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In Brief: Lisocabtagene Maraleucel *(Breyanzi)* for Large B-Cell Lymphoma

IN BRIEF

Lisocabtagene Maraleucel *(Breyanzi)* for Large B-Cell Lymphoma

The FDA has approved lisocabtagene maraleucel (*Breyanzi* – BMS) for treatment of adults with large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, or follicular lymphoma grade 3B who have disease refractory to first-line chemoimmunotherapy, relapsed within 12 months of or after first-line chemoimmunotherapy, are not eligible for hematopoietic stem cell transplantation due to comorbidities or age, or have relapsed or refractory disease after ≥2 lines of systemic therapy. *Breyanzi* is an individualized cellular product prepared from the patient's own T cells, which are genetically modified to express chimeric antigen receptors (CAR) and then infused back into the patient. The CAR T-cell products axicabtagene ciloleucel *(Yescarta)* and tisagenlecleucel *(Kymriah)* are also FDA-approved for treatment of large B-cell lymphoma.[1]

Pronunciation Key
Lisocabtagene maraleucel: lis" oh kab' ta jeen mar" a loo' sel
***Breyanzi*:** braye an' zee

LARGE B-CELL LYMPHOMA — DLBCL is the most common type of aggressive non-Hodgkin's lymphoma. Standard first-line treatment of DLBCL consists of the combination of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). The risk of relapse is highest within one year following treatment.

THE PROCEDURE — Lisocabtagene maraleucel is prepared from autologous T cells obtained by leukapheresis. The T cells are sent to a commercial laboratory, which genetically modifies them using a lentiviral vector to encode an anti-CD19 CAR transgene. *Breyanzi* is supplied in a patient-specific, single-dose infusion bag. Before infusion of the genetically modified T cells, patients usually receive lymphodepleting therapy (cyclophosphamide and fludarabine).

MECHANISM OF ACTION — The genetically modified, autologous T cells bind to CD19 proteins on the surface of B cells, promoting T-cell activation and proliferation and secretion of inflammatory cytokines, which leads to T-cell-mediated destruction of cancer cells.

CLINICAL STUDIES — FDA approval of lisocabtagene maraleucel was based on the results of three open-label trials (TRANSFORM, PILOT, and TRANSCEND). In the TRANSFORM trial, 184 adults with primary refractory or early relapsed (≤12 months) LBCL who were eligible for autologous stem cell transplantation were randomized to receive lisocabtagene maraleucel or standard treatment (3 cycles of platinum-based immunotherapy, followed by high-dose chemotherapy and, in responders, autologous stem cell transplantation). Event-free survival, the primary endpoint, was 2.4 months in the standard treatment arm and was not yet reached in the lisocabtagene maraleucel arm. The complete response rate was statistically significantly higher with lisocabtagene maraleucel (74% vs 43%).[2]

In the PILOT trial, 61 transplant-ineligible patients with relapsed or refractory LBCL treated with one prior line of chemoimmunotherapy received lisocabtagene maraleucel. The overall response rate, the primary endpoint, was 80%, of which 54% were complete responses.[3]

In the TRANSCEND trial, 269 patients with relapsed or refractory LBCL treated with ≥2 lines of prior therapy received lisocabtagene maraleucel. The objective response rate was 73% and a complete response was achieved in 53% of patients.[4]

No head-to-head trials comparing lisocabtagene maraleucel with axicabtagene ciloleucel or tisagenlecleucel for treatment of large B-cell lymphoma are available.

ADVERSE EFFECTS — Fever, fatigue, musculoskeletal pain, and nausea have been reported with lisocabtagene maraleucel. The *Breyanzi* label includes a boxed warning about the risk of cytokine release syndrome (CRS), a common complication of CAR T-cell immunotherapy that can cause hypotension, pulmonary edema, coagulopathy, multiorgan failure and death, and about the risk of neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS). CRS has been successfully treated with the IL-6 receptor antagonist tocilizumab (*Actemra*), with or without corticosteroids. Patients should avoid driving or engaging in hazardous activities for at least 8 weeks after receiving *Breyanzi*.

PREGNANCY AND LACTATION — Lisocabtagene maraleucel has not been studied in pregnant or lactating females and is not recommended for use during pregnancy or while breastfeeding. There are no data on the presence of lisocabtagene maraleucel in human breast milk or its effect on the breastfed infant or milk production.

DOSAGE, ADMINISTRATION, AND COST — Two to seven days after completing a 3-day regimen of lymphodepleting chemotherapy with cyclophosphamide and fludarabine, patients receive an infusion of 90-100 x 10^6 (for patients who received one line of prior therapy) or 50-110 x 10^6 (for patients who received ≥2 lines of prior therapy) CAR-positive viable T cells/kg. The CAR-positive viable T cells contain CD8 and CD4 components; the CD8 component should be infused first. Patients should receive acetaminophen and an antihistamine about 30-60 minutes before the infusion. They should be monitored at the treatment facility for 7 days after the infusion and stay near the treatment facility for at least 4 weeks. The wholesale aquisition cost for one dose of *Breyanzi* is about $447,230 for the drug alone.[5] ■

1. Axicabtagene ciloleucel (Yescarta) for B-cell lymphoma. Med Lett Drugs Ther 2018; 60:e122.
2. JS Abramson et al. Lisocabtagene maraleucel as a second-line therapy for large B-cell lymphoma: primary analysis of the phase 3 TRANSFORM study. Blood 2023: 141:1675.
3. A Sehgal et al. Lisocabtagene maraleucel as a second-line therapy in adults with relapsed or refractory large B-cell lymphoma who were not intended for haematopoietic stem cell transplantation (PILOT): an open-label, phase 2 study. Lancet Oncol 2022; 23:1066.
4. JS Abramson et al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study. Lancet 2020; 396:839.
5. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. June 5, 2023. Reprinted with permission by First Databank, Inc. All rights reserved. ©2023. www.fdbhealth.com/policies/drug-pricing-policy.