Idecabtagene Vicleucel

An HCP Tool from AIM with Immunotherapy

Idecabtagene vicleucel (Abecma®) is a modified autolologous T-cell immunotherapy that is directed against the B-cell maturation antigen. It is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after two or more prior lines of therapy andt least one therapy from these drug classes has not worked or stopped working: an anti-CD38 antibody, an immunomodulatory agent, and a proteasome inhibitor.

Clinical trial results of idacabtagene vicleucel

In a Phase 3 international, randomized, open-label, trial called KarMMa-3 (NCT03651128) of adults with relapsed and refractory multiple myeloma who had received two to four regimens previously, were randomly assigned to receive idecabtagene vicleucel (n=254) or one of five standard regimens (n=132). (Note that the standard regimens for each patient depended on their previous therapeutic regimens and may have been: daratumumab, pomalidomide, and dexamethasone; daratumumab, bortezomib, and dexamethasone; ixazomib, lenalidomide, and dexamethasone; carfilzomib and dexamethasone; or elotuzumab, pomalidomide, and dexamethasone.)

- There was a significant response ($p<0.001$) among 71% of the patients in the idecabtagene vicleucel-treated group (n=181 of 254), compared to a 42% response among patients assigned to the standard-regimen group (n=55 of 132).
- After 6 months of treatment, the progression-free survival was 73% in the idecabtagene vicleucel-treated group versus 40% in the standard-regimen group; the progression-free survival after 12-months was 55% and 30%, respectively.
- The median progression-free survival in the idecabtagene vicleucel-treated group was 13.3 months versus 4.4 months for patients on standard regimens.
- Grade 3 and 4 adverse events occurred in 93% of the patients being treated with idecabtagene vicleucel. Approximately 88% experienced cytokine release syndrome, with only 5% being Grade 3 or higher.

Molecular biology and pharmacology

The class of therapeutics is referred to as chimeric antigen receptor (CAR) T cell therapy. It works by removing white blood cells from the patient with multiple myeloma and then engineering the T cells to express a specific receptor on the surface. In this case, the receptors are designed to bind to the B-cell maturation antigen (BCMA) located on the surface of multiple myeloma cells, plasma cells, and a subset of B cells.

Once the T cells are genetically engineered to express the chimeric antigen receptor targeted to the BCMA, they are reintroduced back into the patient with cancer. The engineered CAR T cells will bind to BCMA-expressing myeloma cells and destroy them. The interaction by the receptor activates the CAR T cells, resulting in T cell proliferation, cytokine secretion, and then cytolytic killing of the multiple myeloma cells expressing BCMA. Within 1 month after infusion, a clinical response should be observed.

DRUG DOSING AND ADMINISTRATION

Prior to infusion

White blood cells from the patient with cancer are collected by leukapheresis. The cells are shipped to a laboratory to engineer the expression of a cell-surface receptor directed against BCMA into the T cells. Sufficient numbers of the CAR T cells are grown up in the laboratory expressing the CAR. The process takes around 4 weeks to complete. Then, the CAR T cells are shipped to the health care facility for infusion.

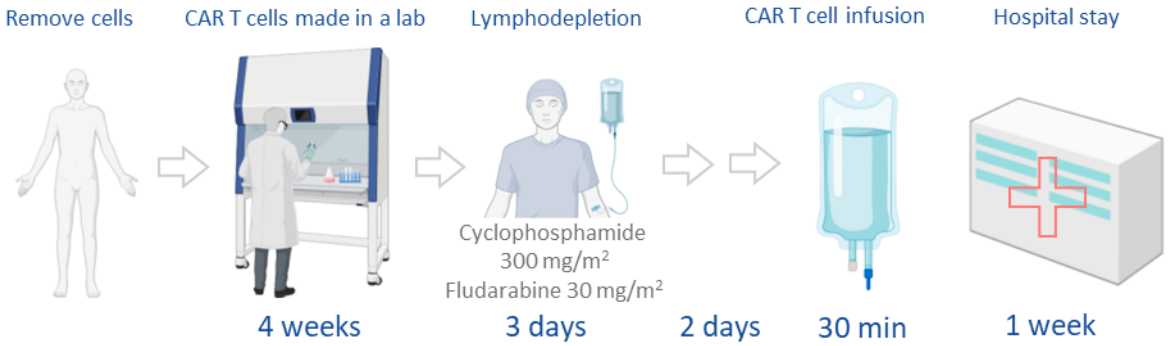
Health care providers need to confirm the availability of idecabtagene vicleucel prior to starting the next phase–lymphodepletion. For 3 days (and 5 days prior to infusion with the CAR T cell therapy), lymphodepleting, cytotoxic chemotherapy is administered to the patient. This is done to clear the system of immune cells, which facilitates the adoption of the CAR T cells by the patient's immune system. The regimen is intravenous cyclophosphamide 300 mg/m^2 and fludarabine 30 mg/m^2 for 3 days. Dose adjustments to the chemotherapy may be needed for renal impairment.

Two days after *completing* the lymphodepletion regimen, the CAR T cell therapy can be administered. (The figure below illustrates the timing of the therapy.) Make sure that tocilizumab is available and emergency resources are standing by before thawing the product. If more than one infusion bag will be used, thaw each infusion bag one at a time. Do not initiate thaw of the next bag until infusion of the previous bag is complete. Infusion bags should be administered within 1 hour of thaw initiation and are stable for 2 hours.

Administration

The CAR T cells are administered using intravenous infusion 2 days after the chemotherapy is finished. Providers must match the labels on the bag with the identity of the patient to make sure that administration occurs with the correct cassette and infusion bag. It usually takes around 30 minutes to infuse the contents of each bag into the patient's system and there may be one or more bags.

Pre-medications include acetaminophen (650 mg orally) and diphenhydramine (12.5 mg IV or 25 to 50 mg orally) approximately 30 to 60 minutes before the infusion. Do not use dexamethasone or corticosteroids as these will interfere.



For 1 week after receiving the CAR T cell infusion, the patient remains at the facility with routine monitoring. (Note that outpatient monitoring may be an option at certain centers.) Then, patients may be discharged from the facility. However, for 4 weeks after receiving the CAR T cell infusion, they are required to remain within 2 hours of the facility where they received treatment.

Patients should not drive, operate heavy machinery, or perform dangerous activities for 8 weeks after infusion. They could manifest problems with memory, coordination, or feel confused, dizzy, sleepy, or have seizures.

Dose

Idecabtagene vicleucel is a single-dose infusion product in one or more bags that contains a suspension of the CAR T cells. The range of cells that are administered is between 300 to 510 x 10^6 cells. Because this is an intravenous solution with a manufactured product, there are no reductions in the dosage.

SIDE EFFECTS AND MANAGEMENT

For 1 week after the infusion of idecabtagene vicaleucel is complete, patients should be monitored regularly for signs and symptoms of adverse reactions in the health care facility that administered the product. Concerns surround the possibility of cytokine release syndrome and neurologic toxicities. For the following 4 weeks, patients should remain within proximity of the health care facility for their safety if a reaction occurs.

In the KarMMa-3 clinical trial, there was a higher percentage of treated patients that experienced early death. Among approximately 25 deaths that occurred, 11 were associated with adverse events.

Black Boxed Warnings

There are 5 warnings associated with idecabtagene vicleucel. These include cytokine release syndrome, neurologic toxicities, hemophagocytic lymphohistiocytosis/macrophage activation syndrome, prolonged cytopenia with bleeding and infection, and secondary T cell malignancies. This drug is available only through the restricted Risk Evaluation and Mitigation Strategy (REMS) called the “ABECMA REMS.”

Cytokine Release Syndrome

Cytokine Relsease Syndrome (CRS), including fatal or life-threatening reactions can occur with idecabtagene vicleucel. Most commonly CRS manifests as pyrexia (87%), hypotension (30%), tachycardia (26%), chills (19%), and hypoxia (16%). However, grade 3 or higher is associated with ARDS, atrial fibrillation, coagulopathy, hemophagocytic lymphohistiocytosis /macrophage activation syndrome, hepatocellular injury, hyperbilirubinemia, hypofibrinogenemia, metabolic acidosis, multiple organ dysfunction syndrome, pulmonary edema and renal failure.

Mild to moderate CRS occurred in 81% of patients receiving idecabtagene vicleucel for relapsed or refractory multiple myeloma in the KarMMa and KarMMa-3 studies. Grade 3 and 4 CRS occurred in 7% of patients and grade 5 in 0.9% of patients.

Median time to onset of CRS is 1 day, but can range up to 27 days. The median duration of CRS was 5 days, but ranged in patients from 1 to 63 days.

The drug should not be administered to patients with active infection or inflammatory disorders. The appearance of CRS may be treated with tocilizumab or tocilizumab and corticosteroids. Confirm that at least 2 doses are on hand prior to thawing the product for infusion into the patient.

For patients with severe or life-threatening CRS, consider ICU-level monitoring and supportive therapy. These patients should be closely monitored for cardiac and organ function until the resolution of symptoms. Consider antiseizure prophylaxis with levetiracetam in patients who experience CRS.

CRS Grade 1 – If the onset >72 hours after infusion, proceed with symptomatic treatment for fever, headache, malaise, myalgia, and nausea. If the onset occurred less than 72 hours after infusion, consider tocilizumab (8 mg/kg IV over 1 hour). If there is no improvement within 12 hours of first-line intervention, such as tocilizumab or tocilizumab and corticosteroids, consider alternate treatment options (i.e., higher corticosteroid dose, alternative anti-cytokine agents, anti-T cell therapies).

CRS Grade 2 – This requires moderate intervention. Patients may have hypotension that is not responsive to fluids, oxygen requirement less than 40% FiO_2, grade 2 organ toxicity, or hypoxia requiring supplemental oxygenation and therefore should be monitored with continuous cardiac telemetry and pulse oximetry.

Administer tocilizumab (8 mg/kg IV) over 1 hour and repeat every 8 hours as needed, if not responsive to fluids or supplemental oxygen. Do not exceed 800 mg tocilizumab and limit to a maximum of 3 doses in a 24-hour period. Consider dexamethasone (10 mg IV) every 12-24 hours.

If there is no improvement at 24 hours or progression, repeat tocilizumab and escalate the frequency of dexamethasone (20 mg IV) every 6 to 12 hours. After 2 doses of tocilizumab, consider alternative agents and do not exceed 3 doses in 24 hours or 4 doses in total. If there is still not improvement within 24 hours or rapid progression, switch to methylprednisolone (2 mg/kg) followed by 2 mg/kg divided 4 times per day.

CRS Grade 3 – This requires aggressive intervention and is associated with fever, an oxygen requirement greater than or equal to 40% FiO_2, or hypotension requiring high-dose or multiple vasopressors.

Administer dexamethasone (10 mg IV) every 12 hours. Identical to grade 2 care, if there is no improvement at 24 hours or progression, repeat tocilizumab and escalate the frequency of dexamethasone (20 mg IV) every 6 to 12 hours. After 2 doses of tocilizumab, consider alternative agents and do not exceed 3 doses in 24 hours or 4 doses in total. If there is still no improvement within 24 hours or rapid progression, switch to methylprednisolone (2 mg/kg) followed by 2 mg/kg divided 4 times per day.

CRS Grade 4 – This grade is life threatening. It comes with a requirement for ventilator support, continuous veno-venous hemodialysis, or Grade 4 organ toxicity.

Administer dexamethasone (20 mg IV) every 6 hours. Identical to grade 2 care, after 2 doses of tocilizumab, consider alternative anti-cytokine agents and do not exceed 3 doses of tocilizumab in 24 hours or 4 doses in total. If there is no improvement within 24 hours, consider methylprednisolone (1-2 g) every 24 hours, if needed, or other anti-T cell therapies.

Neurologic Toxicities

Neurologic toxicities, including immune-effector cell-associated neurotoxicity (ICANS), are associated with idecabtagene vicleucel and may be severe or life-threatening. In the clinical trials KarMMa and KarMMa-3, CAR T cell-associated neurotoxicity occurred in 40% of patients. Only 4.6% of those were Grade 3 or 4. The median time to onset was 2 days, with a range of 1 to 148 days. CAR T cell-associated neurotoxicity had a median duration of 8 days, with a range of 1 to 720 days.

Neurologic toxicities may occur concurrently with CRS, after CRS resolution, or without CRS occurring. Corticosteroids, tocilizumab, anti-seizure medication (levetiracetam), and supportive care are necessary for management. If neurotoxicity occurs concurrent with CRS, administer corticosteroids and more aggressive interventions therapies.

Grade 1 – If the patient has grade 1 symptoms, start non-sedating, anti-seizure medication (levetiracetam). If >72 hours after infusion, observe the patient. If symptoms appear <72 hours after infusion, consider dexamethasone (10 mg IV) every 12-24 hours for 2-3 days.

Grade 2 – In addition to levetiracetam for seizures, dexamethasone (10 mg IV) every 12 hours for 2-3 days can be given, or longer for persistent symptoms. In addition, consider taper for a total corticosteroid exposure of greater than 3 days. (Corticosteroids are not recommended for headaches.) If after 24 hours there is no improvement or the condition worsens, increase the dose and/or frequency of dexamethasone (20 mg IV) every 6 hours.

Grade 3 – In combination with the levetiracetam and dexamethasone from grade 1 and 2 management, neurologic toxicities that persist or worsen may need methylprednisolone (2 mg/kg loading dose, then 2 mg/kg divided into 4 times a day). If cerebral edema is suspected, then consider hyperventilation and hyperosmolar therapy. Additionally, high-dose methylprednisolone (1-2 g, every 24 hours; taper as clinically indicated) and cyclophosphamide 1.5 g/m^2 may be administered.

Grade 4 – This grade is life threatening. All recommendations for grades 2 and 3 should be considered, including levetiracetam, dexamethasone, high-dose methylprednisolone and cyclophosphamide. If cerebral edema is suspected, consider hyperventilation and hyperosmolar therapy.

Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS)

After administration with idecabtagene vicleucel, fatal and life-threatening reactions of HLH/MAS occurred in <3% of patients. Signs of HLH/MAS included cytopenia, hypotension, hypoxia, multiple organ dysfunction and renal dysfunction. The median onset was 6.5 days, with a range of 4 to 10 days. It was associated with ongoing or worsening CRS.

Prolonged Cytopenia with bleeding and infection

After administration with idecabtagene vicleucel, fatal outcomes have occurred related to prolonged cytopenia. Approximately 40% of patients in clinical trials experienced prolonged Grade 3 or 4 neutropenia and 42% experienced prolonged Grade 3 or 4 thrombocytopenia that had not resolved after 1 month following the infusion with idecabtagene vicleucel. The median time to recovery was approximately 1.9 months.

T cell Malignancies

T cell cancers have occurred after the treatment with BCMA-directed genetically modified CAR T cell therapies. In clinical trials, one case of acute myeloid leukemia occurred and four cases of myelodysplastic syndrome. The median time to onset was 338 days with a range between 277 to 794 days.

OTHER TAKEAWAYS ABOUT ADMINISTRATION

- Premedication is required before infusing idecabtagene vicleucel with acetaminophen (650 mg orally) and diphenhydramine (12.5 mg IV or 25 to 50 mg orally).
- Most side effects occur within 9 months following treatment.
- Educate patients and caregivers about side effects and the importance of reporting symptoms as soon as possible.
- Idecabtagene vicleucel is available only under a REMS program.

QUESTIONS & ANSWERS

Q. **Can patients donate blood after receiving idecabtagene vicleucel?**

A. No. After receiving idecabtagene vicleucel for the treatment of recurrent or refractory multiple myeloma, patients are advised not to donate blood, organs, tissues or cells for transplantation. More importantly, patients with blood cancers cannot donate blood, despite receiving therapy.

Q. **What are the most common side effects of idecabtagene vicleucel that I should counsel my patients about?**

A. The most common side effects of idecabtagene vicleucel include chills, confusion, cough, decrease in appetite, difficulty breathing, difficulty speaking or slurred speech, fast or irregular heartbeat, fatigue, fever of 100.4° or higher, headache, and severe nausea or diarrhea.

Q. **What else should I tell my patients who will receive idecabtagene vicleucel?**

A. Patients who receive therapy with idecabtagene vicleucel may have a false-positive test result if they are tested for the human immunodeficiency virus or HIV. Some commercial tests are known to give positive results with a blood sample from the patient.

Taking this product may also increase a patient's risk for getting cancer. Although it is rare, an increase of hematologic (blood) cancers are associated with idecabtagene vicleucel. Health care providers should be monitored for this possibility and increased risk.

There is a small risk for early death within the first nine months of treatment from adverse events associated with the drug. However, the higher rate of early death observed in the clinical trial was progressive multiple myeloma.

Q. **How long does it usually take to get idecabtagene vicleucel?**

A. Once the white blood cells are extracted from the patient and received by the laboratory, the process begins. It will take approximately 4 weeks for the laboratory to engineer the chimeric antigen, in this case BCMA, on the outside of the patient's T cell and then manufacture a sufficient number of cells for treatment. At least one or more infusion bags are sent back to the treatment facility for infusion into the patient after 3 days of lymphodepleting chemotherapy, followed by 2 days of rest. The infusion bags containing a solution of CAR T cells should not be thawed by the clinic until they are ready for administration or within 1 hour of infusion.

The risk of manufacturing failure is approximately 2%. If this occurs, then the patient may need additional treatment while another manufacturing attempt is made.

PATIENT RESOURCES

ADDITIONAL INFORMATION RESOURCES

American Cancer Society
https://www.cancer.org/

Bristol Myers Squibb Medication Guides
Information about idecabtagene vicleucel.
ABECMA.com
1-888-805-4555

NIH: National Cancer Center
https://www.cancer.gov/

FINANCIAL ASSISTANCE

Pfizer Patient Assistance Program
Provides free Pfizer medicines to eligible patients through their doctor's office or at home.
https://www.pfizerrxpathways.com/resources/patients

Cancer Financial Aid Coalition
Facilitates communication, educates and advocates for patients.
www.cancerfac.org

Centers for Medicare and Medicaid Services (CMS)
Apply to determine if you are eligible for government assistance.
www.cms.gov or www.medicare.gov
1-800-633-4227

Lazarex Foundation
Provides assistance with travel costs for clinical trial participation. Ask your social work counselor for a referral if you have been consented to a clinical trial for melanoma.
www.lazarex.org

Needymeds
Database to search for free or low-cost medications, help with medical transportation and other resources.
www.needymeds.org

Patient Advocate Foundation
Provides assistance with mediation, financial stability, and other assistance. Funds subject to availability. Patient must meet their eligibility for financial assistance.
www.patientadvocate.org
1-800-532-5274

The Sam Fund for Young Adult Survivors of Cancer
Assists cancer survivors ages 21-39 with their transition into post-treatment life. This program distributes grants and scholarships in an effort to enable survivors to pursue goals.
www.thesamfund.org
info@thesamfund.org

PRESCRIPTION ASSISTANCE

CancerCare Co-Payment Assistance Foundation
Helps with the cost of medication. Availability of funds for patients with Stage IV melanoma subject to availability.
www.cancercarecopay.org
1-866-552-6729

Medicine Assistance Tool
Database to search for patient assistance resources offered by pharmaceutical companies.
www.medicineassistancetool.org/

Patient Advocate Foundation Co-Pay Relief
Provides direct financial support to patients who medically qualify. Availability of funds for patients with Stage IV melanoma subject to availability.
www.copays.org
1-866-512-3861

Good Days
Formerly known as the Chronic Disease Fund. Provides assistance with insurance co-pays, and prescription medications. Availability of funds for patients with Stage IV melanoma subject to availability.
www.mygooddays.org

HealthWell Foundation
For patients who cannot afford insurance premiums, co-payments, co-insurance, or other out-of-pocket health care costs. Availability of funds for patients with Stage IV melanoma subject to availability. Patient must also meet eligibility for financial assistance.
www.healthwellfoundation.org or grants@healthwellfoundation.org
1-800-675-8416

The Assistance Fund, Inc
Provides prescription copay and financial assistance, including health insurance premiums. Availability of funds for patients with Stage IV melanoma subject to availability.
www.theassistancefund.org
1-855-845-3663

PAN Foundation
Provides financial assistance to cover out-of-pocket treatment costs. Availability of funds for patients with Stage IV melanoma subject to availability.
www.panfoundation.org
1-866-316-PANF (7263)

Patient Assistance Program
Comprehensive database of patient assistance programs offering free medications.
www.rxassist.org
info@rxassist.org

HOUSING

American Cancer Society – Hope Lodge
Provides free housing during treatment appointments. Requires a referral from your social worker.
www.cancer.org/
1-800-227-6333

American Cancer Society – Extended Stay America
Partnership to offer discounted rooms for patients who have to be away from home for cancer treatment.
https://www.cancer.org/about-us/our-partners/extended-stay-america.html
1-800-227-2345

Healthcare Hospitality Network
Connects patients and their caregivers looking for lodging near their healthcare provider
https://members.hhnetwork.org/locate-a-house
1-800-318-8861

Joe's House
Helping patients with cancer find lodging throughout the U.S.
https://www.joeshouse.org/lodging?state=0
1-877-563-7468

National Council of State Housing Agencies
Emergency rental assistance programs available by state. Federal grants still available in some areas.
https://www.ncsha.org/emergency-housing-assistance/

TRANSPORTATION (AIR AND GROUND)

Air Charity Network
Provides access for people in need who are seeking free air transportation to specialized health care facilities
http://aircharitynetwork.org/
1-877-621-7177

Corporate Angel Network
Nonprofit organization that helps cancer patients by arranging free travel on corporate aircraft
https://www.corpangelnetwork.org/
info@corpangelnetwork.org
1-914-328-1313

Medicaid
Ground transportation only. Sets up rides and provides mileage reimbursement for Medicaid patients only.
1-877-633-8747

Mercy Medical Angels
Provides free medical transportation (flights, gas cards, bus and train tickets) for patients with financial needs who need to travel more than 50 miles. Patients must meet their eligibility for financial assistance.
www.mercymedical.org/

Pilots for Patients
Provides free flights to people in need of medical treatment. Patient must be medically stable to fly and be ambulatory. Ask your social worker about a referral.
www.pilotsforpatients.org
1-318-322-5112

ADDITIONAL RESOURCES

ABECMA® (idecabtagene vicleucel). Highlights of prescribing information. Revised March 2025. Bristol Myers Squibb. https://packageinserts.bms.com/pi/pi_abecma.pdf

Mikkilineni L and Kochenderfer JN. CAR T cell therapies for patients with multiple myeloma. *Nat Rev Clin Oncol*. 2021;18(2):71-84. doi: 10.1038/s41571-020-0427-6.

Otero PR, Ailawadhi S, Arnulf B et al. Ide-cel or Standard Regimens in Relapsed and Refractory Multiple Myeloma. *N Engl J Med*. 2023;388:1002-1014. DOI: 10.1056/NEJMoa2213614