Joint Position Paper on Personalised Oncology

Value of personalised oncology treatments and biomarkers

Personalised oncology constitutes administering the right treatment to the right patient at the right time, leading to better outcomes and reduced risk of adverse events. It avoids unnecessary treatment and reduces costs, including the opportunity cost of patients receiving an ineffective therapy. From the healthcare system perspective, personalised oncology brings more certainty on treatment outcomes and improves the sustainability and efficiency of healthcare.

Biomarkers define which patients may or may not respond to therapy, which is crucial to improve treatment standards and efficiency of care. Biomarkers can be objectively measured as indicators of pharmacologic response to therapeutic interventions, and as such hold great potential to predict clinical outcomes and define a personalised treatment strategy. While cancer treatments are traditionally defined by the location or origin of the tumour in the body, it has now become possible to develop treatments that specifically target rare molecular or genomic alterations in the tumour, sometimes even regardless of the location of the tumour itself. Companion diagnostics have the potential to accelerate access to such treatments, reduce development costs, and increase the efficacy and efficiency of treatment.

The benefits to the healthcare system and society are evident from the improvements in patient management and in terms of offsetting costs through reduced use of ineffective treatment, reduced cost of chronic conditions, and reduced hospital stays while delivering better health.

At the same time, personalised medicine in oncology creates challenges, because by its very nature it requires a multidisciplinary approach between different specialties, both clinical (for instance surgery, radiotherapy etc.) and non-clinical (such as bioinformatics or molecular biology etc.). This necessitates the modernisation of national healthcare systems, altering working methods of clinicians and health systems. Health systems and relevant clinical teams are often not currently geared up to cope with providing or making use of personalised medicine techniques, nor putting into action the treatment regimens related to the results of molecular testing.

Challenges to the development and introduction of personalised oncology in Europe

Plenty of access barriers, delays, and disparities for patients exist in Europe. They are driven by a wide range of factors – ranging from a lack of precedence for new treatment paradigms in the regulatory process to incompatible requirements, processes and rules in HTA methodology – that impede the use of effective medicines among clinically eligible patients.

The potential to select therapies according to biomarkers rather than tumour location gives patients treatment options that are specific to their type of cancer, but can also generate challenges for payers in terms of establishing new reimbursement models, such as indication-based pricing.

Another challenge to the introduction of personalised oncology is limited access to biomarker testing, mostly due to limited funding and restrictions on reimbursement. Gaining reimbursement for new companion diagnostic tests can be slow, and the level of evidence required for tests can be unrealistic, with biomarker developers potentially lacking the resources to demonstrate the value of tests. A further issue is that, where multiple diagnostic tests exist, there is no consensus as to how these should be compared. Use of more sophisticated tests, based on next-generation sequencing (NGS) or approaches such as multianalyte assay with algorithmic analysis (MAAA) is currently limited. Implementation of these technologies is challenging, with a need for centralised laboratories, high development costs (and high costs per sample), and the requirement for advanced logistics to keep turnaround times low.

Conducting clinical trials is currently a major challenge in personalised oncology. As personalised oncology is tailored to small groups of patients or even individual patients, traditional development approaches are not always suitable. The more personalised a treatment, the more challenging it is to find the right patients and generate large sets of clinical trial data. This makes it crucial to collect data from other sources, notably real-world data from electronic health records, genomic databases or digital tools and technologies. This requires frameworks for the regulatory use of this data, as well as efforts to improve data quality, interoperability and access.

At the same time, patients will need to be appropriately informed about personalised medicine, since not all patients will directly benefit from personalised medicine. Despite being “personalised”, the tailored treatment pathway in personalised medicine comes down to the results of the molecular testing performed. The treatment regime considered depends on what is available in relation to the result: it could be that a drug to deal with the diagnosis is currently in clinical trials, into which the patient could subsequently be placed, or that the required drug lacks market authorisation in the patient’s home country but that it exists in the neighbouring country or even that such a drug does not exist yet. For this reason, patients need to be better informed by their clinicians of the true nature of personalised medicine and associated access issues.

Recommendations and future directions

It is important to consider the value of personalised oncology in terms of the benefits for patients, healthcare systems and society. Patients can benefit from improved

efficacy and reduced adverse events; healthcare systems can benefit from increased efficiency and improved outcomes; and society can benefit from early treatment of disease and improved efficiency of resource allocation. In addition, personalised oncology can lead to innovation in terms of more effective and more ethical clinical trials, as well as reduced research and development costs.

Overall, realising the potential of personalised oncology for all patients will require close collaboration among all relevant stakeholder groups. More 'joined-up thinking' is needed among oncologists, pathologists and payers to establish the most effective use of personalised therapies and diagnostic tests and ensure that the long-term health economic benefits of personalised oncology are realised. Overall, decisions should be based on what matters most to patients. Paying attention to the patient perspective also results in better use of resources, a goal that should appeal to all personalised oncology stakeholders.

High-quality real-world data and evidence can be the basis of successful clinical use of personalised oncology, as they facilitate and accelerate the development of personalised cancer treatments, contribute to clinical decision-making and support regulatory, reimbursement and policy decisions.

Data can only be used if it is meaningful and at scale. This requires that the right data to be captured for research, development and clinical use, and that the data is interoperable. Connected data systems should be developed by adopting harmonised quality and content standards and linking electronic health record systems and other sources of data across borders. Regulators, payers and policy-makers should agree on clear frameworks for the optimal use of real-world evidence in their decision-making processes.

Co-developing therapies, companion diagnostics and digital tools and technologies is likely to be beneficial: co-development approaches can result in more integrated personalised solutions with benefits for patients, while improving cost-effectiveness, increasing probability of success in drug development and reducing time to approval. This requires close interaction and collaboration among regulatory bodies for medicines and medical devices.

In Europe, the European Medicines Agency (EMA) is likely to play a role, through the new *in vitro* diagnostics regulation, in assessing the performance of tests. From a reimbursement perspective, linking the assessment of therapies and companion diagnostics is likely to be important as it is the combined package that delivers the full value. In general, clear and appropriate evidence requirements are essential to ensure manufacturers know what needs to be submitted for a positive assessment. With large numbers of therapies and diagnostic tests in development, harmonised regulatory frameworks and aligned data requirements will be important to ensure the necessary

evidence can be generated. By contrast, however, reimbursement of new personalised treatments including combinations of immunotherapies may require a more flexible approach to the generation of clinical and economic evidence, incorporating real-world evidence, performance-based reimbursement and early access programmes.

In future, some of the challenges associated with biomarkers and companion diagnostics may be addressed by NGS. Although the infrastructure requirements for NGS are costly and conduct relies on dedicated expertise, once established NGS may be a cost-effective approach to testing; use of comprehensive genomic profiling via NGS to determine treatment would avoid the need for multiple companion diagnostic tests with their associated costs and limitations. Clinically, there would be substantial benefits to NGS becoming part of routine practice.

About the paper

The position paper results from a CDDF multi-stakeholder workshop. Attendees included patient advocacy groups, academics, regulators, payers, HTA bodies, representatives of pharmaceutical manufacturers and molecular diagnostics companies. This summary describes the key themes discussed in the workshop, comprising the value of personalised oncology, current challenges to the introduction of personalised oncology in Europe, and future directions.

The paper was co-authored by Kathi Apostolidis, President of the European Cancer Patient Coalition (ECPC), Professor Francesco de Lorenzo, former ECPC president and board member of the Cancer Drug Development Forum (CDDF), Maurits-Jan Prinz (Roche) and Tobias Helmstorf (Bayer) for the EFPIA Oncology Platform.

About European Cancer Patient Coalition (ECPC)

The European Cancer Patient Coalition (ECPC) is the voice of cancer patients in Europe. With over 400 members, ECPC is Europe's largest umbrella cancer patients' association, covering all 28 EU member states and many other European and non-European countries. ECPC represents patients affected by all types of cancers, from the rarest to the most common.

About the Cancer Drug Development Forum (CDDF)

The Cancer Drug Development Forum (CDDF) is an international organisation, providing a neutral platform to stimulate interactions between all stakeholders involved in cancer drug development. The aim of the not-for-profit organization is to accelerate the delivery of effective oncology agents to patients.

About the EFPIA Oncology Platform

The EFPIA oncology platform brings together EFPIA member companies working to defeat cancer. As well as it members being at the cutting edge of new cancer treatments, the group brings together stakeholders from across Europe's cancer care community to find common solutions to the key challenges in cancer care.