ESMO Perspectives

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ISSUE 8 AUGUST 2019

Boundaries

Think global, act local

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Josep Tabernero

ESMO President

When the ESMO Asia congress was first launched in 2015, our Society made a clear commitment to deliver education without borders. Few years later we can witness that opportunities to keep oncology professionals in the Asia-Pacific region updated with the rapid pace of oncology have increased, thus further expanding cooperation with international colleagues.

This year, our Leaders Generation Programme (LGP) will double its offer. It will take place not only in Europe, in the ESMO Head Office in Lugano, but also in Asia, for the first time aiming to provide talented professionals in the region with the opportunity to develop their leadership skills and grab a chance to become leaders of tomorrow in the global ESMO society.

Today, crossing geographical boundaries is key to the evolution of cancer research and care, and a boost to education is only one of the effective strategies to try to solve discrepancies across countries. More collaborative efforts are also needed, for example, to overcome shortages of anti-cancer medicines posing a threat to patient care, as they can reduce adherence to therapy and limit the ability of physicians to provide effective treatment regimens. ESMO is proud to be at the forefront of this key health policy issue, and a call to action was launched a few months ago at an EU Parliament meeting to ensure that the shortage of anti-cancer medicines remains a top priority on the EU political agenda. Initiatives as such at a global level may have a great impact on the current oncology scenario, however by reasoning with the common principle "Think global, act local", we must also narrow our views to adapt global recommendations to country-specific settings. In this issue of the magazine, we have chosen to explore how National Cancer Control Plans (NCCPs) can help countries to meet global goals, and which is the role of the oncologist in their implementation.

Talking about boundaries, geographic distance is not the only barrier that can affect high-quality cancer care. The sex and gender oncology movement which is emerging in the field as reported by one of our members reinforces my belief that there are also cultural and professional boundaries that we need to cross to achieve better outcomes for patients in the future. Another example is represented by patient-reported outcomes which have been traditionally designed to get clinicians closer to their patients, but that still struggle to be fully integrated into daily practice.

Oncology knows no border, and so we should not as professionals. The stories that we report in this edition offer valid examples on how we can push our boundaries further, by not limiting ourselves and letting us inspire, and by keeping on pursuing our efforts to put our ideas into practice.

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National Cancer Control Plans: **Translating Commitments Into Action**

National cancer control plans or programmes (NCCPs) are crucial to achieve the World Health Assembly-agreed reductions in cancer-related mortality. However, their implementation is still hard to achieve.

The World Health Organization (WHO) defines a National Cancer Control Plan as 'a public health programme designed to reduce cancer incidence and mortality and improve quality of life of cancer patients, through the systematic and equitable implementation of evidence-based strategies for prevention, early detection, diagnosis, treatment, and palliation, making the best use of available resources'.

"82% of the WHO Member States have publicly available cancer-related plans."

There is growing evidence that the concrete way to translate the latest achievements of research and the commitment to cancer into practice comes through the implementation of NCCPs.

In 2013, the World Health Assembly and ministers of health globally agreed plans for the prevention and control of non-communicable diseases (NCDs) and accepted a target of a 25% relative reduction in the overall mortality from NCDs by 2025. "Having global recommendations represents a first step in the achievement of a better cancer care," highlighted **Giuseppe Curigliano from Istituto Europeo di Oncologia (IEO), Milan, Italy**. "The second step is to put them into practice at a national level. The development and implementation of NCCPs, which are comprehensive and evidence-based resource plans, allow countries to translate commitments for cancer into action." There are both political and practical reasons why the development of a country-specific NCCP is crucial to optimising the management of cancer. If a country does not have a structured plan, which takes into account variables including available services and cancer burden, it is unlikely to achieve its goals.

According to a recent review (Lancet Oncol. 2018;19:e546–555), 82% of the WHO Member States have publicly available cancer-related plans, with discrepancies in their development and domains that are part of the plan. "This really depends on a country's priority," said Curigliano. "For some, this will be prevention, for others treatment. Information from cancer registries can provide the picture of a country's disease burden and form the basis of prioritisation of action."

There is no **one-size-fits-all model** for optimal NCCP implementation. The International Cancer Control Partnership (ICCP) – a group of international organisations engaged in cancer control planning efforts – is involved in supporting the development, implementation and evaluation of NCCPs. In addition, for the last two decades, the International Cancer Screening Network – a consortium of countries, organisations, and experts acting as a critical resource for countries that have active population-based cancer screening programs in place – has worked with the National Cancer Institute (NCI) to promote evidence-based cancer screening implementation. **Detailed budget planning and resource allocation** are still major challenges according to **Lisa Stevens, formerly from NCI US Center for Global Health**. "A programme cannot be set up in isolation. For example, if you organise a screening programme, you must make sure that you have the resources to fund not only this but also the treatment that will be required when cancers are detected."

Economically realistic NCCPs not only focus on the most important priorities but also use available tools to help **estimate the costs of proposed strategies**. "One such tool, developed for cervical cancer, uses an algorithm to estimate costs based on healthcare workers numbers and materials used", explained Stevens. "The WHO is currently working on a costing tool for around 20 different cancers in different income situations and is conducting pilot testing." Another way to optimise constrained resources is to target the population most at risk. "For example, the US Preventive Services Task Force has raised the age for mammography in the US to at least 50 years, which avoids over-screening and an unnecessary burden on the healthcare system", continued Stevens. "However, long-term impact will only come with sustained government investment and, as the person who makes the decision to invest is unlikely to be the person in power when the successes start to happen, this is sometimes a hard sell."

The European experience: Spain

José Martín Moreno
University of Valencia, Spain

Spain initially developed its cancer strategy for the national health system in April 2003, when I was Director General of Public Health and Spain's Chief Medical Officer. The plans were updated in 2006 and again in 2010 and a new update is expected in the near future. Spain is a decentralised Member State of the EU and the plans are adjusted for each autonomous community. The overall strategy is comprehensive, containing aspects of health promotion and protection – including primary prevention actions – early detection, adult healthcare, child and adolescent care, palliative care, research and evaluation. However, its weak point is that it does not have a **detailed operating budget**, beyond that for coordination aspects.

Spain is proud of its excellent health system, which is seeing a reduction in cancer mortality at a rate of 1% per year and a cure rate of 60% for cancer patients. In this respect, one of the greatest oncology challenges facing the country in the coming years is **long-term survivorship**: currently, there are more than 1.5 million people who have overcome the disease and who have health needs different to those of the general population, including long-term side-effects and socio-economic requirements. Other areas to be addressed include adapting the strategy in line with new developments and challenges in the field of cancer prevention and control – with an operational budget – and allocating **more investment for cancer research**.

Thanks to joint actions such as the European Partnership for Action Against Cancer, it has been possible to map cancer plans in Europe and the EU and there appears to be reasonable homogeneity throughout the region, at least on paper. The true situation may be a different picture, mainly because written plans do not always develop into operational realities – leading to functional inequalities – and plans without budgets, of which there are many, are in effect wasted paper.

The Latin American experience: Brazil

Felipe Roitberg
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Brazil has had a National Cancer Control Plan (NCCP) since 2005 and it was consolidated in 2017, as part of its non-communicable diseases (NCD) policy. Prevention and early diagnosis are the strongest domains, and **two relevant programmes** are worth mentioning. Firstly, the implementation of an extremely successful anti-tobacco policy, which led to a reduction in smoking-related deaths and new lung cancer cases. Secondly, a programme improving pap-smear coverage and human papillomavirus vaccination, which aims to reduce cervical cancer burden.

The major barriers we have encountered in implementing the NCCP relate to the **monitoring of the plan**, and the fact that the **findings are not presented in a user-friendly way**, making it difficult to gauge the effectiveness of the plan. Importantly, Brazil also needs to find ways to tackle its relatively high number of late diagnoses compared with high-income countries.

It is difficult to compare Brazil's NCCP with those of other Latin American countries, because of the fragmented healthcare systems in the region. The overall Latin American Universal Health Coverage (UHC) index – scoring all indicators of universal health coverage from 0 to 100, with higher total scores indicating a better coverage – is 75, which is quite comparable with Europe's 77. However, when depicting the data, the heterogeneity of the UHC index among Latin American countries becomes apparent, being differently distributed according to four out of five WHO quintiles. Efforts are being made to overcome these issues, such as the implementation of the 'Universal Access with Explicit Guarantees' in Chile, a list of neoplasms for which treatments are covered by the government, and Peru's public health policies focused on primary-care interventions aimed at modifying population behaviours related to obesity, smoking and alcohol consumption, all major risks factors for cancer.

Even though Brazil has a high UHC index, **there are inequities in access to cancer treatments within the system**, reflecting the remarkable regional socioeconomic disparities. So, depending on where you live in the country, "my healthcare system is not your healthcare system".

Brazil has its own essential medicines list, however new and costly approved drugs are not incorporated, and this frequently translates into out-of-pocket expenses. It is worth noting that while Brazil's investment in oncology has risen as much as eight times in recent years, it is significantly lower than high-income countries' per capita investment.

The Asian experience: India

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India has had a dedicated NCCP for over forty years: put in place in 1975, it was most recently updated in 2016. **Treatment is core to the Indian plan**. The government has made significant investment in new treatment centres and there has been also an increase in private and public-private sector collaborations. More recently, the government made a commitment towards providing free treatment for patients within the 'Ayushman Bharat Scheme' and many women and children in India have benefitted through government funding of cancer treatment in 2019. While India is doing much better with its cancer plan compared with other areas in the South Asian Association for Regional Cooperation (SAARC), we recognise that these are relatively low-income countries and that many more structured governmental, civil society and stakeholder efforts are needed to improve access to cancer care in India.

The NCCP recommendations include screening for common cancers and efforts are in place to improve population-based screening by the state governments through the district cancer control programmes. However, much has to be done to make screening acceptable within the community and to raise awareness of the need for it, particularly for women's cancers. **Education of the public** may help to improve uptake of screening, but given the high rate of illiteracy, particularly in the lower socioeconomic classes among whom rates of cervical cancer are higher, programmes that provide one-to-one or small group education are likely to be more successful than written educational literature. These educational programmes would require more health workers within the rural health schemes. The lack of population-based screening results in significant numbers of patients with locally advanced disease, necessitates **strengthening of palliative care** services at district and regional cancer centres and improved access to pain control measures.

Global cooperation is crucial in helping to implement national plans. **Global guidance on areas of importance** helps to direct national efforts. For countries with limited resources, global engagement, including financial assistance, would help them work towards achieving the goals of their cancer plans. India has invested in the development of efficacious, low-cost screening methods, generic drugs and indigenous diagnostic and treatment equipments. These initiatives will help to meet the demand-supply gap for cancer services. Furthermore, international advocacy can strengthen implementation of NCCPs, by promoting focus on defined 5- and 10-year goals, and a list of committed deliverables, and a dedicated budget to ensure implementation.

E-Cigarettes and Cancer

What Should Oncologists Know About E-cigarettes?

Electronic nicotine delivery systems (ENDS) or e-cigarettes were supposedly designed to be a short-term bridge to smoking cessation. Now they are increasingly used by youth and non-smokers and may be a gateway to traditional tobacco cigarettes. Evidence on the long-term use of these devices is lacking and the harm of aerosols is still uncertain. More studies are needed to determine the role of ENDS in cancer development or treatment.

ENDS are battery-powered products that create an aerosol by heating a liquid consisting of propylene glycol and vegetable glycerin and flavouring agents. The liquid may or may not (but usually does) contain nicotine, at variable doses. Differently from conventional cigarettes, there is no combustion of tobacco in ENDS, thus making people think they cause less harm. However, the varying voltage that is applied to the liquid creates a mixture of potentially toxic substances in the aerosols that are then inhaled by users.

While the scientific community is still questioning the health risks associated to the use of ENDS or e-cigarettes, manufacturers are increasing the attractiveness of these devices. Making them more coloured, with glamourous shapes and smelling deliciously tasty, the result is that vaping is often perceived as less harmful than smoking as no tobacco combustion is involved.

The rapidly growing use of ENDS is emerging as a worrying trend globally, thus giving life to what seems to be an **ENDS paradox**: supposedly designed to be a short-term bridge to smoking cessation, some evidence now suggest that they **may be related to a transition to traditional tobacco cigarettes**, especially among youth, raising safety concerns for a long-term use of these electronic devices and dual use with persistent tobacco smoking.

"Although the EU has banned sales of electronic devices containing nicotine to minors, they can buy them on the internet without effective controls", commented **Cinzia De Marco, a researcher of the Tobacco Control Unit of the IRCCSS Istituto nazionale dei tumori in Milan, Italy**. "ENDS are expanding the nicotine market by attracting youth who were at low risk of initiating nicotine use with conventional cigarettes, but many of whom are now moving on to conventional cigarettes. Even if they do not progress, promoting nicotine use to youth is bad public health policy and it is also necessary to consider that more and more young people are using these devices". According to a recent survey of the European Commission, **about 15% of the European population** had tried ENDS at least once in their life in 2017.

The current landscape around e-cigarettes echoes the 1950s when, while smoking tobacco cigarettes was an increasingly popular social habit, the initial evidence on the carcinogenic effects of the substances released by tobacco combustion emerged from research confirming the involvement of tobacco products in cancer development. After some decades, it is now part of common knowledge that smoking is the one of the main avoidable causes of cancer. But what about ENDS?

"About 15% of the European population had tried ENDS at least once in their life"

At the European Lung Cancer Congress (ELCC) 2019 last April, a discussion on ENDS and cancer prevention aimed to investigate **how oncologists engage with this emerging issue** in public health. "As a medical oncologist", commented **David Spigel from Sarah Cannon Research Institute-Cancer Center in Nashville, US**, "I talk a lot about smoking cessation to my patients and their families, but e-cigarettes do not really come up as a topic". In his opinion, **more evidence is needed to clarify the role of these devices in cancer prevention** thus providing guidance to oncologists to deal with their patients' requests or concerns. "When someone asks me if these devices are harmful, my answer is that we don't know, but probably they are due to the many substances in the aerosol. Unfortunately, what we have learnt so far comes from popular press, and there is limited evidence in the traditional medical press. A lot of us assume that somebody must be watching, approving, assuring safety and understanding what these devices are, but this does not always seem the case", he said.

One of the biggest concerns of **Carolyn Dresler, a member of the International Association for the Study of Lung Cancer (IASLC)**, is that people who smoke may become dual users - that is, keeping on smoking both traditional cigarettes and ENDS. "Most people agree that ENDS are less harmful than traditional cigarettes are", she commented at ELCC 2019. "But although we have not much evidence on their harmful effects at the moment, there is one very important message that healthcare providers should deliver to their patients: to quit any kind of smoking as soon as possible." Dresler continued: "This is an area of significant controversy even within our oncology colleagues. Some advocate that patients must stop the known most deadly product - cigarettes, and if they cannot stop with the more traditional smoking cessation products, then, they should try e-cigarettes. Then, they should stop using e-cigarettes. Basically, the important point is for patients to get off of deadly cigarettes, and then, stop the other interventions (medicines or e-cigarettes) as soon as possible."

In this scenario, one of the major problems is that the ENDS market and research proceed at different speeds. While the former is growing rapidly and expanding its offer to attract an increasing number of consumers – it is expected to cross 43 billion USD by 2023 with a 15% steady annual growth rate since 2017 – the latter is still at its early times and many more years will be spent waiting for robust evidence from the studies.

Evidence of the impact of e-cigarettes on human health **are still sparse**. A systematic review in 2017 (CA Cancer J Clin. 2017 Nov;67(6):449-471) reported that short-term use of ENDS does not adversely affect cardiovascular function, apart from the already known effects of nicotine on heart rate. Another review (Cancer Epidemiol Biomarkers Prev. 2017 Aug; 26(8): 1175–1191) showed that ENDS can induce inflammation at the pulmonary level given the toxic and irritating mixture of components in their aerosols, although at a lower rate than tobacco smoking.

Regarding the **carcinogenic aspect of using ENDS**, results will be acquired from epidemiologic studies that will take years. At present ample research demonstrates significantly lower levels of carcinogens from these devices. A recent report from the National Academies of Sciences, Engineering, and Medicine concluded that there is no available evidence whether or not e-cigarette use is associated with intermediate cancer endpoints in humans. "I think that ENDS have much lower levels of carcinogens", said Dresler, "but what about the other constituents in the aerosol? They do not seem harmless, and we need more research particularly in cardiovascular and pulmonary impacts to assess if ENDS use plays a role in the development of other diseases too."

A precautionary approach toward the use of ENDS has been adopted globally. In 2016, the World Health Organisation (WHO) recognised that these devices might be less harmful than conventional cigarettes but called for more regulation to deter their promotion to non-smokers and young people, minimise potential health risks to vapers and non-vapers and prohibit health claims about their use. In Europe, the market is regulated by the recently revised Tobacco Products Directive (TPD) 2014/40/EU, that aims to harmonise the safety and quality specifications for ENDS including but not limited to the volume of the refill container, the nicotine content and the existence of child-resistant refill containers.

While safety and health concerns still need to be assessed, the role of these devices **in smoking cessation** is also questioned. A recent meta-analysis (Annu Rev Public Health. 2018 Apr 1;39:215-235) has reported that vapers are about one third less likely to quit smoking, compared to smokers who do not use e-cigarettes. "We need more research to understand why devices like that would make more sense than those we have already to help our patients to quit smoking", continued Spigel, "because we do not know the long-term effects of this strategy. Also, it would be relevant to understand **what happens in the long-term**. What are the behavioural consequences of moving to e-cigarettes? Does it really open-up to other addictive behaviours? These are the questions we have no answers to and that can have an impact on our role as oncologists".

In cancer patients, smoking cessation has been associated **with improved survival, higher quality of life, and better outcomes** of surgery, chemotherapy, radiotherapy, and biological therapies. According to De Marco, ENDS, if used properly, may represent a useful tool to support patients in early phases of smoking cessation. "It will take several years to have reliable data on the consequences of long-term use", she said. "It is possible that the long-term health benefits associated with their use might outweigh the short-term risks, nevertheless, this aspect would need to be clarified". De Marco concluded, "The greatest difficulty of research in this area, both short and long term, is the possibility for researchers to receive funds not derived from tobacco multinationals companies so as to be **able to conduct independent studies**."

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Patient-Reported Outcomes

Integrating The Patient's Voice Into Clinical Settings

While patient-reported outcomes (PROs) are now an integral part of many phase III trials, their incorporation into routine clinical practice is hampered by economic and time pressures among healthcare professionals. However, with the advent of electronic-based questionnaires, current boundaries are likely to be stretched.

When we look at cancer treatments today we should not just focus on that they are clinically effective and sustainable but also on how they are perceived by patients. In the last few decades, growing attention to disease-related aspects that could not otherwise be captured by objective clinical measurements has resulted in patient-reported outcomes (PROs) with the aim **to get doctors closer to patients** and better understand their experience with the disease and its treatments.

It has been proved that **physicians can often underestimate the impact** of a particular side-effect on a patient's life. In oncology, for example, chronic grade 1 nausea would probably not seem to a doctor to be a particularly noteworthy side-effect. However, patients find it extremely difficult to function with this constant low level of nausea and it can really interfere with their quality of life (QoL). And the reverse is also true, as highlighted by **Nadia Harbeck from the University of Munich, Germany**. She said, "For instance, on paper, objective assessment of the CDK 4/6 inhibitors reveals a high degree of grade 3/4 neutropenic toxicity, which might be expected to result in poor patient acceptability. However, PROs show that because this is a manageable side-effect it does not actually have an impact on patient quality of life."

Having already been used for a long time in clinical trials to assess QoL and health-related QoL, the importance of PROs has grown to such an extent **that phase III trials are now generally required to include a PRO measure** and they are also a particularly important element of health technology assessments. Described as enabling the doctor to hear the patient voice at a greater volume, **PROs have the true potential to get doctors closer to patients**.

"As doctors, we try our best to meet the patient's needs, but we must realise that we cannot do this without the patient's input," said **Emiliano Calvo who leads the Early Phase Clinical Drug Development in Oncology, international programme at START Madrid Group, Spain, at Centro Integral Oncológico Clara Campal (CIOCC)**. PROs are also a more reliable and accurate way of gauging a patient's health than simply talking with them. "Patients may forget, or be too embarrassed, to tell the doctor about a side-effect they had several weeks ago. But if it is recorded on a PRO, it can be used to modify management, if necessary," continued Calvo.

Despite the many benefits of formal questionnaires, **their use is still sparse**. While most doctors are not against their use as a concept, in fact, the **logistics of implementing PROs** in daily practice may represent a major limitation. "Oncologists want to spend their time helping the patient. They already do not have enough time to discuss the results of diagnostic tests, treatment options, side-effects, etc. with patients, and so it is difficult for them to see how PROs can be incorporated into their daily practice," said Calvo. Some physicians may feel that PROs provide no extra information over what can be obtained during the usual work-up and monitoring of the patient. This **lack of awareness** regarding the additional value of PROs needs to be addressed through education and training.

A **lack of standardised** tools also hinders the use of PROs in clinical practice. "Can you imagine how difficult it would be to assess and compare efficacy and toxicity if clinicians worldwide did not use the same standardised scales to measure anti-tumour activity and side-effects?" said Calvo. "This is the situation with PROs." Choosing which PRO to administer can also deter doctors from using them. PROs cover a wide range of parameters – including symptoms, mood, QoL, physical function and distress – and selecting the most appropriate one to use in any setting can be confusing. Although the advice is to individualise choice according to the patient's needs, this can be a hard task.

Electronic PROs may help doctors to overcome major barriers to their use. However, these barriers seem to apply mainly to the relatively outdated paper-based PROs, a format which is unlikely to be fully integrated into clinical practice. **The introduction of electronic PROs** (ePROs), which are digitally-based and can be used by patients remotely, has also come with the promise to change the face of PROs in clinical care. By using these tools to record outcomes on a regular basis, patients' cumulative experiences can be stored digitally and then be discussed with the doctor at the next visit.

Studies have shown that by enabling management to be individualised to the patient, these ePROs can actually improve survival in patients with metastatic cancer (JAMA. 2017 Jul 11;318(2):197–198; LBA9006 Journal of Clinical Oncology 34, no. 18_suppl). "They allow patients to feel that their care is continuous and they help doctors to build a better chronological picture of how patients are coping with their disease and its treatment," said Harbeck. The integration of ePROs into clinical practice will **take time and will require a change of mindset** on the part of healthcare practitioners. "Some doctors may be concerned that by using ePROs they may be legally obliged to continuously monitor a patient's health and may be liable to legal redress if they fail to do so. This issue can be addressed by requiring patients to formally agree that an ePRO is to be used only as a tool for them to prepare themselves for their next visit with the doctor.

"Since the implementation of PROs combined with patient-centred interventions has already been shown to be associated with better health-related QoL, with fewer hospitalisations and even increased survival compared with standard care, these data collections and evaluations should be highly encouraged. How critically patient-reported data are needed becomes even more evident, as it has been demonstrated that clinicians miss about half of their patients' symptoms during treatment."

Karin Jordan
University of Heidelberg, Germany

"PROs collected via validated measures are an important and valuable means of determining if cancer treatments and procedures help rather than harming patients. The benefits of novel therapies expressed as progression-free survival or modest overall survival, which may excite clinical scientists, are often of little or no real value to patients experiencing the burdens of treatment-related side-effects. Quality not just quantity of life must be measured."

Dame Lesley Fallowfield
University of Sussex, Brighton, UK

"The value of PROs lies in their nature; they come directly from the patient and represent his or her health status perception. We know that clinicians might underestimate the incidence of symptoms, therefore PROs need to be included in clinical decision-making. Moreover, to develop patient-centred care we need to further engage patients in the development of care. PROs, ideally combined with patient-reported experiences, could enhance such initiatives."

Manuela Eicher
University of Lausanne, Switzerland

Friedrich Stiefel
University of Lausanne, Switzerland

Putting the patient at the centre of care

The use of PROs is raising more attention about how patients perceive their illness and QoL. What can this tell us about how the idea of cancer has changed over the last decade?
QoL became a consideration with the introduction of cancer treatments, which were often mutilating and associated with severe side-effects. However, progress in acting on this was slow and systematic evaluation of QoL in clinical trials – in order to surpass sole survival assessment – only started decades ago. In the late 1980s, when I started out in oncology, the psychological impact of cancer on patients as a threat to life, for example, was not really appreciated. The subsequent move towards more patient-oriented outcomes has been driven largely by the increased awareness on the part of healthcare providers that cancer is something that affects both the body of the patient and their psyche. For example, pain or disability resulting from cancer and its treatment interfere with the way individuals interact with the world. The increase in survivorship, leading to more patients living with cancer and its physical, psychological and social consequences, highlights the need to address issues important to the patient. The focus on patient-oriented care is also a result of patients being more vocal in expressing their needs, the change in the doctor-patient relationship – with patients becoming less deferential – social change, and research showing the value of PROs. Finally, the traditional collaborative outlook of oncology professionals encourages the contribution of other disciplines relevant to patient-centred care, such as psycho-oncology.

What are the differences in patients' and doctors' perceptions and reporting about symptoms, outcomes and adverse events and why is it important to integrate these subjective and objective perceptions into cancer care?
We need both perspectives. We need the objectifying assessment of symptoms and side-effects by the doctor to detect, diagnose, treat and monitor the disease. However, for patients, it is less about the actual symptom or side-effect and more about the consequences of it on their lives. Two patients who present with the same disease and symptoms may subjectively feel the impact and the burden of a given symptom differently, depending on how it affects their daily life, which again depends on their individual activities and aspirations. We must recognise that objectifying measures do not capture subjective experiences. For example, while a physiological test may indicate to a doctor that there is no change in a sign, for example muscle weakness, the patient may find that they are having greater problems with movement and this causes them distress and embarrassment. It is with and through the body's senses that we experience our world and are affected by it; symptoms interfere with these experiences depending on the way we are in this world.

What are the current major barriers to putting the patient at the centre of care?
The physician should be able to work with the patient to find out what the most important symptom is for him or her and to tailor management appropriately. To achieve this, we need to improve communication between doctors and patients to ensure that doctors understand their needs more clearly, and not only check symptoms, but enter the patient's world.

Neglecting to put the patient at the centre of care is often not only due to lack of efficient communication. So what can a doctor do to really understand the patient's experience?
A doctor needs to have sufficient time to talk to them and this is often not possible in many cost-constrained healthcare settings. In addition, cancer treatment tends to follow a very structured clinical assessment, which carries the risk of hampering the emergence of the patient's subjectivity; changing this requires a change of mindset and of proceeding in the consultation. Added to this, some physicians cope with the emotional demands of their work by distancing themselves psychologically from the patient. Oncologists should thus be encouraged to engage more with the patient, while safeguarding their own mental health. Education and training can certainly help in this respect, as a position paper on the importance of communication training in oncology stated. This paper also outlined the relevant training elements for physicians, which have the potential to improve physicians' capacities to adjust to the patients' needs, without neglecting their own needs (Ann Oncol. 2010 Feb;21(2):204–247). While patients are nowadays much better informed and prepared for discussions than they used to be – largely due to the efforts of patient advocacy groups, which are particularly developed in oncology compared to other disease areas – it is the clinician's responsibility to ensure that each individual patient is given sufficient support and encouragement to discuss his or her needs.

Why We Need To Investigate Sex Differences In Cancer Research

In the era of tailored treatments, looking at sex-related differences may have a great impact in cancer care as biological sex may not only affect tumour biology but also the pharmacokinetics and pharmacodynamics of medicines. Anna Dorothea Wagner, University of Lausanne, explains that a paradigm shift in how studies are analysed, interpreted and, ultimately, designed is required.

Anna Dorothea Wagner
Department of oncology, Lausanne University Hospital and University of Lausanne, Switzerland

An innovative approach

Sex- and gender-sensitive medicine postulates that differences in biological sex, gender identity, role and relations all impact health and disease, and may have implications for prevention, screening, diagnosis and treatment. Its goal is to learn from these differences to improve care and treatment for men and women.

There is a growing body of evidence to suggest that patients' sex can have an impact on the biology and evolution of cancer. However, it is not possible to generalise – there may be no differences in some cancers and large differences in others. With our growing understanding of tumour biology, we can better appreciate such potential differences.

But therein lies the crux, we can only do this if we are actively looking for differences. According to Goethe, *"One only sees what one looks for. One only looks for what one knows."* The consequence of assuming that non-sex-related cancers and their treatments are the same, is that **inter-sex differences in cancer biology and response to treatment** have often escaped our attention.

It is clear that some differences in cancer epidemiology and/or outcomes between men and women can be attributed to differences in past behaviour. For example, in melanoma, differences in the site of tumour development broadly reflect gender behaviour in exposing different areas of the body to the sun – the legs in women and the trunk in men. However, when human melanoma cells are injected into mice, those from men lead to the development of a more aggressive disease than those from women, indicating the involvement of a biological sex effect.

Sex- and gender-sensitive medicine has been taken into consideration by the cardiovascular community for many years but it is relatively new to oncology. I began working in the field around five years ago, quite by chance. I came across young women in my clinical practice with a type of treatment-resistant diffuse gastric cancer that I had not seen in men. In addition, I had the impression that the toxicity of the chemotherapies I was using for gastrointestinal cancers was more pronounced in women. Hoping to find out more about the influence of sex on the development and treatment of cancer, I conducted a systematic literature review about the impact of the patient's sex on chemotherapy toxicity and was astonished to find that it generated only around 40 relevant articles. This made me realise that **the area was indeed insufficiently studied**, and that we would have to conduct our own research to get answers to our questions.

Further research confirmed my initial clinical suspicions. In younger patients with non-hereditary gastric cancer, women suffer more often from poorly cohesive adenocarcinomas (Ann Surg Oncol. 2016 Dec;23(13):4344–4351), which have a very aggressive evolution. This has been observed in different geographical regions (Acta Oncol. 2017 Jan;56(1):39–45). Others have now confirmed that sporadic diffuse gastric cancer has a distinct molecular profile in young women (Gastroenterology. 2017 Aug;153(2):536–549.e26). Another disease subtype, for which patient sex significantly affects the epidemiology – having a significantly higher incidence in males – is adenocarcinoma of the lower oesophagus or gastro-oesophageal junction.

Precision medicine is a much-talked-about goal in cancer management. Patient age, sex and race are fundamental biological variables and while the impact of age on cancer and its treatment have been investigated extensively, the effects of sex and race remain unclear. If we truly want to tailor therapy, we need to challenge **the long-held tradition of treating men and women as if they are biologically identical**. They are not.

For example, men have a higher metabolically active fat-free body mass than women, which is why some chemotherapy agents have higher elimination rates and lower plasma levels in men compared with women. In view of this, we should be questioning if men are receiving sufficiently high doses for optimum efficacy. A trial in elderly men with lymphoma demonstrated that increasing the dose of rituximab – to counterbalance the higher elimination rate – led to an increase in progression-free survival without an increase in toxicity (Br J Haematol. 2017 Nov;179(3):410–420). Another issue of particular interest is that while inter-sex differences in the immune system are well recognised, little has been done to investigate if these differences affect the **relative efficacies of cancer immunotherapy in men and women**.

"We need to challenge the long-held tradition of treating men and women as if they are biologically identical. They are not."

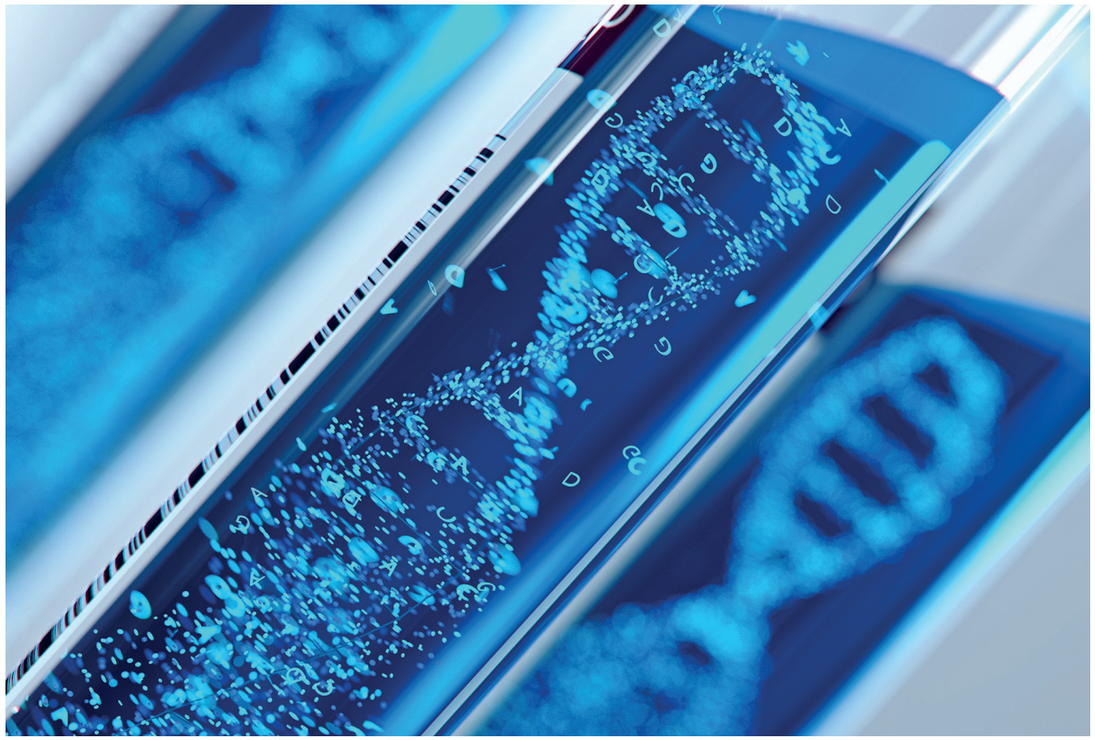
The challenge for oncology today is to look for patterns of how sex and gender affect treatment by investigating potential differences between men and women in cancer epidemiology and outcomes, as well as the pharmacology of cancer therapies and the treatment effects. If such differences are observed, we need to try to understand the **biological basis for these differences** and what can be done to improve treatment outcomes.

It is difficult to power studies to look at inter-sex differences, as their type and magnitude is unknown. What is key is that we analyse the efficacy and toxicity of treatments according to sex, in both the control and experimental arms of existing clinical trials and, crucially, publish these results. Rather than assuming upfront that differences between sexes are due to statistical errors, it should be considered that they may be the result of true biological differences. Medicine targets, but also the optimal dose necessary to hit a medicine target with an acceptable level of toxicity, may be different for men and women (JAMA Oncol. 2018 Jul 1;4(7):1003–1006). Generally, in early studies, patient numbers are too small, and data from large trials or pooled analyses are necessary to understand if inter-sex differences exist, and if they do, to what magnitude.

The **ESMO workshop held in 2018 – 'Gender medicine meets oncology'** – was the first organised discussion about gender medicine in oncology. Featuring some top names in cancer on its faculty, the event was judged a great success by participants and faculty members and we truly hope that it helps to raise awareness among oncologists about the importance of this field. The proceedings are due to be published soon.

Going forward, we need to have broad collaborations, to continue to raise awareness and to increase the involvement of societies if we are to make progress in sex- and gender-sensitive medicine. I personally am very hopeful that a sex-based approach to treatment will improve patient outcomes. And, after a slow start, I am delighted about the current level of interest in the topic – this year, I was invited to present talks on the subject at the Royal Society of Medicine in London, at the ESMO World Congress on Gastrointestinal Cancer and at the International Society of Gender Medicine. All in all, I think that the outlook is very promising for an area that is still very much in its infancy in oncology.

From left to right: Berna C. Özdemir *Department of oncology, Lausanne University Hospital and University of Lausanne, Switzerland;* **Anna Dorothea Wagner** *Department of oncology, Lausanne University Hospital and University of Lausanne, Switzerland;* **Gian Paolo Dotto** *Department of biochemistry, University of Lausanne, Switzerland. Cutaneous Biology Research Center, Harvard Dermatology Department and Massachusetts General Hospital, Boston, US*



Beyond Blood With Liquid Biopsies

Joan Seoane
Vall d'Hebron Institute of Oncology, Barcelona, Spain

Pioneering work by Joan Seoane and colleagues from Vall d'Hebron Institute of Oncology in Barcelona makes use of cerebrospinal fluid (CSF) to detect circulating tumour DNA (ctDNA) in patients with brain tumours. Where blood and plasma analysis have failed, a new era for liquid biopsies based on different physiological fluids for different tumour types is on the horizon.

The focus of our work in the laboratory at the Vall d'Hebron Institute of Oncology is the characterisation of brain tumours with the aim of finding ways to improve the treatment of patients with these cancers. In common with other aggressive tumour types, brain tumours demonstrate considerable intra- and inter-tumoural heterogeneity, and also evolve over time, so accurate characterisation is necessary to determine the best treatment. Unfortunately, tumour tissue samples **are difficult to obtain in brain cancers** and the **procedure can be risky** for the patient. Frustrated by this, we looked for other ways to help characterise brain tumours, and in 2013 we came across liquid biopsies, which at that time were using exclusively blood and plasma.

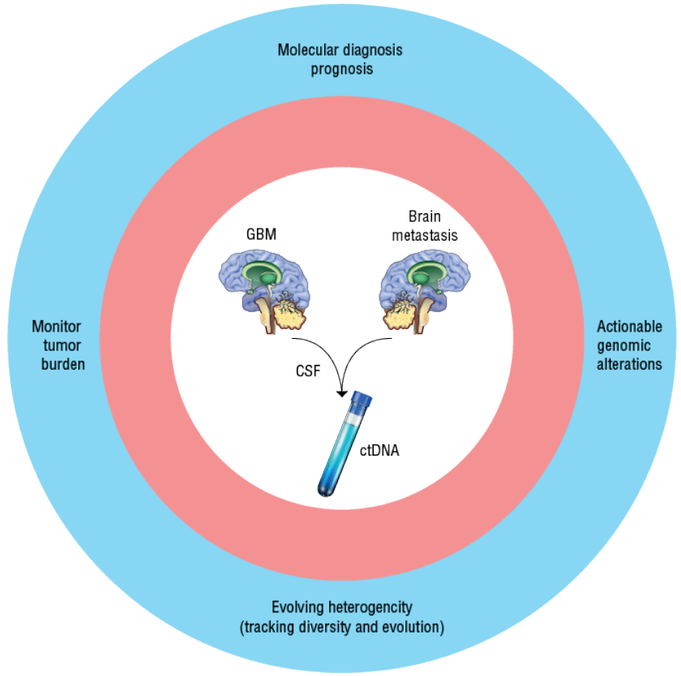
We quickly discovered, however, that patients with **brain tumours do not exhibit tumour DNA in the blood**, so blood or plasma liquid biopsies would be unlikely to yield useful information. That was when we hit upon the idea of using CSF – which is unique in its intimate contact with the brain tumour – as the liquid biopsy medium. Luckily, our position within a multidisciplinary team meant that we could quite easily obtain the necessary CSF samples from patients with brain tumours. The results of our first analysis were startling, showing a clear-cut superiority in the ctDNA content of CSF over that of plasma from the same patient (Nat Commun. 2015 Nov 10;6:8839; Clin Cancer Res. 2018 Jun 15;24:2812).

The advantage of CSF over plasma reflects not just the close contact of CSF with the brain tumour but also the fact that, unlike plasma, **CSF is relatively uncontaminated by normal DNA**. We were so encouraged by the findings from our initial study that we embarked on a joint Spanish project – involving the Hospital 12 de Octubre, the Hospital Clinic de Barcelona and the Vall d'Hebron Institute of Oncology, and funded by the Spanish Association Against Cancer (Asociación Española Contra el Cáncer, AECC) – to investigate the concept further and determine how it could be implemented in clinical practice.

We recently reviewed the evidence for CSF ctDNA for brain tumours and central nervous system metastases (Ann Oncol. 2019 Feb 1;30(2):211–218). The information we get from this approach provides us with a wealth of information about brain tumours that can be used to optimise treatment approaches. First of all, **tumours can be effectively characterised molecularly and any genomic alterations determined**. This enables us to accurately identify tumours with characteristic mutations, such as histone 3 (H3) mutations in midline gliomas, and so complement standard diagnostic techniques without having to perform surgical tissue biopsies. Data can also help us to learn more about intratumoural heterogeneity.

Diagnosis goes hand in hand with prognosis. We are currently looking at using CSF ctDNA analysis in medulloblastoma to distinguish between benign and malignant tumours and then to tailor treatment accordingly. Such a strategy will help to spare patients with benign tumours the often significant toxicities such as cognitive deficiencies and even secondary tumours that can be associated with aggressive anticancer treatment. CSF ctDNA will also allow us to **monitor disease progression or regression and the evolution of tumours**, including the development of mutations that can alter tumour aggressiveness or resistance to treatment. The information will also facilitate the implementation of precision medicine when appropriate, such as in cases of *EGFR* mutation or *ALK* translocations in patients with lung cancer-associated brain metastases. On a similar note, we will be able to detect mechanisms of acquired resistance, for example tumours with EGFR T790M, without the need for intracranial biopsies. Other future possibilities include the prompt detection of disease relapse, which could ensure earlier treatment intervention and an improved chance of an effective response, and the detection of minimal residual disease. Also, we should remember that serial CSF ctDNA sampling can be performed to provide a picture of the tumour over time, in a way that would not be feasible with tissues biopsies.

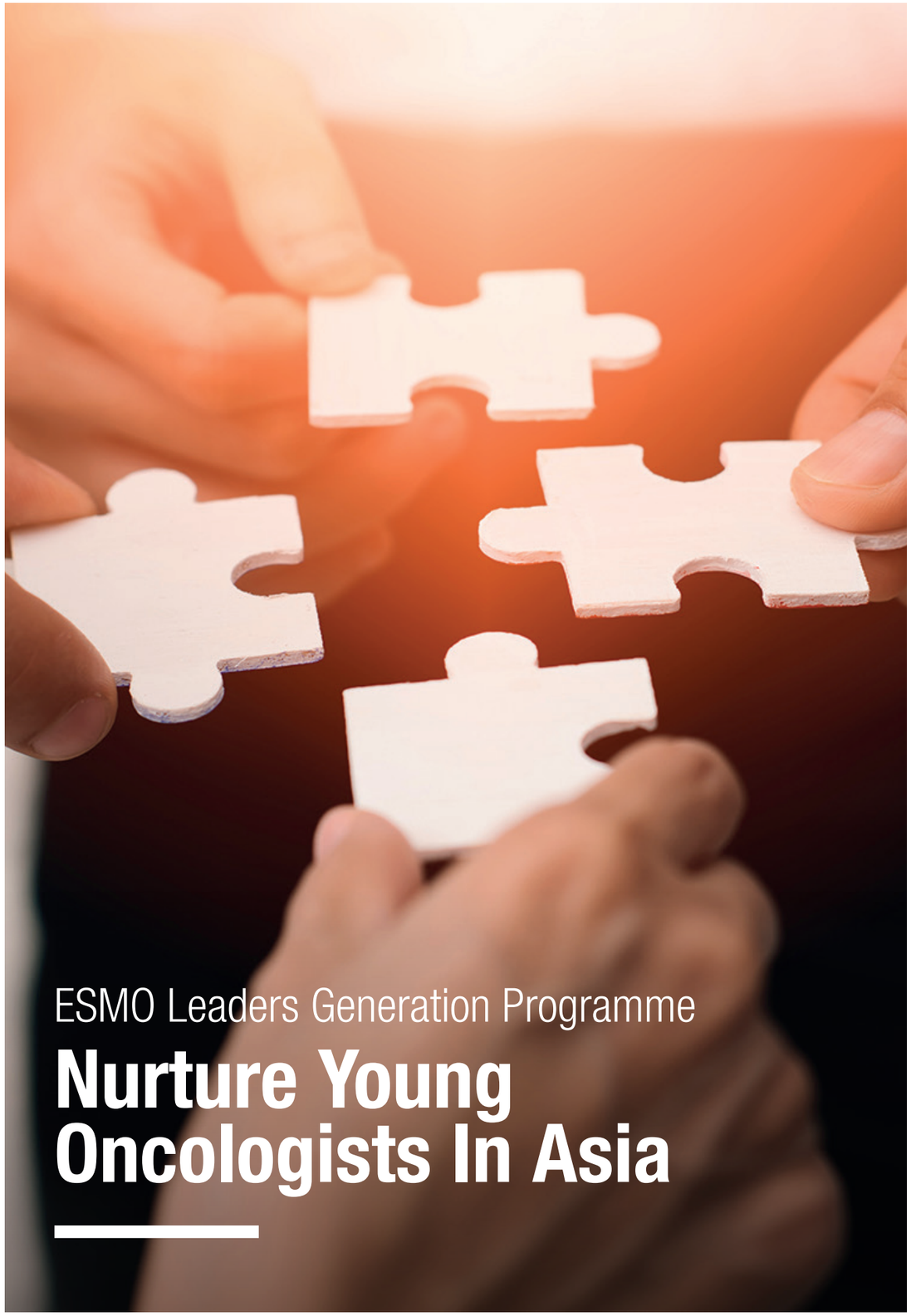
CSF circulating tumour DNA as a liquid biopsy for brain tumours



Annals of Oncology, Volume 30, Issue 2, February 2019, Pages 211–218,
https://doi.org/10.1093/annonc/mdy544

The benefits of CSF ctDNA are clear but there are inevitably some drawbacks too. **Sensitivity is an issue**. We are still not capturing all patients because the levels of CSF ctDNA are below the sensitivity threshold. This is particularly true for patients with low-grade tumours. **Cost is another problem**. In general, whole-exome sequencing is the preferred approach to allow tumour characterisation and to provide diagnostic and prognostic information, but this is expensive and is not available for most doctors to use in daily clinical practice. Finally, centres will need to have both the **technology required to perform the analysis and the personnel trained** to use it.

The use of CSF as a liquid biopsy medium has raised questions about the **utility of other physiological fluids for different tumours**, and groups in Europe and the USA are looking into using other media, including urine and saliva. I think that there will always be a place for tissue biopsies, not least because they provide information not available from liquid biopsies, for example on tissue structure and histopathology. Generally, the role of liquid biopsies will likely be to complement tissue biopsies, although where the risk associated with acquiring a tissue biopsy is considerable a liquid biopsy may be used on its own. Given the pace at which technology is advancing, I am confident that current barriers to the wider use of liquid biopsies – chiefly the need for cheaper and more sensitive equipment – will soon be overcome, and that this type of testing will be available in the clinic in the near future.



ESMO Leaders Generation Programme

Nurture Young Oncologists In Asia

Since 2016, the ESMO Leaders Generation Programme (LGP) – which was conceived to nurture emerging young leaders, to enhance their personal skills and inform them about ESMO's role in oncology – is an opportunity to identify ESMO's future leaders. New this year, the programme will cross geographical boundaries and take place also in the Asia-Pacific region.

The first ESMO Leaders Generation Programme (LGP) Asia will be a four-day course held in Singapore from 18 to 21 November 2019. The course will provide participants with an overview of how ESMO works, offering workshops, discussions and hands-on media and leadership skills training. The programme is aimed at qualified medical or clinical oncologists, working in the Asia-Pacific region and who are ESMO members aged between 31 and 45.

As the world of oncology is getting more complex, young oncologists find themselves needing not only to gain clinical experience and be up-to-date on the latest research findings but also to refine **their ability to network, communicate and lead a team**. With soft-skills training not being part of conventional medical education in any country, the ESMO Leaders Generation Programme (LGP) represents a unique opportunity for its participants to grow as fully fledged leaders-of-tomorrow. Traditionally held in Lugano, Switzerland, where the ESMO Head Office is located, this year the programme will also take place in **Singapore, from 18 to 21 November**. "ESMO is a growing society, with a strong foothold in Europe, but rightly, its work extends worldwide in an all-inclusive encompassing approach", commented **Benedikt Westphalen from the University of Munich and Comprehensive Cancer Centre Munich, Germany**, who participated in the programme in 2018. "Those taking part in the new LGP in Asia will learn a lot about ESMO and how to be an active member. In turn, ESMO and oncology globally will benefit from their contribution and the creation of international networks for the future. Whether in Europe or Asia, I strongly recommend that young oncologists who have a willingness to learn, to grow as a leader and to engage with the Society apply to participate in ESMO LGPs. For me, this programme proved to be both a great social experience and a valuable accelerator for my personal career."

Networking during the LGP has also facilitated Westphalen to **take on greater leadership roles** within ESMO and to be involved in several ongoing scientific projects, as he explained. "Since participating in the programme, I joined ESMO Translational Research and Precision Medicine Working Group and I became a member of ESMO Gastrointestinal Tumours Faculty".

Among the 20 participants who attended the 2018 LGP in Lugano, **five oncologists came from Asia**. "For me, the presence of oncologists from different Asian countries enriched the course," concluded Westphalen. "I believe it is important to look and learn beyond what is happening in our own hospitals and to gain insight from colleagues with different cultural and professional backgrounds who are working under different healthcare systems."

Jyoti Bajpai

Department of Medical Oncology, Tata Memorial Centre in Mumbai, India

Jyoti Bajpai, from the Department of Medical Oncology, Tata Memorial Centre in Mumbai, India, was one of the five Asian participants at the LGP in Europe in 2018.

I heard about the course from the Indian Society of Medical and Paediatric Oncology and thought it would be an exciting experience to boost my career. The programme provided a unique opportunity **to learn about ESMO's structure and governance**, its scientific activities and fellowship opportunities, its role in public policy and how ESMO interacts with other related organisations. The LGP provided me with professional skills **that are usually not a part of the medical school curriculum**, for example, how to better communicate and lead, and how to manage time, priorities and stress. I gained insight into my own personality and got ideas to maximise the efficiency and functioning of my team.

The programme exceeded my expectations and provided a wonderful platform to become more involved in ESMO activities. Since the LGP, I have been invited to become a member of ESMO Sarcoma Faculty and this has really helped my career progression. The course and associated networking have **broadened my horizons** and enabled me to be a greater part of ESMO's extended family.

Cancer care in Asia is generally consistent with that advocated by ESMO in Europe. However, holding a dedicated LGP in Asia will help to encourage the sharing of useful practices, build bridges between Asian societies and ESMO, and inspire even more leaders in oncology for the future.

During my time at the LGP, I also learnt about ESMO Women for Oncology, an initiative aiming to support female oncologists looking to achieve leadership positions. The gender gap is an issue that is particularly relevant in Asia too, and female oncologists should be encouraged to apply to join the LGP to improve their leadership skills.

Click to watch & find out more.

Cancer Medicines Shortages

The Time To Act Is Now

Shortages of inexpensive essential cancer medicines is a growing emergency in Europe, although the size of the problem is still uncertain as data are lacking. ESMO is at the forefront in order to drive concerted and collaborative action. A call to action was launched last April as the issue cannot be tackled by countries individually and establishing a strong European leadership is crucial.

Shortages of essential cancer medicines have a direct impact on patient care. For example, a delay or complete inability to provide chemotherapy as a result of shortages can have significant consequences for patient outcomes, including survival rates. In April 2019, ESMO collaborated with the European Parliament to organise a cross-partisan event entitled 'Shortages of Inexpensive, Essential Medicines: Calling for Tangible Political Commitments in the EU' to ensure this issue remains a top priority on the EU policy agenda. A call to action was launched with recommendations and key steps for the 2019–2024 legislative cycle.

ESMO's 'Call to Action' with recommendations and key steps to address cancer medicine shortages in Europe

RECOMMENDATIONS

1. **Introduce legislation** for early notification requirements for medication shortages.
2. **Establish European strategic plans** for medicine shortages
3. **Introduce incentives for production infrastructure improvements** including financial incentives to address the economic causes of manufacturing issues. Incentives for suppliers to remain in these markets should also be considered.
4. **Develop catalogues of shortages** based on a common minimum set of data requirements, including a common EU definition of medicines shortages.
5. **Develop national essential medicines lists** based on the World Health Organization's Model List of Essential Medicines.
6. **Establish procurement models** designed to prevent medicines shortages, including tender-cylce harmonisation.

KEY STEPS

1. Develop an EU-wide study on the issue of medicines shortages and their overarching impact on the European Union through independent EU advisory bodies on social and economic affairs.
2. Work towards creating a common definition of medicines shortaages in the European Union.
3. Position inexpensice essential medicines shortages as a key political priority for the European Union's 2019–2024 legislature.

In 2019, the Economist Intelligent Unit (EIU) and ESMO prepared a set of reports on the current situation of medicines shortages in 5 countries – **Germany**, **Bulgaria**, **Romania**, **Belgium**, and **Finland**. The five country profiles show that unfortunately there is a lack of data on the extent of the issue and that European and international collaborations are key to facilitate the exchange of products in short supply. This work follows the **EIU-ESMO Report on Cancer medicine shortages** published in 2017.

Here we hear two different perspectives on medicines shortages: from a national society for medical oncology and from a patient advocate on the situation in their country, the proactive actions they are taking, and how they are implementing the ESMO recommendations.

Perspective from a National Society for Medical Oncology

Bernhard Wörmann
Deutsche Gesellschaft für Hämatologie und Medizinische Onkologie (DGHO, German Society for Haematology and Medical Oncology), Berlin, Germany

In line with other European countries, Germany suffers from cancer medicine shortages. After a severe shortage of **melphalan** in summer of 2015, we began to study the problem at the German Society for Haematology and Medical Oncology (DGHO) and we published a report in February 2017. The main causes appeared to be due to **manufacturing problems, global distribution, demand fluctuations, pricing, and market withdrawal.**

Together with other medical scientific societies and partners, in a collaborative effort, we made proposals to help address the issues, which are consistent with ESMO's recommendations. The proposals led to a number of changes, including **several legislative procedures**. A 'Jour Fixe' was established as a regular meeting of all stakeholders, including the Federal Ministry of Health, the Federal Institute for Drugs and Medical Devices – the German equivalent of the European Medicines Agency (EMA) – pharmacists, clinicians, and medical societies. This network improves communication on shortages and facilitates quick reactions. **Mandatory reporting** on any medicine shortage in hospital supply was also introduced.

A **national indispensable medicines** list was developed that is slightly different from the World Health Organization (WHO) Model List of Essential Medicines since it also includes some of the newer cancer medicines, such as immune checkpoint inhibitors. For indispensable medicines that are produced at only a limited number of manufacturing sites, legislature has been introduced to **allow facilitated import** if a shortage is noted. For example, in 2018, a problem was flagged with the supply of arsenic trioxide for the treatment of acute promyelocytic leukaemia, but due to facilitated import the problem was resolved and did not impact on patient treatment.

We firmly believe that establishing **European production sites** for all essential cancer medicines will help to prevent shortages due to manufacturing and quality issues. In line with ESMO's recommendation about introducing **production and supplier incentives**, we are currently discussing ways that minimum pricing may be introduced in Germany and investigating whether it is possible to increase the amount of stocks that are kept for essential drugs.

At DGHO, we are actively supporting the ESMO recommendation concerning establishing a European strategic plan for medicines shortages. We have already had discussions with politicians, and we hope this will be high on the agenda when Germany takes over the EU presidency for the second half of 2020.

Perspective of a Patient Advocate

Vlad Voiculescu
Chair of the ESMO Patient Advocates Working Group

In 2008, while working as a banker in Vienna, I discovered that there were shortages of many essential medicines needed to treat children diagnosed with cancer in my home country, Romania. Initially, I bought medicines myself from Austria and took them to Romania, but when I saw the true extent of the problem, I was compelled to do more and created a network of volunteers to help.

Through further research, it was found that over one-third of the core medicines in the WHO List of Essential Medicines were missing in Romania between 2008 and 2013. Romania is not alone in facing the problem of shortages, which are **common in Central and Eastern Europe**. The causes of the shortages are diverse and range from poor public policies to supply-chain problems.

There can be no solution unless we know the extent of the problem. During my time as Health Minister in Romania in 2016, **reporting mechanisms** were established. When a shortage is noted in a certain hospital, authorities can then determine if it is a local, national or even a regional problem across Europe. In addition to shortage reporting mechanisms, **monitoring of medicine stocks**, particularly using centralised systems, is important.

Shortages occur when prices are set too low and, as recommended by the WHO, **special pricing mechanisms** should be in place for essential cancer medicines. To ensure a reliable supply, manufacturers and distributors need predictability and this can be improved by **dedicated acquisition mechanisms**. There are various initiatives where several countries voluntarily collaborate on pricing and acquisition, and these can increase the negotiation power of individual countries and ensure predictability for suppliers and distributors.

There are infamous examples of medicine shortages due to the active ingredient being produced from outside of Europe and only in one factory. If there is a problem with that factory, then an entire continent may be affected by the shortage. **The range of essential cancer medicines is not large**, and because these medicines are so important to cancer patients, addressing manufacturing issues should be possible in Europe.

The first key step proposed by ESMO to tackle medicine shortages is an EU-wide study to assess their true impact. I wholeheartedly agree with this approach as it was only when we began to research the extent of the problem of medicines shortages in Romania that we were able to start to implement appropriate solutions. The second step, creating a common definition of medicines shortages, is something that we have tried to do previously, but it requires time and focus. By establishing a European-wide collaboration, this may now be possible.

We also need common solutions, which is where the third key step is important, we need to position inexpensive essential medicines as an **urgent priority for the future EU legislature**. There are some issues that can be solved at a local and national level but others, like cancer medicine shortages, which need to be tackled across the board, with strong European leadership.

“Choose The Right Projects And You Will Always Love Your Work”

Françoise Mornex *Université Claude Bernard, Lyon, France*

Françoise Mornex, Université Claude Bernard, Lyon, France, made history this year when she became the first woman to receive the Heine H. Hansen Award, in recognition of her contribution to the field of lung cancer. She talks about her passion for her work and teaching and keeping the flame of interest alight.

Professor of Oncology at the Université Claude Bernard, specialising in radiotherapy and chemoradiotherapy strategies for lung cancer, Françoise Mornex did not set out to work in lung cancer. “I did not choose a specific career. I knew I wanted to treat patients with cancer, because I had seen the positive effects of treatment in this area and there seemed to be a greater chance for curing the disease or alleviating symptoms than in other disease areas I had worked in. I also thought that I would like to be involved in research programmes. Above all, I already had a passion for teaching and I knew that this would have to be a part of my career somehow.” Mornex seems to have just followed the opportunities that came along and made the most out of them. For this, winning the Heine H. Hansen Award – which is annually bestowed by ESMO and the International Association for the Study of Lung Cancer – came as a complete surprise to her. “It is very pleasing to be acknowledged and selected by my peers, among many other candidates. I was lucky enough to meet Heine on several occasions and really admired him.” **Being the first woman to win the award** is gratifying, but in the end it is about being honoured for your work. “It is very satisfying to see women accessing this level of award, because a woman’s career journey is still often more difficult than a man’s is.”

The key to continued enjoyment of work is to choose the right projects. Mornex considers that her work has become more and more rewarding with each passing year. “The trick is to identify and select the tasks you like”, she said. “The pleasure of communication and compassion with patients, the satisfaction of curing a patient, the excitement of research in the lab, the sometimes tedious but ultimately exalting requirements of clinical trials, and the sense of achievement when you find a way to clearly communicate your message in teaching. These are the pleasures of my work.” Alongside her academic achievements – with recognition, appreciation and respect for her work – the relationships she has established with her patients and colleagues and the young oncology residents **who look to her as a mentor** are crucial in keeping alive her love for her job.

Despite her love for her work, there are a few things she wishes the younger Mornex had known. “I wish someone had told me earlier that ‘making it known’ is just as important as ‘know how’, because you are the only person who will champion your cause. Other things I would go back to change include having a better understanding of the difference between efficiency versus efficacy, prioritising clinical research and keeping more time for life outside work.” She has some final **words of advice for women in oncology**. “Know that everything is possible, never limit your dreams and choices, act as a professional, and be true to yourself. For every event or opportunity you think is appropriate, go for it, do it and do it well. This will be recognised and acknowledged.

Portrait: Françoise Mornex

Member Focus

“I Have Learnt How To Be A Global Oncologist”

2019 marks the 30th Anniversary of the ESMO Fellowship Programme, a programme that has helped young oncologists to enhance their careers like Giannis Mountzios, Henry Dunant Hospital Center, Athens, Greece, who had the opportunity to broaden his experience internationally.

I feel privileged to have received an ESMO Fellowship **not once, but twice**. I was awarded my first – a translational research fellowship – **back in 2005**, when I was a young general oncology resident and really wanted to gain some experience in the area of translational oncology. My project focused on identifying the differences in biology of lung adenocarcinoma between smokers and never smokers. It was the era when oncologists started to realise that lung cancer in these settings were a completely different disease entity due to the presence of distinct mutations.

When I applied for the fellowship, I knew I wanted to get a more international perspective of oncology and to spend some time working in a world-renowned centre in a different country. The fellowship enabled me to go to Villejuif, in France, to conduct research at the Institut Gustave Roussy (IGR). I did not realise it at the time, but the year I spent at IGR under the mentorship of Jean-Charles Soria would mark the start of my interest in thoracic oncology. Now, as one of the coordinators of the Lung Cancer Working Group of the Hellenic Co-operative Oncology Group (HeCOG) and in charge of a number of lung cancer clinical trials in my home country, Greece, my passion for lung cancer continues to flourish. This first experience also gave me the valuable opportunity to present our work at ESMO 2006 in Istanbul and results were also published in *Clinical Cancer Research* in 2007. Based on these data my mentor and I were also invited to write a review for *Nature Reviews Clinical Oncology* which was published in 2007.

In 2009 a second fellowship, this time in clinical research, provided me with experience from a very different perspective. It focused on the biology of bone metastasis in patients with solid tumours. With a team at the University of Athens, we measured the levels of several markers of bone metabolism in patients with lung, breast and prostate cancer before, during and after treatment with bisphosphonates (BPN). The results of this study were published in *Scandinavian Journal Acta Oncologica* and in *Annals of Translational Medicine*. These data, among others, led to the identification of the PANKL/OPG axis as an important determinant of bone metabolism and paved the way to the discovery of denosumab, a RANKL inhibitor.

“The ESMO Fellowship Programme gives young oncologists an exciting opportunity to cross multicultural boundaries.”

Both fellowships have helped to foster my career. The first gave me a wider perspective of oncology and taught me how to work as part of a multidisciplinary team. I learnt how to interact effectively on a day-to-day basis with technicians, biologists and statisticians. I also had the opportunity to conduct weekly discussions with the whole study team regarding progress and challenges. It was also a great networking experience; many of the international collaborations I still have today are with colleagues I met when I was in France.

I have to be honest and say that there can be some additional challenges to working abroad. For me it was initially language. I had spent several months learning French before I went to Villejuif, only to find that the academic version my tutor had been teaching me was certainly not the language spoken in my daily life in Paris. However, four months into my stay I knew that I was fluent in the language when I had my first dream in French! Luckily, whichever country you are from, oncologists have a common language of cancer, a common goal to pursue, and this is something that unites us.

The ESMO Fellowship Programme gives young oncologists an **exciting opportunity to cross multicultural boundaries**. Working abroad for a time forces you to step back from your own country and to see the oncology landscape from different perspectives. I am extremely grateful to ESMO for these fellowships and for helping me take my first steps at an international level. My main advice for young oncologists willing to apply for a fellowship is to work hard and if unsuccessful the first time not to be disappointed by initial rejection and apply again. This is what I did and it worked!

Giannis Mountzios among tutors and colleagues, during his Thesis presentation at the Institut Gustave Roussy, France, in October 2006.

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ESMO Perspectives is published by the European Society for Medical Oncology (ESMO).

European Society for Medical Oncology (ESMO)
via Ginevra 4, 6900 Lugano, Switzerland

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