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Plan your strategy to engage eligible patients

5 minutes 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 six 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. 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 CAR T-cell therapy

Currently, CAR T-cell therapy and other ex vivo gene therapies are one-time treatments targeted for a relatively small number of patients. Even so, the cost is high. 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 (beta thalassaemia) – $2,800,000
- Skysona (cerebral adrenoleukodystrophy) – $3,000,000

FDA-approved agents

Kymriah: On August 30, 2017, the FDA approved the first CAR T-cell therapy – a cancer treatment known as Kymriah®, used in patients up to 25 years old who have acute lymphoblastic leukemia, the most common cancer in children. The approval was specifically for those patients who went into remission and then relapsed, or did not go into remission with other leukemia treatments. On May 1, 2018, the FDA also approved Kymriah for the treatment of patients with large B-cell lymphoma that has worsened despite two or more earlier lines of therapy.[4] Additionally, on May 28, 2022, the FDA approved Kymriah for its third indication: the treatment of patients with relapsed or refractory follicular lymphoma.[5]

Yescarta: On October 18, 2017, the FDA approved another CAR T-cell therapy, Yescarta®, for adult patients with certain types of large B-cell lymphoma who have not responded to other treatment or relapsed after such treatment (revised April 1, 2022, to second line therapy).[6] On March 5, 2021, Yescarta was approved for its second indication: relapsed or refractory follicular lymphoma.[7]

Tecartus: The third CAR T-cell therapy, Tecartus®, was approved on July 24, 2020. Tecartus treats patients with mantle cell lymphoma who have not responded to two or more previous lines of treatment. On October 1, 2021, Tecartus was approved for its second indication for all adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia.

Breyanzi: On February 5, 2021, the FDA approved the fourth CAR T-cell therapy. Breyanzi® is the third therapy to treat patients with diffuse large B-cell lymphoma (revised June 24, 2022 to second line therapy).[8]

Abecma: Abecma® was approved on March 27, 2021, and is the first CAR T-cell therapy for multiple myeloma. Specifically, Abecma is for the treatment of adult patients suffering from relapsed or refractory multiple myeloma – following four or more lines of therapy.

Carvykti: The sixth CAR T-cell therapy, Carvykti™, was approved on February 28, 2022. Carvykti is the second CAR T-cell therapy for patients with relapsed or refractory multiple myeloma who have undergone four or more prior lines of treatment.[9]

Zynteglo: On August 17, 2022, the FDA approved Zynteglo® for use in treatment of patients 12 years of age and older with transfusion-dependent betathalassemia, a rare inherited blood disorder.[10]

Skysona: On September 16, 2022, the FDA approved Skysona® for use in treatment of boys ages 4 to 17 who have early, active cerebral adrenoleukodystrophy (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.

Additional costs:

On top of manufacturing expenses, the cost of therapy infusion may vary by facility and could be in an inpatient or outpatient setting. The invoice price does not include other associated direct costs, such as hospital/facility charges or physician fees; and indirect costs, such as invoice markups or business development costs. Additionally, patients may continue other treatments for their underlying conditions during the time it takes to prep them 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 CAR T-cell therapy and other ex vivo gene 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 CAR T or other ex vivo gene therapies?

Sources

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.
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 August 5, 2022.
5. Novartis. FDA approves Novartis Kymriah® CAR-T cell therapy for adult patients with relapsed or refractory follicular lymphoma. novartis.com/news/media-releases/fda-approves-novartis-kymriah-car-t-cell-therapy-adult-patients-relapsed-or-refractory-follicular-lymphoma. May 28, 2022. Accessed August 5, 2022.
6. US Food & Drug Administration. FDA approves axicabtagene ciloleucel for second-line treatment of large B-cell lymphoma. fda.gov/drugs/resources-information-approved-drugs/fda-approves-axicabtagene-ciloleucel-second-line-treatment-large-b-cell-lymphoma. April 1, 2022. Accessed August 5, 2022.
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 August 5, 2022.
8. Bristol Myers Squibb. U.S. FDA approves Bristol Myers Squibb's CAR T cell therapy Breyanzi® for relapsed or refractory large B-cell lymphoma after one prior therapy. news.bms.com/news/corporate-financial/2022/us-fda-approves-bristol-myers-squibbs-car-t-cell-therapy-breyanzifor-relapsed-or-refractory-large-b-cell-lymphoma-after-one-prior-therapy/default.aspx. June 24, 2022. Accessed August 5, 2022.
9. US Food & Drug Administration. FDA approves ciltacabtagene autoleucel for relapsed or refractory multiple myeloma. fda.gov/drugs/resources-information-approved-drugs/fda-approves-ciltacabtagene-autoleucel-relapsed-or-refractory-multiple-myeloma. March 7, 2022. Accessed August 5, 2022.
10. Fierce Pharma. FDA extends decision dates on bluebird bio's gene therapy drugs beti-cel and eli-cel by 3 months. fiercepharma.com/pharma/fda-extends-decision-date-bluebird-bio-s-gene-therapy-drugs-beti-cel-and-eli-cel-by-3-months. January 18, 2022. Accessed August 5, 2022.
11. National Institutes of Health. U.S. National Library of Medicine Clinical Trials search for "CAR T-cell." clinicaltrials.gov/ct2/results?cond=car+t-cell&cntry=US&Search=Apply&recrs=a&recrs=f&recrs=d&recrs=e&age_v=&gndr=&type=&rslt. Accessed July 22, 2022.

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