Realising the potential of genomic technologies in cancer care:

Implementing the ‘Cancer Diagnostic and Treatment for All’ initiative in the EU

The following organisations endorse the content of this report:

European Cancer Patient Coalition

Lung Cancer Europe

eu40®

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Foreword

As a European citizen and a Member of the European Parliament, I firmly believe that the European Union can and must bring tangible health benefits to all citizens across the EU. The COVID-19 pandemic has demonstrated a clear need to work together to protect the health of citizens and strengthen our healthcare systems. Only an EU-wide approach will enable us to build fairer and resilient healthcare systems across Europe, accessible to each individual person.

The EU-wide approach should be applied beyond COVID-19. Cancer is a pandemic of its own, representing a real threat to European citizens and societies. Its already high prevalence is projected to continue to increase. This year's publication of Europe's Beating Cancer Plan has been an important political step to fight cancer. Now we all must throw our full weight to ensure successful and result-oriented implementation of the Plan. This will require different stakeholders to come together - public health experts, academics, researchers, healthcare professionals, patients, and the biopharmaceutical industry.

It is with an eye on collaborative implementation of Europe's Beating Cancer Plan that I support the work presented in this timely report. It discusses the Plan's flagship initiative 'Cancer Diagnostic and Treatment for All' and aims to further explore the potential of personalised medicine as a key pillar for cancer diagnosis and treatment. In this document, national and European cancer experts examine the barriers to personalised medicine across the EU and highlight concrete priorities and activities to overcome them. By defining a way forward, this report adds value towards wider adoption of personalised medicine across the EU, and, specifically, for the implementation of the 'Cancer Diagnostic and Treatment for All initiative'.

I would like to thank the authors who work on the ground every day for having come together in this report. Finally, I call upon the European Commission, my fellow colleagues in the European Parliament and national policymakers to listen to them.

We must ensure that the fight against cancer not only remains a political priority, but also leads to positive outcomes for cancer patients across the EU. I commit to working together with my colleagues in the EU Parliament, Commission and the Council to leverage these expert recommendations to co-create policies that support high-quality cancer care in the EU.

Cyrus Engerer, Member of the European Parliament

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Executive Summary

The impact of cancer across the European Union (EU) is undeniable. Every year, millions of people are diagnosed with cancer and many lose their lives to cancer.[1] Alarmingly, the prevalence of cancer is expected to continue to increase.[2]

Scientific advances have allowed us to improve our arsenal in the fight against cancer, and there is a need for their extensive implementation to fully leverage innovation and successfully combat the burden of cancer. This includes the wide adoption of personalised medicine – the tailoring of medical interventions to each individual patient based on biological characteristics measured through biomarker testing. Making decisions based on the specificities of each cancer can improve clinical outcomes and reduce healthcare costs, offering benefits for individual patients and healthcare systems.[3]

The European Commission published Europe's Beating Cancer Plan in February 2021,[4] providing a commitment to citizens across the EU to increase efforts in cancer prevention, treatment and care. The plan outlines 10 flagship initiatives and several supporting actions to address the burden of cancer. It recognises personalised medicine as a key pillar in the fight against cancer, for example in Flagship 6, the 'Cancer Diagnostic and Treatment for All' initiative.[4] Through this initiative, the European Commission aims to leverage comprehensive biomarker testing technologies to improve cancer diagnosis and treatment and help reduce unequal access to personalised medicine throughout the EU.[4]

Europe's Beating Cancer Plan is a welcome strategy to address the burden of cancer, and it is now time to turn the plan into reality. Leading experts from the oncology community worked through the barriers to the delivery of personalised medicine in the EU and aligned on a vision for the way forward. This report presents their views, including the five priority areas that should be addressed by the European Commission while implementing the Cancer Diagnostic and Treatment for All initiative.

Recommendations

1. **Lead awareness campaigns to increase understanding of the benefits of biomarker testing**

2. **Develop EU-wide guidance on personalised medicine, including recommendations on biomarker testing as an indicator of quality in cancer care**

3. **Build the infrastructure required for optimal uptake of biomarker testing**

4. **Facilitate the development of specialised knowledge, including undergraduate, post-graduate and ongoing professional training in personalised medicine**

5. **Mobilise resources to promote equal access to personalised medicine**

It is encouraging to see the European Commission acknowledge the potential of personalised medicine in cancer care, and it is now imperative that decision-makers help to foster the environment required for its equal adoption across the region. Ensuring access to biomarker testing and wide collaboration with stakeholders in the cancer care environment will be crucial for the success of Flagship 6.

People living with cancer across the EU have waited long enough for diagnostic and treatment innovation. The time for action is now.

The promise of personalised medicine in cancer care

In 2020, 2.7 million people were diagnosed with cancer and 1.3 million lost their lives to cancer in the European Union (EU).[1] The burden of cancer continues to increase with the ageing population and complex genetic and environmental factors, such as exposure to pollution and carcinogenic substances.[2] By 2040, the prevalence of cancer is expected to have almost doubled compared to 2020.[2]

Scientific advances and innovation in cancer diagnosis and treatment can help identify cancer earlier, improve the quality of life of people living with cancer and extend their lives. Therefore, it is crucial to identify strategies to bring innovation to clinical practice and limit the impact of cancer on individual people, healthcare systems and society.

Targeted therapies, often referred to as personalised or precision medicines, are increasingly becoming the cornerstone of cancer care. Personalised medicine utilises biological characteristics (biomarkers, which are characteristics of the body that can be measured), such as molecular information, to support disease prevention, diagnosis and treatment.[5] As it is targeted to the characteristics of each person and cancer, personalised medicine may offer better outcomes and reduce the risk of adverse effects alongside a reduction in healthcare costs and greater efficiencies for healthcare systems.[6]

Biomarker testing sits at the centre of personalised medicine as it provides the necessary information to make individualised clinical decisions on the use of targeted therapies. It can, for example, help predict response to treatment, supporting treatment choice.

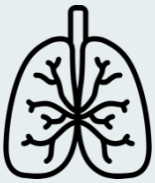
Biomarker testing can be performed by independent tests (single-gene tests) or panels (several genes in one analysis), which can vary in complexity and may be performed by next-generation sequencing (NGS).[6] The choice of the testing approach should be made based on the value created by the different technologies, meaning that while in some cancer types NGS should be preferred to guide decision-making, in others single-gene testing may be a better choice.

The role of biomarker testing in guiding treatment choice

Case study 1. Colorectal cancer

Prognosis of colorectal cancer is often poor,[7] but early diagnosis and treatment choice guided by biomarker testing can play an important role in achieving the best possible outcomes.[7,8] Colorectal cancer cells may have biomarkers that indicate abnormal growth,[9] and these biomarkers can be useful in guiding the best treatment approach.[8] The European Society for Medical Oncology (ESMO) recommends testing for these biomarkers, which helps indicate how effective different treatments are expected to be.[8] This avoids trial-and-error clinical decisions that could signify delaying more effective treatment options.

Case study 2. Non-small cell lung cancer



Lung cancer cells may also have biomarkers that represent genetic changes (mutations) that contribute to tumour growth. Non-small cell lung cancer (NSCLC) accounts for 80–85% of lung cancer cases,[10] and the most common mutation in NSCLC is present in up to 47% of cases.[11] Knowing this – via biomarker testing – can guide treatment choice and contribute to better clinical outcomes. ESMO has published guidelines recommending NGS in NSCLC as it may support clinical decision-making.[12]

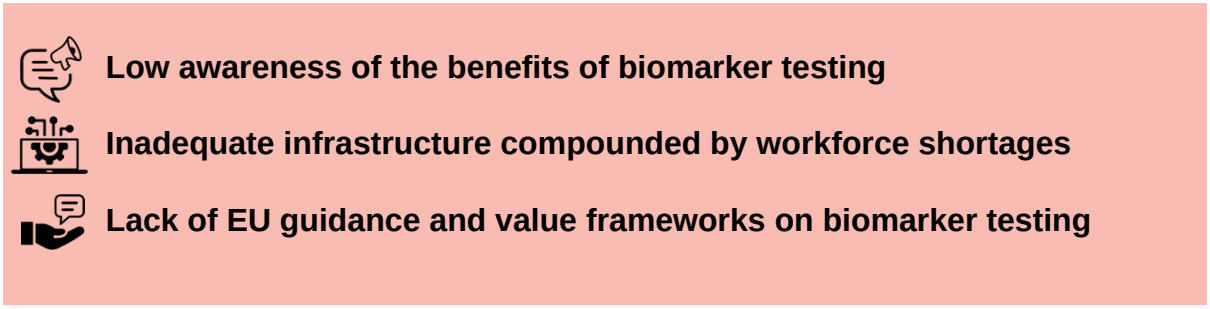
Case study 3. Ovarian cancer

Ovarian cancer is difficult to treat, with most cases diagnosed in late stages,[13] resulting in poor five-year survival rate.[14] There are different molecular profiles in ovarian cancer, which can be assessed through NGS,[12] and results can be used to anticipate response to treatment.[15] This has been recognised in ESMO guidelines, which recommend performing NGS in ovarian cancer samples to guide treatment choice.[12,15]

Barriers to the uptake of personalised medicine in the EU

Despite the benefits for patients and healthcare systems, uptake of biomarker testing throughout the EU remains sub-optimal, and there is variation in access both within and between countries. Many barriers contribute to this (Figure 1).

Figure 1. Barriers to the uptake of biomarker testing



Low awareness of the benefits of biomarker testing

Recognition of the benefits of biomarker testing is still too low – among policymakers, payers, healthcare professionals, patients and the wider public. A 2020 global survey of physicians, nurses, pharmacists and other allied health professionals by the International Association for the Study of Lung Cancer (IASLC) found that just two-thirds of the respondents were aware of recent guideline updates related to biomarker testing in lung cancer.[16] This suggests that some healthcare professionals may not be aware of the clinical value of testing. Clinicians may also be unclear about how to interpret results to create benefits for patients. These factors may contribute to people not being referred for testing even when clinical guidelines recommend doing so.

The suboptimal awareness of the benefits of biomarker testing among healthcare professionals may connect to the limited understanding among patients. According to a survey of people living with cancer conducted by the European Cancer Patient Coalition (ECPC) in 2019, 70% of the respondents said that the importance of biomarker testing was not adequately explained to them by their doctors.[17] If patients are not fully aware of the benefits of biomarker testing, they will likely not feel empowered to discuss this with their healthcare team.

Decision-makers, including policymakers and payers, also seem to have a limited understanding of the clinical utility of biomarker testing, which may result in the poor allocation of resources for this, both human and financial.[18]

Inadequate infrastructure compounded by workforce shortages

There are insufficient laboratory and clinical settings to consistently perform biomarker testing, and in particular NGS, at scale. For example, in some care settings, analyses may take several days or weeks. Cancer can progress quickly, and this delay in getting results of biomarker tests may delay, or entirely prevent, access to the best treatment option. If the cancer has progressed by the time the results are available, the treatment that was optimal in the previous stage may not be suited, or available, in the more advanced cancer stage. A 2021 survey of clinicians found that almost all respondents (98%) expected to receive biomarker testing results in one to two weeks, but 37% had to wait up to four weeks.[19] Of the respondents who waited up to four weeks, over a third initiated a non-targeted cancer treatment. This demonstrates that delays in receiving test results impact clinical decisions and could mean that not all people who would potentially benefit from a targeted therapy are receiving it.

Delays in test results may be explained not only by a lack of sufficient clinical settings and specialised equipment but also a shortage in the specialised workforce required to fully leverage the potential of personalised medicine, as well as knowledge gaps in the healthcare workforce. This may be partially explained by insufficient inclusion of molecular pathology and biomarker testing content in undergraduate courses.

Several professionals are needed to deliver the vision of personalised medicine, including pathologists (who perform biomarker testing analyses), bioinformaticians (who analyse the results) and specialised oncologists (who deliver and action the results). However, the specialised professional to population ratio across the EU is often insufficient – and varying across the region. For example, Europe averages one pathologist for every 32,000 inhabitants, with Iceland having the greatest density at one for every 14,000 inhabitants.[20] At the other end of the scale is Germany, with the second-lowest ratio at one pathologist for every 48,000 residents, and Poland, with just one pathologist for every 63,000 inhabitants. This shows that countries across Europe have not been able to equally support the development and specialisation of the workforce to the required level.

Information technology (IT) infrastructure also needs further development to appropriately support optimal delivery of personalised medicine, including data collection, analysis and sharing between relevant settings. Systems often work in silos, making it difficult to connect the information generated in different institutions.

Funding limitations further compound the infrastructural challenges preventing biomarker testing.

Lack of EU guidance and value frameworks on biomarker testing

There is a lack of guidance at the European level on the importance of biomarker testing. While ESMO has published clinical guidelines for the use of NGS in the management of different cancer types and refers to biomarker testing in cancer-specific guidelines,[8,12,15] further guidance is needed to inform policy decisions at the national level, including funding decisions. A 2021 survey of public hospitals, research centres, private laboratories and universities across nine European countries found only 50% of respondents had regional plans for personalised medicines, which highlights potential inconsistencies in access to biomarker testing throughout Europe and the need for improvement of national policies.[21]

Value assessment and reimbursement frameworks for biomarker testing across the EU consistently fail to recognise the value-add that biomarker testing brings to clinical decision-making and outcomes. They seem to ignore that access to biomarker testing should be a crucial part of cancer care, and that the costs of testing are often a small fraction of treatment costs.[18]

Biomarker testing may help save direct and indirect costs associated with non-targeted treatment options. This has, for example, been shown in advanced NSCLC. In a study conducted in France, analysing the three most common genomic alterations in NSCLC and pursuing a targeted treatment approach in alignment with clinical guidelines was cost-effective compared to a standard care approach without biomarker testing. Specifically, the study found that testing for 'at least one biomarker' compared to none resulted in cost-savings of EUR13,230 per life-year saved.[22] Some stakeholders, including payers, worry about costs of biomarker testing without recognising that performing biomarker testing is an investment in the care for each person – and consequently the healthcare system and society.

Opportunities created by Europe's Beating Cancer Plan

The European Commission launched Europe's Beating Cancer Plan[4] in 2021 to address the growing burden of cancer, outlining 10 flagship initiatives and multiple supporting actions to deliver on this goal. The plan acknowledges the potential of personalised medicine in cancer care and calls for improved access to innovative approaches to reduce costs associated with less effective treatments. With an overall focus on prevention, early diagnosis, treatment and improved quality of life, the plan creates a unique policy context for the recognition of the potential of biomarker testing and the delivery of personalised medicine in the EU.

One of the flagship initiatives in the plan – Flagship 6, the 'Cancer Diagnostic and Treatment for All' initiative – aims to improve the implementation of genomic technologies in cancer care. This initiative intends to create the opportunity to increase access to molecular diagnostics and share genomic profiles between cancer centres to better tailor medical interventions for people living with cancer across the EU.

Europe's Beating Cancer Plan Flagship 6: Cancer Diagnostic and Treatment for All initiative

The new Cancer Diagnostic and Treatment for All initiative aims to help improve access to innovative cancer diagnosis and treatments. According to the European Commission, "it will use the 'next generation sequencing' technology for quick and efficient genetic profiles of tumour cells, allowing Cancer Centres to share cancer profiles and applying the same or similar diagnostic and therapeutic approaches to patients with comparable cancer profiles. The initiative will ultimately help optimise cancer diagnosis and treatment and reduce unequal access to personalised medicine in cancer care, greatly benefitting patients".

The European Commission will dedicate specific funds to the Cancer Diagnostic and Treatment for All initiative as part of EU4Health, an EU funding programme for the period 2021–2027. In October 2021, the European Commission published the calls for proposals related to this initiative.[23]

Recommendations for implementation of the Cancer Diagnostic and Treatment for All initiative

This report recommends five priority areas for the European Commission to consider while implementing Europe's Beating Cancer Plan, in particular the Cancer Diagnostic and Treatment for All initiative (Figure 2). The recommendations highlight key activities required to address the existing barriers to uptake of biomarker testing in cancer diagnosis and care. Where relevant, suggestions on how to leverage other initiatives by the European Commission are included.

Figure 2. Recommendations for successful implementation of the Cancer Diagnostic and Treatment for All initiative

Recommendations

1. **Lead awareness campaigns to increase understanding of the benefits of biomarker testing**
2. **Develop EU-wide guidance on personalised medicine, including recommendations on biomarker testing as an indicator of quality in cancer care**
3. **Build the infrastructure required for optimal uptake of biomarker testing**
4. **Facilitate the development of specialised knowledge, including undergraduate, postgraduate and ongoing professional training in personalised medicine**
5. **Mobilise resources to promote equal access to personalised medicine**

Lead awareness campaigns to increase understanding of the benefits of biomarker testing

There is a need for greater understanding of the importance of biomarker testing in cancer care, which can be achieved through communication, education and awareness campaigns.

The public needs to be made aware of the benefits of biomarker testing and precision medicines, not only through physicians but also direct communication. With improved awareness, people may be more likely to discuss biomarker testing with their physicians upon a cancer diagnosis and disease progression, which would help to involve patients in clinical decision-making and improve outcomes.

Patient organisations play a crucial role in educating and empowering people living with cancer, and therefore there is a strong case for the European Commission to partner with these organisations to deliver messages on biomarker testing to cancer patient communities.[6]

Professional bodies also play an important role in the development of educational materials. The European Commission may consider partnering with organisations such as the Association for Molecular Pathology, which currently provide free to access education content on molecular testing for both physicians[24] and patients.[25]

Decision-makers across Europe also need a greater understanding of the importance of biomarker testing, which calls for awareness-raising at a political level. This will help policymakers and payers at the national level to develop and implement frameworks that recognise the value of biomarker testing.[6]

It is key to address confidentiality and privacy concerns that patients, and the public more generally, may have related to sharing genetic information, such as those related to how data are used.[26] One essential step in this is raising awareness of all the safety measures currently in place to protect health data.

Develop EU-wide guidance on personalised medicine, including recommendations on biomarker testing as an indicator of quality in cancer care

There is a need for EU-wide guidance to support decision-making when it comes to biomarker testing. Guidance should provide an overview of existing genomic technologies and recommendations for approval – for example on data and quality assurance requirements. It should include high-level recommendations for when to perform biomarker testing and should aim to standardise approaches for assessment and reimbursement of biomarker testing across and within Member States. Ultimately, it should define access to biomarker testing as an indicator of quality in cancer care. EU guidance should link to, but not replace, clinical guidelines – for example, it could support recognition and endorsement of European clinical guidelines, such as those developed by ESMO, at the national level.

Several stakeholders should be involved in the development of guidance coming out of the Cancer Diagnostic and Treatment for All initiative, including professional societies, healthcare professionals, patient representatives and the biopharmaceutical industry. The guidance on biomarker testing should evolve with the latest scientific evidence, such as innovation in genomic technologies. It should therefore be updated regularly, and new versions should be communicated clearly and consistently to support their implementation and the continual improvement of cancer care. The European Commission is uniquely positioned to coordinate such a multi-stakeholder effort.

Build the infrastructure required for optimal uptake of biomarker testing

To fully leverage the potential of personalised medicine across the EU, it is essential to have an infrastructure and equipment that facilitate wide access to biomarker testing and that allow for communication and collaboration within and between countries. This includes an increased number of laboratory settings and equipment, and a sophisticated IT system that enables clinicians throughout the EU to learn from data collected in other settings and treatment decisions made by their peers, potentially even in another Member State.[5,6] Information systems and electronic health records currently used in health institutions do not typically allow for this

comprehensive level of communication, which means that there is a need to upscale available systems.

Several existing or upcoming initiatives by the European Commission have the potential to boost infrastructure across the EU. For example, Europe's Beating Cancer Plan Flagship 5, dedicated to the development of an EU Network that links National Comprehensive Cancer Centres,[4] has the potential to increase cross-border collaboration and support the implementation of quality-assured diagnosis and treatment. In addition, the European Health Data Space,[27] an initiative that the European Commission is expected to present at the start of 2022, represents an important opportunity to increase the timely and simplified collection, analysis and sharing of genomic data, such as those collected via biomarker testing. This would allow for the quicker return of results, which is essential to optimise treatment outcomes.

Facilitate the development of a specialised workforce, including graduate, postgraduate and ongoing professional training in personalised medicine

The healthcare workforce must be clear on the benefits of biomarker testing and on the content of clinical guidelines to provide the best possible care for each person living with cancer. Training of healthcare professionals is key to addressing knowledge gaps, accelerating the uptake of biomarker tests and avoiding unnecessary costs on less effective treatments. Biomarker testing and personalised medicine education should start early on, in undergraduate programmes, and continue in medical training and postgraduate programmes. Opportunities for professional training in personalised medicine should be made available to all relevant healthcare professionals, including but not limited to pathologists, oncologists and general practitioners (GPs). GPs often hold the pivotal role of gatekeepers for specialised services, meaning they serve as a link between patients and the care settings that refer them to targeted treatment approaches, making it crucial that GPs are aware of the benefits associated with biomarker testing.

Ongoing professional training in personalised medicine can be achieved through synergies with existing education-related initiatives. The inter-speciality training programme proposed in Europe's Beating Cancer Plan,[4] designed to help deliver a more skilled and mobile cancer workforce through cross-border training and information-sharing, should include modules in personalised medicine, recognising it

as a major component of high-quality cancer care. In addition, Erasmus+ programmes,[28] which support education and training opportunities in Europe, could be used as a delivery platform to increase knowledge among undergraduate healthcare professionals and therefore increase the likelihood of biomarker testing being considered in clinical practice.

In addition to training the healthcare workforce, a specialised forum for discussion of clinical cases, bringing together specialised knowledge on biomarker testing and personalised medicine, can support the uptake of testing and targeted treatments. This can be seen in molecular tumour boards, which interpret testing data and provide genomic-driven, patient-tailored clinical recommendations. Several studies have indicated that clinical decisions made via molecular tumour boards can improve clinical outcomes for people with cancer, including survival.[29] [30] The European Commission should consider leveraging existing molecular tumour boards and supporting the creation of additional groups where needed, while supporting communication between all molecular tumour boards. This can be facilitated by Flagship 5 of Europe's Beating Cancer Plan – the EU Network linking National Comprehensive Cancer Centres.

Mobilise resources to promote equal access to personalised medicine

The steps needed to realise the vision of personalised medicine across the EU – and the vision of the Cancer Diagnostic and Treatment for All initiative – require investment, and the European Commission should dedicate funding to supporting the road ahead. To do so, it will be important to recognise the inequalities across the region and the financial specificities of each Member State. There should be clear ways to measure access to biomarker testing, track progress and identify where additional resources may be needed. This could include, but is not limited to, the following indicators:

- Access to biomarker testing – single-gene and NGS
- Number of pathologists
- Average time between referral and access to biomarker testing, and between biomarker testing and results/follow-up appointment
- Public funding/reimbursement of biomarker testing in indications recommended in ESMO guidelines.

The Cancer Inequalities Registry proposed in Europe's Beating Cancer Plan (Flagship 9)[4] should incorporate these measurements. The registry aims to identify trends, disparities and inequalities between Member States and regions and to determine the level of infrastructural support a country might need. Alongside regular qualitative assessments of the country-specific situation, the registry will identify specific areas of action to guide investment and interventions at EU, national and regional levels. Some existing funding mechanisms, such as the EU4Health Programme[31] and Horizon Europe,[32] should also be ringfenced to help deliver the promise of personalised medicine.

Conclusion

Personalised medicine, through wide and timely access to biomarker testing, has the potential to transform cancer care and provide significant benefits to people living with cancer, healthcare systems and societies in general. It can fundamentally change what it means to receive a cancer diagnosis and live with cancer. Yet throughout the EU, uptake of genomic technologies for biomarker testing remains sub-optimal owing to a range of factors, including low awareness, inadequate infrastructure and lack of EU guidance on the value of testing.

Political commitment to beat cancer has never been so strong in the EU. The European Commission launched Europe's Beating Cancer Plan in February 2021, where it recognises the importance of personalised medicine in cancer care, namely through the Cancer Diagnostic and Treatment for All initiative (Flagship 6). To successfully realise the vision of high-quality cancer care for every person living in the EU, the European Commission must:

- lead awareness campaigns
- develop EU-wide guidance
- build the required infrastructure
- facilitate the development of a specialised workforce
- mobilise resources to promote equal access.

The benefits from personalised medicine are just beginning to be realised, and the next steps will be crucial. It will be important to align political and payer action with regulatory frameworks to ensure continuous access to biomarker testing and personalised medicine. Cross-collaboration with stakeholders across the healthcare environment is essential for the European Commission to help bring the latest innovation to the clinical practice and further advance cancer care.

It is our hope that the European Commission will address the barriers and pursue the actions discussed in this report to help ensure every single person in the EU has access to high-quality cancer diagnosis and care.

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