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Plan your strategy to engage eligible patients

A 5-minute brief on CAR T-cell and other ex vivo gene therapies

Ex vivo gene therapy refers to treatments that involve extracting a patient's cells, genetically modifying them ex vivo (or outside of the body), and returning them back to the patient's body to help treat certain diseases. A new ex vivo cellular gene therapy, known as CAR T-cell therapy, is bringing significant advances in treating and potentially curing certain cancers, such as leukemia, lymphoma and multiple myeloma. Through the end of February 2022, the FDA had approved 6 new cancer treatments using this therapy. Beyond CAR T, other ex vivo gene therapies are potentially coming to market or have recently come to market to treat conditions such as beta thalassaemia, sickle cell anemia and cerebral adrenoleukodystrophy (CALD). For payers, these unfolding developments raise a key issue: What is your strategy for managing these high-cost, clinically complex cases?

How CAR T-cell therapy works

CAR T-cell therapy – chimeric antigen receptor T-cell therapy – reprograms a patient's own immune cells to recognize and eradicate malignant cells. Healthy T cells, a type of disease-fighting white blood cell, are extracted from the patient's blood and engineered in a lab to produce chimeric antigen receptors through gene-transfer techniques. This enables the cells to target specific tumor proteins. The modified cells are then infused into the patient's blood, where they can seek and attack the cancer cells.

Early success

Currently, each type of CAR T-cell therapy is intended to be a one-time treatment. These agents are approved for use when the underlying cancer has recurred or has not responded to more standard treatments, but the timing of treatment and the sequence of treatment with respect to the use of other agents is still being studied. While it's still too early to definitively assess the efficacy of CAR T-cell therapy, early clinical trials have been associated with response rates of over 80%.[1,2,3] Of course, as with any treatment, there may be negative side effects. Treatment with CAR T-cell therapy, for example, may cause cytokine release syndrome, brain swelling and neurological events, which require hospitalization and can be life-threatening.

High cost of therapy

As of September 21, 2022, the invoice prices in the U.S. are:

CAR T-cell therapies

- Kymriah
  - $508,250 (pediatric leukemia)
  - $399,110 (lymphoma)
- Yescarta – $424,000
- Tecartus – $424,000
- Breyanzi – $410,300
- Abecma – $419,500
- Carvykti – $465,000

Other ex vivo gene therapies

- Zynteglo – $2,800,000
- Skysona – $3,000,000

1. Wang D, Wang J, Hu G, et al. A phase 1 study of a novel fully human BCMA-targeting CAR (CT103A) in patients with relapsed/refractory multiple myeloma. *Blood.* 2021; 137(21):2890-2901.
2. Locke FL, Ghobadi A, Jacobson CA, et al. Long-term safety and activity of axicabtagene ciloleucel in refractory large B-cell lymphoma (ZUMA-1): A single-arm, multicentre, phase 1-2 trial. *Lancet Oncol.* 2019; 20(1):31-42.
3. Zhao Y, Zhang J, Yang J, et al. Long-term safety and efficacy of CD19 humanized selective CAR-T therapy in B-ALL patients who have previously received murine-based CD19 CAR-T therapy. *Front Oncol.* 2022; 12:884782.

FDA-approved agents

Agent name	Approval date	Use
Kymriah	August 30, 2017	For patients up to age 25 who went into remission then relapsed or did not go into remission with other leukemia treatments
	May 1, 2018	For patients with large B-cell lymphoma that has worsened despite 2 or more earlier lines of therapy[4]
	May 28, 2022	For patients with relapsed or refractory follicular lymphoma[5]
Yescarta	October 18, 2017	For adult patients with certain types of large B-cell lymphoma who have not responded to other treatment or relapsed after treatment (revised April 1, 2022, to second line therapy)[6]
	March 5, 2021	For patients with relapsed or refractory follicular lymphoma[7]
Tecartus	July 24, 2020	For patients with mantle cell lymphoma who have not responded to 2 or more previous lines of treatment
	October 1, 2021	For all adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia
Breyanzi	February 5, 2021	For patients with diffuse large B-cell lymphoma (revised June 24, 2022, to second line therapy)[8]
Abecma	March 27, 2021	For adult patients suffering from relapsed or refractory multiple myeloma, following 4 or more lines of therapy
Carvykti	February 28, 2022	For patients with relapsed or refractory multiple myeloma who have undergone 4 or more prior lines of treatment[9]
Zynteglo	August 17, 2022	For patients 12 years of age and older with transfusion-dependent beta thalassemia, a rare inherited blood disorder[10]
Skysona	September 16, 2022	For treatment of boys ages 4 to 17 who have early, active CALD, a rare neurodegenerative disease

Looking ahead: Broader impact

Novel therapies, like CAR T-cell therapy, are being driven by rapid advances in biotechnological research. As of 2022, more than 200 clinical trials for CAR T-cell therapy were recruiting, active or completed in the U.S. for a variety of conditions.[11] We can expect to see additional applications of CAR T-cell and other ex vivo gene therapies for more cancer diagnoses and perhaps for immune diseases in the future.

Visit optum.com/business/contact.html#sales to discuss your CAR T-cell therapy and other ex vivo gene therapy options with an account manager.

Additional costs

The cost of therapy infusion may vary by facility and inpatient versus outpatient setting. The invoice price does not include costs such as:

- Hospital-facility charges or physician fees
- Invoice markups or business development costs
- Other treatments for underlying conditions while waiting for CAR T-cell therapy

Considerations for payers

Payers should examine their clinical and network strategies for managing members who may be eligible for CAR T-cell therapy and other ex vivo gene therapies:

- Do you have access to clinical indications for these therapies?
- Do you have a prior authorization process in place that will pick up the service so you can identify a case?
- How will the therapy be reimbursed under your existing provider contracts? Do you know how to analyze the total cost of care for for patients treated with these therapies?

4. US Food & Drug Administration. FDA approves tisagenlecleucel for adults with relapsed or refractory large B-cell lymphoma. fda.gov/drugs/resources-information-approved-drugs/fda-approves-tisagenlecleucel-adults-relapsed-or-refractory-large-b-cell-lymphoma. May 3, 2018. Accessed February 2, 2023.
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7. Gilead. U.S. FDA approves Yescarta® for relapsed or refractory follicular lymphoma after two or more lines of systemic therapy. gilead.com/news-and-press/press-room/press-releases/2021/3/us-fda-approves-yescarta-for-relapsed-or-refractory-follicular-lymphoma-after-two-or-more-lines-of-systemic-therapy. March 5, 2021. Accessed February 2, 2023.
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