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### **OECI President's foreword**

Dear OECI Members, Dear Readers,

the COVID-19 pandemic has impacted almost every facet of our lives and many important congresses and conferences, in the scientific field among others, have been postponed all over the world. In this delicate moment for us all, this issue of the OECI Magazine is not only an important tool of communication but also as a space for reflection.

Like all the other large cancer organisations, OECI has been forced to make the drastic and difficult decision to postpone all its planned activities and events. It is therefore with deep regret that I inform you that the Oncology Days 2020, scheduled in Helsinki from June  $10^{th} - 12^{th}$  have been cancelled and will be re-scheduled in 2021, accordingly with the progress of the pandemic.

However, some administrative and legal obligations cannot be postponed and therefore, after consulting our lawyer and our accountant, a General Assembly must be convened as soon as possible so as to comply with the provisions of the law. In order to be able to validate the General Assembly and approve the items in the Agenda, the Full Members will be requested to send their votes on an electronic form annexed to the convening letter, the agenda and the General Assembly infopack.

Despite the difficulties, it is imperative to continue planning the largest cancer research Programme so far conceived in the history of European research. As a result, the Board and the Assembly of the European Cancer Mission have continued their activity in order to prepare the first calls for Horizon Europe at the beginning of 2021. You may find a brief account of the state of the art in the first article of this issue of the OECI Magazine. This Edition also includes two articles dedicated to the relationship between COVID-19 and Cancer.

Unfortunately, the COVID-19 pandemic has found us unprepared and is creating serious difficulties for our health systems. The situation is particularly delicate for cancer patients undergoing therapy (and therefore are extremely vulnerable), as well for patients waiting for a therapeutic protocol which often must be put off.

This Edition is dedicated to all the health workers who are sacrificing themselves to provide adequate care to all patients affected by the virus. I would also like to offer my deepest condolences to those who have lost their loved ones due to this immense tragedy. I firmly believe that this experience will bring about a greater strength and determination to find new tools to better serve our cause, and efficiently respond to our patients and their families. In this the OFCI Quality Programme, which

patients and their families. In this the OECI Quality Programme, which has already certified 50% of our Members, will be instrumental.

Despite the serious weakness Europe is facing, oncology has proven to be ever more united and deeply European. I am certain that our example corresponds the renewed sense of belonging provided by our politicians, who have the moral duty to carry on the principles set out by the Founding Fathers and to continue building a more cohesive and supportive Europe.



Thierry Philip OECI President



Organisation of European Cancer Institutes

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# Oncology Days

**HELSINKI 2021** GENERAL ASSEMBLY, SCIENTIFIC CONFERENCES AND RELATED EVENTS

> Helsinki, Finland June 16th-18th 2021



## **European Cancer Mission:** an OECI landscape in the **European Union**

#### Thierry Philip<sup>1,2</sup>

- 2. President Organisation of European Cancer Institutes

Mrs. Mariya Gabriel, Commissioner for Innovation, Research, Culture, Education and Youth is responsible to ensure swift agreement on, and full implementation of the future Horizon Europe Research and Innovation Programme. The Pillar 2 of the New Framework Programme includes the Mission to fight

The OECI is strongly involved to promote the participation of its Members in several actions that will be launched as part of the Cancer Mission at the beginning of 2021 with the opening of calls for tenders around actions to fight cancer in Europe with the objective of saving 3 million lives by 2030.

The first version of the Mission Board was discussed in February among the members of the Assembly before the Mission Board. This first document was straightforward with 10 actions ranging from fundamental research to survival and including education and training.

OECI has been very positive about action 7 corresponding to our core activity, namely the Designation of cancer centres through a professionally led Accreditation and Designation process with selfassessment followed by peer review. The interdisciplinarity and multidisciplinarity of comprehensive cancer centres was seen in this first version as a major tool to achieve the objectives of the mission.

After discussion with the Assembly, a second draft, very different from the first, was opened for discussion among the members of the Assembly. The number of actions was increased to 14 (far too many) and action 7 (on quality) disappeared to be found in actions 9 and 11, although completely modified. The Mission promoted the creation of a National Cancer Control Infrastructure and lost the role and place of cancer centres, i.e. professionals.

Recommendation 10, an interesting proposal for a European Network/Infrastructure to share real life data is another example that the Mission has lost the professional works in this second focus.

We think that cancer centres and cancer networks within a university Hospital should be the core of the implementation of the Mission actions. We favour at least one cancer centre or one university virtual cancer centre per country and in large countries a cancer centre every 5 million inhabitants.

Last but not least two very important points:

Paediatric should be individualised because SIOP Europe already works as a mission action. They are linked to the world SIOP (USA, China, South America...). They already produce guidelines and clinical trials at European level; they cooperate with the best basic research institutes (see EU-Life), whilst being linked to patient organisations and pharmaceutical industries and working with underdeveloped countries.

It is in the interest of the Mission to save a certain amount of money for the objectives of SIOP because it is certain to obtain measurable results within 5 to 6 years.

The ageing of Europe's population will lead to a tsunami of cancers in the next ten years. More than 60% of the increase in cancer cases concerns patients over 65 years of age. This group of patients is specific and will deserve specific preventive, screening, diagnosis and treatment procedures. They cannot be found anywhere in the 14 actions and will need specific targets and funding.

#### **APPENDIX**

### ORGANISATION OF EUROPEAN CANCER INSTITUTES FEEDBACK TO THE EUROPEAN BEATING CANCER PLAN

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The Roadmap is ambitious. We suggest to use the term Primary Prevention instead of Prevention. The document should include something more about variability within and between countries, in terms of structure (what we use), process (what we do) and outcomes (what we obtain in terms of health). There should be a greater emphasis on the transfer of already available knowledge and, the subsequent intervention to remove obstacles.

#### **OECI MAIN POINTS**

#### 1. Policy objectives

Two frequently cited policy objectives are: a. Equality of access for patient to high quality cancer care b. Optimal treatment for patients as close to home as reasonable Therefore we need to establish cancer networks based around Comprehensive or large Clinical Cancer Centres in every geography, so that all hospitals diagnosing and treating cancer work together in an integrated infrastructure. Comprehensive Cancer Centres or large Clinical Centres are required to ensure the collaboration of multidisciplinary specialists at a team level to assure best possible diagnostic and treatment decisions, and optimal coordination of patient care. Multidisciplinary Teams (MDTs) have been game-changing in cancer treatment. The object of cancer networks is to extend that expertise to all hospitals treating cancer. Europe needs one Comprehensive Cancer Centre or large Clinical Centre per 5-10 million of the population and at least one in small Member States, fully networked to other hospitals.

#### 2. Instruments for ensuring high quality treatment and care

One of the main instruments for ensuring high quality treatment and care within hospitals is a core set of internationally-recognised core quality standards. These standards should cover MDT working, patient pathways, continuity of care, diagnostic procedures, all modalities of treatment, access to clinical trials, supportive and palliative care, patient involvement and engagement, translational research, and use of patient data for benchmarking and for research purposes. These standards can be used for self-assessment by cancer centres. Ultimate assurance comes from an established external Accreditation Scheme for Cancer Centres. This is best achieved at a pan-European level. Quality Standards should also be applied to cancer networks, so that the quality of the whole infrastructure deployed for patients is assured.

#### 3. Big Data and GDPR

A massive amount of data holding great potential for new discoveries is being generated. This is one of the most powerful available weapons in the fight against cancer. Analysis of large number of patients' data will identify signs of predisposition and risk factors, improving testing capabilities of drugs. Several obstacles still remain. The amount of data is vast, and access to appropriate technological infrastructure is an issue. We encourage high standards of electronic patient documentation using agreed formats. The GDPR Regulation needs to be changed to give greater freedom when, i.e., patient's data are used for retrospective studies.

#### 4. Patient-centeredness and involvement

The EBCP should drive equal access to all EU citizens to prevention and high quality standard therapies. To respect the patient's centeredness, we should refer to 3 different populations: - The patient who is still healthy, reducing incidence by prevention - The patient actually diagnosed, offering the best diagnosis and treatment so as to improve survival and quality of life (equity) and the optimum costs (efficiency and effectiveness) - The patient surviving their cancer, by providing support for their holistic needs and giving them the ability to retrieve as normal a working and personal life as possible. We need appropriate legislation to prevent the knock on effect of cancer and ensure survivors are not discriminated after the disease. Every patient should have a Survivorship Care Plan.

### **COVID-19 and Cancer**

Claudio Lombardo<sup>1</sup>. Stefania Gori<sup>2-3</sup> and Giovanni Apolone<sup>4-5</sup>

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The COVID-19 pandemic has exposed the extreme weakness of our health systems. In the last decades, thanks to the research advancements we have developed new diagnostic, curative and rehabilitative technologies, but we have failed to structure a system that can quickly and effectively react to critical and unexpected situations.

None of us would have ever imagined having to face a challenge like this that puts our patients in front of two terrible fears, cancer disease and COVID-19. We must stand on their side to give them reassurances and certainties, evaluating on a case-by-case basis how to administer the treatments according to their exposure to COVID-19.

The ever increasing demand for health facilities and medical care dedicated to infectious diseases results in leaving certain health sectors, including oncology, unable to operate effectively. Previous epidemics have shown that when health systems are overwhelmed, the death toll from chronic conditions, such as cancer, increases significantly. A series of immediate actions must therefore be put in place in order to re-organise and maintain access to high quality essential health services for all cancer patients<sup>1</sup>.

The outbreak of COVID -19 has alarmed cancer patients: the new coronavirus is not an equal-opportunity killer and it mostly targets individuals with previous pathologies in addition to the elderly. Very little is known about this novel human infection and it is difficult to make assumptions on the pandemic life that may turn in an endemic situation up to the availability of an effective vaccine that may eradicate the virus. As a result, great caution is paramount in offering suggestions that cannot rest on rigorous scientific observations. However, it is possible to provide some indications based on scientific evidences validated mostly in previous infectious and epidemic situations.

Cancer patients are more exposed to the risk of infection and possible complications. However, the specific tumor pathology, the general condition of the patient, the stage of the disease and the therapy they are receiving must be taken into consideration. Although immunosuppressive therapies expose patients to a greater risk of contracting infections<sup>2</sup>, there is currently no reliable data showing that a cancer patient is more at risk of COVID-19. The increased risk regards all infectious diseases, given the patient's vulnerable state of health. The few data about incidence of COVID-19 infection in cancer patients derived by report of Yu J. et al<sup>3</sup> which observed in 1524 cancer patients treated from December 30, 2019 to February 17, 2020 at a tertiary cancer institution in Wuhan (China), an estimated infection rate of 0.79%, higher than the cumulative incidence of all diagnosed COVID-19 cases reported in the city of Whuan over the same period (0.37%).

Therefore, it is safe to say that there is no evidence which may justify to postpone a therapy to a patient COVID-negative, unless the oncology department is exposed to Covid-19.

Experience in China, country which has been hit hard by the pandemic, has shown that COVID-19 infection causes mild symptoms in most cases (81%; i.e., non-pneumonia and mild pneumonia); 14% of the affected population developing severe complications (ie, dyspnea, respiratory frequency  $\geq$  30/min, blood oxygen saturation  $\leq$ 93%, partial pressure of arterial oxygen to fraction of inspired oxygen ratio <300, and/or lung infiltrates >50% within 24 to 48 hours) and 5% require hospitalization in intensive care for respiratory failure, septic shock and/or multiple organ dysfunction or failure³. On the other hand, COVID-19 has been particularly severe for individuals with comorbidity such as cardiovascular diseases, diabetes, chronic respiratory diseases, hypertension and cancer. Mortality was of 2.3% in 44672 confirmed cases against an alarming 14.8% of patients over 80 and 49% in critical cases. Mortality was more elevated among patients with pre-existing comorbid condition: 10.5% for cardiovascular disease, 7.3% for diabetes, 6.3% for chronic respiratory disease, 6% for hypertension and 5.6% for cancer⁴.

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For this reason, all cancer patients, if symptomatic (fever, cough, dyspnea), pauci-symptomatic or cohabiting with COVID-positive family members, must be evaluated for COVID-19 infection by nucleic acid testing of respiratory tract samples. If COVID-19 positive, cancer patients should discontinue (if ongoing) or not initiate anticancer treatment, to prevent even serious complications<sup>5</sup>.

Patients with cancer were observed to have a higher risk of severe events (a composite endpoint defined as the percentage of patients being admitted to the intensive care unit requiring invasive ventilation or death) compared with patients without cancer (39% vs 8%; p=0.0003)<sup>6</sup>.

The outbreak of COVID-19 and the high mortality rate reported in infected oncological patients have consequences on the diagnosis and treatment of oncological patients, and on the clinical research.

There are no international guidelines to address the management of cancer patients in any infectious pandemic. Some recommendations regarding the management of cancer patients during the COVID-19 pandemic are given by groups of oncologists on the basis of the little evidence available so far<sup>1, 7, 8, 9, 10</sup>.

The European Society of Clinical Oncology (ESMO) recently published Guidelines on cancer patient management during the COVID-19 pandemic. These recommendations should be used as guidance for prioritising the various aspects of cancer care in order to mitigate the negative effects of the COVID-19 pandemic on the management of cancer patients (https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic).

Outpatients are advised not to visit hospitals, due to risk of infection. Consequently, some clinical trials are being delayed; enforced quarantine, as is widely the case in Wuhan, complicates hospital attendance for repeated appointments and continuity in care, and when severe complications or emergencies occur in patients with advanced cancers, treatment delays or unavailability are possible concerns. Decisions on whether or not to postpone a cancer treatment need to be made on a patient-by-patient basis and on the risk to the patient, as delays could lead to tumour progression and ultimately poorer outcomes.

Certainly, due to the COVID-19 pandemic and the increased risk of exposure to the virus by going out in public, many hospitals and clinics have changed their policies related to the internal management of patients and their relatives.

Some may allow one visitor per patient, whilst others allow no visitors.

In some hospitals, today all cancer patients are tested for COVID-19 before hospitalization: in a single-center case series of 138 hospitalised patients with confirmed 2019 novel coronavirus-infected pneumonia in Wuhan, China, presumed hospital-related transmission of COVID-19 was suspected in 41% of patients<sup>11</sup>.

Moreover, the patients must be informed that before heading to a medical appointment, they have to check with the clinic or hospital for their current visitor policy. Oncologists should recommend delaying some treatments for supportive care. Cancer screening tests, such as mammograms or colonoscopies, may also be delayed reducing the risks of exposure to the virus.

Oncologists may recommend stretching out the length of time between cancer treatments using medications, such as chemotherapy or immunotherapy or they may recommend delaying starting these treatments, based on cancer diagnosis and the treatment goals, presenting to the patients the benefits and risks of continuing or delaying treatments.

Appointment for a scheduled visit may be replaced conducting the visit under videoconferencing: the patients are often more technologically prepared than doctors!

Each cancer centre, in agreement with other institutions of the region or of the country, should avoid overlapping parallel information mechanisms that cause confusion and increase anxiety with personal and social effects disproportionate to the real threat associated with the pandemic.

Cancer centres have activated and/or implemented procedures for the management of any suspected case. In agreement with the National health authorities, they have also established guidelines to carry out tests and, in case of positivity, have devised instructions to transfer the cancer patients to reference centres/departments adequately equipped.

The patients and their relatives must therefore be duly informed that there are no emergency improvisations and that their diseases are under control even in extreme difficulty situations such as current circumstances.

In time the pandemic will end, and we are certain that we will all have learnt a valuable lesson that will help assist our patients more efficiently in the future. As an example, a telematics filter will be instrumental prior to each appointment at the hospital in order to understand which patients may safe undergo to their planned therapy, thus avoiding unnecessary travel.

All this can and must be done interacting with patient associations. All our institutions are therefore invited to give hospitality to the associations operating at local and regional level by agreeing on practical collaboration protocols.

The recovery process will be long, and co-existence with the virus will oblige us to thoroughly review our approach to a COVID-positive and COVID-negative patient, adopting serological tests under validation by the WHO in collaboration with several European laboratories.

This is not a discrimination but a greater attention to the weakest among the weak and a new safe approach to guarantee our health workers.

OECI should ask itself about this and promote concrete and coordinated actions to demonstrate once again that "health and care" have no borders or different approaches because patients have the rights to receive the best available treatments and health care workers must be able to be guaranteed to operate in safety.

In-fact, it is likely that cancer institutes/centres have reacted in different ways depending from the country, the pandemic severity and its times of appearance.

This is the rationale for proposing an OECI survey, that will be soon circulate, to know and understand how, in this pandemic context, decisions concerning cancer research and care have been implemented and how much impacted the volume, the case-mix and, may be, the outcomes.

Scientific knowledge grows thanks to our experiences that must be shared and disseminated through qualified communication channels recognised by the scientific community. In this regard, we invite you to read carefully the article written by Professor Nicola Silvestri for this issue of the OECI Magazine.

#### References

- 1. van de Haar J, Hoes LR, Coles CE, et al: Caring for patients with cancer in the COVID-19 era. Nature Med 2020. doi.org/10.1038/s41591-020-0874-8.
- 2. Kamboj M, Sepkowitz KA: Nosocomial infections in patients with cancer. Lancet oncol 2009; 10(6):589-597. doi:10.1016/S1470-2045(09)70069-5
- 3. Yu J, Ouyang W, Chua MLK, Xie C. SARS-CoV-2 Transmission in Patients With Cancer at a Tertiary Care Hospital in Wuhan, China. JAMA Oncol. Published online March 25, 2020. doi:10.1001/jamaoncol.2020.0980
- 4. Wu Z, McGoogan JM: Characteristics of and important lessons from the Coronavirus Disease 2019 (COVID-19) outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA 2020 Feb 24. doi: 10.1001/jama.2020.2648.
- 5. Zhang L, Zhu F, Xie L, et al: Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. Ann Oncol 2020 Mar 26. pii: S0923-7534(20)36383-3. doi: 10.1016/j.annonc.2020.03.296.
- Liang W, Guan W, Chen R et al: Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol. 2020 Mar;21(3):335-337. doi: 10.1016/S1470-2045(20)30096-6.
- 7. Al-Shamsi HO, Alhazzani W, Alhuraiji A, et al: A practical approach to the management of cancer patients during the novel coronavirus disease 2019 (COVID-19) pandemic: an International Collaborative Group. The Oncologist 2020; 25:1-10
- 8. Coles CE, Aristei C, CBliss J, et al: International guidelines on radiation therapy for breast cancer during the COVID-19 pandemic. Clin Oncol 2020; 32:279-281
- 9. Banna G, Curioni-Fontecedro A, Friedlaender A, Addeo A: How we treat patients with lung cancer during the SARS-COV-2 pandemic: primum non nocere. ESMO Open 2020; 5:e000765
- 10. Ngoi N, Lim J, Ow S, et al: A segregated-team model to maintain cancer care during the COVID-19 outbreak at an academic center in Singapore. Ann Oncol 2020 Mar 31. pii: S0923-7534(20)36410-3. doi: 10.1016/j. annonc.2020.03.306
- 11. Wang D, Hu B, Hu C, et al: Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Whuna, China. JAMA 2020 Feb 7. doi: 10.1001/jama.2020.1585.

# **COVID-19** pandemia and crisis of health systems at the time of globalization: what have we learnt from the cancer lesson?

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In December 2019 a novel virus characterized by rapid human-to-human transmission and named severe acute respiratory syndrome coronoavirus-2 (SARS-CoV-2) was first detected in China<sup>1</sup>. On March 11<sup>th</sup>, 2020, the World Health Organization declared this new disease caused by the coronavirus (COVID-19) a pandemic<sup>2</sup>. As of April 14<sup>th</sup>, 2020, over 1.8 million COVID-19 cases have been registered worldwide, while the number of deaths exceeded 110 thousand, according to Johns Hopkins' latest update on the global trend of the coronavirus pandemic<sup>3</sup>. The majority of COVID-19-related deaths (75 thousand) were recorded within the European Union, in Italy, Spain and the United Kingdom, although presently the number of deaths occurred in the United States are exceeding any other country hit by the pandemic. After four months since the first cases were reported, we should ask ourselves: what have we learned so far? Never as at this moment could we make Isaac Newton's words our own: "what we know is a drop, what we ignore is an ocean". To date, there are five main features of COVID-19 disease.

The first is its clinical heterogeneity, as regards the severity of the symptoms (from asymptomatic/pauci-symptomatic forms, to extremely serious and fatal cases), the clinical pictures with involvement of different organs and systems, the age of the subjects, and even the highest incidence in male sex.

The second dramatic aspect of this disease is represented by its greater morbidity and mortality in the most fragile subjects, whether they are elderly and / or carriers of other chronic ilnesses (including malignancies).

The third, and probably most notable, characteristic is the absence, to date, of an effective treatment, such as a vaccine capable of protecting the general population from an infection which, as in the pandemics of the past, is no longer only affecting healthcare but is also increasingly taking on characteristics of an economic and social crisis.

The fourth element, at a certain extent a direct consequence of the previous one, is the increasing number of unproven treatments, not supported by any sound evidence, which are nevertheless proposed by several unconfirmed sources; furthermore, beyond this fake news phenomenon, the pressure towards a miracolous treatment coming from all the stakeholders (the general population, the media, the politicians), had also softened the peer review process, even of high impact journals, leading to the publication of preliminary and/or uncontrolled data, ultimately increasing the background noise surrounding the management of the pandemia.

The fifth, and final, element is the extremely rapid spread of the virus, as a result not only of its own features, but also of globalization.

So far, the question could be: how to try to compose such a complex puzzle? We would like to draw attention to these five words (heterogeneity, fragility, incurability, miraculous cures, and globalization) by trying to propose a strict parallelism with the history of the treatment of oncological diseases; indeed, these are five words have also characterized the history of the treatment of cancer. So far, what have we learnt from the cancer lesson? How did we overcome the mirage of the "magic bullet" for

the treatment of tumours? The history of therapeutic successes in Oncology is made up of small steps mediated by an increasing knowledge of the biological and molecular characteristics of the cancer cell, and of the microenvironment that surrounds it<sup>4</sup>. In other words, the improvements achieved over the past decades in the field of cancer are the net result of gradual, but continuous efforts, made with scientific methodology and intellectual rigor, ultimately aimed at achieving a personalization of treatments through a precision medicine approach<sup>5</sup>; despite having not been fully realized yet<sup>6</sup>, this remains our ultimate finish line.

But the potential turning point in this war will be represented by what is also one of the strengths of this virus: globalization. In other words, this infectious pandemic requires a globalization of scientific knowledge and skills (we could say, a "knowledge pandemic"). Namely the research model pursued in oncology: networks within networks, with the ability to create relationships and shared knowledge. In this scenario, European cancer centres and therefore also OECI are called upon to play a key role in this epochal challenge.

The first area of action is represented by sharing knowledge regarding cancer patients and COVID-19 from different centres. Today, no one knows yet how we should deal with these patients. It is increasingly urgent that the experiences of individual cancer institutions could be shared globally, in order not to disperse precious data and experience.

In this regard, I would like to point out an editorial initiative supported also by the president of OECI, represented by a special issue in the magazine Frontiers in Oncology (https://www.frontiersin.org/research-topics/13559/covid-19-infection-in-cancer-patients-how-can-we-help-patients-and-oncologists). The aim of this special issue is to offer a platform on which to gather available data from the "frontlines", as the availability of such data will prove crucial for policy makers and medical practitioners alike. Through this platform, we would like to invite those managing cancer centres to gather, and report data for the benefit of those who will encounter this infection in the coming weeks and months.

Potential issues include, but are not limited to, the following:

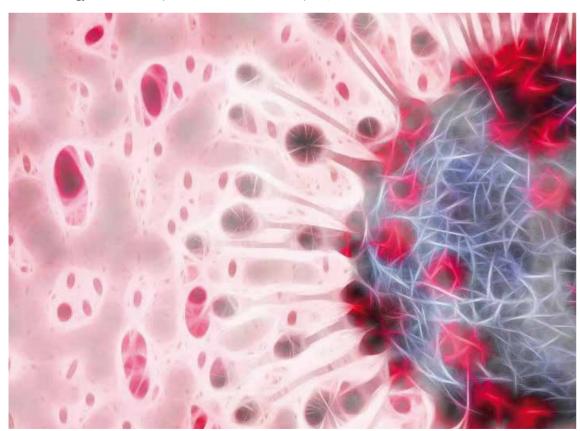
- 1) what are the practical limitations when a patient is found to be positive for COVID-19 (before or) after a session of chemotherapy, immunotherapy, and/or targeted therapies?
- 2) are cancer patients at increased risk of complications or mortality related to COVID-19 infection?
- 3) what policies are being adopted in individual countries (and/or institutions) to manage oncology departments and clinics?
- 4) how (and if) should fragile patients with advanced disease receiving chemotherapy be treated when they are in areas heavily affected by the infection? What ethical and practical implications can be found there?
- 5) Should all candidates to cancer surgery be tested beforehand to assess COVID-19 positivity? moreover, how to behave before an infusion of a systemic chemotherapy treatment? Oncological scientific societies have already started to publish guidelines (or, more correctly speaking, experts' suggestions), in an attempt to answer questions that, from the very beginning of the pandemia, emerged in everyday oncological practice, in order to try to deliver optimal care to cancer patients in such exceptional circumstances<sup>7,8</sup>.

The second challenge to which European cancer centres are called to respond is the need to identify a clear scientific leadership with dedicated oncology teams at international, national, and regional levels coordinated with each other in a hierarchical manner with the objectives of both interacting with health government agencies and to contribute to develop "dynamic" indications capable of responding to the changing needs of a health scenario in constant evolution<sup>9,10</sup>. Moreover, oncology research centres have within their wards technologies used for the study of cancer cells which, in this war, can be converted towards both the study of the molecular characteristics of the virus, as well as its diagnosis.

In conclusion, to win this war we need a strategy which requires what we have learned from research for the treatment of oncological diseases with a paradigm shift through the definition of what we have called "liquid dynamic medicine" <sup>11</sup>.

#### References

- Worldometer. COVID-19 Coronovirus Pandemic. Available at https://www.worldometers. info/coronavirus/#countries. Accessed April 14, 2020
- World Health Organization. Coronavirus disease (COVID-19) Pandemic.
   Available at https://www.who.int/emergencies/diseases/novel-coronavirus-2019.
   Accessed April 14, 2020
- 3) (COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU) https://coronavirus.jhu.edu/map.html accessed April 13, 2020)
- 4) **Grandori, C., Kemp, C.J.** Personalized cancer models for target discovery and precision medicine. Trends Cancer 2018 4, 634-642
- 5) **Prasad V, Fojo T, Brada M.** Precision oncology: origins, optimism, and potential. Lancet Oncol. 2016 Feb:17(2):e81-e86.
- 6) Tannock IF, Hickman JA. Limits to personalized cancer medicine. N Engl J Med 2016;375:1289-1294.
- COVID-19: supporting oncology professionals. https://www.esmo.org/covid-19-and-cancer. Accessed April 14, 2020
- 8) ASCO Statement on Novel Coronavirus (COVID-19). https://meetings.asco.org/am/asco-statement-novel-coronavirus-covid-19. Accessed April 14, 2020
- 9) Al-Shamsi HO, Alhazzani W, Alhuraiji A, Coomes EA, Chemaly RF, Almuhanna M, Wolff R, Nuhad IK, Chua MLK, Hotte SJ, Meyers BM, Elfiki T, Curigliano G, Eng C, Grothey A, Xie C. A Practical Approach to the Management of Cancer Patients During the Novel Coronavirus Disease 2019 (COVID-19) Pandemic: An International Collaborative Group. Oncologist. 2020 Apr 3. doi: 10.1634/theoncologist.2020-0213. [Epub ahead of print]
- 10) **Silvestris N, Moschetta A, Paradiso A, Delvino A.** COVID-19 pandemica and the crisis of health systems: the experience of the Apulia Cancer Network and of the Comprehensive Cancer Center Istituto Tumori "Giovanni Paolo II" of Bari. Int. J. Environ. Res. Public Health 2020, 17 (in press)
- 11) Silvestris N, Ciliberto G, De Paoli P, Apolone G, Lavitrano ML, Pierotti MA, Stanta G. On the behalf of the "dynamic medicine OECI group". Liquid dynamic medicine and N-of-1 clinical trials: a change of perspective in oncology research. J Exp Clin Cancer Res. 2017 Sep 13;36(1):128



# 50 Centres are now in the OECI Accreditation and Designation Programme: a significant milestone

#### Simon Oberst1,2

- 1. Chair of the OECI Accreditation and Designation Board
- 2. Director of Clinical Development Cancer Research UK Cambridge Centre

A few months ago OECI had our 50th application of a cancer centre into the Accreditation and Designation (A&D) Programme. This is a significant milestone for the programme. The programme now comprises 50 of the largest cancer centres in 14 out of 27 Member States of the EU, plus Norway and the UK. 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 1 million new cancer patients since their accreditations. The status of accreditations and designations as OECI Comprehensive Cancer Centres, and OECI Cancer Centres, is depicted in Figure 1.

Figure 1. Status of the A&D Programme at April 2020



The last few years have seen significant growth in the programme in France, with many of the major specialist cancer centres now on board, either accredited or in the process, and further new applications are expected, including in large University Hospitals. Another major area of expansion is Scandinavia, with all the significant Finnish centres already in the programme, and increasing applications from Sweden and Norway.

Interestingly, approximately half of all accredited centres have been designated as OECI Cancer Centres, and half as OECI Comprehensive Cancer Centres. Both designations are tough to achieve as measured by the quality standards, so that all centres provide high quality cancer services and education; the OECI Comprehensive Cancer Centres have a greater volume of translational and clinical research.

But there is much more to be done, as we lead the most extensive quality programme for cancer centres in Europe. Within the context of the EU Cancer Mission and Beating Cancer Plan, mentioned elsewhere in this issue, we would like to extend the network in Spain, the Netherlands, the UK, Denmark, Poland, and central and eastern European nations. Indeed, one of the ideas posed to the EU Cancer Mission Board is for there to be a Comprehensive Cancer Centre or large Cancer Centre for every 5-10 million population in EU Member States, with at least one in each smaller Member State. Our OECI vision is a Europe-wide quality network of the largest and most innovative cancer centres, sharing information on best practices in organising diagnosis and treatment, survivorship and patient involvement, and translational and clinical research. At the centre of OECI, we recognise the need to build upon the peer review and quality improvement service we provide to centres individually, by sharing and publishing data from the aggregate of our cancer centres, and providing benchmarks of best practice.

So in the next few months we will be working on setting up more comprehensive data systems, and consulting our centres about which data we should regularly collect and benchmark across our 50 plus centres. This data collection and analysis needs to be connected to patient outcomes, both clinical and quality of life measures, so that in time we can provide valuable insights into which processes and structures in our centres are producing the optimal outcomes for our patients. It goes without saying that this is a complex project!

Our OECI quality network should share innovative practices, which could range from particular roles and responsibilities of cancer nurse specialists, to models of services co-designed with patients. Our peer review teams have been keeping logs of exemplars of services we have observed in centres undergoing accreditation, and which deserve evaluation of their impact, and then dissemination among all our members. At the same time, the most common improvements which are being actioned by our members are being documented (as described in the related article here) so that we can see how the application of evidence-based quality standards is having an improving impact on cancer centres across Europe. That is the fundamental mission of the A&D Programme.

#### **Recent accreditations**

The following centres/institutes have been awarded OECI Accreditation & Designation Certificates between September 2019 and March 2020). We offer our congratulations to each of them for this achievement.

#### New accreditations

- TAYS Cancer Centre, Tampere (Finland) OECI Cancer Centre
- TYKS Cancer Centre, Turku (Finland) OECI Cancer Centre
- Trinity St. James's Cancer Institute, Dublin (Ireland) OECI Cancer Centre
- Karolinska Institutet and Karolinska University Hospital, Stockholm (Sweden) OECI Comprehensive Cancer Centre

#### Re-accreditations

- Istituto Europeo di Oncologia, Milan (Italy) OECI Comprehensive Cancer Centre
- Cancer Research UK Cambridge Centre, Cambridge (UK) OECI Comprehensive Cancer Centre

# Catalysing quality improvement in OECI A&D Centres: recent findings

#### Willien Westerhuis<sup>1</sup>, Harriet Blaauwgeers<sup>2</sup> and Simon Oberst<sup>3</sup>

- 1. OECI Accreditation and Designation Programme Co-ordinator
- 2. OECI Accreditation and Designation Programme Manager
- 3. Chair of the OECI Accreditation and Designation Board

It is the fundamental mission of the OECI Accreditation and Designation (A&D) Programme to have an impact on quality improvement within cancer centres in Europe, based on applying evidence-based quality standards. A critical part of the process when compiling the Final Report is agreeing the Improvement Action Plan with the centre. This is based on the main opportunities for improvement noted by the peer review team, together with actions addressing the standards scored as only partially or not complied with. So what are the most common improvements which are being actioned by centres in their Action Plans? In which domains is the A&D Programme having impact?

#### **Governance and Organisation**

One of the most common strategic actions for centres to improve is around the structural organisation of the cancer centre. This is a particular challenge when the centre is not a standalone cancer centre, but rather a centre based within a University Hospital, with multiple links to Universities and cancer research institutes. We find that many centres require improvement in overall governance and management to ensure the full integration of cancer research and clinical care.

#### Multidisciplinary Team (MDT) approach and integration

Multidisciplinary co-operation is essential in cancer care. We are pleased to observe that all OECI accredited centres have set up multidisciplinary teams for tumour groups, where specialists from the different disciplines involved in the care for cancer patients are present to discuss their diagnosis and treatment. However, centres are sometimes weak about **consistent organisation of MDTs**, for instance the presence of a common MDT procedure describing the patients who need to be discussed, the disciplines required to be present, data projection and recording of the decisions, as well as the structural presence of nurses and supportive care disciplines.

#### **Outcomes analysis and compliance with clinical guidelines**

We find that many cancer centres are not strong in collecting and analysing the outcomes of their patients by cancer type, stage of disease at diagnosis, and treatment. This requires sophisticated electronic patient records with an ability to build and report cohort data, relating this to compliance or non compliance of the treatment with clinical guidelines. It also requires the discipline of MDTs to hold some meetings in the year devoted not to case conferences but rather to quality analysis and improving pathways. Improving these points is common in action plans.

#### **Quality and risk management**

We find that, although centres keep different records of certain indicators (such as waiting times, Serious Adverse Events, 30-day mortality) very often they do not have a comprehensive quality and risk dashboard. Also, when centres are part of a larger general hospital, the quality indicators are not always specific to cancer patients. OECl audit teams will specifically look at how the data are used to spot systems weaknesses and improve them. Other improvement points often relate to the lack of risk assessments before the introduction of a new technology.

#### **Patient empowerment**

The comparative lack of patient involvement in the strategic and operational issues of cancer services or research is quite often noted in peer review reports as requiring improvement. In some centres patient groups are pro-actively involved in development of patient information brochures, or designing

new patient facilities. Other common improvement points relate to **informing and educating patients** about their illness, the treatment, follow-up and survivorship care. Some centres also have actions to take about providing patients with access to their own medical record.

#### Role and tasks of oncology nurses

Throughout Europe there are differing paradigms of the role and professional autonomy of oncology nurses. Improvement points regarding the roles and tasks of oncology nurses are commonly related to these issues, such as the co-ordination of cancer patients through their pathway, taking action when waiting times could be exceeded, and referring them to supportive care. In some countries in Europe there is no specific education for oncology nurses and it becomes the responsibility of the cancer centre to train the nurses in oncology after they have finished their basic nursing education.

#### Clinical research

Evaluating the structures and processes for clinical research is one of the focal points in the OECI A&D Programme. Common improvement points relate to the lack of an Institutional Review Board to evaluate clinical trial proposals, and weaknesses around the promotion of clinical trials among patients, including public information on what is involved in a clinical trial, and specific trial availability. When examining the eligibility of centres to be designated as Comprehensive Cancer Centres, we find that achieving a 10% accrual rate of patients into prospective interventional clinical trials is a high bar for some centres, but this is a measure which OECI holds very important for these centres as evidence of good translation of science.

#### **Scientific Advisory Board**

Having a Scientific Advisory Board (SAB), consisting of an international group of experts on cancer research, provides centres with an independent and expert view on research and innovation. In several centres an SAB has been found to be non-existent. This improvement point is essential for all centres engaged in cancer research.

#### Conclusion

The A&D Programme has a clear procedure for monitoring the implementation of the Improvement Action Plan in each centre one year after the peer review, and if necessary after that. At the five year re-accreditation the completion of the previous actions is also evaluated. In this way, OECI can be sure that the A&D Programme is being instrumental in spurring these quality improvements in all our centres.

### **A&D Programme and Covid-19 implications**

The year 2020 was originally going to be the busiest year to date for the OECI A&D Programme, with a total of 14 Peer Reviews planned, of which 9 were Italian cancer centres/institutes. Unfortunately, due to the Covid-19 situation in Europe, from February 2020 until the Summer, 5 reviews have been postponed so far. There may also be consequences for reviews planned for September to December 2020, as the centres, which are currently working on their self-assessments, may have difficulties completing the questionnaires within the deadline due to the crisis.

OECI does not want to burden centres with a peer review when their professionals are coping with a health care crisis. Also, our auditors are employed in European hospitals, most of which are also dealing with the Covid-19 crisis, and some of which at the present time do not permit their staff to travel abroad.

As a result, the deadlines will be redefined. The OECI A&D Co-ordination team will work with the centres to see what is feasible and reschedule the visits, starting with the centres that were scheduled for the first half of 2020. For centres working on the self-assessment, we advise them to keep working on it, as far as the situation permits, so that we can plan the visit as soon as the Covid-19 situation is over.

## Big Data, Artificial Intelligence and Real World Evidence

#### Giovanni Apolone<sup>1,2</sup>

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Nowadays Precision/Personalised Medicine has gained attention in several fields of medicine.

After a first definition that emphasizes the objective of offering the patient a therapy (drug) tailored to the genetic-molecular profile of the disease, a definition broadening the meaning from drug therapy to all the various moments of medicine (prevention, early diagnosis, therapy, surveillance and rehabilitation) and including factors related to the macro-environment, the host, the micro-environment, etc. in the profiling variables has been coined. Evidence is also emerging of a multi-factorial nature of the main degenerative diseases that remain among the leading causes of death, such as cancer, with the increasing evidence of the etiopathogenetic and prognostic role of factors related to genetics, metabolism, inflammation and the immune system. As a result, the distinctions between the various diseases are obsolete and require a more transversal research approach. The new multi-factorial and multi-dimensional context increases complexity and emphasizes a necessary holistic approach with greater integration between scientific, social and humanistic disciplines.

Despite continuing advancement in knowledge, along with the new drugs and technologies made available by research, cancer remains a major cause of illness, morbidity, mortality and costs. In the USA and in most European Countries, as a results of the combination of efforts in primary, secondary prevention strategies together with the new drugs, cancer survival has improved. Anti-cancer agents, together with radiotherapy and surgery, contributed substantially to saving lives and curing cancer diseases, both in adult and pediatric patients. This holds true mostly in early stage cases thanks to adjuvant therapy. By contrast, the efficacy of drugs to cure advanced stages is still poor and the small improvements achieved, measured in terms of months, is object of debate. Recent papers have estimated that drug treatments may only account for a small part of these positive achievements, ranging from 20 to 30%. We are waiting for the yield of the targeted agents introduced a few years ago which promise a better risk benefit profile for the lower toxicity, as well as the effect on larger population of new immunotherapy drugs so far active in a few subgroups. We hope that our increased capability to describe the molecular profile of tumors will pave the way for a truly personalized medicine. The ability to identify predictive and prognostic factors that allow us to prescribe the right care to the right patient needs to be improved.

In this complex context, a new movement has emerged promising to be able to quickly and efficiently provide new evidence: the so-called Big Data. Formally, in statistics and computer science this term generically indicates a collection and mass of a very large amount of data and information, both structured and non-structured, that are so extensive in terms of volume, speed and variety to request specific technologies and analytical methods for the extraction of new knowledge. The term is therefore used to analyse or extrapolate and relate a huge amount of heterogeneous information using sophisticated statistical Artificial Intelligence methods, such as machine learning and natural language processing, as the amount, typology and complexity of data cannot be analysed with traditional statistical methods but requires more advanced tools to reveal meaningful information. The purpose is to discover the links between different phenomena (for example correlations) and to foresee the future prognostic of factors. In oncology the matrix of data usually includes factors related to genetics, molecular, metabolism, inflammation, the immune system, treatments and outcome measures. A large amount of data does not mean Big Data. In order to define a large set of records as Big data the following four Vs criteria should be satisfied:

- The size and quantity of generated and stored data (Volume).
- The type and nature of the data that derives from the fusion of different type of information (Variety)
- The speed at which the data is generated and processed to meet the demands, as Big Data is often available in real-time (Velocity).
- The quality and the data value to assure accurate analysis (Veracity)

In oncology there is no shortage of opportunities to exploit the BIG Data and IA methodology to respond to important questions that have not been solved yet with the standard statistical analysis: identifying new targets for new drugs, improving the efficacy of old drugs, ameliorating our predictive and prognostic ability, increasing the capability to identify the best health care policies and, last but not least, increasing the patient and citizen participation in producing data relevant to decision makers, such as Patients Reported Outcome (PRO) and Patients Reported Experience (PRE) Measures.

We do have cases, clinical, molecular and administrative data coming from several sources including clinical outcomes and PRO and PRE measures; in addition, nowadays it is easier to integrate them in a common data set and process them using fast and more user-friendly methods. So, what are the factors that have limited the use of Big Data in medicine and in oncology in particular? They are several, and among them the most important are related to issues pertaining the GDPR, the existence of different institutional and national initiatives that do not interact, the need of funding to create a shared and integrated platform, and the lack of a common European effort. The ongoing Cancer Mission that has the objective to beat cancer and improve outcomes will need a coordinate effort to create a Pan-European consortium to carry out research on data from the real world that will produce new evidence that matters for patients. Big Data and Al are the instruments to do that in such a context.



# **COVID-19 and Nutrition:** from dietary prevention to nutritional therapy

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Coronavirus disease 2019 is an infection of the respiratory tract caused by coronavirus, a viral form closely related to the SARS virus. The current COVID - 19 therapy is exclusively supportive and respiratory failure from acute respiratory distress syndrome (ARDS) is the main cause of death1.

Elderly and especially cardiovascular, diabetic, hypertensive and oncological co-morbidities are factors of increased risk of mortality<sup>1</sup>.

This article analyses the nutritional aspects linked to the epidemics, and try to bring major light into the distinction between dietary prevention and nutritional therapy.

#### 1. PREVENTION

#### Malnutrition

The prevention, diagnosis and treatment of malnutrition are paramount in preventing the complications of COVID-19, particularly in elderly and neoplastic patients.

As recently reported in an ESPEN document, nutritional risks may be assessed by means of the MUST and NRS-2002 criteria in outpatients and inpatients respectively<sup>2</sup>.

According to the "Global leadership initiative on malnutrition" (GLIM), malnutrition is diagnosed by means of two or more phenotypic and etiological factors (see table)<sup>3</sup>.

#### Phenotypic criteria

#### Weight loss (%):

> 5% within past 6 months or > 10% beyond 6 monihs

Low body mass index (kg/m<sub>2</sub>):

<20 if < 70 years or <22 if > 70 years Asia: <18,5 if < 70 years or <20 if > 70 years

#### Reduced muscle mass:

Reduced by validated body composition measuring tecnique

#### **Etiologic criteria**

#### Reduced food intake or assimilation:

50% of ER >1 week or any reduction for > 2 weeks or any chronic Gl condition that adversely impacts food assimilation or absorption

#### Inflammation:

Acute disease/injured, or chronic disease related

From a practical point of view, it is necessary to draw attention to involuntary weight loss, lack of appetite, reduction of the hand strength and slowing down of the gait.

The diagnosis of sarcopenia associated to malnutrition is fundamental as it is associated with increased respiratory and cardiovascular risks.

In order to prevent and treat malnutrition and sarcopenia, a proper diet including proteins with high biologic value is mandatory. Supplements are also recommended so as to boost muscle mass whilst reducing the risks associated with sarcopenia. Indications for respiratory rehabilitation are also needed. Cardiovascular endurance training is suggested, usually in aerobic mode, at 60-80% of the maximum tolerated physical effort or heart rate or up to 4-8 degree of breathlessness according to the Borg scale or fatigue score.

Practically, it is suggested walking, swimming, cycling and similar activities, as well as gymnastic exercises which may be performed at the gym or at home without fatigue.

#### Metabolic and cardiovascular polymorbility

As far as cardio metabolic polymorbility is concerned, prevention should be mainly focused on weight, blood sugar and pressure control by means of a correct diet.

#### Additional preventive factors

The amino acid **arginine** supplementation improves bacterial clearance and T cell function for the immune system. Moreover, it is able to improve the immune response resulting from the proliferation of the cells, strengthen the competence of natural killer cells and the activity of interleukin-2 and its receptor.

The fat-soluble **vitamin A** is called "anti-infective" vitamin and many of the body's defenses against infections depend on an adequate supply. In some viral forms such as measles and viral diarrheas in children vitamin deficiency plays an unfavorable role. Vitamin A inhibits measles replication and improves innate immune responses<sup>4</sup>.

**Vitamin E** is a fat-soluble with an important antioxidant role. Vitamin E deficiency was found to intensify the ongoing myocardial damage of Coxackie B3 virus (a RNA virus)<sup>4</sup>.

**Vitamin D** is another fat soluble which plays an important role in the maturation of immune cells and is associated with various viral diseases<sup>4</sup>. Recent observational reports suggest a significant deficiency of vitamin D in subjects with COVID-19.

**Omega-3 fatty acids** play a very important role in anti-inflammatory processes, and are the substrate for the formation of a group of lipid mediators (resolvins) that mediate the resolution of inflammation.

**Selenium** is a key trace element in defense against infectious diseases as antioxidants. It is a cofactor of glutathione peroxidase, as well as zinc in superoxide-dismutase, which are fundamental enzymes in antioxidation process. The activity of glutathione peroxidase, along with other antioxidant enzymes such as superoxide dismutase and catalase are correlated with viral infections due to an imbalance between ROS production and airway antioxidant defenses. Dietary selenium deficiency can be associated with increased oxidative stress and can alter the viral genome so that a normally benign or slightly pathogenic virus can become highly virulent in the host, in particular in case of influenza viruses and Coxackie<sup>4</sup>.

**Zinc** is an important element in the maintenance and development of immune cells of both the innate and adaptive immune system. A zinc deficiency results in dysfunction of both humoral and cell mediated immunity and increases susceptibility to infectious diseases. Zinc supplementation can effectively impair replication of a variety of RNA viruses<sup>4</sup>.

Finally **iron** may have a negative effect in case of overload as it produces oxidative stress. A reduction in red meat intake is therefore suggested.

#### 2. NUTRITIONAL THERAPY IN PRESENCE OF DISEASE

In malnourished patient with insufficient oral intake, oral supplements (ONS) are suggested (at least 400 kcal per day and 30 g of protein high in essential amino acids and especially in leucine, which is associated with muscle mass stimulation)<sup>2</sup>.

The protein source of ONS should preferably be of high biological index with high anabolic action, in particular whey protein (WP), used for this reason to antagonize the sarcopenia of elderly subjects. Moreover WP contains immunostimulating constituents associated with a wide variety of bioactive functions (in particular anti-infective). WP promotes the synthesis of glutathione (fundamental intranuclear antioxidant) thanks to the high content in glutamine and cysteine<sup>5</sup>. During viral infectious diseases (hepatitis C and HIV) WP has determined an inhibitory efficacy on the viral infection probably in relation to the content of lactoferrine<sup>5</sup>. In HIV RNA virus WP supplementation has significantly increased the synthesis of glutathione (GSH) as well as muscle performance. Multivitamins and particularly vitamin D-250H should be administered at admission<sup>5</sup>.

In oxygenotherapy patients with nasal cannulas (FNC), high flow nasal cannulas HFNC (HFNO) and non-invasive ventilation (NIV) artificial nutrition should be used. The preferred route is the enteral one<sup>6</sup>.

Severe obesity (BMI >40 kg /m²), and diabetes are high risk conditions for the development of serious diseases from COVID-19. Inflammatory-metabolic derangement is linked to insulin resistance and stress hyperglycemia, high levels of free fatty acids and increased protein catabolism<sup>6</sup>.

Diabetes and hypertension have, as minor common denominator, high levels of plasma myeloperoxidase (MPO) that could be linked to pulmonary phagocytic hyperactivation and HLH¹. Interstitial pneumonia causes significant hypoxemia associated with increased aerobic glycolysis (Warburg effect), intracellular acidosis and ROS increase<sup>7</sup>.

Hyperactivation of macrophages, linked to Warburg effect, with the recruitment of monocyte, neutrophils and platelets from circulating blood play a crucial thrombo-inflammatory role, (as recently suggested in COVID-19), by forming neutrophil extracellular traps (NET) formation, and monocyte—platelet aggregates which could be responsible of DIC<sup>7</sup>.

From a therapeutical point of view, the reduction of glucose bioavailability by means of ketogenic diet could hypothetically represent a possible metabolic tool for reducing the Warburg effect of macrophages, neutrophils and monocyte accrual from blood, inhibition of IFN type I production (by lactate) and viral replication (by antiglycolytic effect)<sup>4</sup>.

In this regard, a RCT has been developed at IRCCS San Martino in Genoa, Italy. The open trial involves patients with COVID-19 in medium-severity and hospitalized phase with the use of a normocaloric, normoproteic ketogenic diet. The main endpoint is trying to reduce the evolution towards CSS and ARDS and mortality/transfer to sub-intensive/intensive care or need for CPAP or intubation<sup>7</sup>.

Currently, whilst waiting for the results on the ketogenic diet trial, a diet with reduced carbohydrate content should be activated in case of initial symptoms. In principle, in obese patients, nutritional regimes should include low-calories and relatively high-protein<sup>2,6</sup>.

Moreover, when the respiratory situation worsens, the calorie ratio of lipids/carbohydrates should be increased to 50/50 in order to reduce oxygen consumption and carbon dioxide production<sup>2,6</sup>.

Nutritional treatment should also be considered in convalescence and take into account the long period of inactivity and asthenia which could result in loss of muscle mass and muscle function<sup>2</sup>.

In these patients a strong focus on functional rehabilitation of the motor and respiratory system associated with a good support of proteins with high content of essential amino acids must be evaluated in the long term.

Critical COVID-19 patients can remain intubated for long periods. After estubation, dysphagia can impair the return to normal food intake and a diet with a modified consistency with hyperprotein supplements could be suggested<sup>6</sup>.

In conclusion, the control of malnutrition, sarcopenia and multiple nutrient and micronutrient deficiencies is crucial in the prevention of COVID-19, which should also see an increased focus on metabolic risks, namely on weights and glucose control.

#### Main references:

- 1) **Zhou F, Yu T, Du R, et al**. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020 Mar 11. https://doi.org/10.1016/S0140-6736(20) 30566-3 [Epub ahead of print].
- 2) **Barazzoni R et al.**, ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection, Clinical Nutrition, <a href="https://doi.org/10.1016/j.clnu.2020.03.022">https://doi.org/10.1016/j.clnu.2020.03.022</a>
- 3) **Cederholm T, Barazzoni R, Austin P et al.** ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr 2017;36: 49-64.
- Lei Zhang & Yunhui Liu Potential interventions for novel coronavirus in China: A systematic review Med Virol. 2020;92:479–490.
- 5) **Sukkar SG, lorio E.** Whey proteins. Overview of clinical trials. Progr Nutr [Internet]. 2011Sep.1 [cited 2020Apr.22];13(1suppl):35-4. Available from: <a href="https://www.mattioli1885journals.com/index.php/progressinnutrition/article/view/1341">https://www.mattioli1885journals.com/index.php/progressinnutrition/article/view/1341</a>
- 6) **Bouadma L, Lescure FX, Lucet JC, et al.** Severe SARS-CoV-2 infections: practical considerations and management strategy for intensivists. Intensive Care Med 2020 Feb 26. https://doi.org/10.1007/s00134-020-05967-x [Epub ahead of print].
- 7) **Sukkar SG & Bassetti M**: Hyperglycemia And Covid-19 Cytokine Storm Syndrome: Is There An Immunosuppressive Role Of Ketogenic Nutrition? Submitted to Nutrition.

# Towards a population screening for breast/ovary cancer genetic risk?

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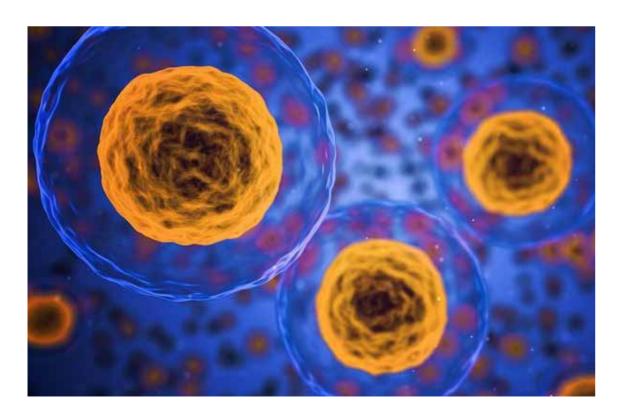
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Breast cancer is the most frequent female malignancy and it represents 25% of all new cases of cancer, while ovary cancer is still one of the most deadly among women.

Most of these tumours are sporadic, while 5-7% are due to a hereditary predisposition. The genes mainly involved and better characterized in the hereditary predisposition of these neoplasms are BRCA1 and BRCA2 genes, two tumour suppressors involved in DNA repair mechanisms and whose mutations confer an increased risk of developing breast and/or ovarian cancer.

The prompt identification of these mutations can bring substantial benefits not only for prevention measures (e.g. prophylactic mastectomy and/or ovariectomy), but also in the management of the disease, including personalized follow-up approaches and targeted therapies. Moreover, it allows to undertake a genetic counselling path for healthy family members, in order to identify those still healthy but at a definitive risk of cancer for BRCA mutations.

The indication to perform the genetic test following the genetic counselling is based on current guidelines which indicate particular features of the personal and family history and clinical criteria conferring a probability of having a BRCA mutation greater than 10% as a threshold for accessing the test. However, besides reducing mortality and social impact, the extension of screening programs also for healthy family members, would allow a huge saving of the rising costs associated with these pathologies, supporting the choice of the "Test" strategy vs a "No Test" one.



The results of analyses carried out on different health systems show that by applying the "Test" strategy on patients and their families, a decrease in breast and ovarian cancer cases is achieved with a substantial decrease in costs and savings in economic resources which are also related to the decreased costs of the clinical management of early detected tumours.

Specifically, as the Italian example shows, it has been estimated that the "Test" strategy decreases the costs for treatment of breast and ovarian cancer cases by  $\in$  7,052,221.00 and  $\in$  18,244,182.13 respectively. It should also be outlined that, against an initial investment of  $\in$  5,719,584.00 for the "Test" approach on a target population of 5.200 new cases estimated for the year 2016, the saving of economic resources is of about  $\in$  25,296,403.13. The cost per case avoided is therefore  $\in$  29,727.50.

Even more remarkable, various studies show that it is rewarding, in particular situations, to provide the BRCA genetic test, despite the guidelines, for example to all patients diagnosed with ovarian cancer and then extend the test to their family members in case of positivity. This strategy has been validated in countries such as United Kingdom, where the extension of the test to family members of ovarian/breast patients with BRCA mutation proved to be a cost-effective approach.

In order to imagine a wider scenario, that considers the significant limitations of family history-based guidelines due to their complexity and limited availability of clinical information-that often lead to inappropriate and inconsistent access to the test with possible loss of more than 50% of subjects carrying BRCA mutations - another different approach, based on population or "mainstream" screening of BRCA genetic test approach represents an advantageous possibility in terms of cost-effectiveness and cost-benefit.

This approach promises that in the next decades it will be possible to decrease the number of deaths for cancer compared to the strategy based on family history alone, and thatif carried out on the entire population, it would allow to intercept mutated but still healthy cases. The more patients will be identified as mutated, the sooner and better they will be treated with the result of a less impact on public health costs due to late care.

# Towards a routine diagnostics NGS workflow including equipment

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#### Introduction

Next Generation Sequencing (NGS) is vital for the diagnosis and treatment of complex diseases while the applications are growing fast. However, NGS mostly needs to be seen as in house developed tests. This makes implementation complex for medical laboratories. Therefore, it is key to develop dedicated diagnostic NGS workflows including equipment.

#### The project

INSTAND-NGS4P is an EU-funded Pre-Commercial Procurement (PCP) project Grant Agreement n°874719 for improving cancer patient's benefit from NGS, which started 1-1-2020, with 18 partners. It will develop integrated standardized NGS workflows, which compile information from gene testing, pharmacogenetics testing and e-medication in one result supporting therapy decision. The EU-cofunded PCP project provides funding to define unmet medical and technical needs based on an Open Market Consultation to form the basis of a call for tenders for companies. Responding companies are evaluated for their ability to answer these needs.

PATHOLOGY

CANCER

#### Consortium

- 7 medical centres with NGS platforms in research and diagnostic led by Medical University of Graz and University of Florence; ERASMUS University Medical Centre, University of Milano-Bicocca, University Clinics of Schleswig-Holstein, St. Anna Kinderkrebsforschung, Centre Léon Bérard and one SME, BioXPedia
- Patient advocacy groups, Italian Patient Association and European Cancer Patient Coalition
- Standardization organization DIN(CEN/ISO),
- Research infrastructures: BBMRI-ERIC through Technical University of Munich and UNIMIB, and ELIXIR through University of Ljubljana
- Partners in NGS-related EU programs: University of Manchester and University of Liverpool- the 100,000 Genomes Project- UK Biobank-pharmacogenomics; Organisation of European Cancer Institutes (OECI) - 92 entities, 13 Clinical Accredited Centres - 18 Accredited CCCs, and University of Helsinki- FIMM network and iPRI

#### Major challenges of the EU Project

- Improving analytical performance by standardizing pre-analytics
- Integrating pre-analytics, analytics and data analytics into a standardized workflow
- Defining genetic variants with medical implications for cancer and pharmacogenetics relevant for cancer drugs
- Meeting IVDR requirements
- Improving NGS benefits for patients and health care

#### How it works

Two innovative NGS workflows from sample pre-analytics to medical decision-making will be developed for routine diagnostics. The workflow's modular design enables also SMEs to contribute. Specifications support the "PCP suppliers" in complying with regulation and standards. To achieve the ambitious objectives, the 7 leading centres jointly procure. 8.55 M€ is allocated to the R&D suppliers, who are selected based on public tenders. The call concerns pre-analytics, sequencing, bioinformatics, e-reporting/e-medication. All activities are in partnership with the European Commission. Stay tuned with our project: http://www.instandngs4p.eu/



### EACR 2020 - Innovative Cancer Science: Better Outcomes Through Research - Postponed to 2021

Jane Smith

Chief Executive Officer European Association for Cancer Research

In light of the global COVID-19 pandemic, the EACR Board has made the decision to postpone all EACR conferences that were to be held in 2020, including the EACR 2020 Congress. We want to be proactive in protecting the safety of the research community as well as the populations of our venue cities. We are already planning ahead for 2021, and we are also working hard to convert some of our 2020 meetings into virtual events for EACR members, so look out for some exciting announcements on this soon.

We have announced that our 2020 Congress will be postponed to the new dates of 09-12 June 2021, in the same venue of Torino, Italy. We will update the programme to reflect new research and developments in the field and we look forward to our community gathering together again in June 2021 for exciting science and networking. The new website will be accessible from **www.eacr2020.org** and registrations will remain open. In the meantime, on 18-19 June 2020 we will hold a virtual EACR Congress. The first day will feature keynote lectures and the EACR awards. The second day will include oral presentations from selected abstracts submitted before 02 March.

In the last edition of the magazine, we told you about the EACR and OECl's long-standing collaboration on the Molecular Pathology Approach to Cancer conference. After delivering eight successful conferences on this important topic in Amsterdam from 2011 to 2018, the conference was paused in 2019 to allow time for a thorough review of the programme and the format, to ensure that it continues to meet the needs of its diverse audience including pathologists, molecular pathologists and pathology residents, researchers in the field of molecular diagnostics and precision oncologists. We planned to relaunch the conference in Lisbon in May 2020. In the light of COVID-19 that conference will now take place in December 2021, in the same venue in Lisbon. Details can be found on the conference website: <a href="https://www.eacr.org/conference/molecularpathology2020/covid-19">https://www.eacr.org/conference/molecularpathology2020/covid-19</a>

It has, and continues to be, a time of uncertainty and change, but we will navigate this unique and challenging situation together as a cancer research community. EACR President Alberto Bardelli wrote recently: "Nobody really knows when we will be able to go back to the lab. To my fellow scientists across the world: be prepared, start prioritizing your experiments and keep in touch. Discovery needs kit, yes, but it truly gets done when minds meet."



### Frankfurt Cancer Conference From Molecular Research to Mechanism-based Cancer Therapy

**Christian Brandts** 

Director University Cancer Center Frankfurt

The novel coronavirus SARS-CoV-2 has brought about many changes in the way cancer researchers all over the world work and collaborate. Nevertheless, we are confident that this year's Frankfurt Cancer Conference, themed "From Molecular Research to Mechanism-based Cancer Therapy", will take place from 23 to 25 September 2020. We are expecting 400 scientists from all over the world to attend the conference.

Numerous internationally renowned speakers from the USA and Europe have accepted the invitation to present their recent findings, including Scott Armstrong, Mariano Barbacid, Craig Crews, Benjamin Ebert, Neta Erez, Tony Green, Joan Massagué, Louis Staudt, Robert Weinberg and Eileen White.

With eight sessions and two poster exhibitions, the conference program covers a broad spectrum of topics in translational cancer research, ranging from immunotherapy, tumor microenvironment, tumor stem cells and preclinical models to innovative approaches in personalized oncology.

The Frankfurt Cancer Conference aims to bring together leading experts in cancer research and in clinical oncology. Participation in the conference offers many opportunities, especially for young researchers to present their work to a larger scientific community, discuss their results with renowned experts in the field, and establish contacts and collaborations for new research projects.

In recent years, numerous cancer research networks have been established in the Frankfurt area making

important contributions to the development of new cancer therapies, among them the University Cancer Center (UCT) Frankfurt, member of OECI, as well as the Frankfurt/Mainz site of the German Cancer Consortium (DKTK) and the Frankfurt Cancer Institute (FCI). Along with international research highlights, promising results from the translational research programs of these three institutions will be presented and discussed at the Frankfurt Cancer Conference 2020.

#### Frankfurt Cancer Conference at a glance:

The Frankfurt Cancer Conference will take place at the Westend Campus of the Goethe University Frankfurt from 23-25 September 2020. It is aimed at scientists in cancer research, oncologists as well as students of medicine, biology and biochemistry. Scientific abstracts for poster presentations and talks can be submitted until April 30, 2020 (also end of Early Bird Registration). The registration deadline for the conference is August 15, 2020. More information on the program as well as registration and abstract submission can be found at:

www.frankfurtcancerconference.org



# Modification to the OECI membership

#### **New Members**

The OECI warmly welcomes 2 new applications for Full Membership and 1 application for Associate Membership.

Their participations will certainly enrich the OECI Accreditation and Designation Programme and will help to better realise the activities promoted by our Organisation.

#### **Full Membership**

#### **Beaumont Hospital**

http://www.beaumont.ie Ireland



#### **IRCCS Ospedale Sacro Cuore Don Calabria**

https://www.sacrocuore.it Italy



#### Associate Membership

#### Sainte-Catherine, Institut du Cancer

https://www.institut-sainte-catherine.org
France



#### Modification of denomination

The OECI Full Members Institut Paul Strauss (Strasbourg – France) becomes: Institut de Cancérologie Strasbourg Europe "ICANS"

#### Modifications of the membership status

Starting from January  $1^{st}$  2021, in relation to the Brexit, the below listed OECI Full Members become **Associate Members Type A** 

The Christie NHS Foundation Trust
 Cambridge Cancer Centre
 King's Health Partners Integrated Cancer Centre
 Imperial College Healthcare - NHS Trust

Manchester - UK
Cambridge - UK
London - UK
London - UK

#### Requests of withdrawal

At the end of the current year the following OECI Members will withdraw from the OECI Membership:

European School of Oncology (Associate Member type A)
 Ente Ospedaliero Ospedali Galliera (Associate member Type A
 Genova - Italy

OECI would like to thank the two Members for their contribution to the life of Our Organisation and is looking forward to further fruitful collaborations.

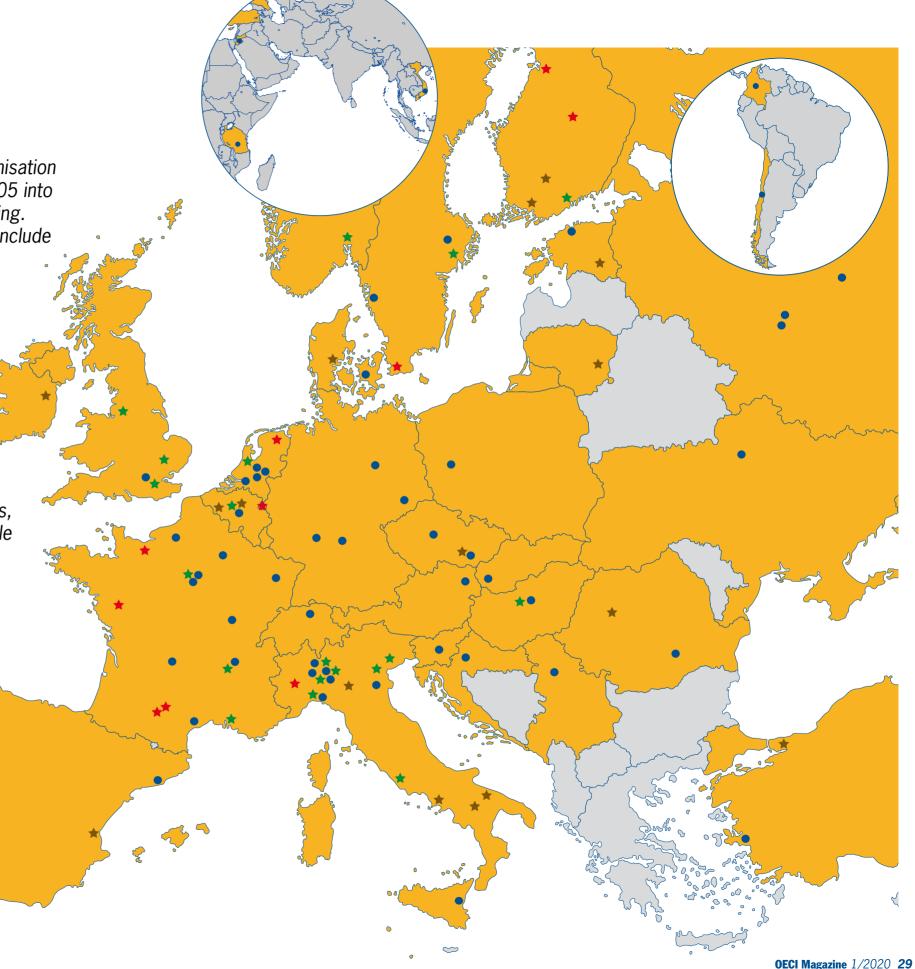
The OECI membership amounts to 102 Members. More information are available via <a href="http://www.oeci.eu/Membership.aspx">http://www.oeci.eu/Membership.aspx</a>



The OECI is a non-governmental, non-profit Organisation founded in Vienna in 1979 and remodelled in 2005 into OECI-EEIG, a European Economic Interest Grouping. Today, the OECI regroups 102 Members, which include some of the most prominent European Comprehensive Cancer Centres. Several major cancer centres from the Chile, Colombia, Jordan, Russian Federation, Tanzania, Turkey, Ukraine and Viet Nam are also members of the Organisation, also to benefit from our Accreditation and **Designation Programme** 

The OECI aim is to accelerate the application of multidisciplinary personalised care approaches, to reduce morbidity and to guarantee an equitable access to care to all cancer patients, avoiding the collapse of the National Health Systems.

- ★ OECI Members A&D certified Comprehensive Cancer Centre
- ★ OECI Members A&D certified Cancer Centre
- ★ OECI Members in the A&D process
- Other OECI Members



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