October 2025

Keytruda & PD-(L)1 LoE: Life after Programmed Death (part 3)

Possessing a new technological approach to oncology does not automatically qualify a product to be priced and commercialised independently of what has gone before it. Payers, in particular, put little emphasis on a new product's mechanism of action, administration method, or the complexities that underpin its R&D and manufacturing, although some do have certain allowances to accommodate these. Ultimately, pricing and access are more contingent upon the clinical outcomes that a new product elicits in patients and particularly how much "better" the new entrant is compared to the existing therapeutic approach.

The loss of exclusivity (LoE) for several of the key market-leading brands will invariably impact how oncology products are appraised and commercialised in the US, Europe, and further afield. At present, there is significant speculation on how payers and access stakeholders will look to leverage the situation in their favour when it comes to decision-making in a peri- and post-LoE PD-(L)1 environment. Based on our CRA expertise, we have developed seven guiding principles that can help build bridges beyond the unprecedented, upcoming patent cliffs. This framework is designed with the end goal in mind: ensuring that oncology remains a thriving hive of activity with meaningful advances in patient outcomes for years to come.

Figure 1: Seven guiding principles for success in a peri- and post-PD-(L)1 LoE environment for branded and biosimilar manufacturers.

1. Be better

- The simplest solution to break away from products undergoing LoE events is simply to demonstrate superior outcomes that go beyond an incremental improvement.
- However, this is easier said than done, especially considering the paradigm-changing efficacy improvements that the range of PD-(L)1 inhibitors bring to numerous cancers and the risks vs rewards associated with head-to-head trials against the branded, incumbent standard of care.
- This is most clearly illustrated by several recent, late-stage trials being discontinued owing to futility against a PD-(L)1 comparator arm, but encouraging evidence is emerging from technologies—including bispecific monoclonal antibodies (BsAbs)—that improvements may be possible.
- However, it is important to map and assess the interplay between being “best in class” and “first in class” and which matters most commercially; whilst the latter may generate faster revenues, long-term success is not necessarily guaranteed by being a first mover.

2. Be safer

- Although not as headline grabbing as significantly boosted efficacy, a reduction in the adverse event profile, fewer tolerability issues, and increased treatment compliance can represent a meaningful, patient-centric advancement in oncology.
- Several of the developments discussed in this article, including subcutaneous PD-(L)1s, oncology vaccines, and BsAbs, all have the potential for benefits in this area.
- Given the challenges presented by combination regimens when it comes to toxicity, having a combination partner that carries a safer profile can make more sophisticated management of tumours a viable option to pursue.
- Although payers have predominantly focused on efficacy upsides in their decision-making, the advent of approaches that have fewer adverse events could meaningfully alter the risk/benefit balance that decision-makers perform and incentivise reimbursement decision-making.

3. Be faster

- Unless there are unforeseen challenges to the LoE date and the arrival of biosimilar PD-(L)1 products, there is a known, finite amount of time remaining for the current price benchmarks to remain intact.
- Where feasible, this presents an opportunity to streamline clinical development and commercialisation efforts to get new products into the market prior to the potentially destabilising effects of LoE.
- Further, launch sequencing could be approached in a manner that affords a new launch with protection from LoE, especially considering that several of the key European patents expire several years after the US equivalent.

- However, be mindful that payers and providers are aware of the savings that can be made from leveraging biosimilars in their negotiations, so their approach to contracting and renegotiation timelines also may change.

4. Be different

- Although the PD-(L)1 class covers a wide range of tumours, their presence is not ubiquitous, nor are they all delivering practice-changing efficacy outcomes in every indication.
- Opportunity therefore exists to target launches—particularly the first ones—to areas that are underserved by PD-(L)1 or other options, or those that are driven by a specific biomarker or oncogene.
- Take for instance Merkel cell carcinoma, for which the current 2024 ESMO-EURACAN guidelines list clinical trials as the preferred first-line option, rather than the currently launched ICIs, which are listed as "alternatives".[1]
- Similarly, brands targeting cancers with limited peri-LoE PD-(L)1 products could also lessen the direct impact of biosimilar entry on pricing.
- Targeting these more open areas and delivering meaningful clinical outcomes for a product's market entry can be an effective means of achieving a price that recognises the high value the product brings.

5. Be competitive

- Setting realistic, achievable pricing and commercial goals at a time of significant LoE in oncology is important for both global and local affiliate country teams.
- Industry can elect one of two routes in this period: either remain competitive on gross-to-net pricing so that new assets do not attract unwarranted scrutiny and do not encounter restrictions or delays in achieving market access, or focus on competing clinically to justify premium pricing relative to the standard of care, despite the pushback this may receive from payers.
- Biosimilar manufacturers, as well as branded product manufacturers—of both PD-(L)1 products and other assets—will have different aims and objectives that must be approached in a manner that reflects a shifting competitive environment.
- However, this is not to say that being ambitious in pricing is not an option. Value-based pricing that recognises innovation will remain a cornerstone of pricing and reimbursement decision-making for payers, making crisp, compelling value narratives critical to encapsulate the patient, societal, and economic benefits of new oncology options.

---

[1] Lugowska, I., *et al*. (2024), Merkel-cell carcinoma: ESMO-EURACAN clinical practice guideline for diagnosis, treatment and follow-up. *ESMO Open*, vol. 9 (5): 102977

6. Be collaborative

- Tackling cancer cannot be achieved in a “one size fits all” manner using a single product, as different tumours adapt differently in response to attack by antineoplastic agents.

- It is likely that overcoming the challenges of cancer biology will take investment in combination regimens, sequencing patterns, and patient profiling, as well as new technologies—some of which may benefit from a post-LoE PD-(L)1 world to foster innovation.
- External partnerships and alliances between pharma and biotech companies will be critical in addressing the various challenges that lie ahead in oncology.
- Additionally, internal cross-functional engagement is necessary amongst medical affairs, commercial, and PMA teams to ensure that manufacturers develop messaging and value propositions that resonate with stakeholders across healthcare systems, including payers and physicians, especially when offerings become more nuanced and complex.
- Further, positioning a future therapy in such a manner that it becomes a building block for future combinations—establishing it as a “future backbone”—could be significant from a clinical and commercial perspective, as we are currently seeing with current PD-(L)1 products and their emerging role in combination regimens.
- Openness to cross-industry collaborations, co-developments, and co-investments will be important for any new product aspiring to secure such a broad “backbone” role, in addition to other important factors, including demonstration of robust monotherapy outcomes.

7. Be forward thinking

- Numerous new technologies, assets, and approaches are emerging on a truly global scale from new and old players alike.
- We have seen significant M&A activity in the antibody–drug conjugate field over recent years, and early signs indicate that we may also see a similar surge in popularity for BsAbs and onco-vaccine technologies, if preliminary outcomes can be robustly confirmed in upcoming trial readouts, suggesting that new investment opportunities should be appraised by manufacturers.
- Ultimately, finding “the next Keytruda” is more a question of “when” rather than “if”, and pharma and biotech’s currently rich pipeline of future options will invariably help us identify which asset(s) could play an important role.
- Whether this future is driven by a continuing role for PD-(L)1 pathway inhibition, either as a combination regimen or a standalone asset, or if it’s driven by another new molecular target, there is reason to be optimistic about the future of oncology for all stakeholders involved in tackling this complex group of malignancies, even at a time of significant change courtesy of PD-(L)1 LoE.

Contacts

Cécile Matthews
Vice President
Cambridge
+44-1223-783-910
cmatthews@crai.com

Aaron Everitt
Principal
London
+44-7920-47-3652
aeveritt@crai.com