Oncology
An Exciting Time of New Hope and New Challenges

Noemi Muszbek, MA, MSc
Senior Research Scientist, Modeling and Simulation, Evidera

Noemi Muszbek

The number of trials ongoing (25% of all medicines in clinical trials in 2013[1]) and the amount spent on oncology within healthcare budgets has led to increasing attention on cancer care. The excitement in cancer care is palpable not only in the medical community, but also in the media. The availability of multiple new treatments and treatment sequences, the move towards a potential cure in some cancer indications with the help of immuno-oncology treatments, such as checkpoint inhibitors, the increasing understanding of the underlying disease biology, research into identifying patients who will benefit from the different treatments with the help of biomarkers, and the faster routes to registration based on earlier data from clinical trials are all contributing to this excitement. However, these developments bring their own set of challenges for all stakeholders, including concerns of the increasing economic burden of the cost of cancer treatments and the challenges emphasized or brought about by the focus on immuno-oncology.

Development in immuno-oncology

One of the most visible differences in immuno-oncology compared to chemotherapies that we have come to expect in some indications is the substantial overall survival (OS) benefit shown by the new checkpoint inhibitors, and the now characteristic plateau in the OS curve. This suggests the potential of some patients being cured of their disease (but, of course, still subject to other mortality). However, the unusual survival curve and the hazard ratio (HR) that seems to increase over time do not lend themselves to the conventionally used methods for extrapolation, therefore requiring new approaches and assumptions on what happens after the end of the follow-up period. In addition, there is limited follow-up with immunotherapies for clinicians to provide guidance on long-term mortality, and historical OS curves with chemotherapies and targeted therapies will likely have very different mortality patterns.

Questions have also emerged regarding the appropriateness of progression-free survival (PFS) as an outcome. PFS is usually based on Response Evaluation Criteria in Solid Tumors (RECIST) or the World Health Organization (WHO) criteria that are commonly reported. The different response patterns seen in immunotherapy agents has led to the development of the immune-related response criteria (irRC).[2-4] However, while irRC may capture benefits more accurately, they are less likely to be accepted by regulatory bodies given their newness. Use of irRC would also impair the use of conventional network meta-analyses (NMA) to establish the relative efficacy of immunotherapies versus chemotherapies or targeted therapies.

Accelerated approval by the U.S. Food and Drug Administration (FDA) and early access programs available in Europe, such as adaptive licensing or Medicines

Adaptive Pathways to Patients (MAPPs), and the early access to medicines scheme (EAMS) in the UK[5, 6] which provided access to ipilimumab, nivolumab and pembrolizumab, enhances these challenges. Evidence initially is often based on single-arm trials increasing the difficulty and uncertainty of projecting and comparing clinical outcomes.

With developing clinical knowledge of the disease biology and the development of biomarkers, the patient population is becoming more fragmented, leading to challenges in the comparative assessment of new therapies relative to older ones.

Focus of the cost of cancer treatments

With the development of new therapies comes the focus on drug costs. Recently, not only payers, but also clinicians, started to look at methods to help in selecting treatments offering the best value. In Europe the use of the current health technology assessment (HTA) frameworks are increasing their focus on assessing efficiency with the help of cost-effectiveness analyses (CEAs).

From the payer side, the role of economic criteria has been increasing in the decision making process for innovative drugs. In the UK, starting in April 2016, all new cancer drugs and significant new licensed indications for cancer drugs are to be referred for health technology appraisal, including CEA, to the National Institute for Health and Care Excellence (NICE), as opposed to just a selection of cancer drugs and indications.[7] In Latin America and Asia, the number of formal agencies has been growing. In the U.S., the Institute for Clinical and Economic Review (ICER) has been providing recommendation on drug prices based mainly on cost-effectiveness and budget impact.[8]

From the clinical side, recent years have seen the publication of different value frameworks, including the Medical Oncology Magnitude of Clinical Benefit Scale[9] (ESMO-MCBS) from the European society for Medical Oncology (ESMO), the American Society of Clinical Oncology (ASCO) Value Framework,[10] the National Comprehensive Cancer Network (NCCN) Evidence Blocks,[11] and the DrugAbacus from the Memorial Sloan Kettering Cancer Center.[12] These have been constantly evolving, with ASCO publishing an update in May 2016; ESMO is currently working on a newer version including structural, technical, and immunotherapy triggered revisions;[13] NCCN releasing assessments of treatments in 22 indications; and, DrugAbacus extending the markets included (U.S. Medicare, U.S. Veterans Administration, UK, Ireland, Belgium, and Canada).

The challenges in these assessment include:

- The definition of value, including the criteria according to which value is measured. In the current frameworks, although not identical, the criteria go beyond efficacy and safety and include unmet need, the severity of the disease, innovation, and the patient's voice.
- The determination of value, currently determined in a variety of ways, for example with the use of quality-adjusted life years (QALYs), the determination of a Care Value (for ICER), scoring systems (ASCO and ESMO) or visually (NCCN).
- The assessment of this value using different tools, including CEAs, budget impact analyses, and a form of multi-criteria decision analyses (MCDA).
- The assessment and determination of decision making rules, such as thresholds, the debate around which has been ongoing for decades among health economists, and has recently seen multiple publications.[14-17]

Meeting these challenges requires combined efforts from the different stakeholders, including payers, clinicians, and patients; the development of the methodology that has both a sound theoretical background and is practical for decision making; and the availability of sufficient data to allow the assessments.

The recent clinical developments in oncology offer hope for patients who have not dared to hope before. As with all new developments, these also bring challenges in assessment of the new therapies and, due to the limited resources, the determination of what offers "value for money." These challenges, however, also provide opportunities for the payers, health economics and outcomes researchers, the clinical community, and patients to work together and start discussions to identify new, better solutions and methods that take into account the different aspects of healthcare.

For more information, please contact Noemi.Muszbek@evidera.com.

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