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Challenges in optimizing EU market access for immuno-oncology therapies

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With CAR-T therapies closer than ever to delivering on their promise but still facing significant obstacles, Eva Marchese (pictured above) and Cécile Matthews from Charles River Associates provide an Expert View on the topic.

Since the approval of Yervoy (ipilimumab) in 2011 for the treatment of melanoma, the idea of mobilizing a patient's immune system to combat a wide range of cancers has been transformed from a promising concept to an emerging standard for oncology therapies.

Today, there are several approved immuno-oncology (I-O) products on the market and many more in clinical development – including monoclonal antibody treatments that target specific immune checkpoint receptors such as programmed cell death protein 1 (PD-1) or programmed cell death 1 ligand (PD-L1).

This class of I-O therapies has demonstrated significant improvements in patient outcomes and advantageous safety profiles in pivotal clinical trials across multiple tumor types.

For example, the positive efficacy and safety profile of Merck & Co's (NYSE: MRK) Keytruda (pembrolizumab) led to its approval in the USA for advanced non-small cell lung cancer, advanced melanoma, classical Hodgkin lymphoma, head and neck squamous cell cancer, and several other types of cancer.

With important advantages for clinicians and patients, the fact that some anti-PD-1 and anti-PD-L1 immunotherapies can be positioned for multiple indications can present some unique challenges for health systems and health technology assessment processes.

Management of indication expansion

For every new I-O therapy indication, each European Union (EU) market must conduct a separate evaluation of the drug or update the evaluation to reflect a new indication and treatable patient population.

For patients and physicians, repeated cycles of product assessment can potentially delay access to many I-O treatments. For manufacturers, additional rounds of negotiation can increase costs associated with the launch of I-O therapies and cause uneven product availability across EU markets, while payers and healthcare systems incur additional fees to re-review the same product.

Some EU markets, including France and Italy, have responded to these challenges by grouping disease indications together into a single evaluation process. While more efficient, this approach can delay access for patients if an immunotherapy is approved for a new indication too close to an initial launch in a prior indication.

For example, the PD-L1 inhibitor Tecentriq (atezolizumab) was approved in Europe in July 2017 for the treatment of metastatic urothelial carcinoma (mUC) and as a second-line therapy for non-small cell lung cancer (2L NSCLC).

In Italy, after 12 months and 10 months of assessments for mUC and 2L NSCLC, respectively, Tecentriq only achieved reimbursement in its lung indication.

Challenges in pricing

Determining the appropriate price of I-O drugs with multiple indications can also be challenging.

Many industry experts are considering entirely new pricing models that could help EU healthcare systems better support I-O drugs while maximizing benefits for both payers and manufacturers.

Although traditional pricing agreements such as discounts and rebates are generally easy to manage from the payer perspective, for manufacturers, this approach might not yield a cost-effective price that accurately reflects a product's inherent value.

In addition, many industry insiders agree that traditional discounting measures are only a short-term strategy for payers to address pricing challenges associated with I-O therapies and that new and innovative solutions will need to be developed and implemented to ensure sustainability.

One potential option is indication-based pricing that would allow manufacturers to be more flexible in their pricing strategies when moving quickly from one indication to the next, though it is widely recognized that this strategy can be difficult to manage and implement within the structure of current EU healthcare systems.

Another potential option is an adaptive pricing model designed to help correlate an I-O therapy's price to the level of evidence collected along the entire drug lifecycle. This approach could potentially benefit both payers and manufacturers if framed in a transparent assessment process that is customized for I-O therapies.

Considerations about regulatory strategy

Another common challenge associated with I-O therapies is determining the best regulatory strategy when drug developers anticipate approvals in multiple disease indications.

Manufacturers might consider first targeting an indication in a narrow patient population to secure a foothold in an EU market and then target indications that represent larger patient populations.

This strategy was demonstrated with the anti-PD-1 therapy Opdivo (nivolumab), which first launched for the treatment of melanoma and then subsequently expanded to more than six indications in the following years. The PD-L1 inhibitor Bavencio (avelumab) also seems to be going through a similar drug development path.

It was approved for the treatment of metastatic Merkel cell carcinoma in March 2017 and is now in development for the treatment of other cancer types including NSCLC and advanced ovarian cancer.

On the surface, these products seem to be success stories for manufacturers. However, as clinical development plans translate into an ongoing series of regulatory approvals across multiple types of cancer, there may be game-changing implications that oncology manufacturers must consider when planning a launch strategy.

One potential risk of expanding from a niche indication to a larger lifecycle indication is that payers might deliberately delay price negotiations in order to set a price based on the larger indication. Combination approvals also could put greater pressure on long-term pricing projections and sustainability.

Conclusion

While the historic progress in development of I-O therapies is obviously great news for many cancer patients, the debates over optimal strategies in value assessments, pricing, and market access will likely continue.

Solutions will require perspectives from a wide range of stakeholders and potentially new collaborations between manufacturers and payers to ensure that both can optimize benefit and manage risk.

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