabine in patients with HER2+ metastatic breast cancer who have received two or more prior HER2-directed regimens in the metastatic setting (NALA)	Medical Oncology 1	Cognetti	3
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
O	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	27
O	Dissecting the role of anti-estrogen receptor alpha autoantibodies in breast cancer	Medical Oncology 2	Vici	12
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	15
O	Feasibility study of hypofractionated radiotherapy in patients that have undergone conservative surgery for breast cancer	Radiotherapy	Pinnarò	420
C	Fulvestrant 500 mg: evaluation of the clinical benefit in patients with hormone-responsive, metastatic mammary carcinoma: prospective, observational cohort study	Medical Oncology 2	Vici	37
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	6

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	0
O	Impact of Hippo Pathway Component in Breast Cancer Patients Treated or to be Treated with Neoadjuvant Chemotherapy	Medical Oncology 2	Vici	45
O	LiqBreasTrack: tracking mutational hotspots in breast cancer patients treated with T-DM1 by liquid biopsy	Translational Research Functional Area	Allegretti/Giacomini	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 1	Fabi	11
O	Neoadjuvant chemotherapy in mammary carcinoma patients: retrospective evaluation of efficacy and tolerability	Medical Oncology 2	Vici	533
O	Observational, retrospective chart review study of treatment patterns, health care resource use, and otcomes in metastatic triple negative breast cancer (mTNBC)	Medical Oncology 2	Vici	0
O	Observational Prospective Study with Eribulin for Breast Cancer with Brain Metastases	Medical Oncology 1	Fabi	2
O	One day antiemeti c prophylaxis of NEPA (netupitant plus palonosetron) and dexamethasone to prevent chemotherapy-induced nausea and vomiting (CINV) in breast cancer paatients reciving a combination chemotherapy of doxorubicin or epirubicin with cyclophosphamide (AC-based regimen)	Medical Oncology 1	Fabi	3
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
O	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	16
O	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	4
O	Randomized study of fulvestrant as maintenance therapy after first-line chemotherapy in HER2 negative postmenopausal metastatic breast cancer patients	Medical Oncology 1	Fabi	6
O	Risk of recurrence in HER2+ mammary tumors. Retrospective, multicenter study	Medical Oncology 2	Vici	326

C	The predictive role of percent changes in fasting glucose on efficacy outcome of metastatic breast cancer patients treated with everolimus-exemestane	Medical Oncology 2	Vici	44
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	15
O	*Identificazione biomarcatori predittivi/prognostici nel carcinoma mammario triplo-negativo. NeoTAZ study*	Medical Oncology 2	Vici	53
O	*Il ruolo del TDM-1 nella real world evidence*	Medical Oncology 1	Fabi	19
O	*Indagine osservazionale sull'utilizzo del test Oncotype dx nella pratica clinica corrente*	Medical Oncology 1	Cognetti	64
O	*Indagine osservazionale sull'utilizzo del test Oncotype dx nella pratica clinica corrente*	Medical Oncology 2	Vici	25
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	2
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	24
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	2
O	*Studio di fase IV, multicentrico, interventistico, a singolo braccio per la valutazione della tollerabilità dell'Eribulina e della sua associazione con alcuni polimorfismi in una popolazione non selezionata di donne con tumore mammario metastatico*	Medical Oncology 2	Vici	1
O	*Studio Osservazionale Longitudinale di Coorte sulle scelte terapeutiche del carcinoma mammario metastatico HER2-negativo nella pratica clinica Italiana*	Medical Oncology 1	Cognetti	25
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	14
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	0

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)*	Nursing Direction	Iacorossi/Fabi	8
O	*Studio osservazionale retrospettivo sul carcinoma lobulare mammario lobulare precoce e avanzato*	Medical Oncology 2	Vici	167
O	*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	18
C	*Studio osservazionale, retrospettivo di valutazione dell'attività clinica e della tollerabilità della combinazione everolimus più exemestane in pazienti con carcinoma mammario avanzato hr+ (studio EVA)"*	Medical Oncology 2	Vici	19
O	*Studio osservazionale, retrospettivo di valutazione dell'attività clinica e della tollerabilità della combinazione everolimus più exemestane in pazienti con carcinoma mammario avanzato hr+ (studio EVA)"*	Medical Oncology 1	Fabi	17
O	*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	8
O	*Studio retrospettivo sulle pazienti con carcinoma mammario metastatico HER2 positivo con metastasi cerebrali*	Medical Oncology 1	Fabi	31
O	*TAZ come biomarcatore prognostico in pazienti affette da carcinoma mammario in fase iniziale. PHOBOS Trial*	Medical Oncology 2	Vici	128
O	*Terapia con nab-paclitaxel in pazienti affette da carcinoma mammario avanzato. Studio osservazionale multicentrico*	Medical Oncology 2	Vici	16
C	*Terapia con T-DM1 in pazienti affette da carcinoma mammario avanzato HER2 positivo. Studio osservazionale retrospettivo multicentrico*	Medical Oncology 2	Vici	17
O	*Validazione prospettica del TAZ-score come biomarker di risposta completa patologica in pazienti affette da carcinoma mammario luminal B/HER2-positivo trattate con terapia neoadiuvante a base di trastuzumab - TRISKELE Trial*	Medical Oncology 2	Vici	70
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	2
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	9

ENDOCRINE				
C	A Multicenter, Randomized, Double-blind Phase 2 Trial of Lenvatinib (E7080) in Subjects with 131I Refractory Differentiated Thyroid Cancer to Evaluate Whether an Oral Starting Dose of 20 mg or 14 mg Daily Will Provide Comparable Efficacy to a 24-mg Starting Dose, But Have a Better Safety Profile	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	0
O	Retrospective molecular study in patients with simultaneous occurrence of medullary and papillary microcarcinoma of the thyroid	Translational Research Functional Area	Blandino/Appetecchia	0
C	*Impatto Prognostico Della Linfoadenectomia e del pattern delle metastasi linfonodali nei pazienti affetti da tumore neuroendocrino polmonare tipo carcinoide: studio retrospettivo multicentrico*	Thoracic Surgery	Facciolo	18
C	*Studio retrospettivo in pazienti con simultanea occorrenza di carcinoma midollare e papillare della tiroide*	Endocrinology	Appetecchia	183
C	*TSH ricombinante: nuova ipotesi di somministrazione*	Endocrinology	Appetecchia	221
GASTROINTESTINAL				
O	A Multi-centre Randomised Clinical Trial of Biomarker-driven Maintenance Treatment for First-line Metastatic Colorectal Cancer (MODUL)	Medical Oncology 1	Zeuli	1
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
C	A Phase 2, Randomized, Double-blind Study of Gemcitabine and Nab-paclitaxel combined with Momelotinib in Subjects with Previously Untreated Metastatic Pancreatic Ductal Adenocarcinoma Preceded by a Dose-finding, Lead-in Phase	Medical Oncology 1	Milella	0
O	A Phase 3, Multicenter, Open-label, Randomized Study of nab-Paclitaxel Plus Gemcitabine versus Gemcitabine Alone as Adjuvant Therapy in Subjects with Surgically Resected Pancreatic Adenocarcinoma	Medical Oncology 1	Milella	9
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	0
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	0

O	A Randomized, Double-Blind, Phase 3 Study of the JAK1/2 Inhibitor, Ruxolitinib or Placebo in Combination With Capecitabine in Subjects With Advanced or Metastatic Adenocarcinoma of the Pancreas Who Have Failed or Are Intolerant to First-Line Chemotherapy (The JANUS 1 Study)	Medical Oncology 1	Milella	0
C	Cologuard™: Case Control Stool Sample Collection Study to Support Ex US Adoption	Digestive Endoscopy	Anti	44
O	CORRELATE - Safety and Efficacy of Regorafenib in Routine Clinical Practice Setting	Medical Oncology 1	Cognetti	2
O	Cytokinesis failure, chromosomal instability and tumorigenicity: HIPK2 role in pancreatic cancer	Translational Research Functional Area	Nisticò/Rinaldo	0
C	Diffusion MR of the liver: optimisation of the IVIM technique for the characterisation of focal liver lesions	Clinical Pathology	Caterino	100
O	Dissecting the Adipose Triglyceride Lipase (ATGL) functions in the pathogenesis of hepatocarcinoma	Hepato-Biliary-Pancreatic Surgery	Grazi	20
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	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	10
O	Extra-telometric functions of TRF2 in malignant transformation	Translational Research Functional Area	Biroccio	0
O	Innovative tools for early diagnosis and risk assessment of pancreatic cancer	Translational Research Functional Area	Nisticò	195
O	Isolation and characterization of tumor stem cells in intra- and extra-hepatic cholangiocarcinoma			
C	MR Imaging Biomarkers in Response Evaluation to Neoadjuvant Chemoradiotherapy in Rectal Cancer Type	Radiology	Caterino	39
O	Phase I/II study to evaluate Nab-paclitaxel in substitution of CPT11 or Oxaliplatin in FOLFIRINOX schedule as first line treatment in metastatic pancreatic cancer	Medical Oncology 1	Cognetti	36

C	Systematic collection of hepatocarcinoma, intrahepatic cholangiocarcinoma and cholangiocarcinoma of the hilus that have undergone hepatic resection in the context of the Italian chapter IT-IHPBA	Hepato-Biliary-Pancreatic Surgery	Grazi	35
O	Toxins produced by intestinal bacteria and predisposing genetic variations: a dangerous link for colorectal cancer development?	Digestive Endoscopy	Stigliano/Oddi	
O	Toxins produced by intestinal bacteria and predisposing genetic variations: a dangerous link for colorectal cancer development?	Hepato-Biliary-Pancreatic Surgery	Oddi	
O	ULTRA sensitive PLAsmonic devices for early CAncer Diagnosis	Translational Research Functional Area	Giacomini	32
O	*Studio caso-controllo sull'aderenza del paziente alla preparazione alla colonscopia*	Nursing Direction	Iacorossi	69
O	*Analisi differenziale dei profili di espressione dei microrRNA in colangiocarcinoma, epatocarcinoma e metastasi epatiche*	Translational Research Functional Area	Grazi/Blandino	131
O	*Registro italiano di resezioni epatiche mini-invasive*	Hepato-Biliary-Pancreatic Surgery	Grazi	10
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	7
O	*La cognizione sociale nell'adulto con epilessia*	Neurology	Maschio	10
GYNECOLOGICAL				
C	Randomized, open label, phase II trial of bevacizumab plus weekly paclitaxel followed by bevacizumab monotherapy maintenance versus weekly paclitaxel followed by observation in patients with relapsed ovarian sex-cord stromal tumours	Medical Oncology 2	Vici	0
O	A multicenter phase III randomized study with second line chemotherapy plus or minus bevacizumab in patients with platinum sensitive epithelial ovarian cancer recurrence after a bevacizumab/chemotherapy first line	Medical Oncology 1	Saverese	0
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	
C	A Phase 3 Randomized, Double-blind, Placebo-controlled, Multicenter Study of AMG 386 With Paclitaxel and Carboplatin as First-line Treatment of Subjects With FIGO Stage III-IV Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancers	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	3

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	A two-part, randomized phase iii, double-blind, multicenter trial assessing the efficacy and safety of pertuzumab in combination with standard chemotherapy vs. placebo plus standard chemotherapy in women with recurrent platinum resistant epithelial ovarian cancer and low HER3 mRNA expression	Medical Oncology 1	Savarese	4
O	Attacking proliferation and chemoresistance in ovarian cancer: therapeutic potential of a new functional link between oct4 and the rb pathway	Pathology	Carosi	14
O	Endometrial Cancer Conservative treatment - A multicentre registry	Ginecology	Vizza	3
O	HPV vaccination in women candiates for undergoing conservative theapy for HPV-correlated dysplastic pathology of the uterine cervix or ano-genital condyloma	Ginecology	Mariani	221
O	Microvesicles' microrna profiling in biological fluid and tissues of ovarian cancer patients	Pathology	Carosi	20
O	Multicenter retrospective study on Minimally Invasive Interval debulking Surgery In Ovarian Cancer	Ginecology	Vizza	50
O	Multicenter, randomized, controlled clinical trial comparing two follow-up regimen at different frequencies of examinations in patients treated for endometrial cancer	Ginecology	Vizza	24
O	Phase II trial on trabectedin in the treatment of advanced uterine and ovarian carcinosarcoma	Medical Oncology 2	Vici	
O	Predictive role of a microRNA signature in relapsed, high-grade serous, ovarian cancer patients rechallenged with platinum-based regimens	Medical Oncology 2	Vici	77
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
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	4
C	*Biomarcatori nel carcinoma della cervice uterina localmente avanzato trattato con radiochemioterapia: valutazione retrospettiva/prospettica di efficacia e tollerabilità*	Medical Oncology 2	Vici	39

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	2
O	*Tumori rari in ginecologia oncologica*	Ginecology	Vizza	0
O	*Studio clinico randomizzato multicentrico sulle deiscenze vaginali dopo isterectomia totale laparoscopica: sutura della cupola per via endoscopica vs. vaginale*	Ginecology	Vizza	0
HAEMATOLOGICAL				
O	Phase II Study of Chlorambucil in Combination With Subcutaneous Rituximab Followed by Maintenance Therapy With Subcutaneous Rituximab in Patients With Extranodal Marginal Zone B-cell Lymphoma of Mucosa Associated Lymphoid Tissue (MALT Lymphoma)	Haematology Oncology	Mengarelli	3
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	
O	"Geriatric Assessment Adapted" Therapy for Ph- ALL Elderly Patients	Haematology Oncology	Spadea	4
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	4
C	A Phase 3, Randomized, Double-blind Study of Duvelisib Administered in Combination with Rituximab and Bendamustine vs Placebo Administered in Combination with Rituximab and Bendamustine in Subjects with Previously-Treated Indolent Non-Hodgkin Lymphoma	Haematology Oncology	Mengarelli	
O	A phase II study of R-CHOP with intensive CNS prophylaxis and scrotal irradiation in patients with primary testicular diffuse large B-cell lymphoma	Haematology Oncology	Pisani	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	
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	
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	3
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	1
O	A Single-Arm, Open-Label, Multicenter Clinical Trial with Nivolumab (BMS-936558) for Subjects with Histologically Confirmed Stage III (unresectable) or Stage IV Melanoma Progressing Post Prior Treatment Containing an Anti-CTLA-4 Monoclonal Antibody	Medical Oncology 1	Cognetti	27
O	Adjuvant Immunotherapy With Anti-PD-1 Monoclonal Antibody Pembrolizumab (MK- 3475) Versus Placebo After Complete Resection of High-risk Stage III Melanoma: A Randomized, Double- Blind Phase 3 Trial of the EORTC Melanoma Group	Medical Oncology 1	Ferraresi	2
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	An observational study to evaluate the effectiveness and safety of Ipilimumab, administered during the European Expanded access programme in pretreated patients with advanced (unresectable or metastatic) melanoma	Medical Oncology 1	Ferraresi	5
O	Beyond tumor cell targeting with pathway inhibitors in human melanoma: role of the microenvironment	Medical Oncology 1	Milella	
O	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	Detection of Poor Mobilizer (PM) in Multiple Myeloma (MM) patients: prospective product registry	Haematology Oncology	Mengarelli	1
O	Eltrombopag for the treatment of thrombocytopenia due to low- and intermediate risk myelodysplastic syndromes. (Eqol-MDS)	Haematology Oncology	Romano	0
O	Front-line treatment of BCR-ABL+ Chronic Myeloid Leukemia (CML) with dasatinib. An observational multicentric study	Haematology Oncology	Romano	1
O	Front-line treatment of Philadelphia positive (Ph+)/BCR-ABL positive Acute Lymphoblastic Leukemia (ALL) with AP24534 (Ponatinib), a new potent tyrosine kinase inhibitor (TKI). A phase II exploratory multicentric study in patients more than 60 years old or unfit for a program of intensive chemotherapy and stem cell transplantation	Haematology Oncology	Spadea	0

O	High-dose chemotherapy and autologous stem cell transplant or consolidating conventional chemotherapy in primary CNS lymphoma - randomized phase III trial	Haematology Oncology	Pisani	
O	Liquid biopsy: circulating micrornaS and tumor DNA(ctDNA) as novel non-invasive biomarkers in diffuse large B-cell lymphoma	Haematology Oncology	Marchesi/Rizzo/Shivangi	39
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	14
O	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	7
O	National Treatment Program for Philadelphia Chromosome-negative Adult Acute Lymphoblastic Leukemia with Pegylated Asparaginase Added to a Lineage-Targeted Risk- and Minimal Residual Disease-Oriented Strategy	Haematology Oncology	Mengarelli	3
O	Next-generation sequencing for BCR-ABL kd mutation screening in philadelphia chromosome-positive leukemias	Haematology Oncology	Mengarelli	
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	3
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	1
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 ematopoietic stem cells support	Haematology Oncology	Mengarelli	3
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	1
O	Pospective collection of data of possible prognostic relevance in patients with indolent non-follicular b-cell lymphomas	Haematology Oncology	Palombi	
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	1

O	Role of Che-1 in multiple myeloma cell growth and progression	Translational Research Functional Area	Fanciulli	62
O	Spanning bcl-2 functions in melanoma models: from microenvironment to microRNA modulation	Translational Research Functional Area	Del Bufalo	
O	*Registro epidemiologico della leucemia mieloide cronica (LMC)*	Haematology Oncology	Romano	
C	*Studio osservazionale retrospettivo in pazienti con leucemia mieloide acuta trattati con Citosina Arabinoside (ARA-C)*	Neurology	Maschio	8
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	3
C	*Studio osservazionale retrospettivo multicentrico italiano per valutare le caratteristiche cliniche e l'outcome di pazienti affetti da linfoma mantellare ricaduti/refrattari che hanno ricevuto Ibrutinib in Italia secondo uso compassionevole*	Haematology Oncology	Pisani	1
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	2
O	*Crioterapia come profilassi della stomatite indotta da melfalan ad alte dosi nei pazienti adulti con mieloma multiplo sottoposti ad autotrapianto di cellule staminali*	Haematology Oncology	Mengarelli	72
O	*Prevenzione della neurotossicità con nutraceutico e EMDR in pazienti affetti da mieloma*	Neurology	Maschio/Mengarelli	28
C	*Studio osservazionale retrospettivo in pazienti con mieloma multiplo trattati con Pregabalin*	Neurology	Maschio	38
HEAD AND NECK				
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	51
C	Diffusion MR with IVIM technique in head and neck tumors (rhinopharynx, oral cavity, oropharynx, hypopharynx) for the predictive evaluation of the response to radiochemotherapy treatments with 3 Tesla MR	Radiology	Vidiri	42
O	Early Diffusion Weighted magnetic Resonance imaging changes to predict tumor response to chemoradiotherapy in HN cancer	Radiotherapy	Sanguineti	30
O	Health and economic outcomes of two different follow up strategies in effectively cured advanced head and neck cancer	Otolaryngology Head & Neck	Spriano	3

C	Identification of novel coding and non-coding transcriptional targets of gain-of-function mutant p53	Translational Research Functional Area	Blandino	51
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	11
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	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
O	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	1
O	Study of of MYC and YAP contribution to mutant p53 transcriptional activity in head and neck squamous cell carcinomas	Translational Research Functional Area	Blandino	
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	40
LUNG				
O	A cross-sectional study to evaluate the effectiveness of XALKORI Therapeutic Management Guide among physician prescribing XALKORI in Europe/A cross-sectional study to evaluate the effectiveness of XALKORI Patient Information Brochure among non-small cell lung cancer (NSCLC) patients receiving XALKORI treatment in Europe	Medical Oncology 1	Ceribelli	0
O	A factorial study comparing pemetrexed with gemcitabine and testing the efficacy of the addition of cisplatin in elderly patients with non squamous advanced, metastatic or recurrent NS	Medical Oncology 1	Ceribelli	0
O	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	1
O	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	43
O	A Phase II Randomized Study of Pembrolizumab in Patients With Advanced Malignant Pleural Mesothelioma	Medical Oncology 1	Cecere	

O	A Phase II, Non-comparative, Open label, Multi-centre, International Study of MEDI4736, in Patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer (Stage IIIB-IV) who have received at least Two Prior Systemic Treatment Regimens Including One Platinum-based Chemotherapy Regimen (ATLANTIC)	Medical Oncology 1	Milella	12
O	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	5
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
O	A Phase III, Randomised, Double-blind, Placebo-controlled, Multi-centre, International Study of MEDI4736 as Sequential Therapy in Patients with Locally Advanced, Unresectable Non-Small Cell Lung Cancer (Stage III) Who Have Not Progressed Following Definitive, Platinum-based, Concurrent Chemoradiation Therapy (PACIFIC)	Medical Oncology 1	Milella	1
O	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	1
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	
O	A Randomized Phase 2 Study of AP26113 in Patients with ALK-positive, Non-small Cell Lung Cancer (NSCLC) Previously Treated with Crizotinib	Medical Oncology 1	Milella	1
O	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 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	1
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	4
O	Decurarization After Thoracic Anesthesia - A Prospective Multicenter Double-blind Randomized Trial Comparing Sugammadex vs Neostigmine Reversal After Thoracic Anesthesia	Anaesthesiology	Coccia/Pierconti	0

O	K-RAS mutations and dna repair function in sclc . BIO-RaRe	Medical Oncology 1	Milella	16
O	Linking tumor stroma to nucleus via cytoskeleton: hMENA isoforms, signal checkpoints and biomarkers of NSCLC relapse	Translational Research Functional Area	Nisticò	168
O	LUMINIST: LUng cancer Molecular Insights Non Interventional Study	Medical Oncology 1	Milella	4
O	Open Label, Multinational, Multicenter, Real World Treatment Study of Single Agent AZD9291 for Patients With Advanced/Metastatic Epidermal Growth Factor Receptor (EGFR) T790M Mutation-Positive Non-Small Cell Lung Cancer (NSCLC) Who Have Received Prior Therapy With an EGFR Tyrosine Kinase Inhibitor (EGFR-TKI)	Medical Oncology 1	Milella	13
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	
O	Randomized Phase III Multicenter Trial of Customized Chemotherapy versus Standard of Care for 1st Line Treatment of Elderly Patients with Advanced Non-Small-Cell Lung Cancer	Medical Oncology 1	Cognetti	1
C	*Impatto prognostico del pattern di invasione linfonodale nel NSCLC con N2 patologico: studio retrospettivo multicentrico*	Thoracic Surgery	Facciolo	
C	*Impatto prognostico della linfoadenectomia nel NSCLC: studio retrospettivo multicentrico*	Thoracic Surgery	Facciolo	100
C	*Outcome nel NSCLC con infiltrazione della parete toracica: studio retrospettivo multicentrico*	Thoracic Surgery	Facciolo	20
O	*Studio multicentrico osservazionale sull'utilizzo della sigaretta elettronica in Italia*	Pulmonary Phisiopathology	Papale	10
O	*Studio prospettico osservazionale multicentrico sulla determinazione delle alterazioni molecolari nei pazienti con nuova diagnosi di carcinoma polmonare non a piccole cellule in stadio avanzato*	Medical Oncology 1	Ceribelli	0
O	*Utilità dell'Agoaspirazione Transbronchiale convenzionale (conventional Transbronchial Needle Aspiration) (c-TBNA) nella diagnosi, staging e caratterizzazione molecolare delle neoplasia polmonari mediante citologia su strato sottile: esperienza in un istituto oncologico*	Pathology	Marino	273
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	Coccia/Pelagalli	0
O	*Ventilazione protettiva versus ventilazione convenzionale durante ventilazione monopolmonare in pazienti sottoposti ad interventi di chirurgia toracica*	Anaesthesiology	Coccia	60
SARCOMA				

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	
O	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	15
O	International randomised controlled trial of chemotherapy for the treatment of recurrent and primary refractory Ewing sarcoma	Medical Oncology 1	Ferraresi	1
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	19
O	Multicentric prospective, randomized, clinical trial for the treatment of patient with relapsed Osteosarcoma (OS)	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	8
O	Targeting telomere replication in ALT tumors	Translational Research Functional Area	Salvati/Biroccio	14
O	*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	23
UROLOGICAL				
O	A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase III Study of ARN-509 in Men with Non-Metastatic (M0) Castration-Resistant Prostate Cancer	Urology	Gallucci	6
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	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	0
O	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	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	**Urology**	Gallucci	6
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	3
O	A randomised, parallel-group, open-label Phase II trial of the immunological effects of three regimens of GX301 vaccination in castration-resistant prostate cancer patients who have achieved response to first-line chemotherapy	Medical Oncology 1	Cognetti	0
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
C	An International Phase 3 Randomized Trial of Autologous Dendritic Cell Immunotherapy (AGS-003) Plus Standard Treatment of Advanced Renal Cell Carcinoma (ADAPT)	Urology	Gallucci	7
O	Analysis of the prognostic value of body mass index in patients diagnosed with hormone refractory prostate cancer receiving chemotherapy: retrospective observational study	Medical Oncology 1	Carlini	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	Control of prostatic cancer progression by microRNAs 15 and 16	Scientific Directorate/Urology	De Maria/Gallucci	208
O	Evaluation of urine miRNAs as non-invasive tool to predicte Bacillus Calmette-Guérin treatment efficacy in bladder cancer	Urology	Costantini/Rizzo	99
O	Observational prospective study to assess time efficiency of intracorporeal orthotopic diversion with robotic staplers after robot assisted radical cystectomy	Urology	Simone	28
O	Observational study for the evaluation of the predictive value of in vitro pharmacosensitivity on cancer stem cells and the phosphoproteomic profiles in patients with advanced renal cell cancer that are candidates for therapy with multi-angiokinase and mTOR inhibitors	Scientific Directorate/Urology	De Maria/Gallucci	208
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	Radium-223 Alpha Emitter Agent in Safety Study in mCRPC popUlation for long teRm Evaluation	Medical Oncology 1	Carlini	2

O	Targeted Therapy With or Without Nephrectomy in Metastatic Renal Cell Carcinoma: Liquid Biopsy for Biomarkers Discovery (TARIBO)	Medical Oncology 1	Milella	0
O	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	26
O	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	Forastiere	60
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	
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	2
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	35
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	
O	*Valutazione dell'associazione tra obesità, sindrome metabolica e tumore della prostata nei pazienti sottoposti a biopsia prostatica e prostatectomia radicale*	Urology	Simone	0
O	*Studio pilota di radioterapia stereotassica pre-operatoria per carcinoma renale operabile in stadio iniziale (Ct1)*	Radiotherapy	Sanguineti/Gallucci	
O	*Cistectomia radicale open versus robotica con derivazione urinaria totalmente intracorporea. Studio prospettico randomizzato mono-centrico*	Urology	Simone	
MISCELLANEA				
O	A panel of biomarkers as novel tool for early detection of radiation exposure	Medical Physics	Strigari	40
O	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	5
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	4
O	Abdominal SepsiS ("AbSeS") sudy: Epidemiology of Etiology and Outcome	Anaesthesiology	Pelagalli	0

O	Analysis of the transcriptional expression profile and microRNAs in brain metastases from primary tumors of various origin	Translational Research Functional Area	Blandino/Telera	81
O	Assessment of the responsiveness of the Rasch-built, CIPN-specific questionnaire (CIPN-RODS) to clinical changes in patients undergoing neurotoxic chemotherapy	Neurology	Pace	25
O	Endothelin axis/?-arrestin-driven actin reorganization: bringing the right network of proteins to direct invadopodia	Translational Research Functional Area	Rosanò	0
O	Evaluation of the eficacy, tolerability, quality of life and compliance of tapentadol in cancer patients with neuropathic pain due to chemotherapy, other antitumor therapies or the tumor itself	Neurology	Galiè	43
O	Experimental models for investigation of interrelationship between cancer stem cells (CSCs) / tumor initiating cells (TICs) and metastasis	Medical Oncology 1	Fabi	0
O	Global, clinical-pathological and molecular characterization of thymic epithelial tumors	Pathology	Marino	25
O	Hematological Malignancies Associated Bloodstream Infections Surveillance	Haematology Oncology	Spadea	28
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	Plastic & Reconstructive Surgery	Valle	8
O	Molecular mechanism of quadruplex-targeted drugs: towards clinical candidate selection	Translational Research Functional Area	Leonetti	
O	Neurophysiological and clinical incidence and typing of chemoinduced neuropathies and evaluation of the associated neuropathic pain, if present	Neurology	Galiè	203
O	Non coding RNA in solid tumors	Pathology	Carosi	
C	Point prevalence survey of healthcare- associated infections and antimicrobial use in European acute care hospitals	Directorate	Puro	145
O	Prospective Observational Trial to Assess the Impact of Mucositis in Patients Treated with Targeted Therapy in Oncology. (PRO-IMPacT)	Medical Oncology 1	Fabi	4
O	Prospective, Observational, Cohort study of Lonquex® (Lipegfilgrastim) used in clinical practice for the prophylactic treatment of chemotherapy-induced neutropenia (CIN) in adult patients with solid tumours receiving myelosuppressive chemotherapy (CT)	Medical Oncology 2	Vici	14
O	Survey of Nasal microbial Interaction with Fungi	Haematology Oncology	Spadea	16

O	*La malattia di Casteman multicentrica: una rivisitazione dello "stato dell'arte"*	Pathology	Marino	3
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	792
O	*Applicazione della Medicina basata sulla Narrazione nel trattamento chemioterapico di pazienti oncologici*	Epidemiology & Tumor Registry	Cercato	
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	49
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	8
O	*Studio prospettico per il monitoraggio delle sindromi mielodisplastiche nei pazienti adulti*	Haematology Oncology	Mengarelli	20
O	*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	80
O	*Localizzazione e distribuzione intracellulare dell'attivatore p53 "Homeodomain-interacting protein kinase-2" (HIPK2) nel timp normale e neoplastico, di altre proteine coinvolte nell'apoptosi e integrazione con la distribuzione di sottopopolazioni cellulari T. uno studio retrospettivo clinicopatologico e immunologico*	Pathology	Marino	32
C	*Consapevolezza di malattia e soddisfazione per le cure ricevute nei pazienti italiani con tumori solidi: uno studio multicentrico*	Psychology	Pugliese	41
MULTIPLE SCLEROSIS				
O	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	0
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	13

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