

Immunotherapy

Paying for patient- specific therapy: à la CAR-T

CAR-T therapies represent a huge leap forward in the treatment cancer

Using the body's own defence mechanisms to overcome cancer is hardly a new idea, beginning with the pioneering work of William Coley in the late 19th century. Advances in the use first of immune checkpoint inhibitors (CTLA4 and PD-1) and more recently adoptive cell transfer techniques, have given new prominence to immunotherapy. Among immunotherapies, chimeric antigen receptor (CAR)-T cell treatments have gained increasing prominence over the last 2–3 years. For some patients, CAR-T therapy can offer prolonged periods of disease-free remission and extended survival.

To date, two CAR-T therapies have been approved for use by the FDA and EMA:

- Kymriah (tisagenlecleucel) for either adults with relapsed or refractory diffuse B-cell lymphoma or children/young adults up to 25 years old with relapsed or refractory acute lymphoblastic leukaemia.
- Yescarta (axicabtagene ciloleucel) following failure to respond to two previous therapies in various B-cell lymphomas – including diffuse B-cell lymphoma.

After culturing of patient-specific cells, treatment is given as a one-off infusion. Early indicators show that response rates to CAR-T therapy are high and prolonged, but limitations in the

clinical trial dataset present challenges for payers and policy makers.

Demonstrating effect: the search for cure

Curative effect is the hope of every oncologist and patient. The most common measure of survivorship is disease free survival at 3–5 years post-treatment. Many therapeutic choices – surgical resection, stem cell transplant, solid organ transplant – are deemed valuable by default; there is minimal oversight or input from payers/policy makers in the considerations of these approaches since they are nominally curative and do not require expensive pharmaceutical treatments.

The CAR-T therapies blur the lines of treatment – being neither truly a surgical intervention nor a pharmaceutical product. They are highly complex and applied in rare diseases where survival has been historically very poor. This leads to an impressive but, never-the-less, limited set of data with small patient numbers, relatively short follow up, and minimal data on rates and types of subsequent treatment requirement.

The evidence reflects the challenge of innovation – very promising early clinical results allow regulatory review and approval but leave gaps in terms of the understanding of long-term outcomes and impact in the real world.

Establishing value

The major concern of payers and health services are the costs associated with CAR-T therapy: a high initial price for therapy coupled with costs associated with hospitalisation and careful long-term patient management.

While initial costs are high, these are balanced by projected outcomes:

- High response rates
- Durable and long-term disease-free periods
- Limited need for long-term chronic care

Regulators have allowed rapid evaluation of the evidence and built new approaches to allow breakthrough products (like CAR-T) to be used more quickly and on less certain evidence. Against this backdrop, there remains significant uncertainty within the long-term outcomes for CAR-T patients.

While the intrinsic value of cure is evident, the uncertainty inherent in extrapolation of non-comparative and short-duration clinical trials to the long-term real-world setting presents questions for payers and for the pharmaceutical industry.

Payers have sought to allow conditional access in early indications (such as through the Cancer Drugs Fund in England and Wales) while manufacturers have offered alternative payment mechanisms and offers to support funding. Others, such as Canada, have allowed review of CAR-T as a surgical intervention/device, lowering the expectation for data and, perhaps, better reflecting the nature of the technology.

Who pays and how?

Given the potential lifelong effect of treatment, the “sticker price” of CAR-T therapies is notably high. High manufacturing costs and complex management of the supply chain contribute to the costs of delivery of CAR-T therapy.

This raises two questions:

- How to accommodate/reward manufacturers in outcomes-based payment schemes in the few cases where treatment fails?
- How to manage the per patient and overall high budget impact?

On the first question, there are many examples of proposed outcomes-based payment schemes that may be particularly relevant. In recent years, outcomes-based schemes have been unpopular with payers given the complexity of gathering evidence on outcomes, flawed financial structures and administrative burden. Never-the-less, the patients in the case of CAR-T therapies are limited in number and, given the nature of their initial disease, closely followed clinically. Furthermore, initial response to CAR-T seems to be a reasonable indicator of long-term success.

Establishing an appropriate access scheme requires a clear, well-documented and structured approach considering all alternatives and gathering input from all relevant stakeholders:

Managing the budget impact, and in particular the effect of an annual planning cycle, presents additional challenges. Manufacturers have already suggested many alternatives – including annuity-based compensation that can spread the cost of therapy over several years. Health services globally will need to be flexible in order to meet manufacturers part way.

Options for alternative payment approaches include:

- National level fixed or capped budgets: giving annual budget certainty but allowing patient access
 - Annuity-based approaches and future payment schedules
 - Service-based payment
 - Shared manufacturing capability and cost
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Other possibilities include extending data exclusivity or establishing further tax and/or R&D incentives for a trade-off in list pricing.

Conclusion

CAR-T therapies represent a huge opportunity for enhanced patient outcomes – and the hope of cure for some.

Establishing a clear understanding of the value of CAR-T and then using a structured approach to engage with key stakeholders to manage the introduction and budget will be critical in launching CAR-T.

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