

Abecma® (idecabtagene vicleucel)

The First CAR T Cell Therapy for Adults with Relapsed or Refractory Multiple Myeloma

What is Abecma?

Abecma is the first-in-class B-cell maturation antigen (BCMA)-directed chimeric antigen receptor (CAR) T cell immunotherapy for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.¹ *Abecma* recognizes and binds to BCMA, a protein that is nearly universally expressed on cancer cells in multiple myeloma, leading to the death of BCMA-expressing cells.²

The U.S. Food and Drug Administration (FDA) approval of *Abecma* is based on data from the pivotal Phase II KarMMa trial of 127 patients with relapsed or refractory multiple myeloma who had received at least three prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. In the trial among patients treated with *Abecma*, the median number of prior therapies was six (range: 3-16), with 85% being refractory to all three major classes of treatment.¹

Abecma is being jointly developed and commercialized in the U.S. as part of a Co-Development, Co-Promotion and Profit Share Agreement between Bristol Myers Squibb and bluebird bio.

What is CAR T Cell Therapy?

CAR T cell therapy is a type of treatment in which a patient's T cells (a type of immune cell) are changed in a laboratory so they will attack target cells with a specific protein on their surface, such as BCMA.³

What is BCMA?

BCMA is a protein found on the surface of normal and malignant plasma cells. In multiple myeloma, the overexpression of BCMA significantly promotes multiple myeloma cell growth and survival. BCMA is part of the tumor necrosis factor superfamily of proteins, which regulates cell proliferation (growth) and survival.²

By targeting BCMA in multiple myeloma with anti-BCMA agents, there is the potential to block multiple myeloma cell proliferation via downregulation of cell cycle progression and the anti-apoptosis molecules, which are important in preventing cell death.²

Treatment with Abecma

Abecma is a personalized immune cell therapy approved as a one-time infusion with a recommended dose of 300 to 460 x 10⁶ CAR-positive T cells.¹



Abecma is prepared from a patient's own T cells, removed through a process called apheresis or leukapheresis in which blood is withdrawn from the patient and T cells are separated from other blood components.³



The collected T cells are shipped to a specialized cell therapy manufacturing facility where they undergo genetic "reprogramming" to become CAR T cells. Receptors (or "hooks") are added to the T cells to help recognize and target BCMA-expressing cells, including normal and cancer cells, where BCMA is overexpressed.⁴



The CART cells are then multiplied to create the appropriate dose consisting of millions of CAR T cells, which then undergo rigorous testing and quality control before being shipped back to a certified treatment center for the patient. At the treatment center, the CART cells are infused into the patient. One to three days before the CART cells are infused, patients typically receive a brief course of one or more chemotherapy agents, called "lymphodepletion." This process helps prepare the patient's body for treatment.⁴



Abecma is available at certified centers through a Risk Evaluation and Mitigation Strategy (REMS) program to support appropriate use of the treatment, including training on the management of side effects.



Patients will be monitored daily at a certified treatment center for at least 7 days after the infusion. Patients should plan to stay close to the treatment center for at least 4 weeks after infusion so their healthcare team can help with any side effects that may occur.¹

Learn more at [ABECMA.com](https://www.abecma.com).

Patient and Care Team Support



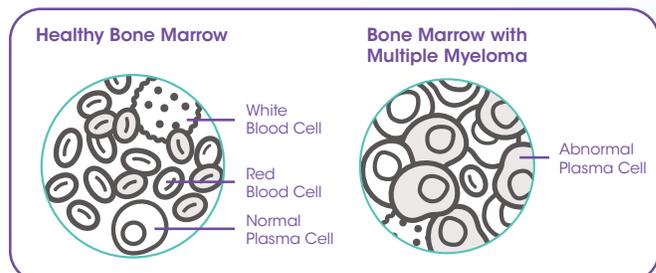
Cell Therapy 360[®] is a comprehensive digital service platform, which provides up-to-date information and treatment support, along with educational resources and support programs for patients, caregivers and care teams throughout the CART cell therapy journey.



Additional resources are available to patients, including logistical support and travel assistance, to help provide an optimal experience with *Abecma*.

About Relapsed or Refractory Multiple Myeloma

In the U.S., more than 34,000 new cases of multiple myeloma are estimated to be diagnosed in 2021.⁵ Multiple myeloma is a blood cancer formed by malignant plasma cells that typically originate in the bone marrow.⁶ Despite advances in treatment, multiple myeloma remains an incurable disease characterized by periods of remission and relapse.⁷ Most patients experience relapse following initial therapies, and depth and duration of response as well as survival outcomes decrease with each successive treatment.⁸⁻¹³



Patients with relapsed or refractory multiple myeloma who have been exposed to all three major drug classes (triple-class exposed), including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody, tend to demonstrate poor clinical outcomes with very low response rates (20% to 30%), short duration of response and poor survival.^{9, 14-16}

Advancing Innovative Treatment Options for Multiple Myeloma

Bristol Myers Squibb has been a pioneer in multiple myeloma research, having developed and delivered new standards of treatment for this incurable disease. Bristol Myers Squibb remains committed to innovating new treatment approaches, including the use of cell therapies, through extensive research to shape a new era of improved outcomes for patients with multiple myeloma.

About bluebird bio, Inc.

bluebird bio is pioneering gene therapy with purpose. From our Cambridge, Mass., headquarters, we're developing gene and cell therapies for severe genetic diseases and cancer, with the goal that people facing potentially fatal conditions with limited treatment options can live their lives fully. Beyond our labs, we're working to positively disrupt the healthcare system to create access, transparency and education so that gene therapy can become available to all those who can benefit.

bluebird bio is a human company powered by human stories. We're putting our care and expertise to work across a spectrum of disorders including cerebral adrenoleukodystrophy, sickle cell disease, β -thalassemia and multiple myeloma using three gene therapy technologies: gene addition, cell therapy and (megaTAL-enabled) gene editing.

Indication

ABECMA (idecabtagene vicleucel) is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

Important Safety Information

BOXED WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAS, AND PROLONGED CYTOPENIA

- **Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients following treatment with ABECMA. Do not administer ABECMA to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.**
- **Neurologic Toxicities, which may be severe or life-threatening, occurred following treatment with ABECMA, including concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with ABECMA. Provide supportive care and/or corticosteroids as needed.**
- **Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS) including fatal and life-threatening reactions, occurred in patients following treatment with ABECMA. HLH/MAS can occur with CRS or neurologic toxicities.**
- **Prolonged Cytopenia with bleeding and infection, including fatal outcomes following stem cell transplantation for hematopoietic recovery, occurred following treatment with ABECMA.**
- **ABECMA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS.**

Cytokine Release Syndrome (CRS)

CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA. CRS occurred in 85% (108/127) of patients receiving ABECMA. Grade 3 or higher CRS (Lee grading system) occurred in 9% (12/127) of patients, with Grade 5 CRS reported in one (0.8%) patient. The median time to onset of CRS, any grade, was 1 day (range: 1 - 23 days) and the median duration of CRS was 7 days (range: 1 - 63 days) in all patients including the patient who died. The most common manifestations of CRS included pyrexia (98%), hypotension (41%), tachycardia (35%), chills (31%), hypoxia (20%), fatigue (12%), and headache (10%). Grade 3 or higher events that may be associated with CRS include hypotension, hypoxia, hyperbilirubinemia, hypofibrinogenemia, acute respiratory distress syndrome (ARDS), atrial fibrillation, hepatocellular injury, metabolic acidosis, pulmonary edema, multiple organ dysfunction syndrome and HLH/MAS.

Cytokine Release Syndrome (CRS) (cont'd)

Identify CRS based on clinical presentation. Evaluate for and treat other causes of fever, hypoxia, and hypotension. CRS has been reported to be associated with findings of HLH/MAS, and the physiology of the syndromes may overlap. HLH/MAS is a potentially life-threatening condition. In patients with progressive symptoms of CRS or refractory CRS despite treatment, evaluate for evidence of HLH/MAS.

Fifty four percent (68/127) of patients received tocilizumab; 35% (45/127) received a single dose while 18% (23/127) received more than 1 dose of tocilizumab. Overall, across the dose levels, 15% (19/127) of patients received at least 1 dose of corticosteroids for treatment of CRS. All patients that received corticosteroids for CRS received tocilizumab.

Overall rate of CRS was 79% and rate of Grade 2 CRS was 23% in patients treated in the 300×10^6 CAR+ T cell dose cohort. For patients treated in the 450×10^6 CAR+ T cell dose cohort, the overall rate of CRS was 96% and rate of Grade 2 CRS was 40%. Rate of Grade 3 or higher CRS was similar across the dose range. The median duration of CRS for the 450×10^6 CAR+ T cell dose cohort was 7 days (range: 1-63 days) and for the 300×10^6 CAR+ T cell dose cohort was 6 days (range: 2-28 days). In the 450×10^6 CAR+ T cell dose cohort, 68% (36/53) of patients received tocilizumab and 23% (12/53) received at least 1 dose of corticosteroids for treatment of CRS. In the 300×10^6 CAR+ T cell dose cohort, 44% (31/70) of patients received tocilizumab and 10% (7/70) received corticosteroids. All patients that received corticosteroids for CRS also received tocilizumab. Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of ABECMA.

Monitor patients at least daily for 7 days following ABECMA infusion at the REMS-certified healthcare facility for signs and symptoms of CRS. Monitor patients for signs or symptoms of CRS for at least 4 weeks after infusion. At the first sign of CRS, institute treatment with supportive care, tocilizumab and/or corticosteroids as indicated.

Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

Neurologic Toxicities

Neurologic toxicities, which may be severe or life-threatening, occurred following treatment with ABECMA, including concurrently with CRS, after CRS resolution, or in the absence of CRS. CART cell-associated neurotoxicity occurred in 28% (36/127) of patients receiving ABECMA, including Grade 3 in 4% (5/127) of patients. One patient had ongoing Grade 2 neurotoxicity at the time of death. Two patients had ongoing Grade 1 tremor at the time of data cutoff. The median time to onset of neurotoxicity was 2 days (range: 1 - 42 days). CART cell-associated neurotoxicity resolved in 92% (33/36) of patients with a median duration of neurotoxicity was 5 days (range: 1 - 61 days). The median duration of neurotoxicity was 6 days (range: 1 - 578) in all patients including those with ongoing neurotoxicity at the time of death or data cut off. Thirty-four patients with neurotoxicity had CRS. Neurotoxicity had onset in 3 patients before, 29 patients during, and 2 patients after CRS. The rate of Grade 3 neurotoxicity was 8% in the 450×10^6 CAR+ T cell dose cohort and 1.4% in the 300×10^6 CAR+ T cell dose cohort. The most frequently reported (greater than or equal to 5%) manifestations of CART cell-associated neurotoxicity include encephalopathy (20%), tremor (9%), aphasia (7%), and delirium (6%). Grade 4 neurotoxicity and cerebral edema in 1 patient has been reported with ABECMA in another study in multiple myeloma. Grade 3 myelitis and Grade 3 parkinsonism have been reported after treatment with ABECMA in another study in multiple myeloma.

Monitor patients at least daily for 7 days following ABECMA infusion at the REMS-certified healthcare facility for signs and symptoms of neurologic toxicities. Rule out other causes of neurologic symptoms. Monitor patients for signs or symptoms of neurologic toxicities for at least 4 weeks after infusion and treat promptly. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed.

Counsel patients to seek immediate medical attention should signs or symptoms of neurologic toxicity occur at any time.

Hemophagocytic Lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS):

HLH/MAS occurred in 4% (5/127) of patients receiving ABECMA. One patient treated in the 300 x 10⁶ CAR+ T cell dose cohort developed fatal multi-organ HLH/MAS with CRS. In another patient with fatal bronchopulmonary aspergillosis, HLH/MAS was contributory to the fatal outcome. Three cases of Grade 2 HLH/MAS resolved. The rate of HLH/MAS was 8% in the 450 x 10⁶ CAR+ T cell dose cohort and 1% in the 300 x 10⁶ CAR+ T cell dose cohort. All events of HLH/MAS had onset within 10 days of receiving ABECMA with a median onset of 7 days (range: 4-9 days) and occurred in the setting of ongoing or worsening CRS. Two patients with HLH/MAS had overlapping neurotoxicity. The manifestations of HLH/MAS include hypotension, hypoxia, multiple organ dysfunction, renal dysfunction, and cytopenia. HLH/MAS is a potentially life-threatening condition with a high mortality rate if not recognized early and treated. Treatment of HLH/MAS should be administered per institutional standards.

ABECMA REMS

Due to the risk of CRS and neurologic toxicities, ABECMA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS. Further information is available at www.AbecmaREMS.com or 1-888-423-5436.

Hypersensitivity Reactions

Allergic reactions may occur with the infusion of ABECMA. Serious hypersensitivity reactions, including anaphylaxis, may be due to dimethyl sulfoxide (DMSO) in ABECMA.

Infections

ABECMA should not be administered to patients with active infections or inflammatory disorders. Severe, life-threatening, or fatal infections occurred in patients after ABECMA infusion. Infections (all grades) occurred in 70% of patients. Grade 3 or 4 infections occurred in 23% of patients. Overall, 4 patients had Grade 5 infections (3%); 2 patients (1.6%) had Grade 5 events of pneumonia, 1 patient (0.8%) had Grade 5 bronchopulmonary aspergillosis, and 1 patient (0.8%) had cytomegalovirus (CMV) pneumonia associated with *Pneumocystis jirovecii*. Monitor patients for signs and symptoms of infection before and after ABECMA infusion and treat appropriately. Administer prophylactic, preemptive, and/or therapeutic antimicrobials according to standard institutional guidelines.

Febrile neutropenia was observed in 16% (20/127) of patients after ABECMA infusion and may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad spectrum antibiotics, fluids, and other supportive care as medically indicated.

Viral Reactivation: Cytomegalovirus (CMV) infection resulting in pneumonia and death has occurred following ABECMA administration. Monitor and treat for CMV reactivation in accordance with clinical guidelines. Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, can occur in patients treated with drugs directed against plasma cells. Perform screening for CMV, HBV, hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in accordance with clinical guidelines before collection of cells for manufacturing.

Prolonged Cytopenias

Patients may exhibit prolonged cytopenias following lymphodepleting chemotherapy and ABECMA infusion. In the KarMMa study, 41% of patients (52/127) experienced prolonged Grade 3 or 4 neutropenia and 49% (62/127) experienced prolonged Grade 3 or 4 thrombocytopenia that had not resolved by Month 1 following ABECMA infusion. Rate of prolonged neutropenia was 49% in the 450 x 10⁶ CAR+ T cell dose cohort and 34% in the 300 x 10⁶ CAR+ T cell dose cohort. In 83% (43/52) of patients who recovered from Grade 3 or 4 neutropenia after Month 1, the median time to recovery from ABECMA infusion was 1.9 months. In 65% (40/62) of patients who recovered from Grade 3 or 4 thrombocytopenia, the median time to recovery was 2.1 months. Median time to cytopenia recovery was similar across the 300 and 450 x 10⁶ dose cohort.

Prolonged Cytopenias (cont'd)

Three patients underwent stem cell therapy for hematopoietic reconstitution due to prolonged cytopenia. Two of the three patients died from complications of prolonged cytopenia. Monitor blood counts prior to and after ABECMA infusion. Manage cytopenia with myeloid growth factor and blood product transfusion support according to institutional guidelines.

Hypogammaglobulinemia

Plasma cell aplasia and hypogammaglobulinemia can occur in patients receiving treatment with ABECMA. Hypogammaglobulinemia was reported as an adverse event in 21% (27/127) of patients; laboratory IgG levels fell below 500 mg/dl after infusion in 25% (32/127) of patients treated with ABECMA.

Monitor immunoglobulin levels after treatment with ABECMA and administer IVIG for IgG <400 mg/dl. Manage per local institutional guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

The safety of immunization with live viral vaccines during or following ABECMA treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during ABECMA treatment, and until immune recovery following treatment with ABECMA.

Secondary Malignancies

Patients treated with ABECMA may develop secondary malignancies. Monitor life-long for secondary malignancies. If a secondary malignancy occurs, contact Bristol Myers Squibb at 1-888-805-4555 to obtain instructions on patient samples to collect for testing of secondary malignancy of T cell origin.

Effects on Ability to Drive and Operate Machinery

Due to the potential for neurologic events, including altered mental status or seizures, patients receiving ABECMA are at risk for altered or decreased consciousness or coordination in the 8 weeks following ABECMA infusion. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, during this initial period.

Adverse Reactions

The most common nonlaboratory adverse reactions (incidence greater than or equal to 20%) include CRS, infections – pathogen unspecified, fatigue, musculoskeletal pain, hypogammaglobulinemia, diarrhea, upper respiratory tract infection, nausea, viral infections, encephalopathy, edema, pyrexia, cough, headache, and decreased appetite.

Please see full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

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