Marc Botteman and Ben van Hout from Pharmerit International discuss how to navigate the value challenges of new cancer treatments like CAR-T with payers.

There has been an explosion in the availability of new and innovative treatments in oncology and pharma’s pipeline progress promises plenty more to come. Breakthrough immuno-oncology treatments are changing the treatment landscape, with mechanisms of action that are very different to more ‘standard’ cancer therapies. Utilising the patient’s own immune system to fight cancer has shown promising results, but these therapies also bring with them a unique set of challenges to payers and the industry.

Patient and disease heterogeneity, the multitude of therapies, combinations of therapies and treatment sequences on offer, and uncertainties around the duration of treatment effects have all made the treatment choice decision a far more complex process. Using standard methods, it becomes more difficult to show that expensive new oncology therapies, while often providing substantial health benefits, offer value for money.

As the likes of CAR-T and checkpoint inhibitors continue to change the environment and add further layers of complexity to treatment choices, it can be very difficult for payers to keep abreast of the benefits associated with each option. New ways of demonstrating value are needed by pharma that can capture the true underlying clinical mechanisms, and thereby reveal the real value of new cancer drugs to payers.
Treatment innovations in oncology

Over the last five to ten years the oncology landscape has seen some major changes as regimens for hard-to-treat cancers like prostate and pancreatic come within our reach and traditional approaches to cancer are revolutionised.

There has also been a recognition that breast cancer, for example, is not a single, homogeneous disease that affects all women in the same way and could have at least four major molecular subtypes. Meanwhile, in blood cancer a deepening appreciation of its biology suggests that physicians will need more than a single intervention or management approach if treatment is to be curative.

“There are a lot of exciting changes happening and these are exciting times – people can feel optimistic about the future of oncology,” says Marc Botteman, co-founder and managing partner of health economics outcomes research and strategic market access consultancy Pharmerit International.

He adds: “There are a lot of breakthrough therapies, and immuno-oncology treatments in particular are a paradigm shift in the standard of care for a lot of cancers as the idea of harnessing the immune system to fight cancer leads to new results.”

“And it’s not just the checkpoint inhibitors that are changing the environment,” Marc says. “Cell-based therapies, like CAR-T and their precision medicine approach, are really having an impact on the patient population.”

Named ‘advance of the year’ at the 2018 American Society of Clinical Oncology (ASCO) meeting, CAR-T, or Chimeric Antigen Receptor T-cell therapy, is perhaps the ultimate in precision medicine. Each course of treatment is specifically developed for an individual patient and involves reprogramming a patient's own immune system cells which are then used to target their cancer. Before that takes place, biomarkers are needed to identify patients that could benefit.
“Where this is all leading us is on a path of extremely complex treatment choices,” says Marc. “These kinds of treatments may work in some populations, but not in others, and a lot of effort is being expended to assess how treatments can be used in combination. It really just explodes the level of complexity in the field.”

Market access challenges

The nature of the changes taking place within oncology makes it particularly difficult for payers to keep up, with knock-on effects for pharmaceutical companies seeking to gain market access for their latest medicines. The rate of change is such that by the time a new drug has gone through a health technology assessment process the resulting decision can easily be out of date as new evidence continually emerges. The challenge for industry is to clearly show where patient benefits reside, not only in terms of their own product but also in the context of all the other treatment options that are available at the time of assessment.

Payers are confronted with new therapies that are expensive. Their effectiveness, while often substantial, is usually seen only in a specific, small population and the evidence base available to show treatment benefit is usually limited. It’s no wonder that demonstrating the value of a new oncology therapy is challenging.

“I tend to think payers will understand the costs of a new cancer drug a lot better than they will fully understand the patient benefits it brings,” says Marc. “There’s so much happening at the moment, and the resources are probably not there to help them understand this, so in general they are likely to need to rely on other groups to simplify their decision-making processes.”

He points to CAR-Ts as one type of therapy that can only be used by a very small patient population and which has fairly high costs. Most payers are not well equipped to deal with these kinds of treatments, although Marc says he is seeing some interesting environmental shifts for payers and pharma in the US with the emergence of pay-for-performance contracts.

Whatever arrangements are put in place, the key question for the pharmaceutical industry is how to generate and synthesise evidence for the new wave of cancer treatments, both those on the market and those waiting in the wings. Traditional clinical trials are not coping well with framing the benefits of these drugs. Patient response is incredibly heterogeneous and benefits in progression-free survival endpoints are not always seen. As such, traditional models may well not work for newer immuno-oncology treatments.

“The trend here is to move away from ever-larger and longer trials and set up ones that use surrogate data. These trials may have response data and data on remission or minimal residual disease, but lack information on the long-term survival impact which is utilised in traditional modelling approaches used to demonstrate value to payers. Even something like real-world evidence, which is much discussed, is still in its infancy.”

Marc continues:

“The existing framework that is used to inform market access decisions is not particularly well suited to understand the change in this paradigm of long-term survival in a heterogeneous patient population. There are a lot of gaps in the data that industry and payers need to work together to fill.”
Modelling developments

One of the ways that these information gaps about new cancer drugs can be addressed is with innovative modelling techniques. These can be trained to capture the underlying clinical mechanisms of the disease combined with the working mechanism of the treatment to reveal the true benefits of a drug.

Ultimately, payers want to understand where different drugs should be placed in a treatment sequence to maximise benefit for a reasonable cost. To do this, they need to understand, based on limited information, how a new treatment compares to all the other treatments that are available. Marc says: “At Pharmerit International we’re using novel techniques to increase our understanding of disease progression and how different drugs work to reach an outcome we have seen in aggregate trial data for a particular drug. This allows us to develop a model structure based on advanced statistical methods that brings together all those underlying mechanisms and accurately reflects the heterogeneities we know exist. We’re able to then better understand what’s happening with all these treatments and make a better prediction about outcomes for a patient or group of patients.”

Pharmerit International’s scientific director Ben van Hout explains further:

“Some of the newer cancer drugs being developed just won’t work in everybody, and that’s most noticeable for immuno-oncology drugs which trigger the body to fight the cancer – in some it works and in others it doesn’t. At Pharmerit International, we’ve developed innovative models that capture the fact that patients are heterogeneous, and that different cancer treatments also differ in their mechanisms of action.”
The future of modelling in oncology

Challenging the existing framework used in market access decision-making by introducing more innovative models that better capture the heterogeneity of diseases, patients and treatment mechanisms provides increased validity and robustness to cost-effectiveness analyses.

Ben says: “By demonstrating that heterogeneity is included in your model extrapolations you reflect what clinicians see in practice – this resonates with them and helps them to better understand your approach. Many payer committees include clinicians – when it comes to market access decision making it is important that they can recognise their patients and their own thought processes in the statistical analyses you are presenting.”

“At Pharmerit International we work hard on methodologies that will provide better analytics on the basis of the data that we see,” concludes Marc. “A pharmaceutical company going to a local or regional HTA body may have a very good understanding of their own product. The challenge they face is to be able to demonstrate to payers the true value of new cancer drugs in the context of all the other products that are out there.”

“ That’s where we help, by looking at all the evidence that’s available for all the other products and organising that information in such a way that the role of the new treatment, and its place in the treatment sequence, can be better understood.”

Ben concludes: “Our pharmaceutical industry is developing impressive and innovative treatments that are constantly improving outcomes for oncology patients. We are excited to help them demonstrate the true value of these products to payers globally.”
About the Authors

Marc Botteman is co-founder and managing partner of Pharmerit and has over 25 years of consulting experience in designing and conducting studies to evaluate the economic value of health care interventions in North America, Europe, and developing countries. Marc’s primary research interests include decision analysis, cost effectiveness analysis, database analysis and strategic reimbursement research. He has applied his research skills to a wide range of therapeutic areas for a variety of sponsors in the private industry and for research foundations and non-for-profit organizations. Marc has authored nearly 100 peer-reviewed publications. Mr. Botteman holds Master’s degrees in economics from Namur University, Namur, Belgium, and demography from Georgetown University.

Professor Ben van Hout combines an appointment as professor of Health Economics at the School for Health and Related Studies of the University of Sheffield with the position of scientific director at Pharmerit. In 1993 he was one of the earliest researchers to apply discrete event models and he was the first to apply a non-parametric method to estimate costs in the presence of censoring. In 1994 he was the first to apply Fieller’s approach to calculate confidence intervals around cost-effectiveness ratio’s and he introduced the acceptability curve, now a well-known concept in cost effectiveness analysis. Ben was one of the developers of the multi-disease modelling approach that is now used by the Dutch government and the WHO. He is one of the founding members of the EuroQol group and currently enjoys chairing the valuation task force within the EQ-5D group. He co-authored the Dutch guidelines concerning costs calculations and pharmaco-economic studies and holds a PhD in health economics and a master’s degree in econometrics, both from the Erasmus University in Rotterdam.