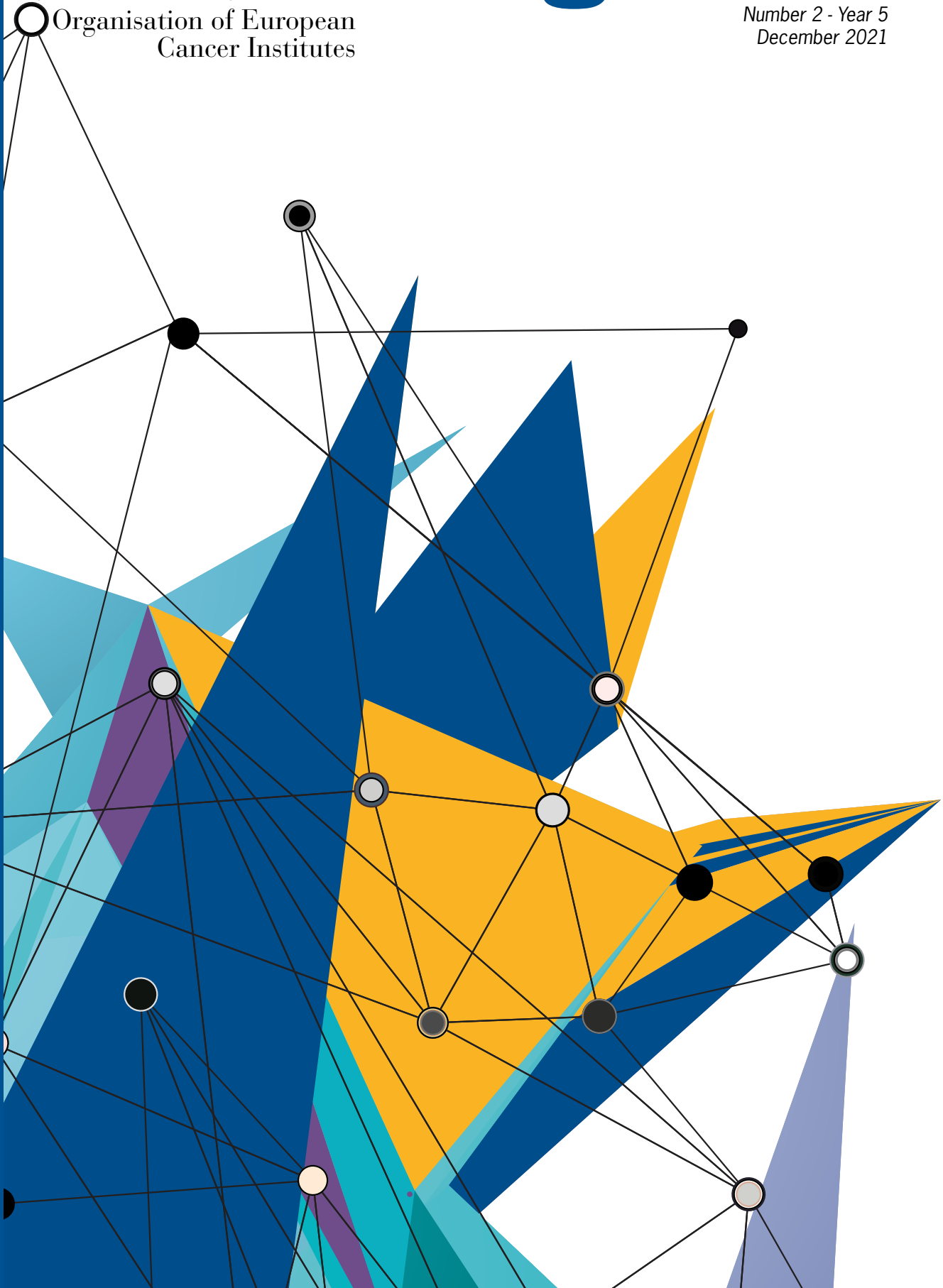




# OECD Magazine

Organisation of European  
Cancer Institutes

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# Oncology Days

OECI 44

**PROMOTING INNOVATION  
AND QUALITY FOR PATIENTS**

## VALENCIA 2022

**GENERAL ASSEMBLY  
AND  
SCIENTIFIC CONFERENCES**

*June 15<sup>th</sup> - 17<sup>th</sup> 2022*



PRELIMINARY  
ANNOUNCEMENT

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# Message from OECI President

## Shaping the future of cancer in Europe



After years of research and bold initiatives to further the understanding of the biological bases of cancer, this disease remains the second leading cause of death in Europe. As the European population is growing and living longer, cancer has become the primary cause of death in both males and females aged 60-79 years - a frightening trend that will soar with Europe's changing demographics. Europe is also home to 1/10 of the world population; nonetheless, a quarter of the world's cancer patients live here, and a 24% increase in the figures is expected by 2035.

Europe needs to capitalize on scientific, technological and AI advances in order to find a predictable and efficient path to bring promising solutions to the patients who need them. Continuing progress against cancer morbidity and mortality requires sustained investment, as well as a better integration of the entire continuum of cancer prevention, diagnosis, research and care.

The European Commission has recognised the need to devise a strategy bringing the relevant stakeholders and information together, and put forward two complementary initiatives: Europe's Beating Cancer Plan and the Cancer Mission, with the latter as part of Horizon Europe. Tailored on three key impact pathways – scientific, social and technological – Horizon Europe aims at wide societal relevance and has raised great expectations.

Strategic alliances are paramount and this is the spirit that should inspire the National authorities, the relevant stakeholders and the OECI, which is currently representing a large cohort of the main actors on the cancer frontline – that is, our Cancer Centres and Institutes.

The stakes are high and the cancer community has pushed towards an unprecedented – and much needed - interaction between health programmes and R&I projects. Hopefully, this time round, the wisdom collected from the entire oncology field will set Europe on the right track. Indeed the volume of calls specific to cancer issued in 2021 from both the Health and Research programmes of the Commission would seem to indicate that within 3-4 years the EU will see many plans turned into action.

In addition, and most importantly today, health systems are still dealing with the stall triggered by the COVID-19 pandemic, another thorn in the side that has severely impacted cancer care, disrupting prevention and treatments. This delay, alongside the increasing costs of cancer diagnosis and care will surely affect health systems. So how do we work out smart solutions to prevent health systems from collapsing?

The role of quality and a better use of accumulated data will play a fundamental role. First, we should identify and disseminate best practices in oncology. We also ought to place greater attention on the quality assessment of our health systems and single out carefully designed indicators that, on the evidence, accurately reflect the quality of care and outcomes. Many different measures continue to be developed by accrediting bodies. Moreover, elaborating quality indicators in oncology is a complex process, and studies demonstrating that a quality or process improvement results in an increase in survival or quality of life are still lacking.

The recognition of a European infrastructure of high quality cancer centres and networks, as predicated by both the Cancer Mission and Europe's Beating Cancer Plan will be key in reducing inequalities and providing each patient with the most effective treatment. The proposed EU network of national Comprehensive Cancer Centres, supported by local comprehensive cancer networks around them, will build on the last two decades work of OECI in quality and accreditation, and the similar initiatives by the German Cancer Society and German Cancer Aid. In particular, it will facilitate the development and accreditation of new cancer centres in those countries in central, eastern, and some southern EU member states which currently lack them.

Europe is currently seeking opportunities to build a unified data hub in order to become more efficient, unlock siloed information and automate processes. Regulations in every Member State are still evolving as institutions continue to adapt. As European Legislation is leading the way, varying national interpretations of the same are bound to hinder cross-country studies. In a nutshell, there are several challenges to overcome, and quality metrics and standards need to be defined in this complex ecosystem. New studies on data and AI give rise to high hopes, but new levels of investment are necessary.

In all these arenas, public-private collaboration should be strongly supported, and the COVID-19 pandemic has demonstrated the need for this. As the world moves towards globalisation, and adapting local realities to central systems is an increasing trend, larger organisations able to host or co-ordinate local bodies may be the best solution to mediate between public entities and industrial players.

Will Europe be able to properly address all the questions laid out above? OECI certainly has the ability to take its place in this scenario but each one of us should take our own responsibilities as part of the whole, where excellence should be allowed to lead our practices without imposing uniformity upon all.

**Thierry Philip**  
OECI President

## A step forward PROmics

**Cinzia Brunelli<sup>1</sup>, Giovanni Apolone<sup>1</sup> and Augusto Caraceni<sup>1</sup>**

1. Fondazione IRCCS Istituto Nazionale dei Tumori di Milano



Recent development of big-data analytics, combined with the spread of electronic data capture, are offering exciting possibilities for the improvement in diagnosis and prediction of individual responses to cancer therapies, and for the development of precision oncology.

Patient reported outcomes and experiences measures (PROMs and PREMs) reflect the self-reported health state directly by the patient, and are fundamental tools to measure the impact of the disease and the effect of treatments and care received, at the individual level. These measures are always relevant to address patients quality of life outcomes, they are the mainstay of management and treatment strategies when disease cure and control are no more viable and are also useful to complement objective disease oriented outcomes. However, the effective integration of PROMs and PREMs within multi-omics personalized oncology is still far to be reached, mainly due to the current fragmented approach to PROMs/PREMs data collection in routine cancer care.

The OECl one-shot project on “Strategies of implementation of PROMS and PREMS in oncology clinical practice and research” is aimed at building the foundation for a network of clinical cancer centres adopting a common platform and common procedures for the routine collection and sharing of PROMs and PREMs data.

A first meeting was held last spring to explore reasons, values and barriers of standardized collection of PROMs and PREMs, as well as to describe real world experiences in some European and non-European cancer centres [https://www.oeci.eu/Attachments/OECI\\_Magazine1\\_2021.pdf](https://www.oeci.eu/Attachments/OECI_Magazine1_2021.pdf)

The next step in this OECl initiative, is to organize an operative meeting addressed to all OECl centres interested in participating in a real world data collection of PROMs and PREMs in their institutions. All OECl centers will receive a questionnaire to explore their experience and use in the field of research and practice with the collection of PROMs and PREMs, as well as their availability to participate in a first exploratory meeting.

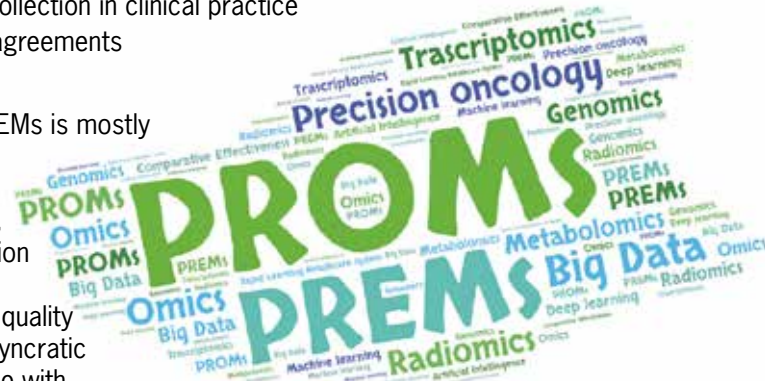
The following relevant issues will be discussed during the meeting:

- wide stakeholders involvement, with a special attention to patients.
- the role of champions in PROMs/PREMs implementation
- PROMs and PREMs tools eligible for the OECD data collection
- qualitative standards for data collection (personnel training, electronic assessment, integration with EHR)
- minimum data sets definition (clinical and socio demographic data to be linked to PROMs/PREMs)
- governance of routine PROMs data collection in clinical practice
- GDPR compliance and data sharing agreements
- Technical data sharing procedures

A standardized adoption of PROMs/PREMs is mostly needed if we aim to promote a

patient-centred approach to cancer care. The development of international, coordinated research and implementation actions in this field can be an effective approach to move from the science of quality of life and PROMs, and from local idiosyncratic applications to a shared clinical practice with multidimensional, multiprofessional and multidisciplinary content.

The lines of activity described above, at the end of the One-Shot Project, could merge into the current WG on Cancer Outcome Research which, at this point, should be reconstituted and redirected.



# Update SEC Trial: Socio-economic consequences of cancer: a patient perspective

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## Introduction

Rising national cancer care expenditures jeopardize the financial sustainability of European health systems<sup>1,2</sup>. The economic health of a member state, its abilities to cover reimbursement, availability of social health insurance, and co-payments for treatments largely affects patients' access to treatment and indirect and direct patient costs<sup>3</sup>. Patient expenses can be affected on multiple levels: increased insurance fee, co-payments, traveling costs but also income loss due to reduced ability to work and falling into debt<sup>4</sup>. Several studies have also indicated that financial toxicity can significantly affect treatment compliance such as avoidance or discontinuation of prescriptions and postponing medical care or follow-up visits<sup>5,6</sup>. This type of behavior has a direct negative impact on the health state and treatment outcome of the patients<sup>7</sup>. Also, high financial burden is expected to be associated with poorer quality of life of patients<sup>8</sup>. Eventually patients find themselves in a vicious cycle of increasing (treatment-related) expenses and loss of household income, which results in (financial) distress and reduced quality of life.

Most of the research regarding patients' socio-economic consequences has been performed in the United States<sup>3,9-11</sup>; the socio-economic impact of cancer in European health care systems, and inter-country variability is poorly understood<sup>12</sup>. Since European studies are lacking, and no data exists on differences between European countries, in 2020 the OECl has decided to sponsor the SEC-trial (Socio-Economic-Consequences of cancer). We aim to explore patients' socio-economic consequences resulting from cancer diagnosis and treatment, in at least 10 European countries.

## Method

A 41-item survey was developed to measure patients' socio-economic impact of a cancer diagnosis and treatment. Next to questions regarding sociodemographic characteristics and coping behavior, two validated questionnaires (Financial Index of Toxicity & EQ-5D-5L questionnaire) are included. The survey is available in 15 languages and accessible on paper and online (QR-code/link). The primary outcome is the level of financial distress among cancer patients, measured by the Financial Index of Toxicity (FIT) score, assessed per country. Explorative multivariate analysis will provide insight in patient and system characteristics related to socio-economic consequences of a cancer diagnosis.

### Status of Accrual

For this study, we aim to include 200 patients per participating country (Table 1). So far, the survey is distributed by 15 hospitals of Organization of European Cancer Institutes (OECI) network and more than 20 patient organizations across Europe. Cancer patients who are currently or were recently treated within the past 2 years with systemic and/or hormonal therapy and/or radiotherapy and/or surgery are eligible for inclusion in this study.

The SEC-trial went live the 28th of August 2021. 60% completion of the survey is required to analyze the FIT score. Currently, 888 cancer patients across Europe have filled in the survey for more than



60%. A total of 656 patients meet the exact inclusion criteria (Figure 1). Until now, the patients that meet our inclusion criteria live in 15 different countries). Most of the patients were included in the Netherlands (N= 240), Spain (N=221) and Denmark (N=127).

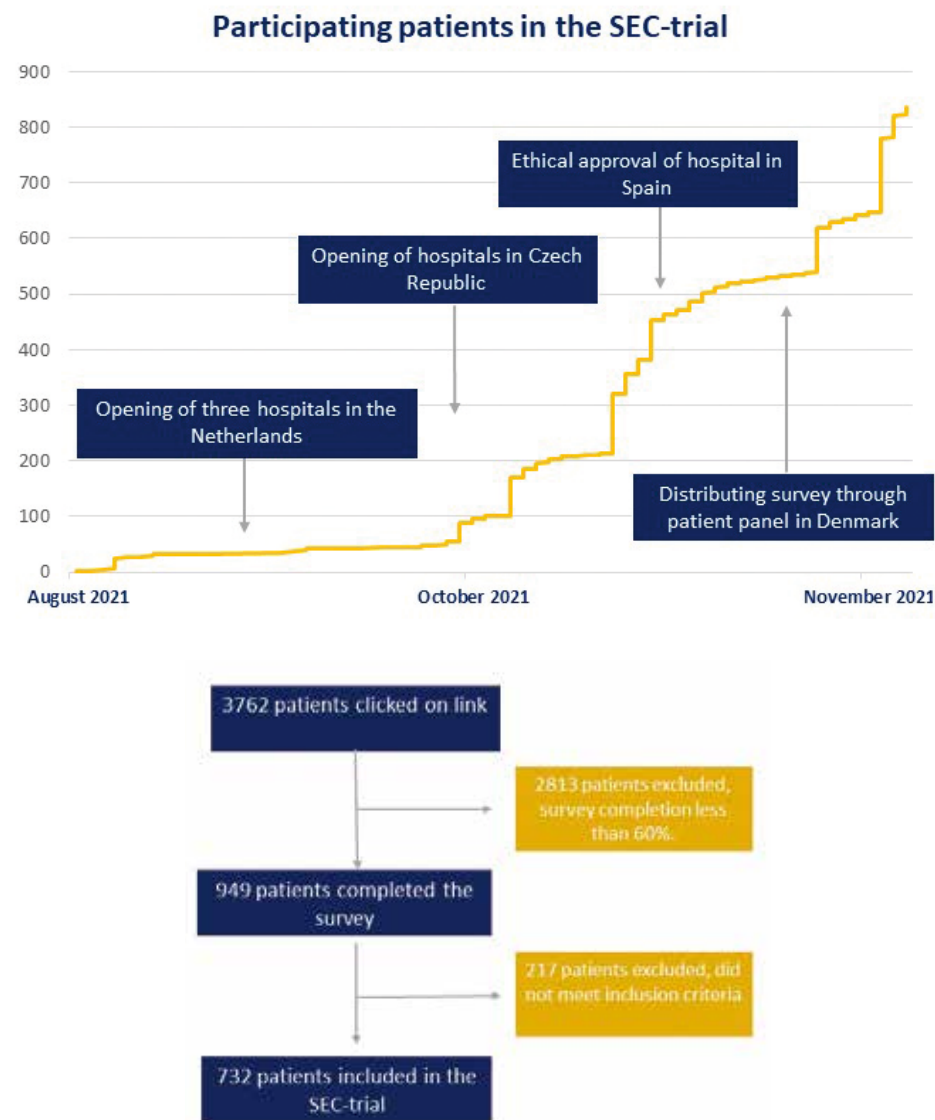


Figure 1: Patients accrual of the SEC-trial

\*A survey is seen as completed if the patients filled in at least 60% of the survey, which allows to calculate the FIT-score.

## Future

Do you want to participate, or do you want more information? Please contact Julie Vancoppenolle (j.vancoppenolle@nki.nl). By sharing our QR-code/link on your platform (newsletter, website, social media or digital patient panel), you can make sure your country is well represented in this study. All participants are welcome, but we have a special interest in collaborations in Greece, United Kingdom and Belgium. With the results of this explorative study, we assess the FIT score of cancer patients in different European countries. We will moreover gather insight in the socio-economic consequences that patients experience after cancer diagnosis. Final analyses are anticipated in Q1-2022.



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# Analysing the hallmarks and data of OECl's first 40 accredited centres

**Simon Oberst**, Chair, Accreditation Board of OECl



The OECl Accreditation and Designation Board has been aware for some time that we hold precious data provided by our cancer centres who are members of the accreditation programme. Whilst preserving the anonymity and confidentiality around those data, we had not published analyses of the trends within our centres since the first 10 centres were accredited in 2014. Accordingly, beginning in 2019, we began analysing the data from more than 1,000 indicators to see what trends could be meaningful in terms of quality across the first 40 centres to be accredited. We wanted this analysis to be qualitative as well as quantitative: that is to say, analysing the scoring compliance with certain quality standards according to our Deming-cycle-inspired scoring system, as well as measuring absolute numbers and percentage quality indicators.

The results of this exhaustive work were published in March 2021 in *Molecular Oncology* – Analysing the attributes of Comprehensive Cancer Centres and Cancer Centres across Europe to identify key hallmarks. We were particularly interested to measure the concentration of translational and clinical research in certain centres – those generally that we designate as “Comprehensive”. We also wanted to test the general level of compliance with standards on multidisciplinary working, to assess how far the practice of multidisciplinary teams (MDTs) working together throughout the patient pathways is embedded, recognising that all centres accredited under the A&D programme have reached a “gold standard” of clinical care.

In a few cases, the analysis was complicated by having data collected according to different manuals even within the last 5 years of the analysis. Nevertheless, after extensive data validation and linking, the analyses are sound.

The results of the analysis make interesting reading. It is heartening to see how the whole practice of MDT working is very well established in all centres (whether Comprehensive Cancer Centres (CCCs) or Cancer Centres (CCs)) only marred by the finding that centres have radically different ways of recording patient pathways, and sometimes not consistently. As with most of our quality work, our view is that what is not properly recorded cannot be relied on as a sound process; the process cannot exist only in the minds of its current practitioners. But our peer reviews involve extensive observation of actual MDT case meetings, and interviews with clinicians and MDT chairs on the exact process of discussion, utilisation of clinical guidelines, decision, patient involvement, and ongoing process.

We found that patient-centredness at an individual patient level, which offers choice, good information and clear communication, is common in most centres. The culture of involving patient groups in co-creating practice developments is also becoming better established. Having said that, consistent analysis of patient outcomes and use of patient reported outcome measures is not adequate in many centres.

The second set of conclusions were around research, and were in one sense not surprising, but in another sense the scale of the concentration of research in centres designated by OECl as “Comprehensive” was greater than we expected. For instance, we found that the median peer-reviewed output of scientific publications from CCCs was nearly four times higher than their CC counterparts. That trend was increased when considering high impact publications. This is despite the general fact that in terms of newly managed patients per year, the median of the CCC cohort was less than 50% larger than its CC counterpart. This would seem to indicate that there are several large-volume cancer hospitals

which are not hugely involved in research.

Similarly, on clinical research, we found that the median CCC had nearly four times more prospective interventional clinical trials open to recruitment than its CC counterpart. As significantly, the rate of patient accrual to those trials was more than seven times the median of CCs. We concluded that it would be important to understand the reasons for the difference between CCCs and CCs and how to improve on trial recruitment rates, which contribute to improved outcomes for patients. Further analysis would be needed in terms of types of trial, especially between commercially-sponsored and investigator-led studies. Overall, the data showed that when restricted to interventional therapeutic trials only, the 10% average patient recruitment rate is quite a high bar, even for some CCCs (the median rate was 13.9%).

As far as we know, no earlier studies of cancer centres involving so many different countries in Europe (18 countries) have been published, especially those using data from both care and research domains, so the analysis – on which OECl can build in subsequent years with increasing levels of detail – is helpful.

A final interesting finding was that the data revealed strong variation in compliance with leadership- and management-related quality standards, even within the CCC cohort, and this variation justifies further research into what constitutes effective governance of cancer centres. Those of us who chair OECl peer reviews did not find this a surprise; indeed, within large centres, especially those around University Hospitals, the governance question remains one of the most potent issues which can either hold back progress of a cancer centre, or, if the challenges are appropriately addressed over time, can accelerate scientific output and the breadth of practice changes into the clinic. As the Cancer Mission and Europe's Beating Cancer Plan swing into action, especially with the Joint Action on the creation of an EU Network of National Comprehensive Cancer Centres, these governance criteria will be of key importance, as Europe seeks to develop and accredit new Cancer Centres to improve the quality of cancer care, education and research right across Europe.

Finally, many thanks to the hard work of the IKNL co-ordination team, the OECl A&D Board, the Accreditation Committee, and all auditors and participating centres, in producing these data and results.





# Molecular Pathology Standardization

Giorgio Stanta and Serena Bonin\*

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There is a change of perspective in oncology diagnostics and research with a rapid and complex development that needs very high attention also at the applied clinical level<sup>1</sup>. In oncology diagnostics, the molecular analyses are mostly not standardized at European level, even if it is very important to obtain reproducible and exchangeable molecular diagnostic analysis. There is also a continuous use of new prognostic and predictive biomarkers, and the interpretation of results of analyses is increasingly complex. For these reasons standardization is today the major issue in molecular diagnostic pathology. We also have to consider that this type of diagnoses is strictly related to the treatment choices especially in oncology.

The Biobanking and Molecular Pathobiology WG of OECl participated directly or indirectly to several activities related to molecular pathology diagnostics standardization and reproducibility in collaboration with European projects. Today, in fact, the technical standardization and evaluation projects in the diagnostic molecular analysis are not performed by the scientific societies but mostly through wide European projects. This is related to the possibility to join specific European expert groups and the availability of grants that cover the expenses of the activities.

Several aspects of molecular pathology should be taken into consideration to reach a real standardization, among these heterogeneity of tumour tissues<sup>2-5</sup>, pre-analytical condition of the biological material<sup>6,7</sup> and analytical methods used.

## The HERCULES project

Heterogeneity in cancer is a basic pattern of the tumours that is necessary to be taken into consideration in the clinical process of molecular diagnosis. There are several types of heterogeneity in tumours: there is a heterogeneity at macroscopic and histologic level related to different level of differentiation of the cells, but also a more functional one related at the position of the cells at the border or in the central part of the primary neoplasia. At molecular level the heterogeneity can be related to a genetic or epigenetic evolution of the cancer clones or to a non-clonal heterogeneity connected with phenotypic functional plasticity that is characteristic of cancer cells or to a less specific stochastic plasticity<sup>2-5</sup>.

In the last four years the HERCULES project on tumour heterogeneity via single cell analysis in a wide collection of high grade serous ovary carcinomas was developed. The final results of the project are on the way to be published and the information could be useful for the OECl institution in the evaluation of tumour heterogeneity at clinical level. The project evaluated heterogeneity at different level such as the primary tumour, in the spreading tissues and in the blood at different time points before diagnosis, during treatment and follow up. Single cell sequencing and deep sequencing data analyses were performed and compared with treatment, chemoresistance and survival.

Several articles have already published so far from the project, open access versions of the publications are accessible<sup>8</sup>.

## The SPIDIA4P project

The SPIDIA4P (Standardisation of generic Pre-analytical procedures for In-vitro DIAgnostics) project and the previous SPIDIA project are related to the pre-analytical processes of the biological material used in molecular diagnostics. These conditions can modify the results of the analyses with the possibility to obtain false negative results. The pre-analytical conditions are related to several medical/diagnostic procedures, starting from the modalities of collection of the tissues, the time of warm ischaemia when the blood supply is stopped during surgical procedures, the cold ischaemia related to the time before of the conservative procedures. The methods of preservation of tissues can be also implicated in the quality of tissues, from the grossing of tissues to the type and time of fixation, the modalities of embedding tissues in paraffin, to the time and conditions of tissue preservation in the archives<sup>6-7</sup>.

Many documents for the pre-analytical conditions of the biological material used for diagnostic purposes have been developed within the SPIDIA4P project<sup>9</sup> in collaboration with the European Standardization Committee (CEN). For this reason the so called CEN technical specifications have been produced. Some of these were already translated to ISO international standards and others are still in development (such as Fine Needle DNA, RNA and proteins, CTC DNA, RNA and cells staining, exosomes and other

extracellular vesicles etc.). The new technical specification documents are submitted to the European Technical Committee 140 "In vitro diagnostic medical devices" (CEN/TC 140). The CEN documents are then considered by the International Organization for Standardization (ISO) for the publication of specific International Standards by the ISO Technical Committee 212 "Clinical laboratory testing and in vitro diagnostic test systems" (ISO/TC 212). The goal of the project is to improve the healthcare systems by the standardisation of pre-analytical workflows applied to clinics. The CEN technical specification can be obtained the same as the ISO international standards by the specific national agencies<sup>10,11</sup>.

## Instand-NGS project

From 2020 the BBMP OECl WG has been participating directly to the Instand-NGS project on the evaluation of NGS (Next Generation Sequencing) products that are present on the market. This project is extremely important for diagnostic molecular pathology as NGS is the most important recent molecular technique used in diagnostics and we are still far away from a real evaluation and standardization of what is available on the market. OECl is directly involved because some of the OECl institutions will be asked to validate the results of the project. This phase can be preliminary to a wide better standardized application of the molecular methods within OECl.

The project is a so called pre-commercial procurement (PCP) project that will identify the best value solutions offered on the market by the examination of competing providers<sup>12</sup>. The evaluation will consider the pre-analytics of biological material examined, the preparation of the library, the sequencing process, the bioinformatics analysis, the e-medication, the actionable items and the integrated report. The project is ongoing and the results will be published.

## The European Molecular Pathology Master

The European Molecular Pathology Master (EMPM) is in development in collaboration with UEMS (Union Européenne des Médecins Spécialistes), that is the European organization for the medical specialties and the University of Nice. The Master has been developed to contribute to the standardization of the molecular analyses results at the European level. This standardization is especially relevant for a better oncology diagnostics and treatment. The Master will start in 2022 and this information will be diffused among the OECl institutions to give the young pathologists and molecular biologists involved in the oncology diagnostics the opportunity to participate. The master was also developed to coordinate the different national initiatives in the field. In fact, many of the people in charge of courses of molecular pathology in the European countries are in the steering committee of the master. This will allow a continuous standardization updating.

In pathology there are three dimensional levels: the macroscopic analysis, the histologic diagnosis and finally the molecular level. The macroscopic and histological levels are mostly internationally codified, but the molecular diagnostics in tissues is in rapid development and standardization of the analyses is still a goal to be reached. This means that results of the analyses could be not easily exchangeable among European institutions. Even more the complexity of the molecular diagnostics is continuously increasing and the weight of the analytical results are very central in the treatment choices. New predictive biomarkers and new sophisticated analytical techniques are continuously proposed.

The objectives of the master is to obtain a more uniform and diffuse preparation of young professionals involved in this field in Europe. Theoretical and practical training will be central and especially addressed to oncologic and infective diseases with high priority for quality assurance and involving bioethical, bioinformatics and artificial intelligence aspects.

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**Dominique de Valeriola**

General Medical Director, Brussels, Belgium

We moved. November 27<sup>th</sup> 2021, the Institut Jules Bordet's teams and patients moved in a new building nearby the general academic Hospital Erasme and the research laboratories of the Faculty of Medicine of the Université Libre de Bruxelles (ULB). All located on the same Campus in Anderlecht with the aim to concentrate the cancer patients and the cancer experts of the two hospitals in the new building and to improve the links with the research lab teams of the ULB. This synergy is taking place through an official grouping of the 2 hospitals and the Queen Fabiola Children's University Hospital where all the pediatric cancer patients of hospitals linked to ULB are treated.

Our new building of 80.000 sqm has been completely designed in order to best fit the clinical pathways of the cancer patients, to facilitate the multidisciplinary as well as the integration of cancer research into care. The capacity of the new Institut Jules Bordet (IJB) is increasing from 160 to 250 beds and the day care unit is doubling. Forty beds are dedicated to hematological patients, 5 rooms to the delivery of radionuclides therapy, a very important emerging field. A complete floor in between the ambulatory care and the hospitalization units has been reserved for all the physicians, the paramedics, psychologists and nurses as well as meeting rooms and all the clinical trials conduct and support units in order to boost multidisciplinary contacts and the integration of research into the entire process of care.



The building is compact to facilitate clinical pathways, to avoid too many steps for the patients and the personal and to promote interactions between healthcare professionals and researchers. Apart of its high technology, it is conceived for the well-being of the patients and their relatives with luminous and peaceful waiting areas and spaces reserved to ensure educational activity in relation to their cancer disease, a room for their children with psychological support, a beauty care space. Six patios bring the natural light in the entire building, even in the basement reserved to the radiotherapy, radiology and nuclear medicine departments. Wood has been widely used for its appealing effect.





400 millions of euros have been spent on the project including the investments for the new up-to-date equipment of which 4 linear accelerators (one MR-Linac) and 2 PET-CT (one for research) as well as three GMP units for the preparation of immune and hematopoietic cells, radiolabeled medications and anticancer drugs, especially those in early phase of development. The Institute also offers intraoperative radiotherapy, radiosurgery by gammaKnife, robotic surgery, high intensity focused ultrasound technique,... We are very grateful to the charity "Les Amis de l'Institut Bordet" for the important donation of 18 millions of euros made in 2021 in support to all the innovative technologies and lab research equipment of the new building.

The concentration of all these technologies and expertise on the same Campus and mostly in the new Bordet will be of particular interest not only for patients suffering of common cancers but also for those with complex and rare cancer and to initiate new clinical trials with innovative anticancer agents or approaches.

Research will stay deeply integrated into care with a specific Innovative Therapy Unit of 12 beds for phase I and II trials and a complete 10.000 sqm floor dedicated to lab research that will host our present teams joined by a new lab on immune-oncology and also satellite sub-teams from other research labs of the ULB, all devoted to cancer.

The move of the activities from the old site to the new one took place in November over a period of 3 weeks, starting with the administrative and research teams followed by some ambulatory activities such radiology or screening consultations in order to test the facilities and medical devices. The hospitalized patients and the last teams were transferred in the new building the 27<sup>th</sup> of November 2021 in close collaboration with the Red Cross of Belgium. Despite the 4<sup>th</sup> wave of the Covid-19 pandemia that impact somewhat our plans, the entire process was successful and we were able to pursue in the wake our activities in the new environment. This was made possible thanks to the good preparation of the move through the "Chrysalide" programme involving more than 80 internal project managers since 2019. Radiotherapy activities will be undergoing on the 2 sites until mid-january.

All our new infrastructures and our increase of capacity will give us the opportunity to help more and more patients and relatives confronted to cancer and also to develop prevention and screening programs as well as to boost our contribution to international clinical and translational research, domains in which the Institut Jules Bordet plays an important role for more than eight decades in close collaboration with many of the cancer centres of OECI and all around the world. All this with the willingness to pursue our goal of quality in care, research and education in the framework of the OECI accreditation programme for comprehensive cancer centres.

Waiting for this new building for more than 15 years, the new Institut Jules Bordet is now a reality. All its teams are devoted to remain essential players in the fight against cancer throughout Europe and beyond.





## Kortrijk Cancer Centre



### Multidisciplinary, integrated and patient centred cancer care to offer the best outcomes

Debruyne Philip<sup>1</sup>, Annelies Courtens<sup>2</sup>

1. Medical Oncologist & Clinical Pharmacologist

2. MScN, RN, Clinical nurse specialist oncology

The Kortrijk Cancer Centre is a division embedded in the General Hospital az groeninge in Belgium, committed to offer high quality multidisciplinary cancer care and continuously working to meet the needs of its cancer patients and their caregivers.

Multidisciplinary oncology clinics are set up based on a group of main cancer diagnosis of the patient and have dedicated physicians, oncocoaches, a data manager and other healthcare professionals who provide 'holistic care'.

Our current portfolio includes medical oncology, haematology, pneumo oncology, digestive oncology, head and neck oncology, surgery oncology, uro oncology, EUSOMA-accredited Breast Clinic, geriatric oncology, gynaecological oncology, neuro oncology and dermato oncology. The cancer centre offers innovative techniques and specialized services: da Vinci robotic and minimally-invasive surgery, PET-centre for West-Flanders, functional MRI, pancreatic cancer surgery programme, intra-hepatic treatment with radioactively labelled microspheres, lutetium-PSMA ligand, abdominal HIPEC, comprehensive geriatric assessment, radiation therapy, pathological anatomy, clinical pharmacology, scalp cooling, onco@home, systemic-anti cancer therapy units, specialized surgery unites and palliative/end of life care unit.

Patients are offered the ability to participate in phases 1 to 4 clinical trials through a dedicated clinical trials office, clinical research unit and involvement in cooperative groups such as EORTC. The cancer centre has the capacity to design clinical trials and to serve as a lead ethical committee.

The hospital and cancer centre actively participates in clinical education of healthcare professionals at different academic levels (bachelor, master, postgraduate, PhD) aiming training of highly skilled and knowledgeable professionals with strong clinical and professional leadership.

Integrated care is provided through the collaborations with colleagues of the first line, second line (E17 Regional Hospital Network covering the South of West-Flanders & East Flanders region) and third line (as member of the Flemish Hospital Network of the Leuven University Hospitals). The cancer centre is a reliable partner resulting in excellent referral pathways and an active consultation practice for rare or complicated cases towards the larger (University) Hospital Cancer Centres.

The cancer centre has a highly developed and integrated palliative and supportive care system. Social counselling, psycho-oncology, nutrition, spirituality and existential services, palliative support team etc. are available in a structured way. In addition we provide supporting programmes such as smoking cessation guidance; oncological rehabilitation; creative therapies; Care for AYA; emotional freedom techniques; facilities for children on the oncology ward and outside the hospital 'Zibi's Boomhut'.

To better fit the priorities of the cancer centre with the unmet needs of our patients and their caregivers, we set up a patient advisory board specifically for oncology. The advisory board is an opportunity to guarantee active communication and participation with our patients and their caregivers. They are an equal partner in striving together for optimal quality care.



## National Cancer Institute of Colombia



### Institutional Arrangements for Transformative Innovation Development

Carolina Wiesner-Ceballos<sup>1</sup>, Álvaro Quintero-Posada<sup>2</sup>

1. MD, MSc, Director General, National Cancer Institute of Colombia

2. MD, Innovation Manager, National Cancer Institute of Colombia

Transformative Innovation (TI) is a deliberate, systemic, long-term innovation process, guided by a vision to change society towards a mode of production, consumption, and care for nature. A bottom-up process is necessary for its development, which involves and supports diverse actors with transformative ideas, who experiment and innovate with systemic alternatives. It implies listening to and valuing different voices and being sensitive to those who could be negatively affected. Due to the uncertainty and variety of alternatives, it requires experimenting with sustainability routes to bring about systemic change. The concept of experimentation includes producing demonstrative prototypes that may inform new paths and generate deep learnings through formative assessment (Ramírez, 2020). For the National Cancer Institute of Colombia (INC), a public organization in the process of transformation towards excellence, it is necessary to redirect Science, Technology, and Innovation in Cancer Control so that they are truly socially and environmentally beneficial, for which profound changes are required in the socio-technical health system.

TI can be developed through processes (Robledo Velásquez, 2017) that contribute to the formation of culture:

- **Modeling, Simulation, and Prediction:** Facing social challenges requires processes and projects that allow modeling, simulating, and predicting complex phenomena (Dyer, Gregersen, & Christensen, 2011), using flexible mechanisms.
- **Knowledge Valuation:** The agencies involved in experiments join with a diverse set of knowledges, which probably are valued differently by each; this inequality of valuations could become a source of development when put at the service of adequate problematic phenomena.
- **Innovation Assessment:** It requires the application of formative assessment techniques, which involves monitoring and follow-up processes of the trajectories of experiments and, above all, the ability to adjust as quickly as the state of intervention demands.

The INC, member of the **Latin American and Caribbean HUB of Transformative Innovation Policy**<sup>1</sup>, has designed the Transformative Experiment "Co-Creation Laboratory for Innovation in Cancer Control Colombia", which will initiate in 2022, with the participation of our patients and in the hope of having the support of the OECD-EEIG, as an essential contribution to new forms of innovation in Cancer Control in Colombia.

1. <https://hubinnovaciontransformativa.net>

#### References

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# Instituto Oncológico Fundación Arturo López Pérez (FALP)

Mauricio Petri<sup>1</sup>, Hugo Marsiglia<sup>1</sup>

1. Instituto Oncológico Fundación Arturo López Pérez



Cancer is the second leading cause of death in the Americas. In 2018, some 3.8 million cases were diagnosed and 1.4 million people died from this disease. The incidence of cancer in some regions has seen a significant increase due to some economic activities with high environmental impact, added to the increase in smoking, alcohol consumption, sedentary lifestyle and low consumption of fruits and vegetables rich in antioxidants. In Chile, cancer is the leading cause of death; 53K new cases are registered per year with an incidence of 217/1000 inhabitants. In the Americas, the most frequently diagnosed types of cancer are: prostate (21.7%), lung (9.5%), and colorectal (8.0%) in men, and breast (25.2%), lung (8.5%), and colorectal (8.2%) among women.

Since 1954, the challenge of the Arturo López Pérez Foundation to “Promote cancer prevention and fight against it with all means, providing care and assistance to all cancer patients, especially the most socio-economically vulnerable”<sup>1</sup> has been its most important mission, putting the patient at the center, researching, accumulating experience and providing our Cancer Institute with the highest technology and infrastructure for early diagnosis and treatment, designing a non-profit, sustainable and inclusive model.



The foundation's strategic plan aims to strengthen these pillars in its search for excellence. For this, since its incorporation as an OECI member, the Foundation has begun a learning and cultural change to become a reference center in Latin America.

Work projects are constantly multiplying to achieve operational excellence. Such as clinical pathway projects that aim at standardizing the best diagnosis and treatment practices based on our multidisciplinary teams' experience, derived from the latest validated clinical guidelines, thus reducing process variability and making them safer and more efficient; or research projects and monitoring of clinical studies to ensure the use of the latest cancer treatments and offer our patients the best results. Despite the pandemic, 2021 presented an improved scenario and gave us the opportunity to advance with the OECI Cancer Center accreditation guidelines, that are a challenge for all of us who work at FALP, and are a reference framework based on the best practices from the most prestigious centers in Europe.

For the Foundation, the cultural change has already begun. It entails changing the way we do things, better strategic projections, more teamwork, better communication, supporting decision-making with solid data (tumor registry project), making risk management a work habit and giving our patients a shared space for co-design.



For all these reasons, this year we took up the challenge of advancing in the OECI Accreditation project, forming a solid Coordination team led by our International Medical Director, Dr. Hugo Marsiglia, PM Mauricio Petri and advisor Nordiana Baruzzi.(picture)

During the month of August, work teams were empowered for each chapter of the manual, as chapter leaders, which favored the diagnosis of GAPs with process owners. Subsequently, opportunities for improvement and SMART objectives were planned for each standard. For this we used the IHI2 model for health organizations, which is an excellent model to define improvement tests with associated Drivers. This triggered new projects, now clearly focused on standards but with the aim of transforming them into the Foundation's work habit, since we are convinced that this is the way to establish a Culture of Quality and Patient Safety.

Over the years, the Foundation has developed evidence-based strategies for the prevention, screening, early detection and treatment of cancer. It has made diagnosis accessible to everybody through mobile clinics reaching populations in the most remote and inaccessible places in Patagonia, helping to reduce treatment accessibility and delay of 5K patients in Chile.(picture)

The Foundation has started a process of profound cultural transformation that includes the challenge of applying the highest standards and adapting them to the socio-economic context of the region. For this, our Leadership, putting collaborators in the center, decided to implement the AHRQ Culture SOPs<sup>3</sup> survey. This survey measures Patient Safety Culture, which is defined as the extent to which the culture of an organization supports and promotes patient safety. It refers to the beliefs, values and norms shared by health professionals and other personnel throughout the organization, which influence their actions and behaviors.

We are certain that this profound transformation will create spaces for a larger participation of our patients and will reinforce the most valuable patterns of the Foundation's culture, such as empathy and compassion for our patients. Voluntarily participating in this challenge fills us with pride and dedication to improve the quality of life for all of them.

<sup>1</sup> Ana Ross, widow of Arturo López Pérez. Valparaíso, 1885 - París, 1974.

<sup>2</sup> <http://www.ihl.org/resources/Pages/Tools/PlanDoStudyActWorksheet.aspx>

<sup>3</sup> <https://www.ahrq.gov/sops/index.html>



# Masaryk Memorial Cancer Institute



**Olga Sapoznikov<sup>1</sup>, Jiri Sedo<sup>2</sup>, Anna Svobodova<sup>3</sup>, Tomas Kazda<sup>4</sup>**

1. MMCI, Head of International Accreditation Unit

2. MMCI, Deputy Director for Strategy, Communication and Education

3. MMCI, Spokesperson

4. MMCI, Director for Science & Research

## General Center Information

The Masaryk Memorial Cancer Institute (MMCI, [www.mou.cz](http://www.mou.cz)) is a highly-specialized national oncology center based in Brno, the second largest city in The Czech Republic. The Institute is one of the two national cancer centers in the Czech Republic and it provides comprehensive cancer care to adult patients with solid tumors.

Every year, experts in the MMCI perform 250,000 outpatient procedures and carry out almost 10,000 hospitalizations.

## Domains of the MMCI

### Comprehensive Cancer Care

The Institute focuses on prevention, diagnostics and all the main modalities of anticancer care. The MMCI Department of Comprehensive Cancer Care implements the latest procedures in systemic cancer treatment and supportive care.

The Department of Radiation Oncology of the MMCI currently operates 5 linear accelerators and is the largest radiotherapy facility in the Czech Republic.

The Department of Surgical Oncology is divided into four units - Surgical Oncology, Breast and Skin Surgery, Gynecology and Urology. The Department possesses 6 operating theaters, one of which houses the daVinci robotic operating system since 2018.

### Research

The MMCI team focuses on scientific research activities, including basic research, and outreach activities aimed at the general public. Research teams are involved in European and world-involvement clinical trials, which evaluate the effects of new anti-cancer drugs (including phase I trials).

Recent examples of publication activity, which arises from research done at the MMCI, shall include such topics as second primary malignancies in colorectal cancer patients, protein dynamics of an ancestral luciferase<sup>1</sup>, and clinical practice guidelines for diagnosis, treatment and follow-up of gastrointestinal stromal tumors.

The Research Centre for Applied Molecular Oncology (RECAMO), which is located in the MMCI, has several ingenious research groups that work in first-class modern facilities. The Institute also possesses the Bank of Biological Material. It is the head of BBMRI-CZ, the Czech national node of the European Research Infrastructure Consortium BBMRI-ERIC (Biobanks and Biomolecular Resources Research).

### Education

The MMCI provides pre- as well as postgraduate education for physicians and other health care professionals. The Institute includes three departments of the School of Medicine of Masaryk University (located in the city of Brno).

### National and international cooperation

The Institute is involved in national and international cooperation projects, exchanges and discussions on policy recommendations at different levels. The MMCI is working with much effort on expansion in this field.

1. Halamkova J. et al. Second primary malignancies in colorectal cancer patients. *Sci Rep.* 2021 Feb 2;11(1):2759.

# Motol University Hospital (MUH)



Department of oncology MUH is well recognized as one of the two National Oncology centres in the Czech Republic focusing on treatment of rare cancers and coordinating the cancer health policy in the Czech Republic. The Department of Oncology is a member of two EORTC working groups for sarcoma and GI tumours. It is involved in the European SPECTA project focusing on personalized medicine. The department also collaborates closely with the Czech Academy of Sciences in different projects of basic research like the development of new targeted cancer therapies, molecular markers of pancreatic cancer and colon cancer and others. The collaboration with the State Institute of Health is focused on identifying the principles of hormonal resistance in patients with breast cancer. The Department of oncology is a member of ERN- EURACAN (sarcoma, head and neck cancer, female genital organs and placenta). The cooperation with Proton Therapy Centre in Prague is ongoing and focuses on the development of new radiation protocols and clinical trials.

The Department of Oncology collaborates with the Institute of Immunology of MUH which developed dendritic-cell based immunotherapies for various solid tumours and tested new therapies in a clinical setting up to the phase I clinical studies. This project is further developed by Czech biotech company Sotio which continues in successful cooperation with MUH on clinical trials testing above mentioned cellular therapies and other immunotherapeutic products.





## East Tallinn Central Hospital



### Baltic Centre of Ophthalmic Oncology

**Artur Klett**, MD PhD FEBO  
**Delis Linntam**, MD

During Soviet times, the ophthalmic oncology for Baltic countries - Estonia, Latvia and Lithuania - was concentrated in Moscow. With independence in 1991, it became impossible to send our patients there and we were facing a necessity but also an opportunity to start building up our own oncology services.

With the support of developed European countries, Estonia was the first of the three Baltic countries to take steps towards establishing a modern ophthalmic oncology centre. First trainings in this field took place in Hamburg (prof. Guthoff), Essen and Berlin and later in Helsinki (prof. Kivelä) and Utrecht (prof. Mourits). Within 1992, all preparations and equipment purchases had been made for starting plaque brachytherapy with Ru-106 for intraocular tumours in Tallinn. Given the small population of the Baltic States, economic considerations and, most importantly, expected slow experience gain in the eye oncology field in 1993 a singular centre was created for all three countries. The ophthalmic oncology, including treatment of all intraocular and orbital tumour patients and complex eyelid tumour cases became concentrated in Tallinn.

The eye oncology services provided in East Tallinn Central Hospital include all intraocular, eyelid and orbital tumour treatments. The most common adult intraocular malignancy is uveal melanoma. During 1993-2021, there have been 885 cases of primary uveal melanoma that have been treated with plaque brachytherapy and 73 eyes have been enucleated.

The most common childhood intraocular tumour is retinoblastoma. The eye salvaging local treatment options in Tallinn include brachytherapy, transpupillary laser therapy and cryotherapy. Since 2016, all children with retinoblastoma are treated with systemic chemotherapy and local therapy. Thanks to great collaboration with Lausanne University Hospital Eye Clinic (prof. Munier), government-funded intra-arterial chemotherapy is also available for our patients.

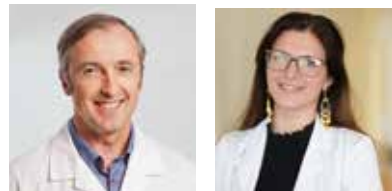
All epibulbar tumours, most of them conjunctival melanomas but also squamous cell carcinomas (SCC) are offered surgical resection with additional brachytherapy and topical chemotherapy.

More advanced eyelid malignant tumours and all orbital tumours from the three countries are treated in Tallinn by surgical resection and plastic reconstruction.

East Tallinn Central Hospital is a member of International Society of Ocular Oncology (ISOO) since 2004 and European Society of Ophthalmic Plastic and Reconstructive Surgery (ESOPRS) since 2000. In 2010, our centre received accreditation from the European Board of Ophthalmology (EBO) as an European Teaching Centre. Since 2016, we are a full member of the European Reference Network of Rare Eye Diseases (ERNE-EYE).

To keep the centre up to standards, we have continuously attended fellowships and trainings in bigger centres. All young colleagues starting in the field are offered trainings in other European centres. As a teaching centre, we in return have had many young colleagues from nine different countries in Europe, mainly interested in learning ophthalmic oncology and reconstructive surgery in Tallinn.

Thanks to liaisons and collaboration with other European centres, today we have not only access to the science-based management guidelines but also the opportunity to consult the most difficult cases with top experts from more experienced centres.



## TAYS Cancer Centre Tampere University Hospital



### Multidisciplinary teams – a standardized platform for quality improvement

**Annika Auranen<sup>1</sup>**, **Sari-Marja Hytönen<sup>2</sup>**, **Maarit Bärlund<sup>3</sup>**

1. Chief Physician, Tays Cancer Centre, Tampere, Finland

2. Quality Director, Tays Cancer Centre, Tampere, Finland

3. Chief Physician in Oncology, Tays Cancer Centre, Tampere, Finland

In Tays Cancer Centre, multidisciplinary cancer meetings were implemented in routine cancer care in the 1990s. During the OECl accreditation process, we noticed that in our hospital setting, in most cancer types the diagnostic, surgical and oncological procedures were performed by different specialists in different divisions. The patients travelled a long road from first admission and diagnostic examinations to end of oncological therapy and follow-up, but it was often the case that the professionals treating the patient in the beginning of the path actually never even discussed with the professionals at the end of the path. Although the different clinical multidisciplinary meetings along the path gave guidance to treatment, quality control, process development and general improvement of the treatment process was not really possible.

In 2017, we started to develop a Team model, which expanded the tasks of the MDTs from clinical decision making to officially defined tasks in quality improvement and effectiveness evaluation. We wanted to create a uniform Tays Cancer Centre platform for quality assessment, quality improvement and monitoring. Our Quality Director Sari-Marja Hytönen was the main driver in implementation of the model. The first step was an open discussion with the personnel about the basic strategic values of the Team action. The personnel chose patient centeredness, effectiveness and personnel work satisfaction as their strategic values. OECl quality standards guide the activity.

The cancer teams are formed around a particular cancer (e.g. breast cancer team, lymphoma team). Participants are collected from all treating units and several professional groups, and include physicians of various specialties, nurses, physicists, nutritional therapists, geneticists, secretaries and other relevant supporting personnel. Patients are involved in team activities, such as building patient pathways. When a cancer team is started, the team creates a team agreement, to which all team members are committed. The team agreement specifies the task, partners, responsibilities, dates of the team meetings, structure of the meetings, goals, working rules and delegations. One of the goals of the teams is to optimize the processes and resources, identify and manage both under- and over treatment and plan and improve patient information and patient participation throughout the whole treatment process.

The teams follow effectiveness with different measures, such as using Clavien-Dindo classification in reporting surgical complications and QoL monitoring with ECOG classification, digital symptom monitoring and standardized QoL questionnaires. Geriatric G8 questionnaire is used to identify frail patients, who would benefit from oncogeriatric consultation.

Today, we have 13 cancer teams and 6 teams in the implementation process. The teams meet at least 4 times yearly to discuss performance of the team. The memos from the meetings are openly available in the hospital intranet. All personnel participating in cancer treatment processes can present improvement suggestions electronically. During 2020, over 100 improvement action suggestions were discussed in the teams, of which 80 proceeded to implementation. We have discovered that early problem identification and rapid solutions lead to the best results.

It has been rewarding to see that the personnel have very rapidly become enthusiastic about this kind of teamwork, as they have realized that this model enables them to do meaningful improvement activity towards better treatment of patients and improvement of their own professionalism. They have also identified that the work they put on the improvement process, is actually an investment on their own wellbeing and work satisfaction.

# Helsinki University Hospital Comprehensive Cancer Center

*Johanna Mattson, Director of HUH CCC*



## Description of the Centre and history

The first department of radiotherapy in Finland started its activities in Helsinki in 1936 and since then the unit has continuously grown to become the first Nordic and second European CCC in 2014. HUH CCC was redesignated as the OEI Comprehensive Cancer Centre in 2021. HUH CCC is also a member of the European reference network (EURACAN).

HUH CCC is responsible for the oncological treatment of cancer throughout the area of the Hospital District of Helsinki and Uusimaa (HUS), with a population of approximately 1.7 million. It is Finland's largest cancer center and one of the largest in the Nordic Countries.

Each year, CCC treats over 30 000 patients, of whom approximately 10 000 are new patients. The center employs 580 health care professionals, more than 120 of whom are physicians.

HUH CCC co-ordinates also cancer diagnostics and oncological surgery by having the chair of the HUH Steering Board for Cancer Care.

The new modern cancer hospital building will be taken in use in 2023.

## First class quality

As part of the OEI accreditation HUH CCC developed its activities and pioneered in Finland by publishing access to treatment, founding patient advisory board and scientific advisory board. To increase patient involvement also in the planning of research activities and clinical a scientific patient advisory board was created.

Additionally, the first formal cancer nurse training programs were launched in collaboration with the Helsinki Metropolia University of applied Sciences. Moreover, all multidisciplinary teams have adopted comparable practices and all specialities share similar key oncology specific performance indicators. Providing real-time, real world outcomes data has been in the focus since the implementation of EPIC in November 2020.

The portfolio of services has expanded to include digital services and remote e-visits /tele meetings when appropriate. Collaboration with the patient advisory board, experience specialists and patient societies continues to improve the treatment and other services according to the needs of the patients and their families

Despite the Covid19 pandemics, the access to treatment has been good and all cancer treatments have been given as earlier. Also the amount of clinical trials has increased. Patient satisfaction rates have been extremely high and the NPS (net promoter score) the highest at HUH.

## Highly educated and dedicated personnel

As a university level teaching hospital, HUH CCC is an active training site for physicians, nurses and physicists. It engages in teaching cooperation with universities and other educational institutes. The Center participates in the basic education of physicians in cooperation with the Faculty of Medicine of the University of Helsinki. Additionally, HUH CCC trains specialists for medical oncology, radiotherapy, hematology, palliative care and breast surgery.

Special attention is paid to the standard early orientation and training of trainees and other new personnel. All trainees have a named senior doctor at the department. Every morning they go through the trainee's patient cases of the day and additionally, the trainee can consult the senior whenever needed.

Cancer nurse training programs were launched in 2014 in collaboration with the Helsinki Metropolia University of applied Sciences. The programs have been extremely popular and include various levels of education starting from basic and then skilled level and up to mentoring and superior skills. Leadership

and management education is provided for leaders and managers to reach better management. The Cancer nurses are educated to take more responsibilities of in person follow-up visits, calls and digital contacts where appropriate.

All employees are offered professional guidance in a group of peers.

As a university hospital, protected time for research is offered for clinicians, physicist, therapists and nurses who do research work as well. Protected time for research is partly funded by sponsored projects in addition to joint clinical research positions with the University of Helsinki and research grants. The research nurse pool is partly funded by HUH and partly by centrally administered sponsored research projects.

At CCC we have the lowest turnover rate of personnel at HUH.

## Modern radiotherapy unit

The department of radiotherapy is among the most modern in Europe. It carries out all radiation therapy techniques currently available, centralized to university hospitals, with the exception of proton therapies. Available techniques include common and special external beam therapy techniques: 3D-conformal with photons and electrons, intensity modulated, stereotactic SRS and SBRT, adaptive therapy, gated therapy and total body irradiation. In addition to EBRT, there is brachytherapy with both HDR (Ir-192) and LDR (Ru-106, I-125) methods, and radionuclide therapies with several different nuclides and carriers.

MR-guided external beam radiation therapy will be available in 2023. It includes the ability to deliver ablative doses with tight margins through real-time soft-tissue visualization and on-table adaptive therapy. With MRI-guided RT, HUH CCC will be able to treat tumors that were previously untreatable with radiation therapy.

The most common treatment targets for internal radiation i.e. brachytherapy are the prostate gland, gynecological cancers and liver tumors. Intraocular radiation therapy is provided in collaboration with HUH Department of Eye disease.

The radiotherapy unit provides an extensive range of cancer targeted radionuclide therapies. In addition to traditional thyroid carcinoma radioiodine therapy, Ra-223-chloride therapy for skeletal metastases, Lu-177-octreotate against NET tumors, Lu-177-PSMA against metastatic prostate cancer, and Y90-SIRT therapy for the treatment of hepatic lesions are available. The unit has two SPECT-CT gamma cameras and a radiopharmaceutical production area according to GMP cleanroom requirements.

A globally unique, novel accelerator-based and first ever in-hospital boron neutron capture therapy (BNCT) device is being built and commissioned at HUH CCC in collaboration with Neutron Therapeutics. BNCT is biologically targeted radiation therapy. At the beginning of therapy, the patient receives intravenous inactive boron-10 which accumulates in the tumor with the help of a delivery vehicle. By radiating the boron-enhanced cancer cells with a low-energy neutron shower, a fission reaction occurs releasing large amounts of energy, which destroys the cancer cells. The first target group for the therapy are patients with recurrent head or neck cancer. However, the therapy can be used to treat other tumors as well, provided that the boron uptake of the tumor is high enough and the tumor's location is suited for BNCT therapy. Building the device itself started at HUS in the summer of 2018, and the first trial therapies will start in 2022.

## Advanced cancer medicine

At HUH CCC systemic therapies for both solid tumors and hematologic malignancies are given. Allogeneic and autologous stem cell transplantations as well as CART-therapies are also carried out at CCC. A novel cell therapy center will be launched at CCC in 2022.

Clinical Trial Unit was set up in 1995 and the Early Phase Trial Unit in 2016 for the efficient and rapid translation of cancer drug innovations into clinical care. In addition to phase I-IV clinical trials, also first-in-man studies are conducted.



In 2021 developing of the clinical trial unit of CCC has been one of three strategic projects at the whole HUH. The unit has adopted novel procedures and consequently increased the number of clinical trials despite the Covid19 pandemics.

Many cutting-edge research projects like individualized systems medicine in cancer are ongoing.

### Top-class oncological surgery

In the field of oncological surgery, the HUH breast surgery unit is one of the largest in the Nordic countries with around 1,500 annual breast cancer operations. The long tradition of systematic gathering of clinical outcome data as part of MDT collaboration and the use of quality registers has produced multiple very highly cited articles on breast cancer.

Also in all other areas of oncological surgery the whole cancer pathway is integrated and the MDTs share similar procedures in patient care. Top-class clinical and translational research is done by all MDTs.

High-class palliative and supportive care

The holistic care of cancer patients is one of the priorities of HUH CCC. Early integrated palliative care with wide spectrum of supportive services is essential for maintaining the quality of life and physical functioning of patients during the cancer treatments. Systematic symptom assessment including physical, psychosocial and spiritual symptoms/problems and functional impairments with defined procedures for referral to supportive and palliative care services is a part of our clinical practice.

Easy access to individualized psychosocial support is available for all patients. A special program has been designed for young patients and patients with young children. Occupational therapist services for young adolescents, and supervised peer groups for patients and separately for their spouses have been launched. In addition to remote visits and the digital services include also mobile software for psychosocial support.

For elderly patients, geriatrics counselling is systematically organized. Collaboration with primary care providers improves the supportive and palliative care. High-class hospice services are delivered in close collaboration with the non-profit third sector actor Terhosäätiö.

EU funded and HUH CCC co-ordinated international Bounce project aims at modeling and piloting targeted services to support the recovery of breast cancer patients.

### Innovative digital services

HUH CCC developed an electronic patient-reported outcome (ePRO) software for cancer patients together with a Finnish start-up company. The Noona software is a web-based application for cancer patients to contact cancer nurses between appointments and self-report symptoms, adverse events of treatments or reply to queries or questionnaires via computer or smart mobile devices.

This technology allows follow-up of cancer patients easily for longer periods. Additionally, PROMs may help to detect disease recurrence or severe adverse events earlier and improve treatment outcome. Lately, software for mental support was developed and digital coaching is under development. With the help of mobile services and telemedicine the treatment may be planned centrally with top expertise but delivered locally near the patient and her family.

Digital solutions have been taken in use in the whole patient path. With smart digital software and digital patient pathways, some of the outpatient visits have been substituted by remote contacts during Covid19.

In addition, globally the first mobile prostate cancer follow-up programme was developed and implemented by the HUH urologists.

The modern IT-systems with data-lakes and predefined items enables gain of real life data and outcomes in real time.

### Cutting-edge research

Research at HUH CCC covers a wide range of different areas from first-in-human and other early phase

trials in the clinical trial unit to larger phase III trials and from surgery to medical oncology and from hematology to radiation therapy studies as well as palliative care and rehabilitation.

HUH Comprehensive Cancer Center has been in the forefront of personalized medicine by engaging fruitful collaboration with basic and translational cancer scientists and by setting up an active early phase clinical drug study center for efficient and rapid translation of research innovations into patient care. Consequently, the number of first-in-man and Phase III studies is increasing as is the scientific output of the research talent at the Center despite the Covid19 pandemics.

To facilitate efficient drug discovery and repurposing for individual patients, we perform molecular profiling and largescale ex vivo drug testing platform consisting of >500 anticancer compounds. This systems medicine approach developed in collaboration with research groups at FIMM (Institute for molecular medicine Finland) has proven to be highly successful for preclinical drug research, predictive biomarker discovery and in novel personalized medicine clinical trials. In addition to hematologic malignancies the systems precision medicine approach has been expanded to include solid tumors using innovative organoid and cancer-on-a-chip technologies. Artificial intelligence and deep machine learning algorithms are needed to further facilitate treatment/trial matching to cancer patients especially in precision medicine programs. To further expand precision medicine in solid tumors HUH CCC has joined the European platform with the Finnish FinProve study.

FinProve is a multi-center, multi-drug, pan-cancer basket trial in which patients with an incurable malignancy, who have exhausted standard treatment options, are treated off label with registered targeted therapies and immune checkpoint inhibitors, based on their tumor molecular profile. The study includes pharmaceutical partners who provide study drugs for free. The European platform allows for data sharing across countries to the benefit all patients. To identify suitable patients systemic sequencing of circulating tumor (ctDNA) and metastatic tumor DNA as well as RNA are performed to discover actionable targets.

HUH has built a strong infrastructure for research i.e. biobanks, IT solutions and datalakes. The Finnish government has also strongly supported the growth of healthcare sector in legislation. HUH CCC has expanded research and development by closely engaging with all major stakeholders - university, pharma, biotech (local SMEs in particular), and patient organizations.

HUH has heavily invested in this area with innovative PPP (public-private-partnerships) solutions, such as iCAN (digitalprecisioncancermedicine.fi), FinnGen (finngen.fi) and CleverHealth ecosystem (cleverhealth.fi). iCAN ie. the digital precision cancer medicine project funded partially by the Academy of Finland is based on the collaboration of clinicians, basic and translational research groups and companies. Patients are also important stakeholders in iCAN studies and activities. FinnGen is a genomic profiling project that uses biobanked patient samples. The project brings together Finnish universities, hospital, hospital districts, THL (National Health Agency), Blood Service, biobanks and international pharmaceutical companies and hundreds of thousands of Finns. Cancer is one of the disease in the main focus of FinnGen and HUH CCC researcher take actively part in this project.

Within the HUH datalake a platform for systemically and prospectively assess the cost-effectiveness of new cancer therapies is being built. As part of this real world data platform also sequential biobanking samples will be collected in addition to patient reported outcomes on adverse events, quality of life, performance status and ability to work. Clinical data can be collected from the hospital data lakes and the Finnish Cancer Registry while costs of treatment are collected from the hospital registries and registries of Kela (Social Insurance Institution of Finland).

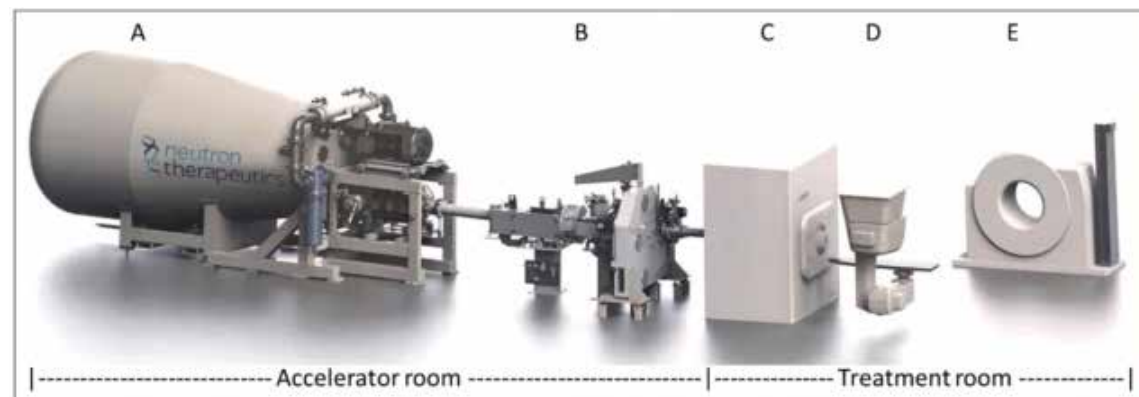
In the field of radiotherapy, HUH CCC develops boron neutron capture therapy (BNCT), where first clinical trials are being initiated using globally novel BNCT technology. Besides clinical trials, establishment of BNCT technology at the center will make HUS CCC also poised to start cutting-edge translational studies on BNCT biology and boron carriers.

### In the future

HUH CCC is extremely committed to continuously improve cancer care and increase high-class scientific research to improve outcomes for cancer patients and their families.



The new BNCT treatment room at the Helsinki University Hospital CCC, showing the beam-shaping assembly (left), robotic couch (centre) and in-room CT scanner (right).  
Courtesy: Neutron Therapeutics.



The key enabling technologies in the Helsinki University Hospital CCC's BNCT facility.  
A compact proton accelerator;  
B proton beam optics;  
C beam-shaping assembly;  
D robotic couch;  
E rail-mounted CT scanner.  
Courtesy: Neutron Therapeutics.



## Institut du Cancer de Montpellier (ICM)



**Marc Ychou<sup>1</sup>, Vanessa Guillaumon<sup>2</sup>**

1. General Director of Montpellier Cancer Institut – Director of SIRIC Montpellier Cancer  
2. General Secretary of SIRIC Montpellier Cancer

Montpellier Cancer Institute (ICM) has rapidly expanded over the last ten years, rising as one of the top-performing Comprehensive Cancer Centres in France and in Europe. Directed by Prof. Marc Ychou, it is the only French cancer centre to combine a cancer hospital, a biomedical research institute and a centre dedicated to cancer prevention in a single organisation, thus ensuring its fourfold mission of patient care, research, prevention and education in a fully integrated approach. Combining excellence and humanism, it offers the most advanced medical expertise supported by cutting-edge technologies and an innovative organisation that places comprehensive care at the heart of the care pathway, as evidenced by a newly created 1,500m<sup>2</sup> building dedicated to supportive care. With nearly one thousand employees, including 120 physicians, it has an active file of about 30,000 cancer patients per year. It is a member of UNICANCER, the first French hospital group exclusively dedicated to the fight against cancer.

Research activities on ICM campus range from basic science to clinical research and population studies. Basic and applied research is carried out at the Montpellier Cancer Research Institute, which hosts within a 4,500m<sup>2</sup> area 17 research teams that work in strong connection with ICM clinicians. Altogether, their scientific output includes the identification of new tumour biomarkers and micro-environmental parameters involved in carcinogenesis or resistance to treatments, the development of novel bio-drugs, and the improvement of cancer treatments such as personalised radiotherapy, chemotherapy and immunotherapy. From this cancer research core, ICM on behalf of the "Montpellier Cancer" consortium has been one of only eight Integrated Cancer Research Sites (SIRIC) awarded by the French National Cancer Institute in recognition of their medical-scientific excellence since 2013. Bringing together the complementary expertise of nearly six hundred research professionals from the ICM, Montpellier University Hospital, Inserm, CNRS and the two universities of Montpellier, the SIRIC Montpellier Cancer is developing world-class research, encompassing the entire continuum of basic research, translational research, clinical research and human and social sciences. Three integrated research programmes focused on colorectal cancer, radiotherapy and tumour escape form the backbone of its scientific strategy. Several flagship achievements with strong potential for clinical application have resulted from this work, placing the SIRIC teams at the forefront of innovation in the fields of circulating biomarkers, radiobiology and radiotherapy, therapeutic antibody engineering, genome biology, cancer prevention and supportive care.

Thanks to this dynamic ecosystem and strong political support, the ICM's current initiative is to build an Oncology Innovation Transfer Centre by 2024, which will combine cutting-edge patient-centered translational research with biotech companies dedicated to entrepreneurial innovation in oncology. By uniting basic biology, translational research, clinical research, interdisciplinary expertise and industrial partners on its campus, ICM aims to develop a leading European oncology innovation ecosystem, whose synergies will boost the translation of scientific discoveries into patient care and cancer prevention. It is around this strategy that ICM will build the cancerology of tomorrow, for the benefit of all patients.





## A Data Journey at Institut Curie

**Xosé M Fernández, PhD**  
Chief Data Officer, Institut Curie

Institut Curie starts from a place of strength as our journey towards a digital hospital set off at the turn of the century. First came the design and implementation of a comprehensive electronic patient record system (EHR), a system securing access to patient data by the treating teams. A hospital group treating 52,000+ patients and managing 107,000+ consultations every year poses some challenges when it comes to implement a digital strategy. Creating the foundations of a system digitising legacy documents required an investment of several million euros over seven years and a clear path to allow the full interoperability of the heterogeneous medical system. Transforming healthcare processes (a complex ecosystem using 60 distinct information systems when the project started), improved the quality of care, and supported the transition towards a paper free hospital in the 21st century.

### Institut Curie breaking new ground

We treat our patients thanks to the lessons learnt from past patients, nobody would question the imperative to learn from current patients this is a core ethical principle of medicine since Hippocrates. Yet the success of such endeavour passes by up-to-date access to real world evidence and this requires expensive technologies and infrastructures capable of handling the growing amount of data generated. In order to integrate these highly heterogeneous datasets we need multidisciplinary teams. In 2017, Institut Curie embarked on the big data dynamic by creating a Direction des Data and hiring a Chief Data Officer with the mission of managing the digital transformation, enabling the utilisation of information as an asset, in order to exploit our growing data collection for the use of scientists and clinicians, and ultimately for the benefit of patients. Today, a multidisciplinary team of data scientists, bioinformaticians, engineers and data managers ensure alongside clinicians that we deploy the relevant tools to capture the longitudinal history of our patients tracking disease progression or identify the cohorts required to test various hypothesis. A successful tandem (clinician/data scientist) which enable us to collaborate with numerous companies and participate in ambitious European consortia such as BigMedilytics.

Medicine today is inherently experimental because therapies rely on experimental results. Collected data provides an empirical basis for understanding what to expect in our patients, to gain insight beyond what experimental data can provide. Hence, the tools provided to the medical practitioner should be more precise, going to the molecular profile level. We have witnessed some developments in this domain with computer systems capable of answering questions posed in natural language (examples such as Consore, discussed later, allow complex queries and aims to accelerate clinical trial enrolment).

Clinical data is often trapped in silos incompatible by different standards and semantics. Information exchange is often limited due to lack of standardisation (different vendors are not using the same technical standards resulting in not interoperable systems), but data sharing is also restricted by structural and technological issues, including access, re-usability and interoperability. Health information architectures face major changes handling an increasing number of solutions and integration points.

But the digital revolution is not only driven by the abundance of data, but also our capability to collect, store and analyse the information to make the data speak. Digital systems underpin the delivery of modern clinical research. They can help to design and deliver protocols, identify and recruit research participants. These systems go hand-in-hand with accessible, interoperable and high-quality data – to

better understand disease and unlock advances in the future of patient care.

### Attract Top Talent

Our **digital transformation** demands a **cultural and organisational change** compared to traditional medicine. It is a **comprehensive** and integrated information, management and research process based on technological solutions and data tools, which seeks to achieve a model based on the generation of knowledge to obtain value.

More than ever, the ability to manage torrents of data is critical as it will be of limited value until it has been integrated with other data and transformed into information that can guide decision-making. Information architecture governs the processes and rules that convert data into useful information, these “plumbing” aspects of data management are vital to high performance.

### A federated architecture model

One of the key drivers of growth of the current digital transformation was an expansion of data processing in the cloud. In Europe healthcare lags behind as there are additional hurdles to cloud adoption (regulations in various countries require specific certification to healthcare data hosting infrastructures). Perhaps a **European Health Space** proposition simplify data governance, and provide incentives to encourage robust data sharing, some initiatives are currently being outlined.

As biomarkers are incorporated into clinical practice guidelines, clinicians need easy access to a patient’s genotype or molecular profiles without having to wade through volumes of genomic data to learn the results of a given test (alongside some information on the quality score for the data provided). The **OSIRIS** minimum dataset has been developed in this context of large precision medicine clinical trials to empower such analysis (supported by the French National Cancer Institute, **INCa**). OSIRIS provides an event-based data model incorporating a combination of clinical and omics concepts, organised into a temporal model of cancer events compatible with searches through the longitudinal changes associated with disease progression and resistance to therapeutic interventions.

OSIRIS is the technical solution proposed to collect and structure clinical and genomic data to improve data sharing and interoperability, it captures the disease course in the context of precision medicine in oncology. An event-based data model of a minimal set of clinical and genomic items using international standards and terminologies enabling a strong interoperability.

This approach should enable an effective decentralised real-world data ecosystem by deploying a data standard, which could improve the compatibility, quality, and consistency of electronic health records. Our data approach provides organisations with a secure federated repository for querying genomic health records, fostering data exchange. Thus, data can be combined from multiple instances when needed collating information from multiple sites to seek new insights.

**Consore** is another extremely useful tool we put at the fingertips of our clinicians, a search engine capable of sifting through millions of patient records across the Unicancer hospital network to identify those matching the search criteria. Moreover, it lists the required clinical details: patient details, clinical narrative reports, chemotherapy administration, tumour characteristics (progression), biological samples, clinical trials... providing a comprehensive overview of a patient history. Each Consore instance is deployed locally in a dedicated environment, which is not accessible from outside. Federated queries across the network must come from approved nodes. A tiered access approach allows data discovery without exposing identifiable information, as no data representations or annotations are shared in the process.

How far will big data and algorithms take us? Will we witness long-term changes in disease progression for our patients, or will these gains ultimately be reversed. On the hope to fuel observational research to improve our health systems, we have been working towards the establishment of the European Digital Institute for Cancer Outcomes Research (**DIGICORE**).

## SIOP Ependymoma II – An international clinical program to improve the diagnosis and treatment of children, adolescents and young adults with ependymoma

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The clinical management of patients with ependymoma remains challenging and the clinico-bio-pathological correlates of outcome are poorly understood. This international SIOP Ependymoma II (SIOP EPII; NCT02265770) program aims to improve the diagnosis and treatment of children, adolescents and young adults with ependymoma. The program has been activated in more than 160 participating sites, including OEI certified centers, over 14 different European countries.

SIOP EPII includes a "staging phase" in which any patient <22y at diagnosis with ependymoma is registered and stratified by age, tumour location and quality of the initial surgery. Centralized pathology and imaging reviews have been implemented at a national level for diagnosis confirmation and staging based on the presence of a possible tumour residue. According to the conclusions of this staging phase and on the suitability to receive radiotherapy, the SIOP EPII program proposes an inclusion in one of three randomised independent interventional studies. Patients ineligible for interventional strata are followed-up in an observational study. The staging phase aims to determine if central neurosurgical and radiological post-operative MRI reviews increase resection rate. Indeed, patients for whom the central radiological review evidences a tumor residue are proposed for a second-look surgery conducted either by the local surgeon or by a central surgeon from a panel of predefined expert neurosurgeons. (Figure 1.).

Patients ≥12 months with i) no significant residual disease and able to receive radiotherapy are randomly assigned in a phase III trial to evaluate the efficacy of post-radiation (focal 59.4 Gy) 16-week chemotherapy (VEC+CDDP) on Relapse-Free Survival (Stratum I); ii) centrally confirmed measurable inoperable residual disease are allocated to randomised frontline chemotherapy phase II study (VEC vs VEC+high-dose methotrexate) and considered for a second look surgery (stratum II). In case of persistent significant tumour residue despite possible second surgery, patients receive an additional 8 Gy radiotherapy boost after focal radiotherapy. iii) Patients <12 months (18 months in UK) or not eligible to receive radiotherapy are randomised in a phase II study to receive alternating blocks of myelosuppressive or not chemotherapy, with or without valproate used as histone deacetylase inhibitor (Stratum III). Secondary outcomes include overall survival, quality of life, neuropsychological and neuroendocrine outcomes, safety, and an integrated biological study aiming to identify key prognostic biomarkers (BIOMECA).

This program emphasizes the current development of central expertise and the need for an improved access to international experts (e.g. European reference network (ERN) and more specifically in paediatrics ERN PaedCan (<https://paedcan.ern-net.eu/home/about-ern-paedcan/>)).

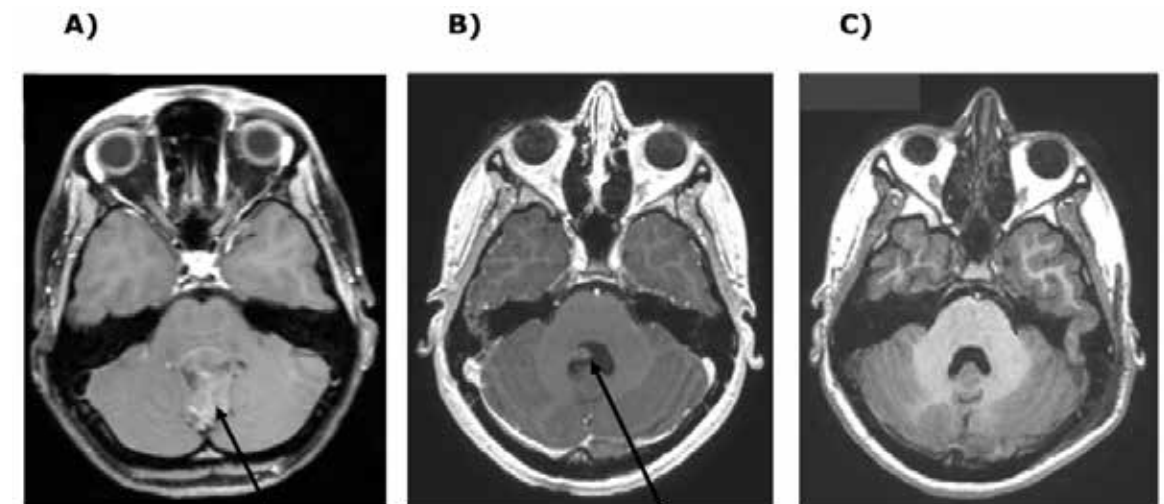


Figure 1. Imaging of one patient with ependymoma, at different time. A) At diagnosis, Preoperative MRI showing a tumour in the 4<sup>th</sup> ventricle. B) Immediate post-operative imaging (axial T1-weight with Gadolinium) showing a significant tumour residue. C) Post-operative imaging after second look surgery, no residual tumour.

As of Oct 31st 2021, 600 patients have been registered in the staging phase, including 321 in the interventional strata (Stratum I: 236/320; Stratum II: 37/60; Stratum III: 48/100) and 217 in the observational study.

Results from SIOP Ependymoma II program are highly expected to provide new insights in the treatment of patients with ependymoma. Indeed, preliminary results from the American Clinical Neurophysiology Society (ACNS) 0831 trial recently suggested a clinical benefit combining radiotherapy and chemotherapy in children older than 1 year following a complete resection.

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## University Cancer Center Frankfurt (UTC)



### Interdisciplinary patient care, translational and clinical cancer research, education and outreach networks for all cancer patients in Hessen

**Stefanie Graf<sup>1</sup>, Felicitas Cremer<sup>2</sup>, Christian Brandts<sup>3</sup>**

1. University Hospital Frankfurt

2. Goethe University, Frankfurt,

3. University Cancer Center Frankfurt (UCT)

At first glance, Frankfurt and Marburg have little in common: here the densely populated urban area and there the large rural region. From the standpoint of their Comprehensive Cancer Centers (CCC), this is just one aspect of their complementarity. As part of a long-term strategic decision, both sites joined forces in 2019 and founded the University Cancer Center (UCT) Frankfurt-Marburg, underwent the international review process of the German Cancer Aid as a CCC consortium and are now one of 14 designated German “Oncology Centers of Excellence”.

The UCT Frankfurt received its first designation as an “Oncology Center of Excellence” by the German Cancer Aid in 2010, and has held this status ever since. As a matrix cancer center within the University Hospital Frankfurt and Northwest Hospital Frankfurt, ten multidisciplinary disease teams work together in tumor boards, establish patient pathways, consent standard operating procedures and regularly undergo extensive external accreditation processes. Furthermore, they coordinate research initiatives, their clinical trial portfolio, and education and training. Over the past 6 years, the CCCs in Frankfurt and Marburg have formed a large outreach network of regional hospitals and oncologists in private practice with the goal of offering cancer patients the best possible care close to their home. As a logical consequence of this productive collaboration, both sites decided to formalize their union with the foundation of the UCT Frankfurt-Marburg in 2019. The cancer center now combines three sites – the University Hospital Frankfurt, Northwest Hospital Frankfurt and the University Hospital Marburg – and is constantly improving multidisciplinary patient care, translational and clinical research, as well as their education and training programs.

In all these areas, the UCT Frankfurt-Marburg organizes and structures the cooperation of its sites by combining their complementary strengths and opportunities, thereby creating unique synergies. Importantly, the Marburg site brings specific expertise to the joint UCT Frankfurt-Marburg. This includes the Marburg Ion Beam Therapy Center offering proton and carbon ion radiotherapy, a fully staffed institute of human genetics with a focus on cancer predisposition syndromes, and a strong cancer research community around the Center for Tumor Biology and Immunology. As a result, the UCT Frankfurt-Marburg offers a full portfolio of high-quality diagnostics and treatment options for more than 35,000 cancer patients per year, with the most modern therapeutic methods in Germany, especially within the framework of clinical trials. Its patient-centered cancer care also features extensive supportive therapies to improve quality of life, including psychooncology and palliative care, social services, as well as sports therapy, music and art therapy.

Apart from patient care, the UCT Frankfurt-Marburg is deeply invested in basic, translational and clinical cancer research. It offers the research community an extensive biomaterial bank and access to a curated database of all cancer patients, covering all available clinical, laboratory and molecular data. Under the guiding principle “*turning molecular information into novel cancer therapies*”, scientists aim to identify novel biomarkers, understand the molecular causes of cancer, develop innovative preclinical models, develop novel cellular immunotherapies, perform academic drug development and initiate early phase I trials. As part of the ambitious outreach network, the UCT Frankfurt-Marburg anticipates to make use of the large population base within the larger Rhine-Main region for innovative phase II-III clinical trials, as well as to enhance early detection and prevention strategies.



A glimpse at the biobank of the German Breast Group (GBG), one of the largest breast cancer groups worldwide, in Marburg. © UCT Frankfurt-Marburg



Inside the Marburg Ion Beam Therapy Center © UCT Frankfurt-Marburg



## German Cancer Research Center (DKFZ)

Dr. Sibylle Kohlstädt

DKFZ Strategic Communication and Public Relations



Research at the German Cancer Research Center (DKFZ) covers the entire translational continuum from discovery of fundamental causes of cancer to the development of disruptive preventive, diagnostic, and therapeutic approaches, up to innovative clinical trials. DKFZ is one of the leading cancer centers worldwide and has particular strengths in the basic research areas stem cell research, neuro-oncology, cancer genomics, and tumor immunology.

Since its establishment, prevention research has been one of DKFZ's hallmarks. The best-known example is the work of Harald zur Hausen, whose research laid the foundation for the development of the vaccine against HPV-induced tumors, a contribution that was acknowledged by awarding the Nobel Prize in 2008. We are currently intensifying our activities in the areas of primary prevention and early detection with the establishment of the National Cancer Prevention Center (NCPC) which we founded together with German Cancer Aid. NCPC will not only conduct outstanding research, but also pursue an integrated strategy to maximize its impact on cancer care.

The heart of the NCPC will be a Prevention Outpatient Research Clinic that will advise citizens and enroll patients in experimental trials and prospective cohorts. Research activities will be accompanied by innovative education programs. The Prevention Outpatient Research Clinic will be established and further developed in Heidelberg and then jointly expanded into other sites with the Deutsche Krebshilfe and other partners.

DKFZ has built a unique portfolio of preclinical and clinical imaging technologies, including emerging technologies such as photon counting CT or ultra high field MR imaging. In parallel, we are driving the development and validation of AI based methods for the analysis of radiological data. Key achievements in radiopharmaceutical sciences include the development of the first-in-class-tracer PSMA 617 for radioligand therapy of prostate cancer.

DKFZ takes an integrative approach to research and combat of infection- and inflammation-related cancers that is unique and sets DKFZ apart from other cancer research centers worldwide. While fundamental studies on oncopathogen-host interaction conducted at DKFZ have deciphered direct mechanisms of infection associated tumorigenesis, we now know that additional co-factors are required, the most important one being chronic inflammation giving rise to a mutagenic microenvironment.

DKFZ has developed a strong translational pipeline to develop prophylactic strategies to prevent infections with oncopathogens and therapeutic concepts to eliminate persistent oncogenic infections. Prime examples are an improved HPV vaccine allowing vaccination in low-income countries, our contributions to the development of a curative antiviral therapy for HPC infection, and of a novel therapeutic vaccine against HPV induced cancers. DKFZ has launched several investigator-initiated trials for tumor therapy based on oncolytic parvovirus and measles virus vectors.

In the field of precision oncology, DKFZ combines cutting-edge multi-omic experimental and computational approaches to develop new discovery and clinical platforms and to initiate innovative clinical trials, thus improving early detection and treatment of cancer.

To fully exploit the potential of identifying novel genetic factors involved in cancer, DKFZ is conducting several precision oncology trials that are internationally regarded as highly competitive (i.e. CATCH, RECOGNITION, MASTER, N2M2). One of these, INFORM (INdividualized Therapy FOr Relapsed Malignancies in Childhood), is the largest transnational genome sequencing program for children with cancer in Europe, with the aim to identify molecular targets that may open up new treatment options for children with relapsed cancers.

With its translational research, DKFZ is active nationwide in Germany: We jointly conduct research in the field of precision oncology with our distinctive clinical partner sites, which we have established with leading University Medical Centers: The National Centers of Tumor Diseases (NCT), the German Cancer Consortium DKTK, the Hopp Children's Cancer Center, the Helmholtz-Institute HI-TRON and the DKFZ-HECTOR Cancer Institute.

The DKFZ's Cancer Information Service is also active throughout Germany. The service provides cancer information for patients, their families, the general public, and health care professionals. The information is free of charge, independent, and up-to-date with the latest scientific findings.

## RE Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology (IEPOR)



of National Academy of Sciences of Ukraine

### Innovative cancer research for good medical practice

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Design of approaches to individualization of cancer patients' treatment based on relationship tumor-organism is the priority research area of RE Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology of National Academy of Sciences of Ukraine (IEPOR). Comprehensive long-term studies using experimental systems in vitro, in vivo, as well as ex vivo on clinical material allowed to discover additional mechanisms of tumor growth, to identify metabolic, molecular, genetic and epigenetic criteria of heterogeneity associated with the malignant tumors' development and progression at system level. We select 2 most innovative IEPOR designs aimed at improving the cancer patients' diagnosis, treatment; proposed for implementation in cancer centers; and have high investment potential.

1. We designed panels of prognostic and predictive nontumoral biomarkers of the most common malignant neoplasms as innovative strategy for personalized cancer course monitoring. The technology is basing on studying the profile of highly sensitive, tissue-specific epigenetic tumor markers – circulating miRNAs. The approach provides rapid non-invasive prediction of effectiveness and sensitivity of the recommended neo- and adjuvant chemotherapy regimens; identify patients at high risk of tumor progression that allows timely treatment regimens' correction and outcomes' improvement. The results of clinical validation and implementation of the developed strategy in leading cancer centers of Ukraine indicate its use advisability for predictive prognosis for the most common cancers.

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2. Our research activities also cover the novel treatment programs' design, especially those based on innovative nanotechnologies principles, including creation nanocomposite (NC) as vector systems for therapeutic agents' targeted delivery to increase the chemotherapy effectiveness. We developed the technology for obtaining antitumor ferromagnetic NC of new generation "Фероплат™ (Feroplat)" – the conjugate of nanoparticles of magnetic fluid with cisplatin. This is the tool for targeted delivery of cytostatics directly to tumor tissue, which ensures its maximum entry into cells and enhances the therapeutic effect. There are no analogues of this design. According to the Ukrainian legislation on preclinical studies, we developed methods for analyzing NC quality, conducted research on its characteristics, stability, and drew up laboratory regulations for its production. Now it is ready for clinical trials. Pharmacology of NC safety, evaluation of its toxicity and specific antitumor activity against solid tumors of different histogenesis indicate its significant pharmacological advantages over the official form of cisplatin and less toxicity to normal cells that opens the prospect for increasing the selectivity of its action and overcoming chemoresistance.

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Following the launch of Ireland's 'Cancer Strategy 2017 – 2026'; increasing focus has been placed upon cancer patient pathways and the importance of nursing competence within such pathways. Within the Trinity St. James's Cancer Institute (TSJCI) the utilisation of 'career pathways' enable registered nurses to pursue and develop specialist competencies and qualifications in a structured format. A defined career pathway with established goals and opportunities enhances competencies to advance within career development, coupled with a focus on maintaining a highly qualified and motivated nursing team.

In April 2019, nursing was acknowledged as 'exemplary' during an OECl site visit, and the TSJCI was accredited as a designated cancer centre. This achievement has emboldened the nursing team to pursue endless strides towards nursing excellence and innovation.

A dual ethos of 'patient first' and 'patient-centred care' exists within the Institute, and the OECl pillars of Education, Clinical Trials, Research, Clinical Care and Consistent quality improvement are key. We are also working-towards the accreditation of a "Magnet 4 Europe" status, to echo and reinforce our steadfast commitment to OECl standards and continuous quality improvement.

Our 'Cancer Nursing Council' convenes on a monthly basis, and membership encompasses medical oncology, haematology, cancer surgery and radiation nursing from across the TSJCI. On a monthly basis, a nominated speaker delivers a presentation on a topic deemed of relevance to the TSJCI – the purpose being for information sharing and lessons learnt. Research is encouraged within the Cancer Nursing Council and it engages with multiple higher education Institutes to facilitate and initiate cancer nursing research. In addition, the cancer nursing membership are regularly invited to present at national and international cancer nursing fora, and utilise oral and poster presentations. As part of our cancer nursing team health prevention, promotion and cancer awareness initiatives for patients, staff and public are provided with relevant literature and guidance on cancer care and prevention.

An additional pillar of our nursing success in TSJCI is education. It is deemed as key in motivating, recruiting and retaining staff within cancer care. We deliver a diverse and relevant training portfolio which includes but is not limited to;

- 'Cancer Care & Haematology Foundation Course', accredited by both Trinity College Dublin and the Nursing Midwifery Board of Ireland (NMBI), is offered nationally and is instrumental towards ensuring that the care provided to haematology/oncology patients is standardised to a high-quality level. Students are assessed through scenario simulations, in collaboration with the Trinity School of Nursing & Midwifery.
- 'Fundamentals in Cancer Surgery' programme – Pilot education programme in November 2021 the first of its kind in Ireland.
- Post Graduate Diplomas are achieved by many of our cancer nursing staff.
- There has been an increase in cancer nurses undertaking Masters Programmes.
- As CAR-T Cell therapy services will be offered to haematology patients by year-end 2021, the development of a nurse's education pathway has been undertaken by the Haematology Oncology nursing team in collaboration with the Trinity College Nursing and Midwifery department.

While such achievements and collaborative initiatives/projects are laudable - the wellbeing of staff working with cancer patients is paramount. We have navigated through the past two years of the COVID-19 pandemic and its' many challenges, and the health and well-being requirements and support tools for staff are key. Nurses can also avail of our employment assistance programme which augments our in-house support capabilities. We initiate regular education and well-being sessions (facilitated by

a Psychologist from our Psychological Oncology service), and work with creative and artistic supports on-site within the TSJCI.

Collaboration and quality care delivery remain at the forefront of all we do within nursing at the TSJCI. These aims have been attainable and constant thanks to the tools and motivation which we have been afforded by the OECl and its accreditation program.



*We take pride in our daily provision of nursing excellence at TSJCI. We always place our patients first.*



# IEO European Institute of Oncologia

## COVID-19, a new challenge on the management of clinical trials at the European Institute of Oncology

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The COVID-19 pandemic has significantly impacted all aspects of clinical care, including cancer clinical trials. During this global health emergency, providing care to patients, particularly oncological patients, has been extremely challenging. Cancer patients have a higher risk of morbidity and mortality than the general population<sup>1, 2</sup>. Therefore, the oncological community has faced many difficulties regarding the management of oncological patients and cancer treatments with respect to the risk of exposure to Sars-CoV-2.

Healthcare facilities had to prepare, adapt and transform in a short time in order to minimize the risk of COVID-19 infection<sup>3</sup>. COVID-19 and the contingency measures taken to preserve and protect patient safety inevitably impacted also on clinical trials and their conduct. In oncology, clinical trials represent a fundamental component of modern practice, providing the crucial evidence to evaluate the efficacy of new therapies<sup>4</sup>.

This paper aim is to examine the experience of the European Institute of Oncology (IEO) in Milan, Italy, regarding the management of clinical trials and activities during COVID-19 pandemic. The IEO is a comprehensive cancer center, where health care of oncological patients also involves clinical research. The Institute is very structured and well-organized. A Clinical Trial Office (CTO) composed of a study coordinator, study nurse, and data entry operator manages the clinical trials operations from their activation to their closure, passing through all the activities in between.

The Institute implemented several strategies from the restrictions suggested by the WHO guidelines regarding sanitation and disinfection<sup>5</sup> to the provisions set out by the European Medicines Agency (EMA) on the Guidance on the management of clinical trials during the COVID-19 (coronavirus) pandemic, such as telemedicine and delivery of investigational products<sup>6</sup>.

According to these rules, at the European Institute of Oncology, patients wearing masks can gain entry to the Institute only after hand sanitation, and body temperature detection through a thermo-scanner. Entrance is limited only to patients. The caregiver must wait outside the hospital, except in the case of patients who are unable to move without assistance<sup>7, 8</sup>. The Institute created the Family Board system that allows the caregiver and family members to follow the patient path in real time from the operating room to his/her return to the ward. This service guarantees patient privacy, since the access is granted only through a personal PIN that the patient receives on confirmation of admission to the IEO.

Cancer patients eligible to undergo treatments in the ward itself are allowed into our facility only after a COVID-19 negative swab.

Cancer outpatients can gain access to the IEO only after a phone call on the previous day in order to assess their conditions and any symptoms that may lead to a suspect COVID-19 infection.

For patient in follow up with no critical symptoms, on the other hand, hospital visits were postponed or converted to remote visits (eg, telemedicine or phone consultation) in order to reduce the number and duration of the on-site visits. Several facilities reported equivalent experiences<sup>7, 9, 10, 11</sup>.

Cancer patients who cannot return to the hospital due to Travel restrictions or quarantine measures are able to have remote visits as is the case in several hospital around the world<sup>7, 10, 11, 12</sup>.

Telemedicine was also used to assess patient conditions the day before therapy, or to evaluate

possible adverse events resulting from treatment<sup>7</sup>. Telephone triage procedures became a reality not only for our Institute, but also for other facilities, such as the Comprehensive Cancer Center in San Francisco. They developed a tool that included the most common signs and symptoms of COVID-19, questions about risk factors and exposure to COVID-19 positive individuals, the assessment of medical conditions, and treatment status<sup>13</sup>.

At the Institute, remote visits are associated with the possibility to perform laboratory analysis and imaging assessment in local facilities<sup>14</sup>. In addition, the laboratory reports can be emailed to the specialists at the IEO who can thus evaluate pre-treatment patient conditions, and establish whether or not to continue with the investigational product<sup>7</sup>.

Moreover, in response to the emergency, the EMA authorized hospitals according to the Sponsor and Ethical Committee to deliver Investigational Medicinal Products (IMPs) directly to the patient's home<sup>6</sup>. The EMA's decision was endorsed by the Italian Medicines Agency (AIFA), the European Society for medical oncology (ESMO) and the European Cancer Organisation<sup>15, 16</sup>.

The European Institute of Oncology in Milan in accordance with these measures produced its own standard operating procedures for home delivery of investigational medicinal products.

The procedure was applied particularly for oral drugs<sup>7</sup>. After a request to the sponsor and receiving the authorization, the study nurse can decide with the patients about the delivery. The data manager organizes the shipment in collaboration with the sponsor. Finally, the IMPs are delivered directly to the patient's residence, where under physician instruction, the patient can be easily treated, assuring therapy and reducing the risk of COVID infection that would otherwise arise from travel and access to public places.

At the Institute, medical practice is focused also on clinical trials. The activities related to trials were at no point suspended, including the enrollment. Based on data regarding the enrollment in clinical trials extracted from our internal database, over the past years (Fig. 1), we observed a constant increase of patients enrolled in clinical trials.

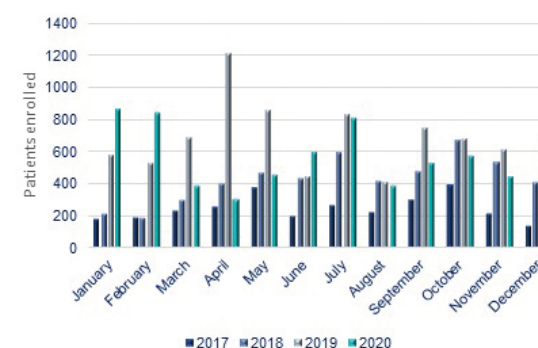


Figure 1a. IEO 2017-2020 enrollment trend per month

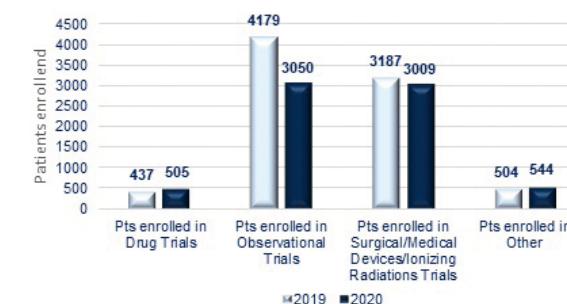


Figure 1b. IEO enrolled patients 2019 vs 2020

Figure 1a shows the enrollment trend per month in 2017-2020 period. Focusing on data from 2019 and 2020, we assessed that the enrollment trend follows exactly the pandemic spread course.

In January and February 2020, the enrollment was constantly growing with respect to the same months in 2019.

After the Italian outbreak at the end of February, the government established a hard lockdown from March to May 2020. For these months, the histogram chart shows a decline in enrollment. As of June 2020, the government has eased the lockdown measures in response to a decrease in the spread of the infection<sup>17</sup>. As a consequence, from June to August, the trend was better or in line with previous year's trend.

Afterwards, the enrollment started to decrease again, due to the worsening of the pandemic in the September-November period with the exception of December, which registered an increase in patient enrollment in clinical trials.



An overall perspective is given by Figure 1b, which show the variation in the number of ongoing trials and enrolled patients comparing 2019 and 2020 in its entirety. The enrollment in surgical/medical devices/ionizing radiations trials reached almost the level of the pre-Covid era. The number of enrolled patients in drug trials and other trials overcame the 2019 trend. Only the enrollment in observational trials showed a shrinkage of 37%. In our opinion, observation trials were perceived by patient as unessential.

In conclusion, The European Institute of Oncology during the outbreak managed to remain a COVID-free hub for oncological patients, by implementing several strategies. Patients who needed therapy necessitating ward admission could access the facility only after a negative swab, and patient who needed outpatient visits could access after a telephone triage carried the day before in order to assess potential COVID-19 symptoms. Conversely, follow-up visits were delayed where possible or converted to remote examinations during which physicians evaluated patient conditions on the basis of laboratory and imaging analyses that had been performed in facilities near the patient's residence. Remote visits thus became a very effective way to assess patient medical conditions and the efficacy of the investigational medicinal products. In cases where travel restrictions or quarantine measures prohibited patients from return to the site for visits, the Institute focused on the patient problem of IMP resupply. To resolve this, the oral IMP was couriered directly to the patient's home. Regarding the activities trial-related, they were at no point suspended, enrollment included. Despite several sponsors and institutions decided to put enrollment on hold<sup>18, 19</sup>, the IEO continued, because halting treatment would be even more dangerous for cancer patients<sup>20, 21, 22</sup>.

According to our data, the enrollment trend in 2020 represents perfectly the trend of the COVID-19

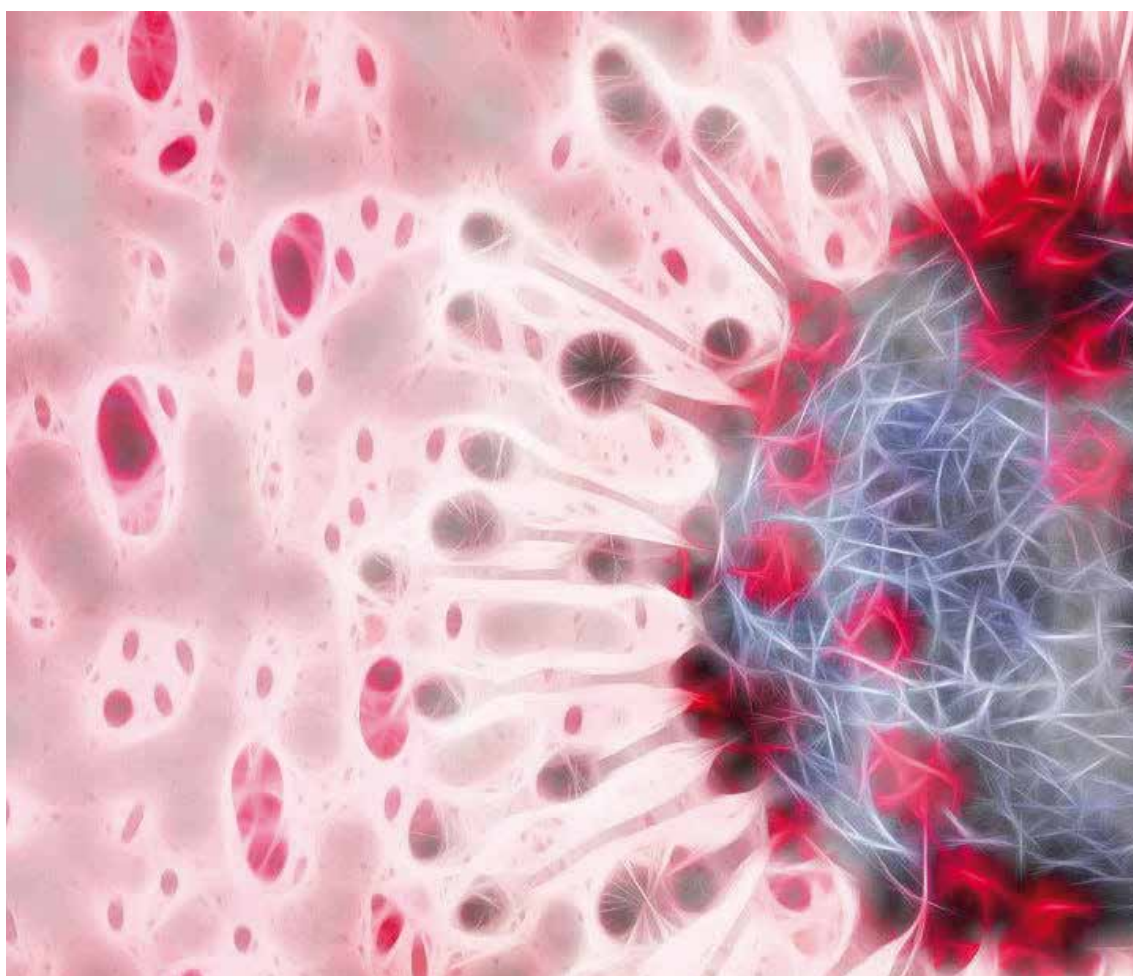
spread in Italy and the anti-contagion restriction established during the year.

The studies that experienced a decline during the covid period are the observational studies. Nevertheless, we observed that at the end of 2020 a positive trend was registered regarding the number of ongoing trials, patient enrollment in drug, surgical/medical devices/ionizing radiations, and other trials.

Therefore, the IEO proved that treatment of cancer patients can be guaranteed during a pandemic preserving the patient rights to the best care possible.

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# Humanitas Research Hospital



**A. Santoro<sup>1</sup>, R. Bui<sup>2</sup>, M. Lagioia<sup>3</sup>**

1. Cancer Center Director

2. Cancer Center Manager

3. Medical Director Humanitas Research Hospital

“Istituto Clinico Humanitas” is a highly specialized polyclinic hospital, with a level II DEA, recognized by the Ministry as an IRCCS. It is a center of clinical and scientific research, strongly integrated with the Humanitas University, in order to combine hospital activities with the training of new generations of professionals.

Humanitas Cancer Center, active since 2010, is a constantly growing reality. It counts 300 doctors, 200 nurses and healthcare professionals, 17 multidisciplinary groups. The strategic objectives are expressed in the **development of leadership at a national level** in pathways with high epidemiological incidence, achievement of **high standards of quality, clinical research**, improvement of **services to patients** also through **innovation** and **formation** of enhancement plans for **clinical talent**.

Humanitas Cancer Center stands out for:

– **Number of patients treated:** ranked among the top 5 Italian centers for volumes of oncological surgery, for all the pathologies with medium / high epidemiological incidence (e.g. Breast, Lung, Prostate, Colorectal, Brain, Liver, Pancreas). Between 2018 and 2019, the number of patients under treatment increased from 6500 to 7000. In 2019, 4300 patients have been treated with surgical interventions, 2100 patients with chemotherapy and 2900 with radiotherapy, registering an increase of 10% compared to previous years.

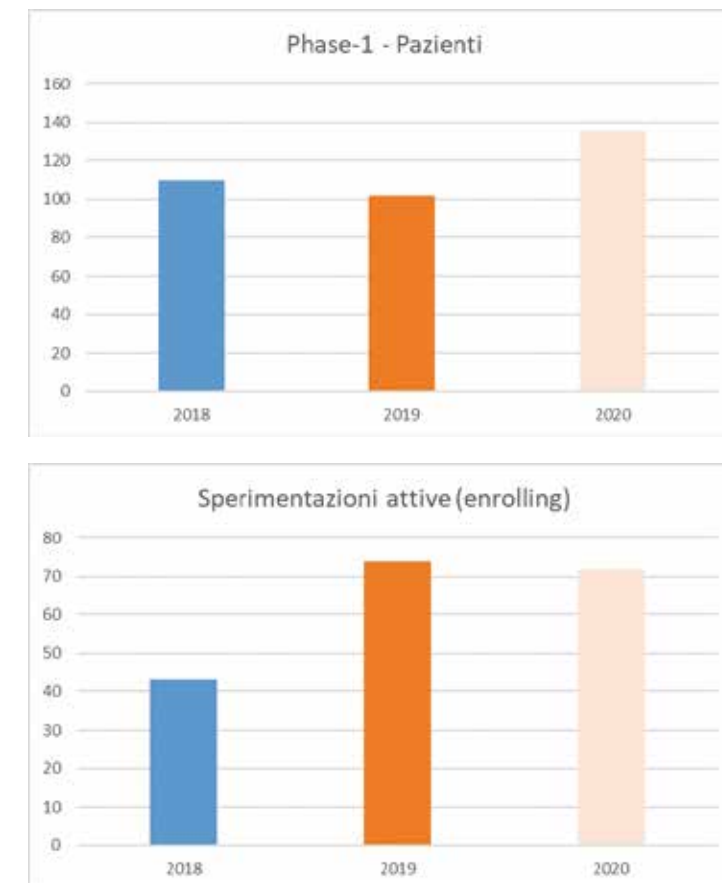
In 2020, during its most acute phases, the pandemic had a significant impact on the hospital. Despite this, the continuity of treatment was guaranteed by the Cancer Center. The activities of Chemotherapy, Research and Radiotherapy did not stop (instead recording a growth) as well as the oncological surgeries, to which priority was given, to guarantee access to treatment.

– **Clinical quality:** according to the National Outcomes Plan (PNE), coordinated by “AGENAS”, Humanitas Cancer Center is positioned in the top decile for all qualitative indicators monitored: mortality 30 days after surgery, re-operations after 120 days and readmission after 30 days.



Below it is represented the growth in recent years in terms of active trials and Phase-1 patients

– **Clinical research:** in order to ensure the best experimental therapies for patients, the increase in protocols and the number of patients to be enrolled is one of the strategic objectives. The activity is extended to most of the pathologies treated, recording a progressive growth in Phase-1 studies. Humanitas Cancer Center covers important positions in all the pathologies. In particular, is leader in Lung and Liver pathologies. Below it is represented the growth in recent years in terms of IF and number of jobs:



– **Multidimensional innovation:** several strategic investment choices have been implemented, aimed at developing distinctive skills and acquiring excellent technologies, such as:

**NGS:** the Ion Torrent Genexus integrated sequencer, active in Humanitas since January 2021, is the first next-generation sequencing solution that simplifies the workflow, automating preparation, sequencing and genetic analysis, allowing the identification of multiple types of Bio-markers, in 24 hours.

**CAR-T:** Humanitas is among the few Italian Centers active (since November 2019) in the treatment with CAR-T cells: an innovative therapy based on T lymphocytes and aimed at patients affected by diffuse large B cell lymphomas and primary mediastinal lymphomas unresponsive to conventional treatments or to patients with acute lymphoblastic leukemia.

**Phase-1 Unit:** Humanitas is an accredited center for the treatment of patients in Phase-1 experimental studies.

– **Integration with the university,** fostering synergies and allowing a direct transfer of skills, from Cancer Center professionals to Humanitas University students and a push towards Research.

At Humanitas Cancer Center, there are about 70 postgraduates, in a rotation program, from the University



## Istituto Tumori Giovanni Paolo II Istituto di Ricovero e Cura a Carattere Scientifico

### The Institutional Biobank

**G. Pelagio\***, **A. Tufaro\***, **G. De Palma\***, **R. Divella\***, **A. Sabatelli\***, **A. Paradiso\***

\* IRCCS Istituto Tumori Giovanni Paolo II Bari-Italy



The Institutional Biobank (BBI) at the “Giovanni Paolo II” Cancer Institute in Bari-Italy, an OECI accredited research Hospital, is an innovative state of the art and purpose-built biorepository and archiving facility that holds expertise and compliance to regulatory quality and audit standards, with full data management and sample retrieval to ensure the validity of research assets.

Built on a 250 square feet facility on two levels, it collects and stores biological material, such as urine, blood, tissue, cells, DNA, RNA, and protein, from cancer patients for use in research allowing to improve understanding of health and disease. At the present date more than 20.000 biological samples are currently stored in our Biobank.

Managed by the Biobank Director, under the supervision of an Institutional Technical Committee, it occupies 5 full time professionals that assure continuous monitoring and all activities regarding collection, handling, storage and distribution of high quality biological samples and related clinical data.

Every sample stored in the facility has patient consent and distribution is subject to approval by a Local Ethical Board.

The facility is divided in ground floor, where offices and labs are located, and a lower level storage room with quality controlled physical storage in 11 ultra low temperature mechanical freezers, 4 liquid nitrogen vapor storage tanks and a controlled rate freezer, with a liquid nitrogen emergency backup system that prevents sample damage in case of freezers mechanical failure, controlled by a remote real time monitoring system with alarms and alerts. Sample data is managed by a dedicated software application and sample status and general Biobank activities are reported every semester.

Quality is assured by updated Standard Operating Procedures in accordance to international recommendations (BBMRI) and ISO 9001:2015 certification has been obtained with regular internal and external audits, whereas, ISO 20387:2019 accreditation is ongoing.

More than three thousand biological sample have been distributed to researchers worldwide allowing to carry out numerous clinical trials and research projects within our Institute and in external institutions.



## Ospedale San Raffaele (OSR)



OSPEDALE SAN RAFFAELE

**Alberto Briganti<sup>1</sup>**, **Stefania Biondo<sup>1</sup>**, **Eleonora Bossi<sup>1</sup>**, **Alessandra Bulotta<sup>1</sup>**, **Stefano Cascinu<sup>1</sup>**, **Consuelo Corti<sup>1</sup>**, **Michele Reni<sup>1</sup>**, **Anna Maria Rossetti<sup>1</sup>**

<sup>1</sup>. IRCCS Ospedale San Raffaele

The Cancer Center (CC) of the IRCCS Ospedale San Raffaele has been formally established in 2021 aimed at promoting synergies and communication between Research and Clinical activities in Oncology as well as at ensuring equal, standardized and high quality access to cancer patients while pursuing advances in patient outcomes and quality of life. The CC takes advantage of several available infrastructures and facilities available at IRCCS Ospedale San Raffaele which represent key factors in management of patients with cancer. Main strengths of our CC include: 1. Availabilities of state of the art facilities for patients with cancer 2. Research activities and clinical trials, clinical network and patient involvement 3. Education.

### 1. Availability of state of the art facilities for patients with cancer

The IRCCS Ospedale San Raffaele is fully equipped with state of the art facilities for the treatment of patients with oncological diseases, including PET/CTs and PET/MRIs, Center for Omics sciences, Biobanks, Experimental Imaging, Advanced Technology Health and well-being. These facilities allow for a comprehensive assessment of patients with cancers from diagnosis to treatment and follow-up.

### 2. Research activities and clinical trials, clinical network and patient involvement

In 2020 our research Institute has been involved in 50 national and international granted projects and 525 peer reviewed manuscripts were published (IF 4290,576). Overall, 258 clinical, patient-oriented trials have been conducted in oncological and onco-ematological patients, including Phase 1 studies. The clinical research activities are fully supported and coordinated by the Clinical Trial Center (CTC) which is dedicated to supporting clinical researchers in designing and carrying out high-quality clinical trials. CTC helps promote innovative research that will lead to new medical advances, improving health around the world. The CTC also functions as a liaison between researchers, funding agencies, regulatory agencies, and CROs. Moreover, the research infrastructures of our IRCCS include Divisions, Institutes and Centers focusing also on cancer research. Finally, the IRCCS Ospedale San Raffaele is fully involved and member of esteemed cancer networks including the Michelangelo Foundation for cooperative studies in breast cancer, EORTC, ARCAD group, Italian Alliance Against Cancer, AISP, IMI, GISCAD.

### 3. Education

Since its foundation in 1998, the Faculty of Medicine and Surgery of the Vita-Salute San Raffaele University (UniSR) has grown to become a vital part of the IRCCS Ospedale San Raffaele healthcare and research system. UniSR offers an International Medical Doctor (IMD) Program and the Residency in Medical Oncology. Moreover, UniSR which is currently top-ranked among Universities in Italy, offers a PhD course in Molecular Medicine aimed to provide excellent guidance, support and training to graduate students interested in understanding the molecular processes underlying human diseases and in designing new approaches for their treatment. The PhD program operates within IRCCS Ospedale San Raffaele, enabling the students to do their practical training in the hospital facilities. The PhD course is split into four main research Curricula including Basic and Applied Immunology and Oncology.

# Vall d'Hebron Barcelona Hospital Campus



## Research at VHIO-VHIR-HUVH: translation towards precision oncology

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1. Vall d'Hebron Institute of Oncology (VHIO)

2. Vall d'Hebron University Hospital; Vall d'Hebron Hospital Campus, Barcelona, Spain

If a picture is worth a thousand words, the rapidly emerging landscape of precision medicine paints entire chapters, particularly in oncology. With the irrepressible explosion of novel data, the rapid advancements in novel genomic technologies as well as exciting treatment modalities, the promise that lies ahead cannot be summarized in so few words! Importantly, such progress can only be translated into real benefit for cancer patients within an environment that provides the appropriate infrastructure, combined expertise, essential interconnectivity and cross talk between all specialists en force.

The Vall d'Hebron Barcelona Hospital Campus represents a hotbed and hub of biomedical research of excellence, with translational science at its core. The Vall d'Hebron University Hospital (HUVH), is flanked by two research institutes of international reference; the Vall d'Hebron Institute of Research (VHIR), and the Vall d'Hebron Institute of Oncology (VHIO). Our Hospital affords our investigators direct access to patients as well as the entire spectrum of healthcare professionals who care for them. This privileged environment promotes the swift translation of scientific discovery into benefits for patients in the clinic, with the oncology field as a forerunner in precision medicine.

Located mere meters away from HUVH, VHIO's CELLEX Building is home to our cancer researchers who closely collaborate and interact with Vall d'Hebron's physician-scientists and expert healthcare teams. Translational science and clinical research are therefore tightly connected which promotes interaction and teamwork which, in turn, accelerates advances in oncology.

Founded back in 2006 VHIO was created to champion a purely translational, multidisciplinary cancer research model. The dual set up of the Medical Oncology Department at Vall d'Hebron and VHIO facilitated the integration of patient care within a unique program where optimal cancer treatment is conciliated with innovative translational research. Aimed at dynamically transforming discovery into clinical benefits for patients, this purely translational approach continues to be at the very heart of VHIO's philosophy. Our Institute's multidisciplinary teams, including clinicians and investigators at Vall d'Hebron's Medical Oncology Department, seamlessly bridge preclinical and clinical research in order to foster a continuous virtuous cycle of knowledge from bench to bedside and back.

In the current era of precision medicine, the translational approach is nothing new and clearly facilitates the detailed and direct study of each patient and each tumor. This successful model of marrying excellence in clinical practice with applied research has since been adopted by many other hospitals in Spain and around the world.

By embracing a more comprehensive approach to combating cancer, VHIO has been able to develop its multidisciplinary cancer teams to ensure patients are cared for by as many different specialties as required for their particular type of disease including surgeons, medical oncologists, radiation oncologists, radiologists, pathologists, psychiatrists, other medical specialists and nurses. The privileged environment of our Hospital affords VHIO direct access to patients as well as the entire spectrum of oncology professionals who care for them, as well as a second-to-none appreciation of how cancer science can translate into more powerful, targeted treatments and better practice for the care of patients.

But it's not just about location or ambience. In addition to the collaborative, multispecialty mindset of Vall d'Hebron and VHIO teams, our cutting-edge programs, facilities and technologies also drive improved survival and quality of life for cancer patients today, and in so doing turn research into more effective, personalized treatments and better practice for the future.

### Driving drug development and targeted therapies against cancer

VHIO-HUVH continues to establish itself as a leading reference in advancing drug development and targeted therapies against cancer. Our Research Unit for Molecular Therapy of Cancer (UITM) – CaixaResearch, is located at the very heart of our Hospital. Founded in 2010 this Unit has rapidly become one of the few comprehensive facilities in Europe to translate discovery into improved outcomes for patients.

With a large portfolio of novel targeted agents against most tumor types, this early phase facility tightly connects Vall d'Hebron's healthcare professionals, VHIO researchers and clinical investigators, to identify novel predictive markers of response to anti-cancer therapies and markers of primary resistance (de novo) and secondary treatment. Further, in order to align the identification of the right therapy to the right patient, our array of preclinical cancer models have been developed to test new anti-cancer therapies, diagnostic and prognostic tools. These studies are not only critical in the design of novel strategies and approaches against cancer but also provide deeper insights into the mechanisms that trigger cancer and enable its resistance to current therapies, progression and spread.

Conducting complex clinical trials with drugs in early development (Phase I and early Phase II), focused on novel targets, clinical research at this Unit is linked with the different research areas carried out by various VHIO preclinical and translation groups. This synergy is key to connecting molecular biology and the best tumor models with pharmacology and innovative clinical science. Driven by our Early Clinical Drug Development Group, research focuses on the development of novel agents based on tumor molecular profile as well as the optimization of therapies using combinations of new drugs with existing ones.

### On target

These efforts have contributed to the development of several targeted agents including trastuzumab, pertuzumab, cetuximab, panitumumab, ramucirumab, trifluridine/tipiracil, gefitinib, osimertinib, ceritinib, crizotinib, loratinib and everolimus, among others. As a direct result of the Unit's clinical studies since 2012, the FDA has approved over 30 new therapies against several tumor types, which are becoming increasingly more targeted thanks to cancer discovery driven by precision medicine in oncology.

Notably, throughout 2020 and during the COVID-19 pandemic peaks, the Unit led 195 ongoing phase I plus Basket clinical trials. It is thanks to the dedication of the expert professionals across VHIO's Transversal Clinical Trials Core Services and Units, including Vall d'Hebron's clinical research oncology nurses, that despite the challenges posed by COVID-19, activity was successfully maintained, and in some instances even surpassed, in order to respond to the needs of our patients.

### Spearheading next generation clinical trials in oncology

The advent of novel, adaptive clinical studies including the so-called basket and umbrella clinical trials, among others, aim to address the current challenges in oncology including the globalization of clinical research, and the use and implementation of emerging health technologies. While randomized controlled trials are considered the gold standard for studying the efficacy of treatment approaches and anti-cancer therapies, they do not allow for the 'real time' and necessary adaptation in tune with the rapid pace of cancer discovery – especially in the academic setting.

To overcome this challenge, VHIO-HUVH investigators at the same Unit pioneer novel clinical trial designs that promote the optimization of biomarker-drug co-development towards more precisely tailoring therapies to each disease setting, each individual patient. In short, these 'smarter' contenders seek to more effectively identify the optimal treatment for the right patient, at the right time, and promise to overcome the rigidity and limitations of traditional clinical trials.

Our teams also advance multi-modular studies in oncology through their (co) leadership of/participation in European and international consortia and projects of excellence. Alongside researchers from other comprehensive cancer research centers, these efforts have led to more dynamic, 'responsive' clinical study designs matched to the molecular makeup of individual patients' tumors.



### Multi-center consortia & cross border collaboration of excellence

VHIO is dedicated to forming, fostering and developing strong, multi-center partnerships globally. These essential collaborations combine the necessary expertise and pooled resources to more rapidly advance cancer discovery, improve outcomes for cancer patients, and avoid costly duplication of efforts.

These projects aim at driving important improvements in the treatment and care of our patients. Two illustrative examples are the WIN - Worldwide Innovative Networking in personalized cancer medicine Consortium and its first WINTHER clinical trial, coordinated by VHIO, and the ongoing studies led by our Institute in collaboration with other investigators belonging to Cancer Core Europe (CCE).

The WIN Consortium, initiated by Gustave Roussy Cancer Campus Grand Paris (Villejuif, France) and The University of Texas, MD Anderson Cancer Center (Houston, USA) is a non-profit, non-governmental organization incorporating 39 leading organizations, including VHIO, which collectively represent all stakeholders in personalized cancer medicine. Covering 21 countries and 4 continents, the partners are united by their vision to deliver on the promise of effective, personalized cancer medicine to patients worldwide.

WIN members collaboratively design and carry out global studies designed to achieve breakthroughs for cancer patients across the globe. In 2019, the eagerly anticipated results of the WINTHER Consortium's first clinical trial, Genomic and transcriptomic profiling expands precision medicine, were published (Rodon et al. Nat Med. 2019). Findings showed that RNA profiling together with DNA testing matches more patients with advanced cancer to personalized anti-cancer therapies than DNA profiling for tumor mutations alone.

Coordinated by researchers of our early phase UITM-CaixaResearch Unit, the WINTHER investigators reported that patients treated with a drug or regimen more closely matched to the molecular profile of their respective tumors, do better. By assessing RNA as an important adjunct to DNA profiling for determining precision treatments, this study rang in a new era for clinical trial design and personalized medicine in oncology.

Cancer Core Europe (CCE) is a unique partnership aimed at addressing the cancer care research continuum. This working consortium represents a critical mass of activity for the successful exchange integration of all cancer care information, clinical research and outcome research, led by 7 partners and European comprehensive cancer centers of excellence: the Gustave Roussy Cancer Campus Grand Paris (Villejuif, France), Cambridge Cancer Centre (Cambridge, UK), Karolinska Institute (Stockholm, Sweden), Netherlands Cancer Institute – NKI (Amsterdam, The Netherlands), National Center for Tumor Diseases – DKFZ-NCT (Heidelberg, Germany), The National Cancer Institute of Milan (Italy), and VHIO.

Endorsed by CCE and led by our VHIO-HUVH investigators, the Basket of Baskets (BoB) two-stage clinical trial study steps up as a more flexible and adaptive model in order to significantly accelerate patients' access to an array of novel therapeutics. As the first European multi-modular academic trial, BoB integrates molecular prescreening, the development of novel diagnostic tests including ctDNA, with the assessment of targeted therapies matched to those patients who will be most likely to benefit from them.

BoB is divided into two separate parts: advanced molecular diagnosis or screening, i-Profiler, and the therapeutic phase, i-Basket. First, patient tumor samples are analyzed for genetic profiling to identify the specific alterations of each individual tumor, followed by bioinformatics analyses to gauge the clinical relevance of a particular treatment tailored to these alterations, with the option of adding extra modules with other anti-cancer medicines currently under development.

Patients identified with the alteration/s included in BoB's i-Basket, and who meet the inclusion criteria, enter the second part. Each module focuses on a different treatment (either as monotherapy or in combination), and has a different sponsor/coordinator.

Building on the BoB adaptive trial, the EU-funded Cancer Core Europe Consortium-Building Data Rich Clinical Trials (CCE-DART), recently launched. Coordinated by VHIO, and carried out in collaboration with other leading experts belonging to CCE, this project harnesses and incorporates powerful cutting-edge technologies, methods and platforms to design and develop the next generation of data rich, dynamic studies in oncology.

CCE-DART will further enhance BoB's harmonized, molecular multi-tier profiling platform to more precisely match patients to novel anti-cancer medicines based on the genetic specificities of their individual tumors. In parallel, the researchers will continue to develop multiple treatments in genomically-selected populations.

Just like many of our other research endeavors and activities, without our direct access to cancer patients at Vall d'Hebron these pioneering studies would simply not be possible.

### The development & application of empowering platforms and technologies

At the core of VHIO's research activities are its cutting-edge core technology platforms for the application of next-generation whole-genome sequencing in precision oncology. By sequencing panels of genes or entire genomes in cancer patients, we are now better equipped than ever before to identify specific molecular risk factors and better predict the potential efficacy of specific agents matched to the molecular specificities of individual patients' tumors.

### Molecular profiling & personalized cancer treatment

Our Molecular Prescreening Program, which is powered by one of our Institutional Programs, the FERO Foundation's Institutional Advanced Molecular Diagnostics Program (DIAMAV), catalyzes precision medicine at VHIO. Over the past decade, our molecular prescreening has provided access to advanced molecular diagnostics to more than 5,000 patients, and is critical in matching targeted therapeutic approaches with hundreds of clinical trial opportunities.

This program also counts on the expertise provided through our early phase clinical trials Unit. Representing a key driver of clinical-molecular correlative research at VHIO-HUVH, this program includes different teams like Oncology Data Science ODysSey Group, the Cancer Genomics Group, the Molecular Oncology Group and the Early Clinical Drug Development Group, among others. The team regularly convenes to explore existing molecular tests developed in-house, and novel biomarkers of potential interest for future inclusion.

In addition, our cancer researchers and genomicists participate in weekly tumor board meetings with HUVH's medical oncologists to provide guidance on the interpretation of NGS results as well as discuss new markers for clinical testing in patients eligible for inclusion in our early phase clinical studies.

These teams collaborate together to perform molecular profiling in up to 1500 patients each year, establishing VHIO as one of the few centers in Europe to run such a comprehensive program.

These efforts are also extended to an increasing number of patients through collaborations with other centers, across borders. As an example, we participate as partner in the American Association for Cancer Research's (AACR) Project Genomics Evidence Neoplasia Information Exchange (GENIE).

### Generating novel insights into the mechanisms of resistance & response to immune-based therapies

The relatively recent emergence of immune-based therapies against cancer should be rightly celebrated, but much work still needs to be done to better predict those patients who would most likely benefit from them, extend their early promise to more patients as well as tumor types (either as monotherapy or, most likely, in combination), and tackle important concerns regarding safety and toxicity.

This will only happen by further potentiating and personalizing this anti-cancer armory to successfully unleash the power of the immune system in a greater number of individuals to attack disease. Our investigators work together to deliver the robust immune data required to better guide treatment decisions that benefit all patients and not just the so-called 'super-responders'.

Supported by the BBVA Foundation, VHIO's Comprehensive Program of Cancer Immunotherapy & Immunology (CAIMI), centers on advancing research into the natural mechanisms governing how T lymphocytes react to cancer and how to use these antitumor responses to develop more personalized and potent immune-based therapies and treatment strategies.

Representing an important forward step in advancing agents that inhibit checkpoint regulation of the

immune system, this program aims at achieving a deeper understanding of mechanisms of resistance and response to these therapies, and prioritizes the early clinical drug development of those treatments and combinations that show most promise.

Over the past years, CAIMI has enabled the development of various translational projects linked to the early clinical development phases of immunotherapy. Just some focus areas include the development of cell-based therapies such as killer T cells for non-responders to current immunotherapies, characterizing hyperprogressive disease with immunotherapy to advance insights into this phenomenon, as well as establishing a radiomic signature to predict response to immunotherapy, led by the investigators at the Radiomics Group). This team is now exploring how this correlates with the genomic evolution in patients.

These groups have also worked together to finalize the clinical grade validations of tumor-infiltrating lymphocytes expansion for the treatment of certain cancer patients at Vall d'Hebron. Most recently, these groups filed an investigational new drug (IND) application to the AEMPS Spanish Regulatory Agency towards treating patients with metastatic epithelial or immunotherapy refractory tumors with neoantigen-reactive TILs. By enriching for neoantigen-reactive lymphocytes, the aim is to fortify the efficacy of TIL therapy in epithelial cancers.

### Where to next?

Translational oncology undoubtedly continues to mark many important milestones and celebrate significant progress towards solving cancer sooner, but the vast complexity and heterogeneity of this disease still represents a major challenge.

While the quality and depth of today's research is certainly reducing the serendipity of cancer science, the oncology research community should continue to raise the bar in its ambitions. Only then will we collectively be able to better validate markers, unravel the vast amount of genetic and pathway data to apply it clinically: the acme in advancing personalized and targeted therapies against cancer for the benefit of our patients today, the future of those tomorrow.

In parallel, cancer treatment and care can will only continue to more rapidly advance through the equal involvement and cross-talk between all oncology professionals from different specialties as dynamic, multidisciplinary cancer teams within a setting that provides the appropriate infrastructure, expertise, and interconnectivity.

At VHIO we consider ourselves very fortunate. Our Vall d'Hebron University Hospital provides us with the ideal environment through which to foster, nurture and promote such essential collaboration. As importantly, we join forces together in applying the same dedication and fight in beating cancer.



## Biomedical Research Center of the Slovak Academy of Sciences



**Miroslav Chovanec**, Scientific Director

Cancer Research Institute, as a part of the Biomedical Research Center of the Slovak Academy of Sciences, conducts cancer research in a complex and multidisciplinary way. State-of-the-art methodologies of cancer research are well-established and routinely used at the Institute. Our Institute consists of five departments, each having an expertise in the particular field of cancer research, supported by the corresponding infrastructure.

Department of Genetics studies DNA damage types and repair mechanisms that play a crucial role in cancer development and progression, as well as in cancer treatment response. OMICS data are the basis for identification of biomarkers that are able to stratify urogenital cancer patients in terms of predicting their prognosis. Cell lines derived from these cancer types with a wide range of sensitivity to chemotherapeutics are used to identify and verify these biomarkers and clinical samples are utilized to validate their clinical applicability. Epigenetic alterations in endometrial and breast cancer, and the role of gut microbiome in cancer development and treatment are also studied at the Department of Genetics. Finally, mechanisms of posttranslational regulation of processes involved in gene expression, DNA repair and chromosome segregation are delineated, with the primary interest in the protein kinases and phosphorylation.

Department of Tumor Immunology is devoted to multiple aspects of translational hematological research to study the mechanisms of development and progression of hematological malignancies. Research is directed on tumor sub-clonal heterogeneity by a large-scale high-dimensional profiling of tumor cells combining cellular and molecular approaches. By mapping the tumor microenvironment, immune modulations, immunological mechanisms and immune checkpoint molecules, we aim to reinforce anti-tumor immunity and/or abrogate the tumor-promoting signals that may translate into an improved overall survival of patients.

Department of Molecular Oncology has a long-term experience with in vitro and in vivo preclinical cancer research (colorectal, breast and pancreatic cancer, germ cell tumors, and melanoma). Research is focused mainly on the establishment of advanced research models derived from patient tissue (organoids, patient-derived xenografts), therapy resistance, tumor microenvironment, tumor-targeting via nanocarriers and DNA methylation changes associated with metastasis.

Department of Nanobiology focuses on the molecular and cellular interactions between nanomaterials and biological systems, thus contributing to the development of new safe-by-design nanomaterials for potential biomedical use including anti-cancer therapy. Besides the impact of potential nanotherapeutics on genome integrity, the biodistribution, pharmacokinetics, and biosafety after long-term accumulation in the body are investigated as well.

Department of Radiobiology performs research in the field of ionizing and non-ionizing radiation working in line with modern trends of radiobiology, providing radiobiological expertise to authorities. New emerging possibilities of using ionizing and non-ionizing radiation in medicine on one side, and increasing health risks from exposures on the other, are also area of our research interest.

An effect of radiation on the development and etiology of leukemia with focus on hematological stem cells is another aspect followed at this department.





## Challenges and Opportunities in developing a Comprehensive Cancer Centre within a University Hospital context – the experience of Maastricht

**Bernd Kremer<sup>1</sup>, Manon van Engeland<sup>2</sup>, Marja Vermeeren<sup>3</sup>**

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3. Quality and safety manager of the Maastricht Comprehensive Cancer Center, the Netherlands

Prior to 2016, oncological care and research were not completely integrated at Maastricht UMC+. Care took place in the Oncology Center of the hospital and research in the GROW research school of the faculty of health, medicine, and life science of Maastricht University. Despite numerous and intensive collaborations, there was no explicit shared vision and strategy and the connection between clinicians and scientists needed to be improved.

The Oncology Center and GROW decided to merge in 2016 and work together to obtain the OECI accreditation as a 'Comprehensive Cancer Center'. Thus, the aim was to inextricably link care, research, and education with one common vision and strategy.

A first conference for clinicians and scientists was organized together with patients mid-2016. At the same time, the 'Looking at the other's point of view' program started up, in which doctors and researchers visited each other at their workplaces. The conference was aimed at meeting each other emotionally and together with patients to see what we stand for.

The circle of innovation® (COI) instrument developed by MUMC+ was used to make our translational work in the field of 'survival with preservation of function' visible. Using the COI (reading it clockwise starting in the right upper quadrant) we show how we acquire new knowledge, how we translate this knowledge into the clinics, how we implement it, and how this contributes to improving health in the region or to knowledge utilization.

### Link to booklet circles of innovation

In a second conference a number of excellent COI's were presented and discussed and those present were invited to develop a COI for their own tumour lines.

A larger number of newly developed COI's representative of our vision and strategy were presented in a third conference. Symposia for nurses and other employees were organized in parallel. Simultaneously, preparations for the OECI accreditation were started.

Researchers and clinicians who visited one other gained insight into and admiration for the other's work. Researchers literally reported with tears in their eyes that they now know the reason why they're doing their research and clinicians responded that it's unimaginable where we can be in 5 years. During the first conference together with our patients the theme of 'survival with preservation of function' arose. The (emotional) connection had arisen.

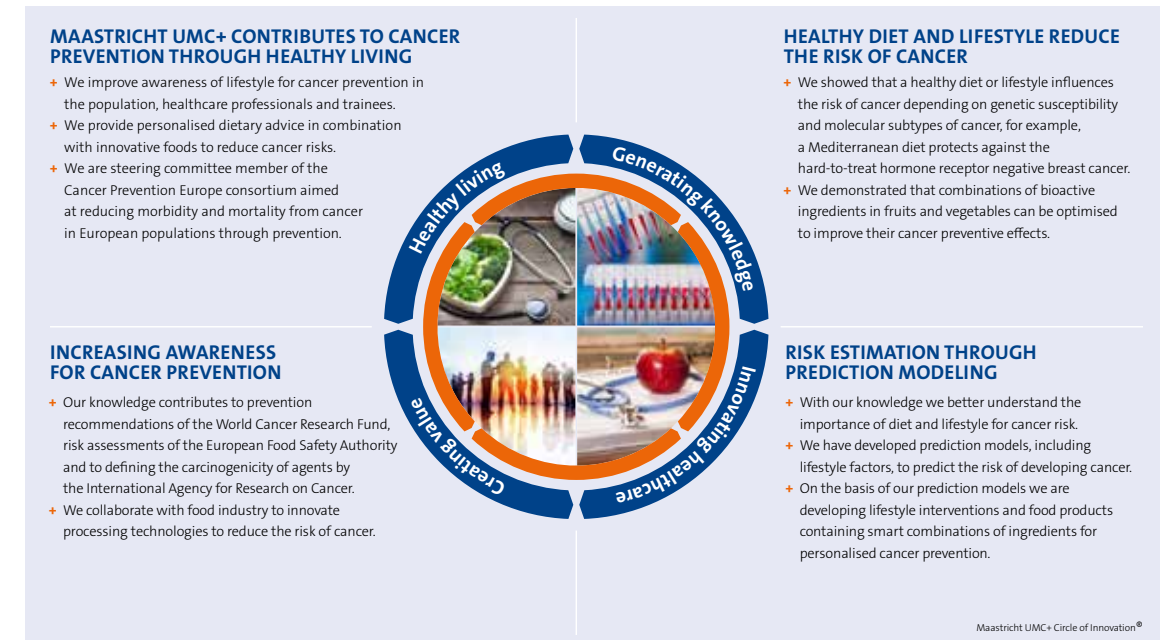
Defining the COI strengthened the substantive connection between scientists and clinicians and the focus on translation of knowledge.

After the second conference there was cooperation from almost all tumour lines and after the third conference there was broad support for our vision and the COI instrument.

During the preparation of the OECI accreditation, the quality of clinical care, research, and education was further strengthened and an appropriate governance and financing structure implemented. Further, the common vision was made more explicit and the collaboration with other partners in the field of oncology reinforced.

Critical success factors were the emotional connection in addition to the already existing substantive connection and the use of the circle of innovation® to promote and make visible the translation of knowledge to implementation and to facilitate the conversation between scientists and clinicians. Besides, the exemplary role of a number of figureheads played an important role in getting the other colleagues on board. Finally, sharing success (almost all tumour lines showcased their successes in a COI), but also the process of the OECI accreditation, were partly responsible for the broad dissemination of our vision.

### Circle of Innovation: Primary prevention of cancer



 Maastricht UMC+  
More knowledge, better life





## Preventing radiation-induced toxicities using a model-based, fully automated continuous learning system

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### Introduction

Radiotherapy (RT) plays a pivotal role in the treatment of many cancers by improving local tumour control and overall survival. However, RT results in a wide variety of acute and late toxicities that have a major impact on daily functioning and quality of life.<sup>1</sup> The overall outcome of cancer patients is increasing due to improvements in cancer screening programs and intensified and more personalised treatment approaches. Therefore, the prevalence of cancer survivors at risk for late toxicities is increasing as well. Consequently, prevention of these late toxicities becomes increasingly relevant.

Radiation technology is continuously improving, allowing for better sparing of healthy tissues without affecting target dose. Classical methodological approaches like randomized controlled trials are less suitable to assess the added value of these new technologies for various reasons (e.g., no real current standard, technology-user-interplay effect and short technology life cycles). Therefore, the department of Radiation Oncology of UMCG developed an alternative evidence-based methodology, referred to as the "Model-based Approach (MBA)", specifically for radiation technologies that primarily aim at reducing toxicities.<sup>2,3</sup>

### Model-based approach (MBA)

The MBA applies Normal Tissue Complication Probability (NTCP) models (i.e., prediction models describing the relation between RT dose to multiple organs-at-risk (OARs) and the risk of toxicities, to guide RT dose optimization (**model-based optimization**).

Additionally, NTCP-models are used to select patients for more advanced technologies like protons (**model-based selection**).<sup>2,3</sup> To this purpose, a comparison is made between optimized photon and proton plans to assess the difference in dose ( $\Delta$ Dose) in which the clinical relevance of  $\Delta$ Dose is assessed by using NTCP-models to determine a  $\Delta$ NTCP-profile. These  $\Delta$ NTCP profiles indicate the expected reduction in toxicity rates between protons and photons and thus can be considered a biomarker for the expected clinical benefit of protons over photons.

Finally, the added value of new RT technologies to prevent toxicities can be evaluated by **model-based validation**, which consists of two components:

1) model validation, and 2) model-based clinical evaluation).<sup>3</sup> Model validation refers to continuous NTCP-model validation as they may change over time with new RT technologies or changes in population mix. In model-based clinical evaluation, the added value of new RT technologies can be validated by comparing the observed toxicity rates after treatment with the new technology (e.g., protons) with the predicted toxicity rates (NTCP) based on the dose distributions derived from the old technology RT plans.

To support the MBA, we developed a fully automated IT-infrastructure allowing for a continuous learning system that results in a gradual but significant reduction of radiation-induced toxicities.

### Figure 1: RT Continuous Learning System (RT-CLS)

The backbone of the RT-CLS is the prospective data registration programs in which all relevant patient, tumour and treatment variables and follow up data are prospectively collected as well as acute and late toxicities, and patient-rated outcome measures (Figure 1).

The RT-CLS allows for all components of the MBA, including NTCP-model development and validation, model-based optimization, model-based selection and model-based validation. RT-CLS have been implemented for head and neck, CNS, lung, oesophagus and breast cancer and over 10,000 patients have been included already with a yearly accrual of approximately 1,100 new patients per year. All

data are automatically extracted from Mosaik, EPIC and RayStation and linked in a central database (Redcap) according to the FAIR-principles.

### ProTRAIT-project

The RT-CLS is now being extended to all 3 proton therapy centres in the Netherlands, providing one central database in TraiT for all proton therapy patients and allowing for federated learning.<sup>4</sup>

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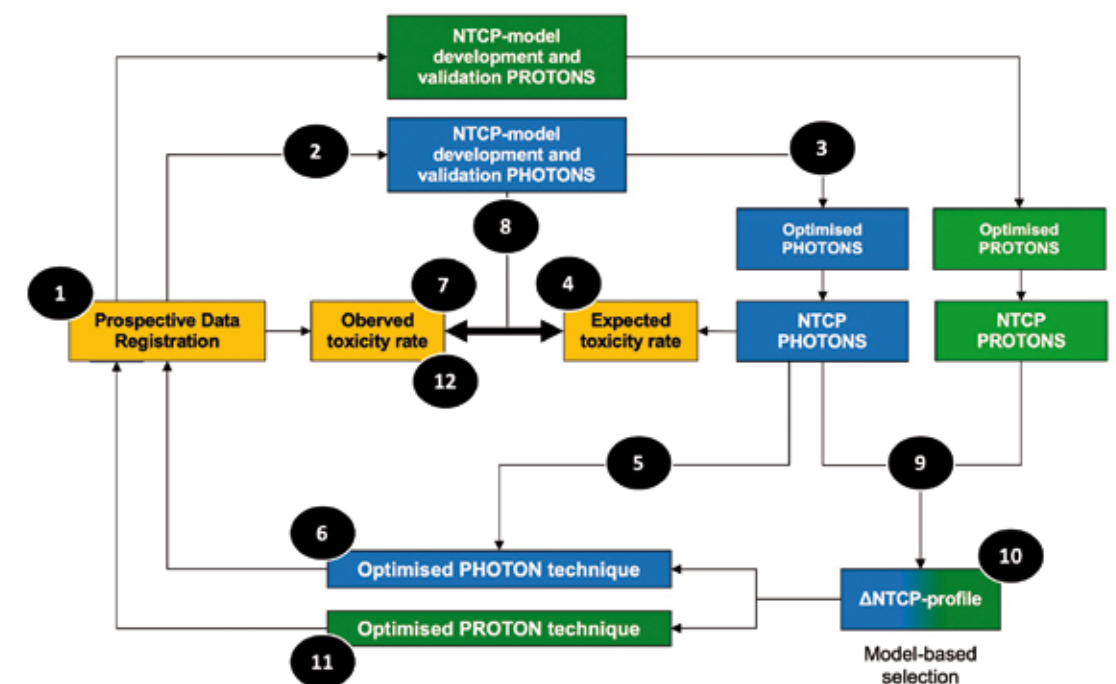
Figure 1: RT Continuous Learning System

The backbone of the model-based approach is the prospective data registration (1). Data from this registry are used for the development of NTCP-models and for NTCP-model validation in subsequent patient cohorts treated with photons (2). The dose parameters in these models are then used for model-based optimization (3), leading to optimized photon plans. For each photon plan, an NTCP-profile is created, indicating the full spectrum of expected toxicities (4).

Patients who are not eligible for protons follow shortcut (5) and are treated with the optimized photon technique (6) and are included in the prospective registry (1). NTCP-model validation is continuously done by comparing the expected toxicity rates (4) with the observed toxicity rates (7). NTCP-models can be adjusted according to a standardized procedure (8).

When patients meet the general eligibility criteria for proton therapy, a plan comparison is made (9), in which the NTCP-profiles for photons and protons are transferred into a  $\Delta$ NTCP-profile, which is a biomarker for the expected benefit of protons over photons. When the criteria for proton therapy are met (national indication protocol), patients can be treated with protons (11) and are also included in the registry (1).

The data from these patients can be used to validate the NTCP-models for protons and can also be used for model-based clinical evaluation in which the expected toxicity rates from the photon plans (4) are compared with the observed toxicity rates after proton therapy (12).





# Final Conference of the iPAAC JA - Cancer Control in Europe: Finding Sustainable solutions

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Innovative Partnership for the Action Against Cancer Joint Action (iPAAC JA) will finish its work with the end of 2021<sup>1</sup>. iPAAC JA brings together 44 institutions from 24 European countries and is co-financed (80%) by the European Commission in the framework of the Third Health Programme (2014-2020). The general objective of the iPAAC JA is to develop innovative approaches to advances in cancer control and is focused on implementation, reflected in the key deliverable: the Roadmap on Implementation and Sustainability of Cancer Control Actions, which will support Member States in implementation of iPAAC and Cancer Control (CANCON) JA recommendations.

The innovation that is covered within the JA consists of further development of cancer prevention, comprehensive approaches to the use of genomics in cancer control, cancer information and registries, improvements and challenges in cancer care, mapping of innovative cancer treatments and governance of integrated cancer control, including a new analysis of National Cancer Control Programmes in Europe. In the past ten years European Commission co-financed three cancer projects from the JA group, the European Partnership for Action Against Cancer - EPAAC JA, CANCON JA and iPAAC JA whose coordination was entrusted to the Slovenian National Institute of Public Health, located in Ljubljana, Slovenia<sup>2</sup>. The project's last conference, entitled Cancer Control in Europe: Finding Sustainable solutions will be one of the final steps in the frame of the iPAAC JA. The event will be an opportunity to meet stakeholders in cancer care and control with the aim of discussing the outcomes of the project in the light of the Europe's Beating Cancer Plan (EBCP) implementation and the forthcoming activities<sup>3,4</sup>. The conference is scheduled for 13 and 14 December 2021 and is adapted to the international events in times of the COVID-19 pandemic<sup>4</sup>.

The final conference will be opened by the Slovenian Minister of Health, Dr Janez Poklukar. European Commissioner for Health and Food Safety, Dr Stella Kyriakides will talk about the development of policy on cancer at EU level and iPAAC JA Scientific Coordinator, Dr Tit Albreht will give us an overview of iPAAC JA and its objectives. The conference will continue with the presentations of work package leaders and the achievements of their teams in the fields of cancer prevention, genomics in cancer control and care, innovative therapies in cancer, challenges in cancer care, cancer information and registries and governance of integrated and comprehensive cancer care. Panel discussion with important opinion leaders will follow every above mentioned presentation.

The panel discussion entitled Cancer Prevention & Early Detection – Putting knowledge into action will be chaired by Dr Satu Lipponen. The panel will be enriched by the panelists Dr Carolina Espina, IARC, Dr Pekka Jousilahti, Dr Ahti Anttila, Cancer Society of Finland and Dr Partha Basu, IARC. Innovation towards the future: ELSI aspects on genomics and horizon scanning approaches is the title of the panel discussion chaired by work package leaders Dr Marc van den Bulcke, Sciensano and Dr Marianne Duperray, INCa. Ms Chloe Mayeur and Dr Dawn Craig will be among the invited panelists.

Dr Roberta de Angelis, ISS, will chair the panel entitled The Role and development of Cancer Registries & the European Commission Knowledge Center on Cancer. Among the panelists there will be Dr Elizabeth van Eycken from the European Network of Cancer Registries, Dr Isabelle Soerjomataram from the IARC and Dr Manola Bettio from the Joint Research Center.

The panel regarding cancer survivorship and the right-to-be-forgotten, an important topic due to the high number of cancer survivors in EU will be chaired by Prof Francoise Meunier. His own real-life story will share Dr Jaka Cepec from Slovenia. Professors Josep Borras and Joan Prades from Barcelona will chair the panel entitled Challenges in care: Integrated and Comprehensive approaches. Dr Roberto Grilli, Dr Yolande Lievens University of Ghent, Dr Augusto Caraceni, INT, and Dr Francesco Sclafani will be their invited panelists.

Governance of Comprehensive Cancer Care – patient pathways, patient-reported outcomes, quality indicators, sets of standards, framework for quality assurance in Comprehensive Cancer Care Networks, National Cancer Control Programmes is the title of the panel, which will be chaired by Dr Simone Wesselmann and Dr Ellen Griesshammer from DKG. Among the discussants there will be the Founder of Melanoma Patient Network Europe & Member of Horizon Europe's Cancer Mission Board, Dr Bettina Ryll, Dr Ulrich Keilholz from Charité Berlin, Prof Giovanni Apolone from the Organization of European Cancer Institutes (OEI) and Dr Jean-Baptiste Meric, Director of Public Health and Care at INCA.

Final and probably the most important iPAAC deliverable – Roadmap on Implementation and Sustainability of Cancer Control Actions will be presented by Dr Regine Kiasuwa Mbengi from Sciensano, Belgium. There is a great expectation on highlights of the high-level panel discussion entitled Action, cooperation and implementation at EU and MS level of the recommendations of the iPAAC JA, CanCon JA and EPAAC JA which will be chaired by Dr Tit Albreht, iPAAC Scientific Coordinator. His guests will be important European officials and opinion leaders, Dr John F Ryan, the Director of Public Health, Country Knowledge and Crisis Management for DG SANTE, Prof Christine Chommiene, vice-chairperson the Mission on Cancer, Dr Antonella Cardone, Director of the European Cancer Patient Coalition, Dr Wendy Yared, Director of the Association of European Cancer Leagues and Dr Guy van den Eede from the JRC. Prof Walter Ricciardi, Chairman of the Mission on Cancer and Dr Marc van den Bulcke, Head of Service of the Cancer Center Sciensano, Belgium will chair the last panel, the cherry on the cake, entitled Future Challenges in Cancer Policy and Cancer Control at Member States Level, which will be introduced by Dr Matthias Schuppe from DG SANTE presenting the Implementation Plan for the EBCP.

The iPAAC JA final conference will be therefore a great opportunity to discuss the outcomes of the JA in the context of the EBCP as well as of the future of cancer control and overall cancer management in Europe.

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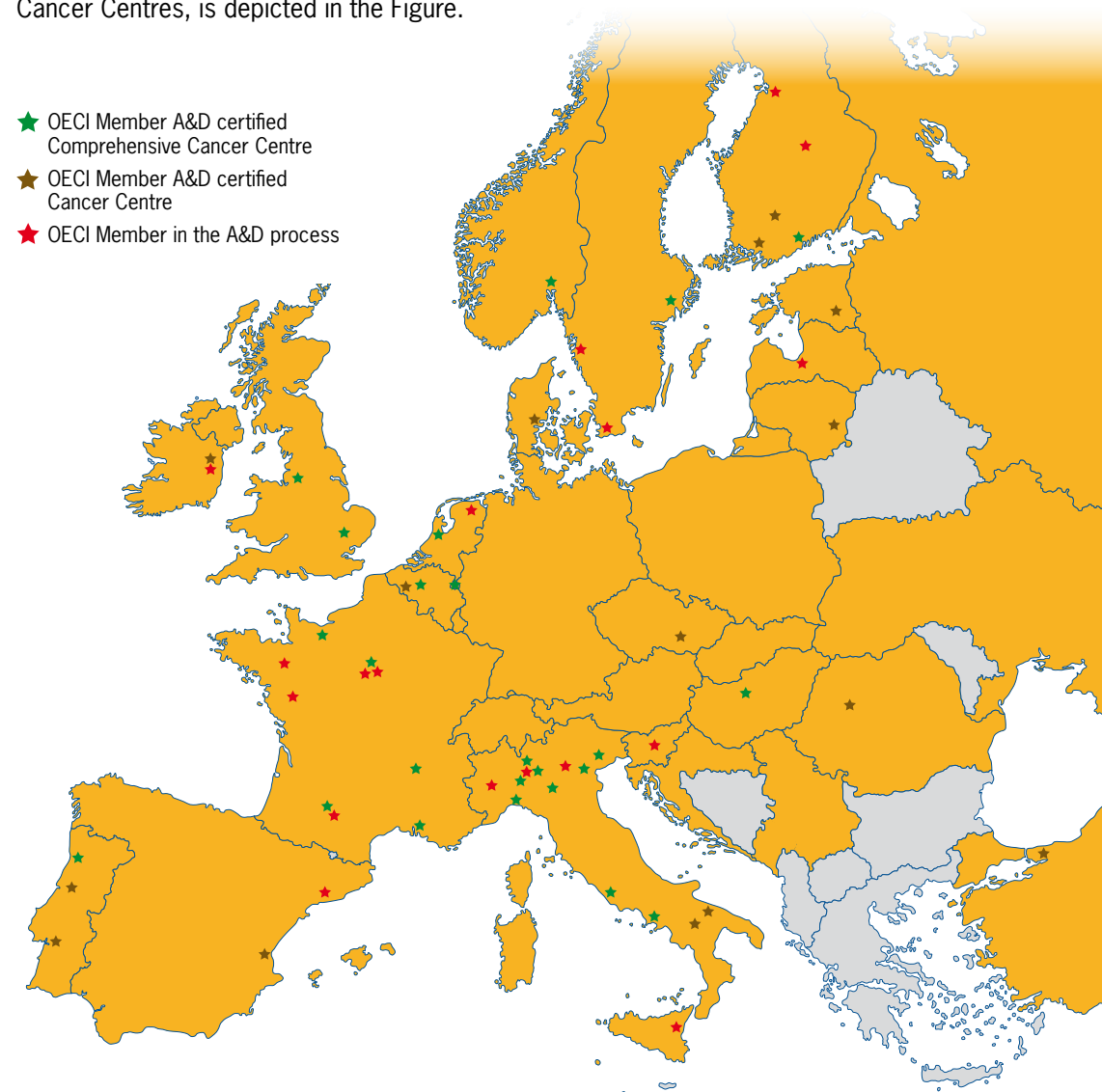
# News from the A&D Programme

Accreditation is a process in which an independent organisation evaluates a centre and certifies that it meets certain quality standards. OECI has specialised its A&D Programme in multidisciplinary integrated cancer care and research, with a major focus on comprehensiveness.








The OECI A&D Programme now comprises 57 of the largest cancer centres in 18 out of 27 Member States of the EU, plus Norway, Turkey and the UK.

In a review of 40 of these centres with a final designation: these centres produce more than 12,400 peer reviewed publications on cancer research annually, have total annual research budgets of well over €1 billion, and have treated more than 210,000 new cancer patients per year. This is a significant milestone for the Programme.

The status of accreditations and designations as OECI Comprehensive Cancer Centres, and OECI Cancer Centres, is depicted in the Figure.




## In 2021 seven OECI Members and 1 cancer centre under approval for the membership, applied for the A&D Programme

- **Beaumont Hospital**  
Dublin, Ireland 
- **Centre de lutte contre le cancer Eugène Marquis**  
Rennes, France 
- **Institut Universitaire de Cancerologie AP-HP Sorbonne Université**  
Paris, France 
- **Istituto Oncologico del Mediterraneo**  
Catania, Italy 
- **Ospedale San Raffaele**  
Milan, Italy 
- **Vall d'Hebron Barcelona Campus Hospitalari**  
Barcelona, Spain 
- **Riga East University Hospital Cancer Center**  
Riga, Latvia 

## Recent accreditations - updated November 30<sup>th</sup> 2021

The following centres/institutes have been awarded OECI Accreditation & Designation Certificates in 2021. We offer our congratulations to each of them for this achievement.

### New Accreditation

- **Maastricht UMC+**  
Maastricht, The Netherlands 

### Re-Accreditations

- **Azienda Unità Sanitaria Locale di Reggio Emilia IRCCS**  
Reggio Emilia, Italy 
- **Helsinki University Hospital**  
Helsinki, Finland 
- **Istituto Oncologico Veneto IRCCS**  
Padua, Italy 
- **Fondazione IRCCS Istituto Nazionale dei Tumori di Milano**  
Milan, Italy 
- **Istituto Nazionale Tumori IRCCS "Fondazione Pascale" (INT Pascale)**  
Naples, Italy 
- **Istituto Nazionale Tumori - Regina Elena**  
Rome, Italy 
- **IRCCS Centro di Riferimento Oncologico della Basilicata (CROB)**  
Rionero in Vulture (Potenza), Italy 



# New auditors for the OECI Accreditation and Designation Programme

The OECI Accreditation & Designation Programme is designed to help European cancer centres implement a quality system for oncology, and provide cancer patients in Europe with equal access to high quality cancer care.

In order to be certified within the A&D Programme, a multidisciplinary team of professionals in oncology visits cancer centres for a peer review. Performing a peer review visit is paramount to examine all aspects of the Cancer Centre, both the organisation at the management level and at the clinical and laboratory level for all disciplines and ensure quality improvement in the applicant Cancer Centre.

The OECI auditors are highly skilled in their own fields, and are also trained in how to perform a peer review audit for OECI in such a way as ensures complete consistency within the Programme.

OECI auditors learn how to perform a peer review and how to use relevant tools for auditing during a two-day training, which focuses on interview techniques and techniques how to interpret the questionnaires. As the A&D Programme is ever-growing and comprises now 57 of the largest cancer centres in 18 EU countries, plus Norway, Turkey and the UK, OECI has been looking to expand its team of expert auditors.

On the 25<sup>th</sup> – 27<sup>th</sup> of October 2021 a group of 16 new candidate auditors participated to the 2021 Training Course in Inveruno,

Italy, at the beautiful location of the Villa Verganti-Veronesi near Milan. The participants come from cancer institutes all over Europe (Czech Republic, Finland, Ireland, Italy, Latvia, Norway, Portugal, Spain Sweden).

The training course was provided by Patrick Corstiaans (check this) from KERTEZA an independent training company for auditors. In particular, the two training days included:

- Introduction in quality management and auditing
- Introduction of the OECI quality standards, procedures and tools
- Roles and responsibilities of auditors and chair of an audit team, as well as the OECI coordinator
- Theoretical background and practical exercises on preparation of an audit, teamwork as an audit team
- Role plays in performing an OECI audit

This now means that we have around 65 trained auditors!

We would like to wish the new OECI auditors a warm welcome to the OECI community!



## Dr. Dominique de Valeriola left the OECI Board

We would like to thank our friend Dominique for the services she has rendered to OECI over the past 9 years.

Dominique served as OECI President from 2015 to 2018, leaving the chair to Thierry Philip on June 2018 at the OECI General Assembly in Poznan. During her Presidency the OECI Membership has significantly increased. In addition, under her helm, in 2018 the A&D WG was transformed into a Programme, which is now the core activity of our Organisation.

Jules Bordet has just inaugurated a new facility and it is also thanks to all the efforts done by Dominique that Brussels has now a renewed cancer centre where our patients may access cutting-edge treatments and care.

We can't thank Dominique enough - the first woman to cover the Presidency of the biggest worldwide network of cancer centres.

Today, she is chairing the Working Group on Collaboration for Good Practices with Patients. We hope to continue enjoying her support and friendship for a long time.



*Thanks Dominique*

## Three new Members co-opted to the OECI Board

During a recent OECI Board held in Inveruno on October 5<sup>th</sup> 2021, the Board members approved at unanimity the President's proposal to co-opt to the OECI Board three new Members. The three candidacies will be brought to the formal approval of the OECI General Assembly at the next meeting in Valencia on June 17<sup>th</sup>

Below the three new entries

We congratulate with the three new co-opted Members



**Cemažar Maja**, Institute of Oncology Ljubljana

**Iwona Lugowska**, Maria Skłodowska, Curie National Research Institute of Oncology, Warsaw

**Jacqueline Stouthard**, Netherlands Cancer Institute, Amsterdam

# Oncology Days - June 2022

June 15<sup>th</sup>

## Accreditation and Designation Session

### Striving for excellence in Comprehensive Cancer Care, Research and Education

#### Part I

The session (open to everyone) will be an opportunity to hear the latest developments in the Accreditation and Designation Programme and the wider OECI initiatives in cancer quality improvement. This is also an opportunity for OECI auditors (and prospective auditors) to renew their knowledge and discuss key practical issues arising in Peer Reviews:

- Present state of play of the Accreditation Programme
- Developing support processes, excellent practices, and benchmarking of our Centres

#### Part II

- Participation in EU Actions to advance the vision for comprehensiveness in cancer care and research
- Skills development and experience for OECI Peer Reviews

June 15<sup>th</sup>

## Outcomes cancer research WG Session

### A step forward PROmics™

"PROmics and PREMs are part of the broader chapter of the health-related quality of life (HR-QoL) assessment.

For years, several and standardized tools have been available, widely used in clinical practice and research protocols. A lot of evidence is available on their validity and reproducibility and about what are the factors that influence the feasibility in the two areas but their added value is still open when used in the context of the new scenarios where the key factors are data sharing and integration, big data and artificial intelligence".

- PROMs objectives and implementation (clinics and research)
- Implementation standards and organizational issues
- AI & digital therapeutics: are we ready for that?
- Do we need to develop new quality of life tools?
- The role of OECI in EU funding on Quality of Life calls in the Cancer Mission

June 15<sup>th</sup>

## Cancer Economics and Benchmarking WGs Session

### Costs and Consequences of Personalized Cancer Treatment

Personalized and (combined) targeted treatment come with considerable costs, challenging the financial sustainability of health systems. We present findings from a survey on combined targeted treatments in 10 EU countries and from an economic experiment on transparency in price negotiations.

Currently there is little data on the socio economic consequences (SEC) of cancer and its treatment. for patients. We present data from the OECI on shot project survey on this topic in 15 EU countries. There is a need for consensus on valid instruments to asses SEC. An interim report from- and discussion with the OECI taskforce on socioeconomic consequences of cancer ends this session.

- Introduction
- Developments in costly Cancer treatments
- Targeted treatment combinations
- Transparency as a solution to high prices
- Socio Economic Consequences of Cancer
- Methods and Instruments in Analysis of Socio Economic Consequences
- Discussion and consensus

# Oncology Days - June 2022

June 15<sup>th</sup>

## Biobanks and molecular pathobiology WG Session

### Molecular Pathology Standardization

Today one of the major problem in oncology diagnostics is that the molecular analyses are not standardized to perform reproducible and exchangeable molecular diagnostic analysis. This is even more pressing because of the continuously increased use of prognostic and predictive biomarkers, directly related to treatment choices and the interpretation of results of diagnostics and clinical research molecular analysis is increasingly complex.

- Introduction
- Molecular Pathology Standardization
- Tissue treatment and preservation
- DNA preservation and analysis standardization RNA preservation and analysis standardization Proteins preservation and analysis standardization
- General discussion

June 15<sup>th</sup>

## Collaboration for Good Practices with Patients WG Session

### Moving from Patient Involvement to Co-Creation with Patients

OECI cancer centers are collaborating with patients and their close ones to enhance the quality of care and research. Indeed, patient experience is improved when patient perspectives are taken into account in the redesign of cancer centers activities. In this session, we will give an update on the recent changes in patient involvement practices, and we will make a focus on cancer centers which started a new from collaboration: co-creation with patients.

- Involving patients in quality improvement processes
- Impact of patient perspectives on the patient journey
- Can we mix "expert-driven" and "patient-led" approaches?
- What is a cancer center open to co-creation with patients?

## A&D Board meeting

June 16<sup>th</sup>

## Scientific Conference

### Artificial Intelligence: a tool in modern and future oncology

Opening and welcome of the authorities

Comprehensive cancer centers in Europe: OECI and European alignment.

#### SESSION I

##### AI in diagnostic procedures

- Artificial intelligence and computational pathology
- Artificial intelligence application in cancer diagnostics
- Radiomics in Oncology: A Practical Guide

#### SESSION II

##### AI in clinical outcome prediction

- AI and tumor molecular profiling
- May AI replace classic statistical approaches to predict clinical outcomes?
- Deep learning NMR and outcomes prediction
- AI in computational biology: tackling the difficulty of integrating complex datastreams from different diagnostic

Key Lecture  
BIG DATA & AI

#### SESSION III

##### AI Future Directions

- A new vision for collaborative RWD studies
- AI and Big Data in Cancer Outcome Research
- Big Data: may pharma companies and academy be allied?
- Large-scale predictive model development and validation using data standardised to the OMOP Common Data Model

#### SESSION IV

##### Applications of AI in Oncology

- Experiences of AI in cancer surgery
- AI in Radioation Oncology
- AI in drug development
- Drug repurposing in oncology

Key Lecture: The challenge of AI for OECI Members



The participation is free  
Registration from February 1<sup>st</sup> 2022 at:  
<http://www.oeci.eu/Assembly.aspx>

#### THE OECI 2022 SCIENTIFIC COMMITTEE

##### President

Thierry Philip and Antonio Llombart Bosch

##### Members

Giovanni Apolone, Maja Cemažar, Christian Brandts, Dominique de Valeriola, Manuel Llombart Fuertes, Claudio Lombardo, Jozsef Lovey, Iwona Lugowska, Simon Oberst, Gunnar Sæter, Giorgio Stanta, Jaqueline Stouthard, Wim van Harten

#### THE OECI 2022 NATIONAL SCIENTIFIC AND ORGANISING COMMITTEE

##### President

Antonio Llombart Bosch and Manuel Llombart Fuertes

##### Members

José Antonio López-Guerrero, Tomás Quirós

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