



Time to Accelerate. Access to Genomic Tumour Testing

ACTION REPORT



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1. Community 365 is a group of charity, philanthropy, and industry contributors to the Focused Topic Networks of the European Cancer Organisation. Community 365 provide ideas, guidance, practical support, and resources for our work in convening stakeholders and building consensus in the European cancer community. Community 365 contributors do not have a decision-making role in our policy work. Rather, policies of the European Cancer Organisation, such as those represented in this document, are agreed by our Board after consultation with our Member Societies and Patient Advisory Committee, via our Policy Pathway process. More information here: <https://www.europeancancer.org/community-365>
 2. More information here: <https://www.europeancancer.org/events/250:community-365-roundtable-meeting-on-improving-access-to-genomic-tumour-testing-across-europe.html>
 3. European Cancer Organisation's Policy Decision Making Process: <https://www.europeancancer.org/2-%20uncategorised/24-policy-decision-making>.

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Executive Summary of Recommendations

- With the growing applicability of approved and targeted therapies towards a greater range of cancer tumour types, the need to address the evident lack of access across Europe to associated genomic tumour testing becomes ever more politically urgent.
- Separate investigations into levels of access to genomic tumour testing across Europe signal that common and primary barriers to access include:
 - Difficulties in reimbursement processes, including lack of integration between reimbursement for therapies and reimbursement for tests;
 - Lack of awareness of new genomic biomarkers and,
 - Ongoing needs to achieve required laboratory infrastructure, pathology workforce capacity.
- To move beyond the reimbursement barrier will require enhanced understanding by payers of the costs of not making use of genomic tumour testing in cancer care, to which health economists have an important role. It is also hoped that future EU harmonisation in fields such as HTA assessment could assist in generating more common understanding about the range of cost and health service benefits achieved by deploying more targeted treatment approaches.
- Other barriers to access discussed during the roundtable included the need to achieve wider understanding and knowledge about genomic tumour testing among the range of professions typically involved in delivering multidisciplinary cancer care, and among the patient and citizen community, who are very often the real drivers of policy change in cancer.
- Good practices in achieving improved access to genomic tumour testing should be shared and replicated across Europe. Examples highlighted during the roundtable included the approaches undertaken in countries such as Germany, Belgium and Ireland, in which clear strategies have been developed and related actions committed to those strategies thereafter implemented.
- Such actions can include national guidelines, coordination of expert centres to help provide laboratory and knowledge structures across a country. National level coordination of approach can also assist in ensuring quality assurance of testing, including that tests are fully complete and conducted at the right time.
- The needs of data collection connected to genomic tumour testing were also highlighted, including establishing centralised national and potentially European data collection to harness clinic-genomic data gathered during testing to advance the understanding of genomic alterations and their role in driving cancer.
- Future opportunities are also identified in:
 - Making use of digital pathology techniques in genomic tumour testing to assist with pathology capacity challenges, including assistance from artificial intelligence techniques;
 - Working at EU level to meet identified unmet needs in genomic tumour testing, including via well formulated and relevant Horizon Europe funding calls;
 - Making information about what tests are available in which countries for which tumour types to assist cancer patients and their families in discussions with their treatment teams.
- A major unresolved, and ever more evident, barrier to patients in Europe being able to access targeted therapy supported by genomic tumour testing is the ongoing difficulties in achieving a smooth implementation of the EU In Vitro Diagnostic Regulation (IVDR). Evidence is now available about the lack of coordination of IVDR related trial and conformity assessment applications across countries which are delaying relevant trials and future authorisation and availability of diagnostics to identify patients for innovative targeted treatments and tests. Possible solutions, such as a voluntary harmonisation procedure, are currently being discussed at political level and should be a priority area of focus for national governments and the European Commission in 2024.

Introduction

Genomic tumour testing is a means by which a clinical care team for a cancer patient can check for gene mutations in an individual's cancer to better predict how the tumour might behave, including how fast-growing the cancer may be and how likely it is to spread. Genomic testing can be performed on biopsied tissue, tissue from an entire cancerous tumour that has been removed and sometimes also in ctDNA extracted from blood (liquid biopsy). Tumour profiling can then permit greater personalisation of the individual's cancer treatment, with oncologists better able to match treatments more likely to provide positive outcomes.

The October 2023 a roundtable took place in a context of stakeholder concern that too many cancer patients in Europe continue to lack access to such testing, requiring examination of the persistent barriers to such access and how they might be overcome.

AIMS OF THE ROUNDTABLE

- To explore the potential of genomic tumour testing to improve outcomes for cancer patients.
- To identify the obstacles in the effective implementation of genomic tumour testing.
- To generate policy recommendations on overcoming the access challenges, grounded in the insights and perspectives shared during the roundtable discussions.

Genomic Tumour Testing in Europe in 2023: The Current Landscape

Co-chaired by **Cecilia Schott**, Vice-President, Global Head Precision Diagnostics, Novartis and **Mark Lawler**, ECO Board Member (2022-2023) and Chair in Translational Cancer Genomics, Queen's University Belfast



Cecilia Schott introduced the first session of the roundtable, which had the aim of providing an overview of the current landscape of genomic tumour testing in Europe.

Dr. Nicola Normanno, Director of Cell Biology and Biotherapy Unit, Director of the Translational Research Department, INT Fondazione Pascale, Naples, gave the first presentation of the session, sharing some key research findings about access to biomarker associated therapy from the International Quality Network for Pathology initiative (IQN Path⁴).

Dr Normanno emphasised the role of biomarker associated therapies in both increasing the efficacy of cancer treatment, but importantly too, in reducing toxicity and side effects. He was therefore

heartened by the ever-broadening applicability of biomarker associated therapies, with a growing proportion of cancers becoming relevant in this respect.

As well as increasing patient access to such testing, Dr Normanno also spoke to the need to ensure the quality of biomarker testing. With this in mind, IQN Path survey research activity has sought to provide better information on how both matters are being addressed presently in Europe. The survey activity has involved laboratory managers, cancer patients, physicians and payers.

Access to and quality of 12 biomarker tests and liquid biopsy analysis were evaluated, for both Tier 1 and Tier 2 biomarkers (Table 1).

Table 1. Biomarker tests covered by the research. Tier 1 tests were covered in all countries, while Tier 2 tests were covered only in 'focus' countries.

Tier 1	Tier 2
Single biomarker IHC / FISH	Single biomarker IHC / FISH
<i>PD-L1</i>	<i>HER2</i>
Single biomarker molecular	<i>ALK</i>
<i>BRCA</i>	<i>MMR / MSI</i>
<i>EGFR</i>	<i>ROS1</i>
<i>NTRK</i>	Single biomarker molecular
Complex genomic signatures	<i>BRAF</i>
<i>NGS hotspot (up to 50 genes) / targeted panel</i>	<i>KRAS / NRAS</i>
<i>NGS comprehensive panel</i>	Other
	<i>Liquid biopsy (ctDNA / plasma)</i>
Covered for EU27 and UK	Germany, France, Italy, Spain, UK, Belgium, Netherlands, Sweden, Poland, Greece

The mapping revealed significant variations in both medicine and test access, as well as test quality across Europe.

Reflecting on the results relating to medicines access, and potential causation factors, Dr Normanno identified the problem of delay between the European Medicines Agency providing an approval to a new therapy and the subsequent

periods of delay thereafter as individual countries make determinations about the reimbursement of such therapies.

In respect to results on access to biomarker testing, Dr Normanno pointed to problems caused by a lack of diagnostic laboratory infrastructure. Results of IQN Path's research suggested this was a particularly present problem in some countries in

4. <https://www.iqnpath.org/>

Table 2. Biomarker tests covered by the research. Tier 1 tests were covered in all countries, while Tier 2 tests were covered only in 'focus' countries⁵.

	Tier 1 biomarker tests	Tier 2 biomarker tests
Single biomarker tests: immunohistochemistry (IHC)/Fluorescence PD-L1 in situ hybridisation (FISH)		HER2 ALK MMR/MSI
Molecular (MDx): includes Polymerase Chain Reaction (PCR) and single biomarker next generation sequencing (NGS)	BRCA EGFR NTRK	BRAF ROSI
Multi-biomarker test technologies: complex genomic signatures	NGS hotspot (up to 50 genes)/targeted panel NGS comprehensive panel (more than 50 genes)	N/A N/A
Other	N/A	Liquid biopsy (ctDNA/plasma)

the eastern part of Europe. Meanwhile, in the south of Europe, a more limiting factor appeared to be lack of budget provision for testing.

More positively, Dr Normanno reported that Germany, Denmark, and Belgium are three countries that can demonstrate leadership in improving patient access to precision cancer

Figure 1. The current status on quality and access to biomarker testing in Europe: (A) Medicines access; (B) Single biomarker test access; (C) Multi-biomarker test access; (D) biomarker test quality.

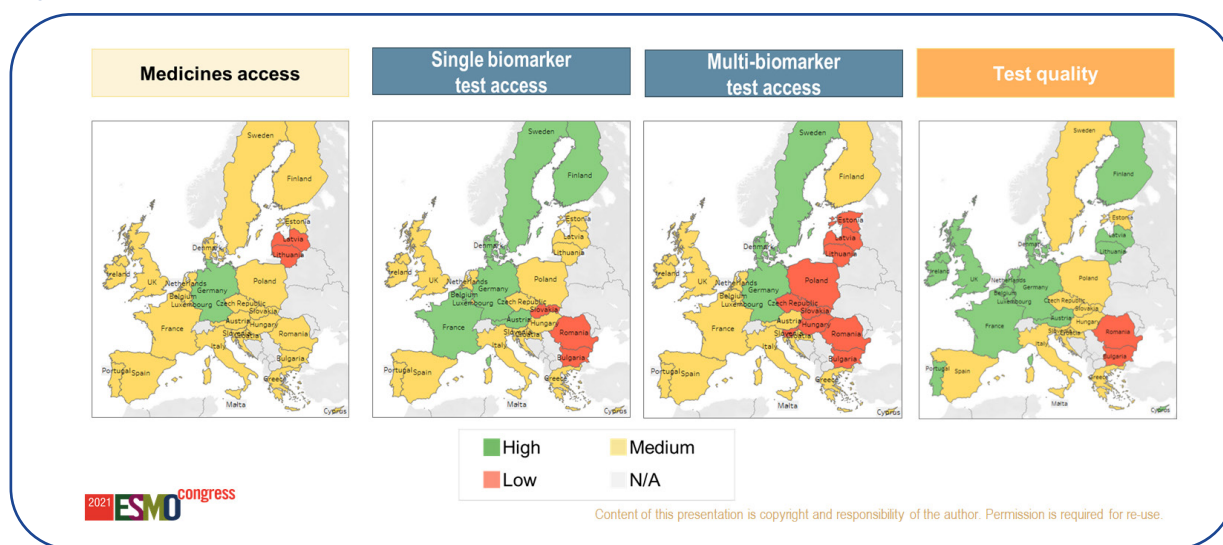
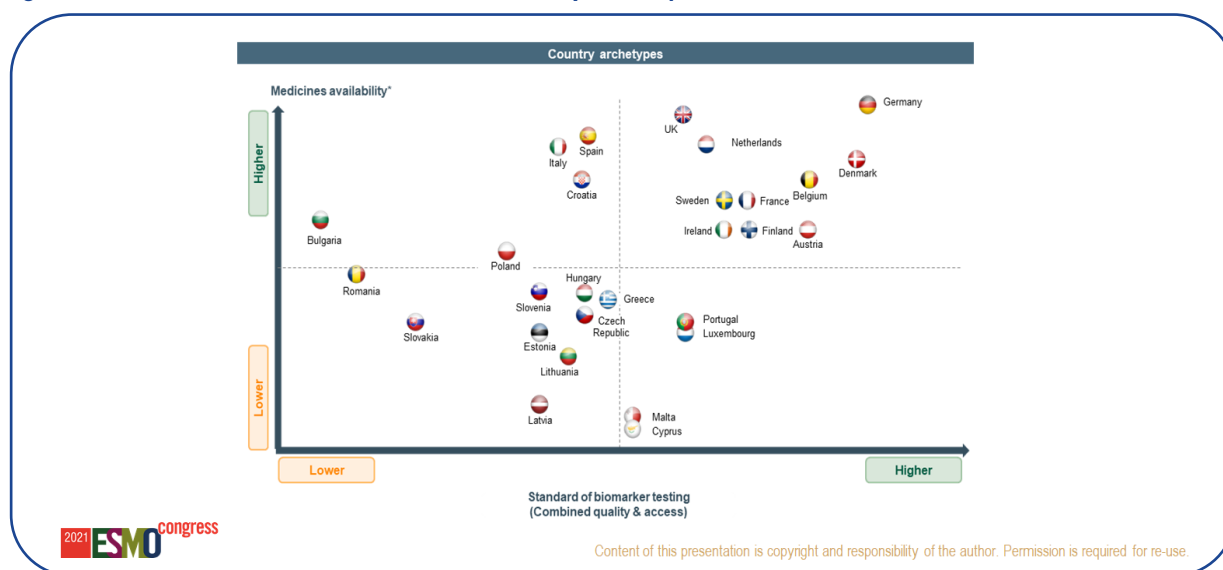


Figure 2. Biomarker test and medicine availability in Europe.



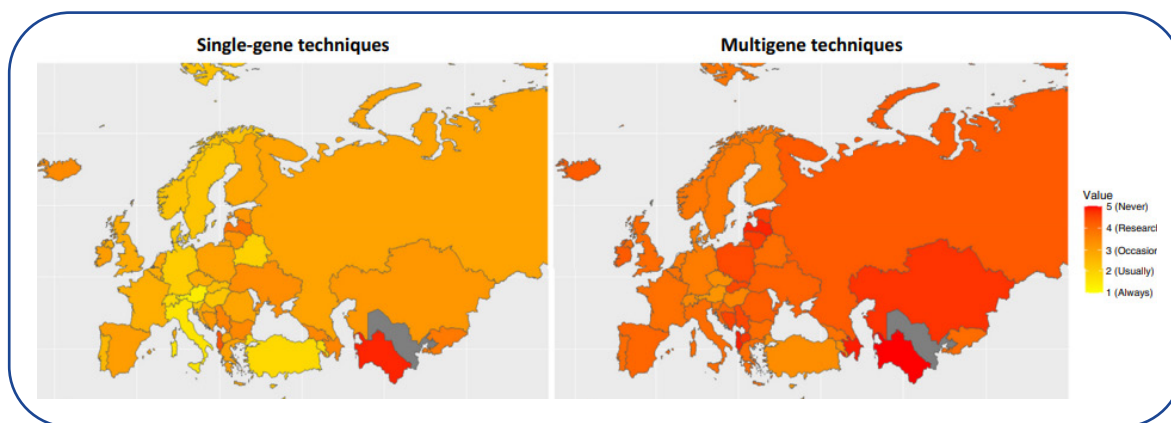
5. Normanno N, Apostolidis K, Wolf A et al. Access and quality of biomarker testing for Precision Oncology in Europe. *European Journal of Cancer* 2022;176:70–7.
6. Normanno N, Apostolidis K, Wolf A et al. Access and quality of biomarker testing for Precision Oncology in Europe. *European Journal of Cancer* 2022;176:70–7.

medicine and related tests. Figure 2 depicts this, where medicines availability was plotted against standard of biomarker testing (combined quality and access).

Based on these identified barriers, a list of eight short-term policy recommendations have been proposed by IQN Path. These are:

1. **Parallel approval of the medicine and associated genomic testing:** Developing a process for the parallel approval of the medicine and associated testing (both for regulatory and reimbursement approval).
2. **National system for biomarkers test value assessment:** Developing an efficient value assessment process for new biomarker tests which defines clear criteria for determining their value. This would of course consider the broader health system benefits of biomarker testing and enable the incorporation of new data as they are generated (either in clinical trials or through real-world evidence).
3. **Dedicated biomarker test budgets:** Introducing dedicated diagnostic budgets to support reimbursement of all biomarker tests, removing regional variation and inequality in access.
4. **Mandatory ISO accreditation and EQA scheme participation:** Mandating that laboratories pursue ISO accreditation and participate in EQA schemes covering all precision biomarker tests/test techniques. Dedicated budgets
5. **Regional testing centres:** Encouraging the creation of regional testing centres to drive cost efficiencies, development of technical expertise and investment in test technologies, and allow for fast turnaround times due to high sample throughput and expertise, with standardised approaches to internal and external quality assurance.
6. **Stakeholder education:** Ensuring that key stakeholders at every level (i.e., physicians, pathologists, payers, patient advocacy groups, policy makers) are provided with comprehensive and most up-to-date education on the utility of biomarker testing, testing pathways and reimbursement sources, while keeping in mind that the ultimate aim is improving patient outcomes. The ESMO/ESP guidelines should also be actively promoted by member states' cancer and medical societies.
7. **Centralised national data collection:** Establishing centralised national and potentially European data collection to harness clinic-genomic data gathered during testing to advance the understanding of genomic alterations and their role in driving cancer.
8. **Horizon scanning:** Establishing processes for horizon scanning for future testing needs, as well as emerging tests to better anticipate future demand and funding requirements.

Figure 3. Availability map of single versus multiple genes techniques (all countries, n = 48).



Rosa Giuliani, Consultant Medical Oncologist, Guy's and St Thomas' NHS Foundation Trust provided an overview of an ESMO study on the availability and accessibility of biomolecular technologies in oncology in Europe⁵, recently published in the *Annals of Oncology*. The study was based upon reporting by 201 individuals from 48 countries, of whom 143 were oncologists (73%), 44 biologists or pathologists (22%) and 14 other professionals (7%).

The study was performed as a survey and covered six key domains: the existence of health organisation for biomolecular technologies,

the availability of biomolecular technologies in cancer, the presence of laboratories or platforms performing biomolecular testing, the use of technologies in pre-specified cancer types, the pricing and reimbursement of the tests and the barriers to utilisation.

In a similar manner to studies by IQN Path described by Dr Normanno, the recently published ESMO study has also found that the availability of multigene techniques across Europe is, overall, much more limited than would be hoped for.

7. <https://www.sciencedirect.com/science/article/abs/pii/S0923753423007603>

Table 3. Availability of techniques across countries by region⁸.

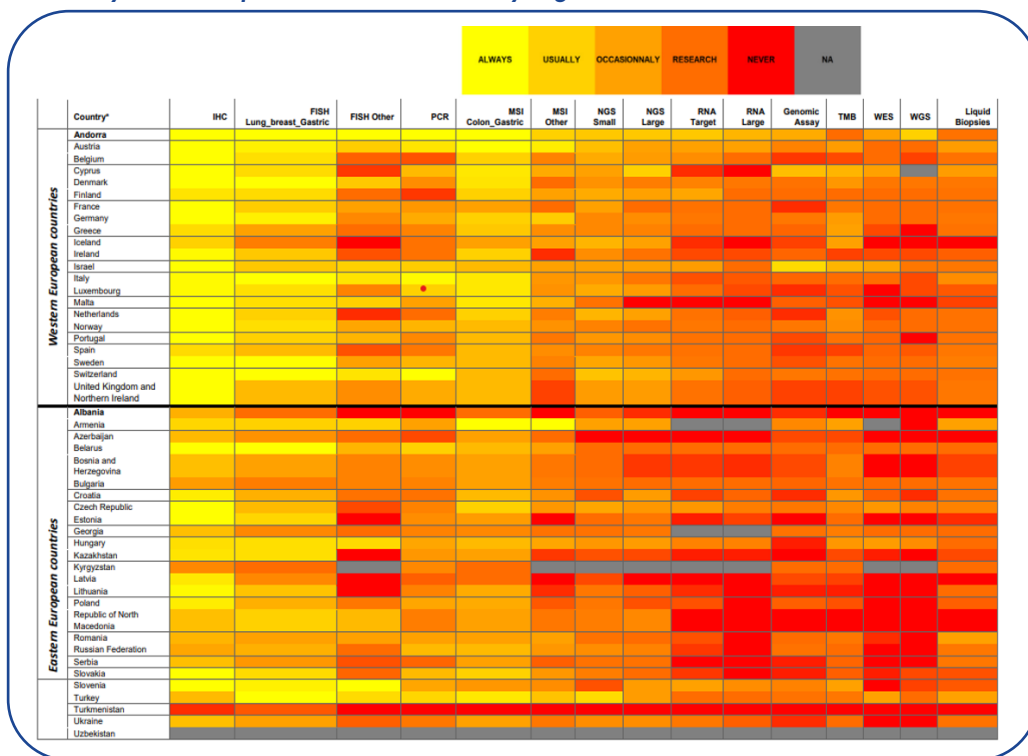
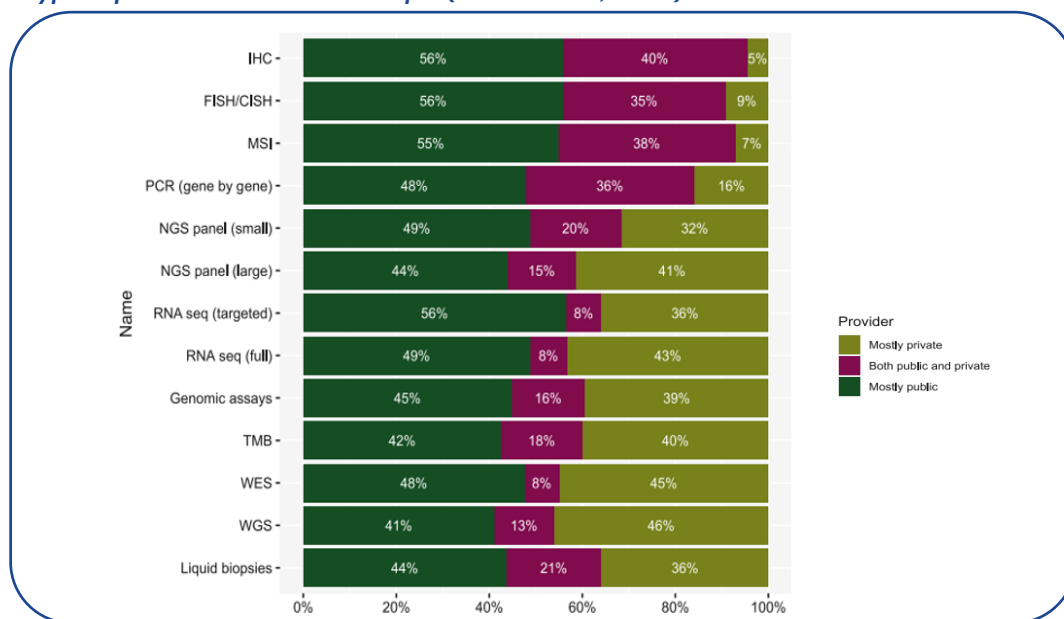


Figure 4. Type of provider for each technique (all countries, n = 48)⁹.



Dr Giuliani also identified testing access trends according to service provider. For example, as compared to simple techniques like immunohistochemistry (IHC), complex techniques, like whole genome sequencing (WGS), are usually provided by the private sector.

Reflecting on the results of the ESMO study in respect to availability of different techniques for testing, Dr Giuliani considered that when looking at the findings on access to some of the more complex testing techniques, the study suggests access to these are presently confined more to the research domain than to general overall cancer patient population.

8. Bayle A, Bonastre J, Chaltiel D et al. ESMO study on the availability and accessibility of biomolecular technologies in oncology in Europe. *Annals of Oncology* 2023;34:934–45.
9. Bayle A, Bonastre J, Chaltiel D et al. ESMO study on the availability and accessibility of biomolecular technologies in oncology in Europe. *Annals of Oncology* 2023;34:934–45.

When examining barriers to access, financial reimbursement issues remain a significant challenge to overcome. Figure 5 gives an indication of this. Of all the recognised barriers to the equal and fair use of genomic tumour testing in Europe, financial reimbursement was ranked by the study reporters as the major limitation.

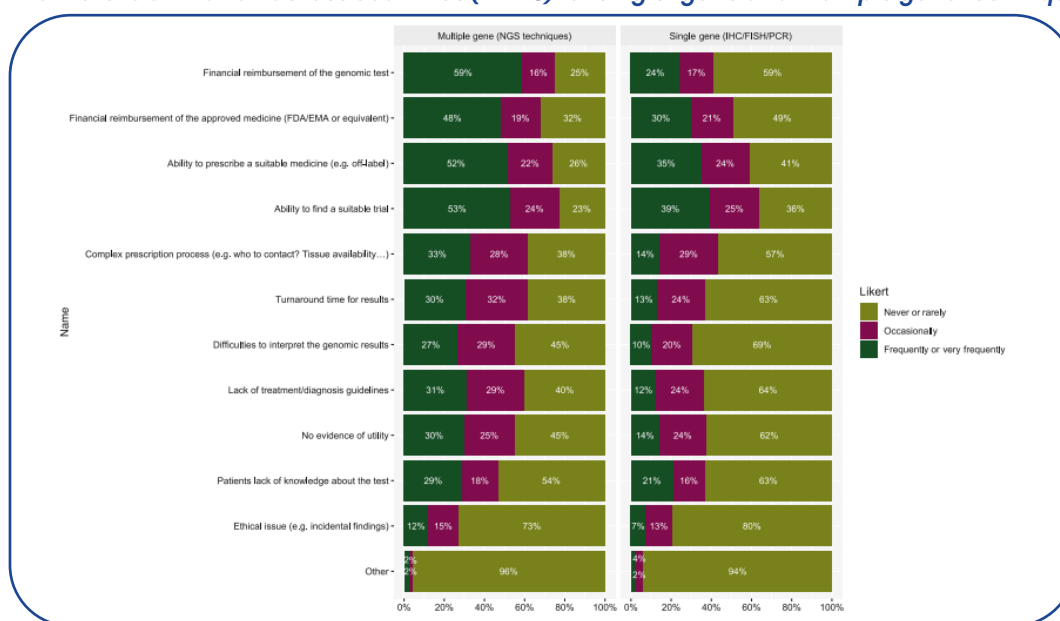
The survey highlighted that large next-generation sequencing panels remain largely inaccessible in routine clinical practice in Europe at the present time. In too many cases, access remains mostly provided to patients via clinical trials and research activity.

However, simple validated biomarkers (i.e. simple techniques, not requiring extensive panels), do appear to be more widely tested across countries.

Besides financial reimbursement for tests, Dr Giuliani emphasised the next key barrier as being the availability of a suitable drug for treatment after genomic profiling.

Concluding her remarks, Dr Giuliani called for a shift in our angle of observation when considering genomic tumour testing. Instead of thinking of 'the cost of' genomic tumour testing, we should consider the impact of 'the cost of not' testing. In this case, the pathway of the evidence generation model also needs to be rethought, with clear and consistent monitoring of the use of genomic tumour testing in routine practice post-approval.

Figure 5. Barriers to utilization across countries (n = 48) for single-gene and multiple gene techniques¹⁰.



At a political level, Dr Giuliani called for:

- Global cooperation in making access to genomic tumour testing a shared agenda and priority for countries; and,
- Inclusion of implementation plans for genomic tumour testing within national cancer plans.

During a Q&A with Dr Normano and Dr Giuliani, a roundtable attendee emphasised the need to grow general and public understanding of the role of genomic tumour testing in improving cancer treatment to generate greater political momentum for increased access to it. Dr Normano especially agreed with this, describing patients as “the real drivers of change.”

Cecilia Schott concluded the session by emphasising on some reflections following the presentations and discussions. This included:

- Promoting concepts of parallel reimbursement, in respect to not isolating and separating reimbursement of a medicine and reimbursement of a test linked to that treatment.
- Improving the horizon scanning activity and general education about genomic tumour testing, especially in view of the increasing application of biomarker associated cancer treatment across tumour type.

10. Bayle A, Bonastre J, Chaltiel D et al. ESMO study on the availability and accessibility of biomolecular technologies in oncology in Europe. *Annals of Oncology* 2023;34:934–45.

POLICY RECOMMENDATIONS

- With the growing applicability of approved and targeted therapies towards a greater range of cancer tumour types, the need to address the evident lack of access across Europe to associated genomic tumour testing becomes ever more politically urgent.
- Separate investigations into levels of access to genomic tumour testing across Europe signal that common and primary barriers to access include:
 - Difficulties in reimbursement processes, including lack of integration between reimbursement for therapies and reimbursement for tests;
 - Lack of awareness of new genomic biomarkers and,
 - Ongoing needs to achieve required laboratory infrastructure, pathology workforce capacity

Developing the Infrastructure for Delivering Genomic Tumour Testing: Where Are We Now and Where Do We Need to Be

Co-chaired by **Patrycja Rzadkowska**, Vice-Chair of the ECO Patient Advisory Committee, and **Achim Escherich**, Global Technical Companion Diagnostics Lead, Market Access, Menarini Stemline.



Achim Escherich introduced the second session of the roundtable, which had the aim of investigating further the infrastructural needs associated to improving cancer patient access to genomic tumour testing.

Reinhard Büttner, Professor and Chairman for Pathology, Institute for Pathology, University of Cologne, gave an opening speech aimed to support the presentations of the roundtable. It explored the ways in which some of the infrastructural conditions for improved access to genomic tumour testing might be better met.

Before doing so however, he reflected that one matter that perhaps had not come through in the IQN Path and ESMO studies about access is some of the underlying issues of knowledge. Lack of knowledge about tumour testing may be underappreciated to a degree as there is often reticence by individuals to openly signal their personal limits of understanding on a topic. Yet cancer treatment is inherently, and at its best, multidisciplinary. This indicates a need for a level of knowledge about the importance and role of genomic tumour testing across a multidisciplinary clinical team. Otherwise, decisions about the optimal therapeutic pathway for a patient may be missed.

To illustrate how science is driving change in approach in the field of genomic tumour testing, Professor Büttner provided the example of lung cancer, where there are now more than 25 genes that should be sequenced for biomarker analysis. A further example is given by the growing development of liquid biopsies but which remains rarely provided to patients outside of research.

As a means of meeting these evolutions in need, Professor Büttner illustrated how Germany has built up 6 centres of special expertise across the country. The centres are acting as knowledge transfer hubs and in so doing hope to increase access to technologies such as liquid biopsy for metastatic breast cancer (mBC) patients. This network of centres are also helping to ensure quality assurance of genomic testing for Estrogen Receptor 1 (ESR1) mutations in ER+/HER2- mBC. This includes ensuring that tests are conducted for the right patient at the right time using the right technology and infrastructure.

Paul Hofman, Chair of the Working Group for Pulmonary Diseases, European Society of Pathology

(ESP), gave the perspective of ESP on meeting the need to improve access to genomic tumour testing in Europe. In particular, he presented ten headline recommendations on the topic from the European Society of Pathology. These are:

1. Organise regularly workshops and webinars (educational programmes) at the EPS's dedicated to genomic tumour testing (including topic on bottleneck for testing access).
2. Set up annual joint meeting sessions with the Molecular Pathology WG of the ESP at the European Congress of Pathology (next Florence 2024).
3. Setting up a MSc European Masters of Molecular Pathology under the umbrella of the ESP, the European Union of Medical Specialists (UEMS) and the Organisation of European Cancer Institutes (OECI).
4. Information among the European pathologists concerning the European Society for Medical Oncology (ESMO) recommendations and guidelines for Next Generation Sequencing (NGS) testing in solid tumours.
5. Information on the evolution of the ESCAT (ESMO Scale of Clinical Actionability Targets) classification, to be updated each year.
6. On site training in expert centers for molecular biology in Europe thanks to the Giordano fellowships from the European Society of Pathology.
7. Strong participation of advocates and patients association for dissemination of molecular testing best practices and equity in Europe.
8. Interaction with different organisations, such as the International Quality Network for Pathology (IQN Path), meetings with the European Alliance for Personalised Medicine (EAPM).
9. Publication of position papers for European recommendation.
10. Publications regarding mandatory, emerging and exploratory predictive biomarkers in different European journals (Ann Oncol, ESMO Open, Lung Cancer, Virchows Archiv).

Reflecting more widely, and upon previous presentations in the roundtable, Dr Hofman saw special opportunity in advancing digital pathology and the use of artificial intelligence in the field of genomic tumour testing.

Tanja Spanic, President of Europa Donna - the European Breast Cancer Coalition provided the perspective from the breast cancer patient community in respect to meeting the infrastructure needs associated to improved genomic tumour testing access.

Commenting towards previous exchanges in the roundtable about the importance of assisting patients and the patient community with knowledge about genomic tumour testing, Spanic remarked on a serious of challenges within this, including:

- That genomic tumour testing is an ever-developing scientific field. This means new and relevant information about testing is often becoming available, making the education and awareness goal something of a moving target;

- That there is lack of access for patients to credible and up-to-date information about access to genomic tumour testing, especially whether testing is available in their country, for their cancer;
- That the subject area is riven with a multitude of scientific terms, sometimes referring to the same thing, or sounding similar but meaning different things. This makes the topic more opaque and less easy for an ordinary citizen patient to engage with.

Spanic also highlighted case studies related to the reimbursement challenge, whereby she is aware of breast cancer patients being eligible to reimbursed biomarker related treatment, but not the test associated to it. The patient then has to pick up this out-of-pocket expense. Policy is not following the science in this respect.

A BELGIAN PERSPECTIVE

Developing the infrastructure for delivering genomic tumour testing

Marc Van den Bulcke, Head of Service, Belgian Cancer Centre, Epidemiology and Public Health, Sciensano, Belgium, then provided an overview of how his country was responding to the challenges involved with providing greater levels of access to genomic tumour testing.

In the last ten years, there have been significant advancements in Belgium to improve diagnostics in cancer. In 2015, a national Working Group on personalised medicines developed a "road book" to bring omics into routine diagnostics in oncology through ten actions. The first was to create a common approach – a set of guidelines. A commission of technical and medical experts was created as a multidisciplinary approach to supervise the work. Additionally, improvement in the linkage between reimbursement of testing and treatment was also made.

Allied to these developments, was a strong recognition of the need to support the integration of cancer care delivery with cancer research, including in the field of genomic tumour testing. To this end, Belgium, with the support of the

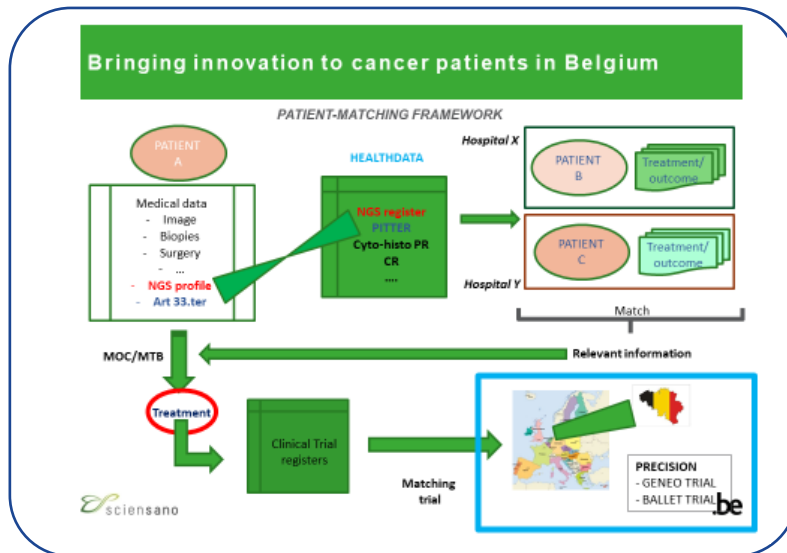
Belgian Society of Molecular Oncology, launched a precision medicine platform, to support more patients being brought to relevant clinical trials.

At a more international level, Belgium has been active with the European Commission's Horizon Europe programme to help stimulate research towards unmet needs in genomic tumour testing, including for more cost-efficient and fully inclusive forms of testing.

A further EU supported project, being conducted under the auspices of Europe's Beating Cancer Plan, and coordinated by Sciensano, is CAN.HEAL. The project aims to establish recommendations for EU health systems that improve access to prevention, diagnosis, and treatment of cancer through personalised medicine to individuals and patients. Involved in this, is an assessment of readiness for various technologies in the field of personalised medicine for wider adoption and uptake in healthcare systems.

Moreover, Belgium is taking a very positive and constructive approach towards EU level initiatives, one being the European Health Data Space. Many other projects being taken up via the EU Cancer Mission and Europe's Beating Cancer Plan, such as the European Cancer Imaging Initiative, can help in supporting countries to meet the general challenges of personalised medicine adoption.

Figure 6. Belgium Status NGS implementation 2023.



In helping to conclude the session, Achim Escherich pointed out some key messages he had heard in the interventions. This included giving focus to knowledge and education on genomic tumour testing and biomarkers as a critical need. This is underlined by the understanding that cancer care is multi-professional in its nature. Wider awareness and understanding about genomic

tumour testing across professions would therefore be helpful. Patrycja Rzadkowska connected closely to remarks in the meeting, and the online chat, that emphasised a universal understanding of how important patient organisations and patient advocates can be in improving understanding about genomic tumour testing and driving policy change.

POLICY RECOMMENDATIONS

- Identified opportunities to improve access to genomic tumour testing include:
 - Making use of digital pathology techniques in genomic tumour testing to assist with pathology capacity challenges, including assistance from artificial intelligence techniques;
 - Working at an EU level to meet identified unmet needs in genomic tumour testing, including via well formulated and relevant Horizon Europe funding calls;
 - Making information about what tests are available in which countries for which tumour types to assist cancer patients and their families in discussions with their treatment teams.

The Value of Genomic Tumour Testing

Co-chaired by **Patrycja Rzadkowska**, Vice-Chair of the ECO Patient Advisory Committee, and **Elizabeth Sheppard**, Global Pricing & Market Access Director, Oncology Diagnostic AstraZeneca.

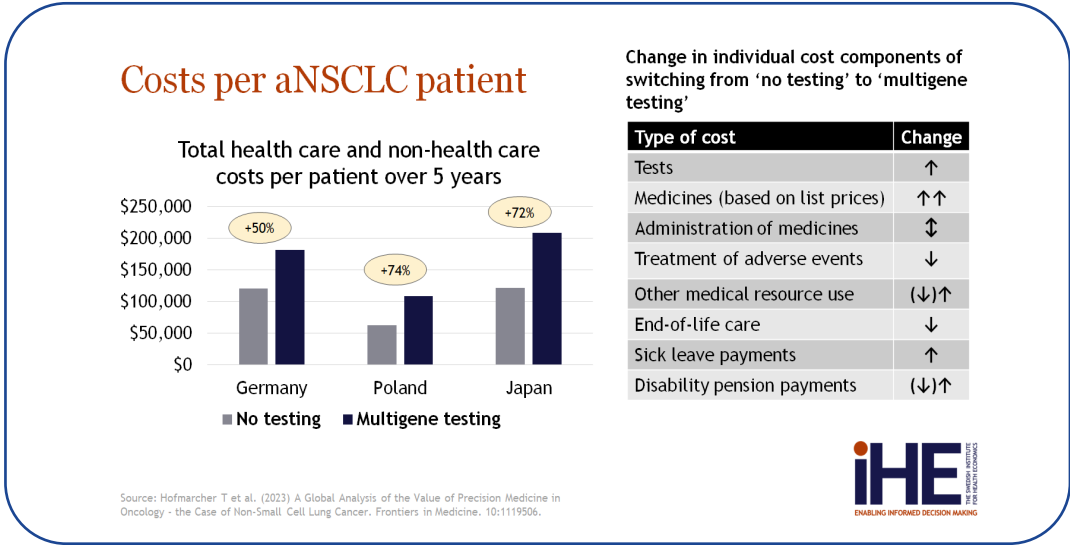


Introducing the session, **Elizabeth Sheppard** highlighted the pertinency of the interventions to follow, based on the already identified issues in the roundtable about overcoming reimbursement challenges associated to genomic tumour testing, as well as making appreciation of both opportunities and potential threats represented by the present implementation of the EU Health Technology Assessment (HTA) regulation. It was noted that to overcome access challenges we need to have access to comprehensive molecular testing by investing in broader access to biomarkers. The early collaboration with patients, the industry regulatory bodies on evidence generation, the standardisation of the assessment of evidence and the use of real world data cross border are all crucial in augmenting the accessibility of biomarkers. Precision reimbursement also needs to be supported by novel outcome-based payments that also support diagnostic reimbursement.

Thomas Hofmarcher, Research Director, Swedish Institute for Health Economics (IHE) gave a health economic perspective on the assessment of value in precision medicine, including genomic tumour testing, with lung cancer as a case study.

Hofmarcher opened his presentation with some reflections about key principles of value-based healthcare, which means looking at both costs (direct and indirect) of treatment in balance to the outcomes they deliver. Inherent in this are questions about which costs are included and how, and which outcomes are taken into account and how. In this context the choice between, and balance between, indicators such as overall survival and progression free survival become highly relevant. Further to this, in academic literature there can also sometimes be methodological issues in making pronouncements about cost-effectiveness of treatment depending on what price metrics are used. Many such studies, for example, make use of list prices of medicines, when the actual price will be quite different.

Figure 7. Costs per aNSCLC patient.



This provided some background to his institution's study into cost-effectiveness in personalised medicine, with an aim of giving consideration to factors such as occasions when personalised medicine might achieve efficiencies in care delivery or lead to reductions in other forms of healthcare cost that would otherwise be incurred. Commentary from roundtable attendees on this point including giving consideration as well to the tax contributions that can result from successfully treated cancer patients returning to a "normal" life and employment.

Lung cancer is a good case study to review in this sense as over the past 15 years lung cancer has been a particular pioneer area in the field of personalised medicine with increasing levels of targeted therapies now available dependent on gene-targeting and biomarker testing.

Figure 7 provides an indication of some of IHE's analysis of cost-effectiveness of personalised medicine in lung cancer. Commentary that Hofmarcher provided to this slide included indicating that many of the personalised therapies are administered orally which brings savings to

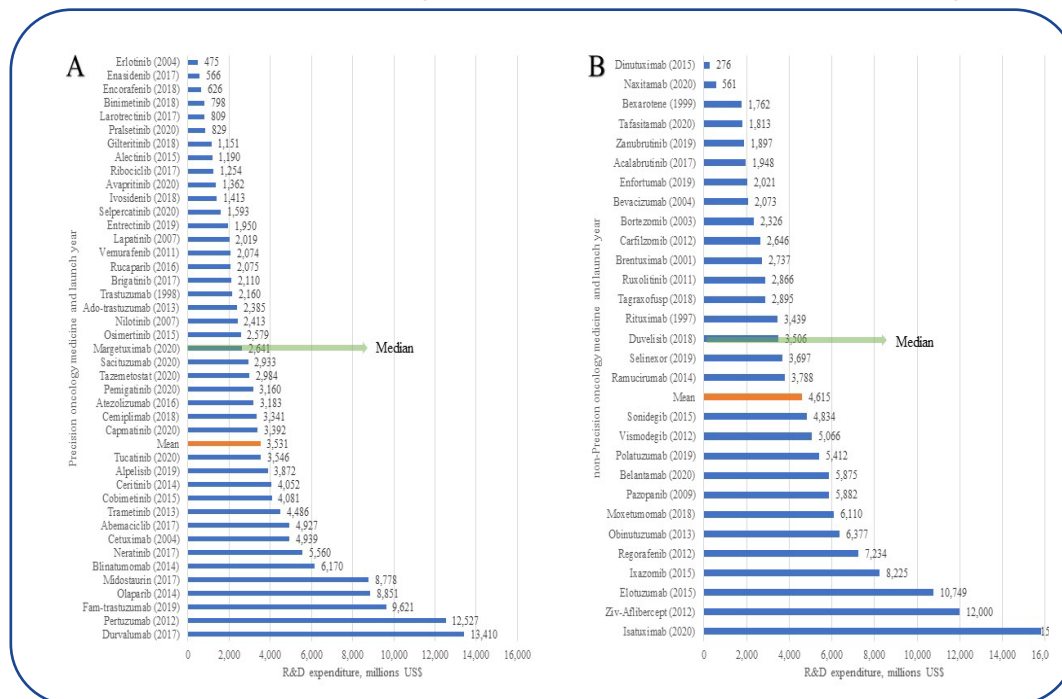
healthcare resources compared to intravenous administration of chemotherapy requiring more significant appointment burden for healthcare institutions. The number of adverse events is typically also reduced, due to the targeted nature of personalised therapies compared to chemotherapy, which results in cost savings. Improved survival of patients leads to a decrease in the need and costs for end-of-life care. It should also be recognised that a move towards personalised medicine will increase costs for genomic testing, but these testing costs are minor in relation to the costs for the targeted therapies that require those tests to be performed. Concluding his presentation, Hofmarcher emphasised that, in historic terms, personalised medicine is still in the early years of moving towards full deployment, with many key learnings still being taken on board. Among these include the critical needs to:

- Address laboratory infrastructure for genomic tumour testing, and also capacity in terms of pathology workforce; and,
- Complete a shift away from single biomarker testing towards multi genome testing, and maybe whole genome sequencing in the future.

The health-economic value of biomarker testing in oncology deserves greater attention to facilitate its adoption in clinical practice.

Professor Mark Lawler, ECO Board Member (2022–2023) and Chair in Translational Cancer Genomics, Queen’s University Belfast presented a publication of a study exploring the economic benefit of precision medicine in treating cancer. of the work reviewed precision oncology medicines in the marketplace, examining their economic impact compared to traditional oncology medicines¹¹.

Figure 8. R&D spend for 42 precision oncology medicines versus 29 non-precision oncology medicines.



The study shows that R&D spending for 42 precision oncology medicines is \$475M to \$13,410M – Median \$2,641M vs. 29 non-precision oncology medicines which is \$276M to \$15,821M – \$Median 3,506M. It may surprise some to understand that the median R&D spend of precision oncology medicines is indicated to be less than that of non-precision oncology medicines. Moreover, the probability of success (POS) for precision vs. non-precision oncology medicines was \$1,486.6M v \$2,077.9M, respectively, a difference of \$591.3M.

Increased POS associated with a Companion Diagnostics (CDx) in clinical trials is linked to employment of a CDx approach vs. non CDx approach increases POS by a factor of 2.5. The analysis indicated that there was a 27% increase in

the return on investment (ROI) of precision oncology medicines over non-precision oncology medicines.

Key results of the study include:

- Over \$1 billion less were spent in R&D to develop a medicine guided through clinical trials in a precision oncology approach, compared to a “one size fits all” approach.
- A CDx -guided approach can deliver health benefits at a potentially affordable cost, lowering expensive clinical trial attrition rates and sparing patients from ineffective treatments with significant side effects.

11. <https://pubmed.ncbi.nlm.nih.gov/37408046/>

- Treating patients based on their genomic make-up is the travel direction/pathway that we should be pursuing.
- This study highlights how it can be achieved in an efficient and cost-effective way. A \$50M investment in better genomic testing would be transformational. For every \$1 million invested, an additional \$100 million+ in additional revenues could be realised.

Precision medicine can be a cheaper, more efficient way to treat cancer. However, if a CDx-guided approach is not deployed, there is a strong risk that a huge opportunity to deliver the best, most affordable care to our patients will be missed.

The deployment of a CDx at the earliest stage substantially lowers the cost associated with oncology medicines development, potentially making them available to more patients, while staying within the cost constraints of cancer health systems.

Marco Marchetti, from the National Center for Health Technology Assessment (HTA), at the Italian National Institute of Health (ISS) spoke to his work and involvement with other country representatives in bringing forward the implementation of Regulation (EU) 2021/2282 on health technology assessment.

It is hoped that the regulation can lead to improving the availability for EU patients of innovative technologies in the area of health, such as personalised cancer medicine, by strengthening the quality of HTA and fostering better collaboration and harmonisation across Member States in HTA methods and application.

The application of the HTA regulation, including aspects such as the conduct of Joint Clinical Assessments, is managed by the Member States through an HTA Member States coordination group which will make decisions such as how a particular technology will be evaluated, and the timing of the evaluation. Member States choosing not to make use of any Joint Clinical Assessment in their own national reimbursement decisions will need to explain carefully the reason for this. With the regulation coming into full application in 2025 there is now significant work underway in constructing the systems and procedures for its operation.

Overall, Marchetti envisaged the new framework for value assessment for new health technologies, to be supportive of a better and clearer means of addressing reimbursement decision-making, including for treatments requiring genomic tumour testing to support their use.

POLICY RECOMMENDATIONS

- To move beyond the reimbursement barrier will require enhanced understanding by payers of the costs of not making use of genomic tumour testing in cancer care, to which health economists have an important role. It is also hoped that future EU harmonisation in fields such as HTA assessment could assist in generating more common understanding about the range of cost and health service benefits achieved by deploying more targeted treatment approaches.

Genomic Tumour Testing: Looking Into the Future

Co-chaired by **Professor Mark Lawler**, ECO Board Member (2022-2023) and Chair in Translational Cancer Genomics, Queen's University Belfast, and **Olivia McDermid**, Senior Manager Global Health Policy – HTA & Oncology, Amgen Zug.



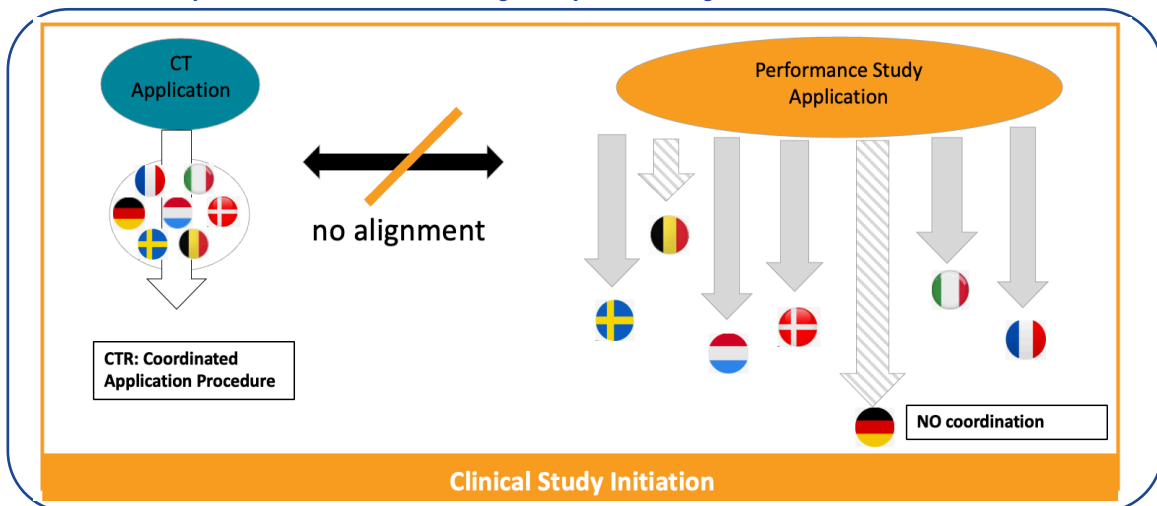
In opening the session, **Olivia McDermid**, gave an overview of the many relevant political developments in the field of personalised medicine already current, and projected in 2024. A particularly concerning point in this regard is ongoing and unresolved problems in the implementation of the EU In Vitro Diagnostic Medical Device Regulation (IVDR regulation), which has particular impact in the field of companion diagnostics and genomic tumour testing. Clinical trials are being frustrated and access to targeted therapies delayed.

Audrey Wolf, Associate Director Healthcare Systems and SMEs, European Federation of Pharmaceutical Industries and Associations (EFPIA) provided

her perspectives on the present status of IVDR regulation implementation and its impacts for clinical trials and personalised medicine access.

Explaining the regulation's intention for better coordination of In Vitro Diagnostic Medical Device assessment across Europe, the reality remains that there is little to no alignment and coordination still between EU member state authorities in charge of clinical trial applications and performance study applications. This situation, therefore, creates important delays to the launch of clinical trials in Europe.

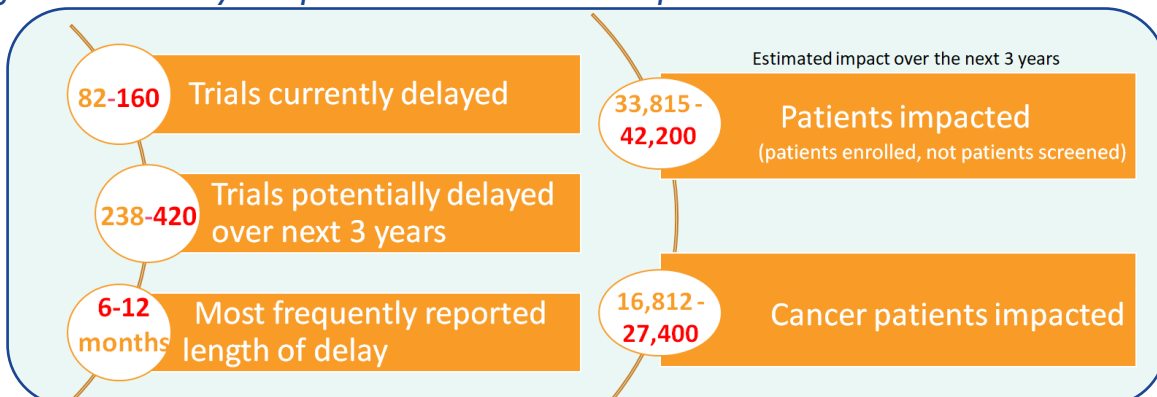
Figure 9. Adverse impact on other initiatives e.g. Europe's Beating Cancer Plan, ACT-EU.



In 2023, EFPIA conducted a survey on the impact of IVDR on clinical trials and patients. The survey was addressed to EFPIA members. Data from this survey reveals that between 82 to 160 clinical trials are currently being delayed because of the impact of

the implementation. EFPIA Members estimate that over the next three years, between 238 to 420 trials are expected to be delayed if the situation does not improve. The length of delay reported by the survey is between 6 to 12 months. Additionally, over the

Figure 10. EFPIA Survey on Impact of IVDR on clinical trials & patients.



next three years, it is estimated that approximately between 34,000 – 42,000 enrolled patients will be impacted, including between 17,000 – 27,000 cancer patients.

EFPIA is working on a set of complementary solutions which include postponing the application of IVDR to clinical trials using IVD which would solve a lot of issues but would require a change in the legislation which is currently not a priority for the European Commission.

Table 4. EFPIA proposed complementary solutions until coordinated process is in place.

Proposals	Challenge(s) addressed	Impact level (H/M/L)	Timelines (short/long-term)	Lead
1. Postpone application of IVDR to clinical trials using an IVD	All – provides the opportunity to implement other solutions until coordinated process is available	H	Short term	European Commission
2. Voluntary Harmonisation Procedure across Member States	PSA submissions to each Member State, inconsistent process, timelines	H	Long term	HMA, MDCG
3. Common Set of Principles for Performance Study Submission and Review	Divergence & lack of clarity, inconsistency of approach Role & Responsibilities not clear	H	Medium term	MDCG (guidance being drafted)
4. Risk-based Approach to Performance Studies	Infrastructure challenges; Burden of PSA	M	Long term	European Commission
5. Under Article 92: Temporarily Accept Non-conformity to PSA Requirements	PSA submissions to each MS in absence of needed infrastructure and coordination	M	Medium term	MDCG
6. Clarify Definitions of In-House Test to Broaden Scope	Burden of PSA, Enrolling early phase studies in Europe	M	Short term	MDCG

Another solution could be to put in place a voluntary harmonisation procedure across Member States, which would solve many of the issues related to inconsistency and lack of coordination. However,

this solution would need to be put in place swiftly and requires strong political support from various key stakeholders to implement in a timely fashion.

AN IRISH PERSPECTIVE

Genomic Tumour Testing: Irish National Healthcare System

Maeve Lowery, Professor of Translational Cancer Medicine at Trinity College Dublin and Consultant Medical Oncologist, St James Hospital presented on how Ireland has responded at the political level to the challenge of improving access to personalised cancer medicine, with reference to the Irish national cancer plan and other initiatives.

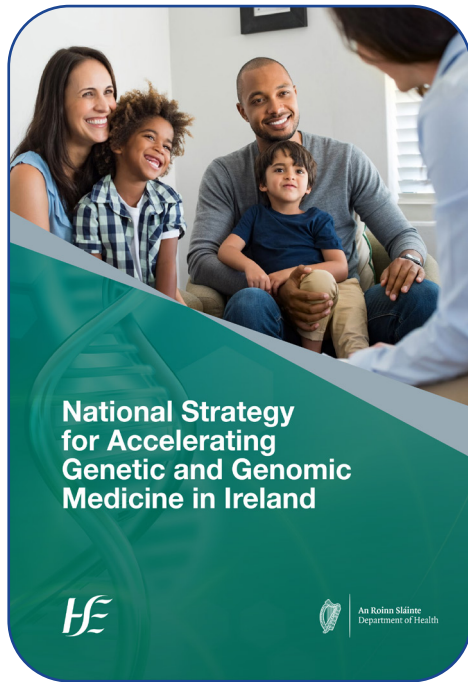
In Ireland, it had been politically recognised that a coherent strategy and funding to develop cancer diagnostics services was missing. This need has been highlighted by observations that, for example, in the last 5-7 years, an increasing number of approved cancer medicines do require a companion diagnostic, such as genomic tumour testing, to be used effectively.

In part in response to this, the Cancer Molecular Diagnostics Advisory Group was established in May 2017 under the National Cancer Control Programme

in Ireland. The group of experts comprised a multidisciplinary membership with the objective of evaluating the companion diagnostics that should be deployed for informing precision oncology treatment.

Then in 2022, the *National Strategy for Accelerating Genetic and Genomic Medicine* in Ireland was published. As part of the strategy, the Advisory Group submitted a Framework for developing cancers related diagnostics services. The strategy highlighted the need to consolidate the expertise that is already in the country and to have a consolidated approach across cancer centres and suggested to follow a tiered centre approach. Building on observed practices from other countries in Europe, among the goals is fostering collaboration rather than competition between cancer centres in respect to test access. Recognising knowledge needs, the strategy includes facilities for centralised bioinformatics support.

Figure 11. Framework for National Precision Cancer Molecular Service.



Michele Calabrò, Director of the European Regional and Local Health Authorities (EUREGHA) highlighted the value of including regions and local health authorities in the discussion around genomic tumour testing infrastructure and access. Experiences of countries such as Ireland are important case studies to bring forward for harmonisation across Member States.

Moreover, it is crucial for regions to understand what the impact of challenges is related to genomic tumour testing and to collaborate with European regional authorities to overcome such issues.

It is crucial for regions to have geographical representatives in the European framework and to select specialised centres in the topic.

Digitalisation plays an important role in facilitating the connection between different elements of the strategy and infrastructure in relation to genomic tumour testing across Europe.

In closing remarks, Michele emphasised the value that the European Union can play in facilitating and financially supporting cross-border cooperation methods for common health challenges, such as access to genomic tumour testing, inclusive of regional health authorities.

Concluding the session, Olivia McDermid re-emphasised the significance of concern among stakeholders about the impact that delayed implementation of the IVDR regulation is having on the field of companion diagnostics and the need to elevate political attention to available solutions. Olivia also reflected on a learning from the session as including the value of sharing best practices across countries, as evidenced in the presentation by Maeve Lowery.

POLICY RECOMMENDATIONS

- Good practices in achieving improved access to genomic tumour testing should be shared and replicated across Europe. Examples highlighted during the roundtable included the approaches undertaken in countries such as Germany, Belgium and Ireland, in which clear strategies have been developed and related actions committed to those strategies thereafter implemented.
- Such actions can include national guidelines, coordination of expert centres to help provide laboratory and knowledge structures across a country. National level coordination of approach can also assist in ensuring quality assurance of testing, including that tests are fully complete and conducted at the right time.
- A major unresolved, and ever more evident, barrier to patients in Europe being able to access targeted therapy supported by genomic tumour testing is the ongoing difficulties in achieving a smooth implementation of the EU in vitro diagnostic medical device regulation (IVDR). Evidence is now available about the lack of coordination of IVDR related trial and conformity assessment applications across countries which are delaying relevant trials and future authorisation and availability of treatments and test. Possible solutions, such as a voluntary harmonisation procedure, are currently being discussed at political level and should be a focus for national governments and the European Commission in 2024.

