

Clinician's Guide to ABECMA[®] CAR T Cell Therapy Process

Includes information on the ABECMA process, patient eligibility, leukapheresis, manufacturing, and adverse events.

2L=second line; CAR=chimeric antigen receptor.

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 two or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAS, PROLONGED CYTOPENIA and SECONDARY HEMATOLOGICAL MALIGNANCIES

- 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.
- T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA
- ABECMA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS.

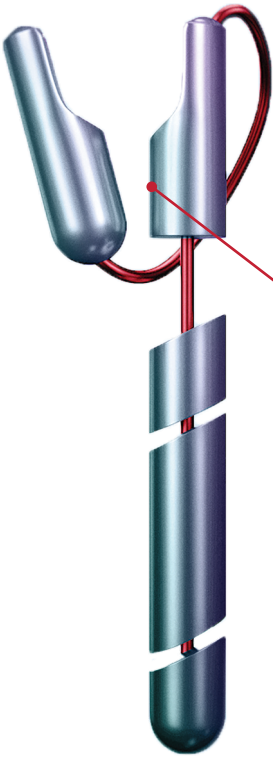
Please see Important Safety Information throughout and [click here](#) for full Prescribing Information, including **Boxed WARNINGS** and [Medication Guide](#).

ABECMA[®] Is the First CAR T Cell Therapy for RRMM¹



A personalized immune cell therapy that targets BCMA with a one-time infusion^{1*}

ABECMA consists of T cells transduced with a CAR lentiviral vector.



The CAR construct includes an extracellular **scFv-targeting domain that binds specifically to BCMA**, a cell-surface antigen expressed at significantly higher levels on malignant plasma cells of MM.^{1,3†}

TARGETING BCMA

BCMA expression is largely restricted to plasma cells and is uniquely overexpressed on myeloma cells, making BCMA a promising target antigen.^{1,3†}

Following ABECMA infusion, the CAR-positive cells proliferate and undergo rapid multi-log expansion followed by a bi-exponential decline. ABECMA can persist in peripheral blood for up to 1 year post infusion.¹

*Treatment process includes leukapheresis, manufacturing, administration, and adverse event monitoring. A single dose of ABECMA contains a cell suspension of 300 to 510 x 10⁶ CAR-positive T cells in 1 or more infusion bags.

†BCMA is expressed both on normal and malignant plasma cells.

BCMA=B-cell maturation antigen; MM=multiple myeloma; RRMM=relapsed/refractory multiple myeloma; scFv=single-chain variable fragment.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions:

Early Death: In KarMMa-3, a randomized (2:1), controlled trial, a higher proportion of patients experienced death within 9 months after randomization in the ABECMA arm (45/254; 18%) compared to the standard regimens arm (15/132; 11%). Early deaths occurred in 8% (20/254) and 0% prior to ABECMA infusion and standard regimen administration, respectively, and 10% (25/254) and 11% (15/132) after ABECMA infusion and standard regimen administration, respectively. Out of the 20 deaths that occurred prior to ABECMA infusion, 15 occurred from disease progression, 3 occurred from adverse events and 2 occurred from unknown causes. Out of the 25 deaths that occurred after ABECMA infusion, 10 occurred from disease progression, 11 occurred from adverse events, and 4 occurred from unknown causes.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

ABECMA REMS¹

Due to the risk of CRS and neurologic toxicity, ABECMA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS.

The required components of the ABECMA REMS are:

- Healthcare facilities that dispense and administer ABECMA must be enrolled and comply with the REMS requirements
- Certified healthcare facilities must have on-site, immediate access to tocilizumab
- Ensure that a minimum of 2 doses of tocilizumab are available for each patient for infusion within 2 hours after ABECMA infusion, if needed for treatment of CRS
- Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense, or administer ABECMA are trained on the management of CRS and NT
- Further information is available at www.AbecmaREMS.com, or contact Bristol Myers Squibb at 1-866-340-7332

CRS=cytokine release syndrome.

IMPORTANT SAFETY INFORMATION (cont'd)

Cytokine Release Syndrome (CRS): CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA. Among patients receiving ABECMA for relapsed refractory multiple myeloma in the KarMMa and KarMMa-3 studies (N=349), CRS occurred in 89% (310/349), including \geq Grade 3 CRS (Lee grading system) in 7% (23/349) of patients and Grade 5 CRS in 0.9% (3/349) of patients. The median time-to-onset of CRS, any grade, was 1 day (range: 1 to 27 days), and the median duration of CRS was 5 days (range: 1 to 63 days). In the pooled studies, the rate of \geq Grade 3 CRS was 10% (7/71) for patients treated in dose range of 460 to 510 x 10⁶ CAR-positive T cells and 5.4% (13/241) for patients treated in dose range of 300 to 460 x 10⁶ CAR-positive T cells.

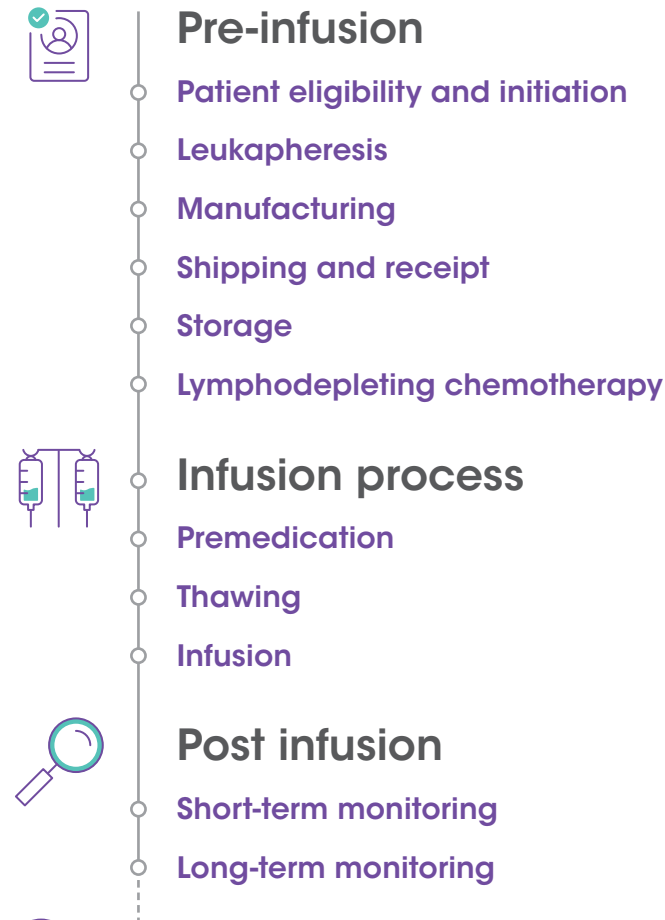
The most common manifestations of CRS (greater than or equal to 10%) included pyrexia (87%), hypotension (30%), tachycardia (26%), chills (19%), hypoxia (16%). Grade 3 or higher events that may be associated with CRS include hypotension, hypoxia, hyperbilirubinemia, hypofibrinogenemia, ARDS, atrial fibrillation, hepatocellular injury, metabolic acidosis, pulmonary edema, coagulopathy, renal failure, multiple organ dysfunction syndrome and HLH/MAS.

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.

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The ABECMA[®] Process

An overview of the ABECMA process¹



At any point during the ABECMA process, you can visit the Scheduling and Apheresis Portal at www.CT360.com for appointment and product status information.

IMPORTANT SAFETY INFORMATION (cont'd)

Cytokine Release Syndrome (CRS) (cont'd): Of the 349 patients who received ABECMA in clinical trials, 226 (65%) patients received tocilizumab; 39% (135/349) received a single dose, while 26% (91/349) received more than 1 dose of tocilizumab. Overall, 24% (82/349) of patients received at least 1 dose of corticosteroids for treatment of CRS. Almost all patients who received corticosteroids for CRS also received tocilizumab. For patients treated in dose range of 460 to 510 x 10⁶ CAR-positive T cells, 76% (54/71) of patients received tocilizumab and 35% (25/71) received at least 1 dose of corticosteroids for treatment of CRS. For patients treated in dose range of 300 to 460 x 10⁶ CAR-positive T cells, 63% (152/241) of patients received tocilizumab and 20% (49/241) received at least 1 dose of corticosteroid for treatment of CRS.

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Patient Eligibility and Initiation

Determining eligibility for ABECMA^{1,2}

Eligible adult patients include those with RRMM after 2L who are:

- Triple-class exposed who have received two or more prior therapies*
- Have received 2 kinds of treatment regimens that include an immunomodulatory agent, a PI, and an anti-CD38 monoclonal antibody
- Clinical fitness (eg, ECOG PS 0 or 1[†] and adequate organ function)

Pivotal trial population^{1,3}

KarMMa-3 was a phase 3, open-label, randomized, multicenter trial that evaluated ABECMA vs standard regimens[‡] in 386 patients with RRMM. Patients had received 2 to 4 prior regimens including an immunomodulatory agent, a PI, and daratumumab, and were refractory to their last regimen.

In KarMMa-3, ABECMA was studied in patients of varying ages and risk profiles:

- 30 to 81 years of age (median age: 63 years)
- 100% were triple-class exposed
- 59% were R-ISS disease stage II
- 95% were daratumumab refractory
- 24% had extramedullary disease
- 28% had high tumor burden
- 42% had high-risk cytogenetics[§]

One-time ABECMA infusion in KarMMa-3: 175 to 529 x 10⁶ CAR-positive T cells (n=254)

ABECMA offers unlimited slot availability and the MOST locations near you.^{4||}

*Received an immunomodulatory agent, a PI, and an anti-CD38 monoclonal antibody.

[†]All the patients had an ECOG score of 0 or 1 at screening, but the score may have been greater than 1 at baseline (randomization).

[‡]The standard regimens consisted of 5 antimyeloma treatment options: DPd, DVd, IRd, Kd, or EPd, selected by investigator contingent upon the patient's most recent antimyeloma treatment.

[§]High-risk cytogenetic abnormalities included del(17p), t(4;14), and t(14;16).

^{||}Lots manufactured January 2023–November 2023. Manufacturing success rate is calculated as patients successfully treated with conforming product/patient apheresed.⁴

DPd=daratumumab, pomalidomide, dexamethasone; DVd=daratumumab, bortezomib, dexamethasone; ECOG PS=Eastern Cooperative Oncology Group Performance Status; EPd=elotuzumab, pomalidomide, dexamethasone; IRd=ixazomib, lenalidomide, dexamethasone; Kd=carfilzomib, dexamethasone; PI=proteasome inhibitor; R-ISS=Revised International Staging System.

IMPORTANT SAFETY INFORMATION (cont'd)

Cytokine Release Syndrome (CRS) (cont'd): Monitor patients at least daily for 7 days following ABECMA infusion at the REMS-certified healthcare facility for signs or symptoms of CRS and monitor patients for signs or symptoms of CRS for at least 4 weeks after ABECMA infusion. At the first sign of CRS, institute treatment with supportive care, tocilizumab and/or corticosteroids as indicated. Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of ABECMA. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

Neurologic Toxicities: Neurologic toxicities, including immune-effector cell-associated neurotoxicity (ICANS), which may be severe or life-threatening, occurred concurrently with CRS, after CRS resolution, or in the absence of CRS following treatment with ABECMA.

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Leukapheresis

Collecting your patient's T cells through leukapheresis is the first step in the ABECMA[®] treatment process^{1,2}

Before leukapheresis begins:

- Perform screening for CMV, HBV, HCV, and HIV in accordance with clinical guidelines before collection of cells for manufacturing
- Confirm that your patient has been given adequate time after their last anticancer treatment

Washout periods before leukapheresis in the KarMMa-3 pivotal trial⁵

Systemic MM therapy

Stopped ≥ 14 days
prior to leukapheresis

Corticosteroids (>20 mg/day prednisone or equivalent)*

Stopped ≥ 14 days
prior to leukapheresis

Following leukapheresis, your patient's T cells are sent to a manufacturing site.¹

*Physiologic replacement, topical, intranasal, and inhaled steroids were permitted in the KarMMa-3 trial. CMV=cytomegalovirus; HBV=hepatitis B virus; HCV=hepatitis C virus; HIV=human immunodeficiency virus.

IMPORTANT SAFETY INFORMATION (cont'd)

Neurologic Toxicities (cont'd): In patients receiving ABECMA in the KarMMa and KarMMa-3 studies, CAR T cell-associated neurotoxicity occurred in 40% (139/349), including Grade 3 in 4% (14/349) and Grade 4 in 0.6% (2/349) of patients. The median time to onset of neurotoxicity was 2 days (range: 1 to 148 days). The median duration of CAR T cell-associated neurotoxicity was 8 days (range: 1 to 720 days) in all patients including those with ongoing neurologic events at the time of death or data cut off. CAR T cell-associated neurotoxicity resolved in 123 of 139 (88%) patients and median time to resolution was 5 days (range: 1 to 245 days). One-hundred and thirty four out of 349 (38%) patients with neurotoxicity had CRS. The onset of neurotoxicity during CRS was observed in 93 patients, before the onset of CRS in 12 patients, and after the CRS event in 29 patients. The rate of Grade 3 or 4 CAR T cell-associated neurotoxicity was 5.6% (4/71) and 3.7% (9/241) for patients treated in dose range of 460 to 510 x 10⁶ CAR-positive T cells and 300 to 460 x 10⁶ CAR-positive T cells, respectively. The most frequent (greater than or equal to 5%) manifestations of CAR T cell-associated neurotoxicity include encephalopathy (21%), headache (15%), dizziness (8%), delirium (6%), and tremor (6%).

At the safety update for KarMMa-3 study, one patient developed fatal neurotoxicity 43 days after ABECMA. In KarMMa, 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.

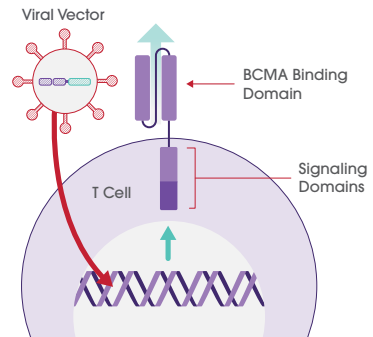
Cerebral edema has been associated with ABECMA in a patient in another study in multiple myeloma. Grade 3 myelitis and Grade 3 parkinsonism have occurred after treatment with ABECMA in another study in multiple myeloma.

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Manufacturing

At the manufacturing site¹

- The patient's T cells are transduced with a CAR lentiviral vector targeting BCMA
- The transduced T cells are expanded, formulated into a suspension, and cryopreserved



Bridging therapy during manufacturing^{1,3}

Bridging therapy can be used in some patients at the physician's discretion for disease control during the manufacturing process.

- 85% of patients received bridging therapy in the KarMMA-3 trial

ABECMA is provided as a single dose for infusion containing a suspension of CAR-positive T cells in 1 or more infusion bags¹

- The recommended dose range is 300 to 510 × 10⁶ CAR-positive T cells
- ABECMA is an autologous product
- Of 249 patients who underwent leukapheresis, 3 received CAR-positive T cells that did not meet product release specifications for ABECMA, and in 3 patients there was an inability to manufacture ABECMA

The median time from leukapheresis to product availability was 35 days (range: 24 to 102 days)^{1†}

[†]Manufacturing turnaround times may vary.

IMPORTANT SAFETY INFORMATION (cont'd)

Neurologic Toxicities (cont'd): Monitor patients at least daily for 7 days following ABECMA infusion at the REMS-certified healthcare facility for signs or symptoms of neurologic toxicities and monitor patients for signs or symptoms of neurologic toxicities for at least 4 weeks after ABECMA infusion and treat promptly. Rule out other causes of neurologic symptoms. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed. Counsel patients to seek immediate medical attention should signs or symptoms occur at any time.

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Chain of Identity

To ensure patient safety, Bristol Myers Squibb requires chain of identity (COI) at 4 key points in the treatment process^{1,6}

1. **When you receive the liquid nitrogen (LN₂) dry vapor shipper**
 Shipper contains Release for Infusion (RFI) certificate and frozen product in LN₂ container. Verify patient identifiers on product RFI certificate match across patient medical records.
2. **After transferring ABECMA® to on-site storage***
 If on-site vapor phase LN₂ storage is qualified, transfer product container to on-site storage. Verify patient identifiers, including JOIN,[†] match on product RFI certificate and on product labels.
3. **Prior to thawing ABECMA**
 Verify product containers match product RFI certificate. Verify patient identifiers across all product labels, including JOIN.[†]
4. **Prior to ABECMA administration**
 Prior to administration, verify patient identifiers match product RFI certificate and patient medical records. Verbally confirm patient identification with patient.

*Applies to institutions that have demonstrated capacity and have been prequalified for on-site storage.

[†]The JOIN is a unique identification code that is assigned to the patient's specific cellular material and is the link between the patient and their cells throughout the manufacturing process.

IMPORTANT SAFETY INFORMATION (cont'd)

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

In patients receiving ABECMA in the KarMMa and KarMMa-3 studies, HLH/MAS occurred in 2.9% (10/349) of patients. All events of HLH/MAS had onset within 10 days of receiving ABECMA, with a median onset of 6.5 days (range: 4 to 10 days) and occurred in the setting of ongoing or worsening CRS. Five patients with HLH/MAS had overlapping neurotoxicity. The manifestations of HLH/MAS include hypotension, hypoxia, multiple organ dysfunction, renal dysfunction and cytopenia.

In KarMMa-3, one patient had Grade 5, two patients had Grade 4 and two patients had Grade 3 HLH/MAS. The patient with Grade 5 HLH/MAS also had Grade 5 candida sepsis and Grade 5 CRS. In another patient who died due to stroke, the Grade 4 HLH/MAS had resolved prior to death. Two cases of Grade 3 and one case of Grade 4 HLH/MAS had resolved.

In KarMMa, one patient treated in the 300 x 10⁶ CAR-positive T cells 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.

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 guidelines.

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Receiving the ABECMA Shipment

Cryopreserved ABECMA is shipped to your site in a qualified LN₂ dry vapor shipper⁶

- ABECMA will be shipped on the scheduled date directly to the infusion site's assigned address and/or department, as specified on the Cell Therapy 360[®] Scheduling Portal

1. When you receive the LN₂ dry vapor shipper⁶

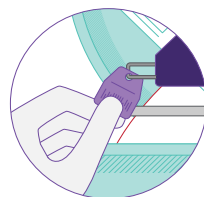
STOP AND CONFIRM PATIENT ID

Two site staff are required to verify the patient information listed on the RFI certificate matches the information listed on the treatment center's patient medical records:

- Patient's first and last name
- Patient's date of birth
- JOIN[†]

In case of any questions or concerns with the RFI certificate, contact Bristol Myers Squibb at **1-888-805-4555**.

- Confirm the LN₂ dry vapor shipper is free of damage and the tamper-evident tag is intact
 - If the tamper-evident tag is cut or the tag numbers do not match those listed on the RFI certificate, contact Bristol Myers Squibb at 1-888-805-4555



Note the shipper expiration date and time on label inside shipper, and ensure expiration is after the planned date of ABECMA infusion or transfer to on-site storage.

Unless preapproved for on-site storage, do not open the inner container until ready to prepare ABECMA on the day of infusion.

IMPORTANT SAFETY INFORMATION (cont'd)

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 contact Bristol-Myers Squibb at 1-866-340-7332.

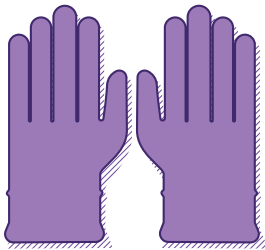
Hypersensitivity Reactions: Allergic reactions may occur with the infusion of ABECMA. Serious hypersensitivity reactions, including anaphylaxis, may be due to dimethyl sulfoxide (DMSO) in ABECMA.

Please see Important Safety Information throughout and [click here for full Prescribing Information](#), including **Boxed WARNINGS** and **Medication Guide**.

General Guidelines for Safe Handling

Before handling ABECMA[®], ensure the appropriate safety measures are taken and that personnel have been trained according to institutional practices⁶

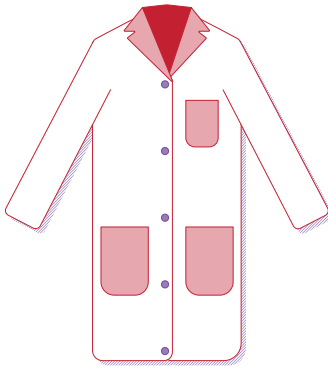
Wear the following personal protective equipment (PPE)



Waterproof thermal protective gloves



Safety glasses with side shields



Lab coat

IMPORTANT SAFETY INFORMATION (cont'd)

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.

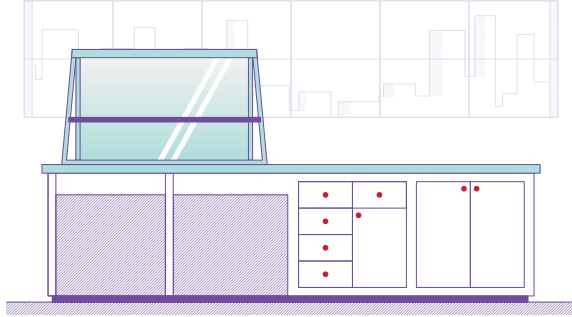
In all patients receiving ABECMA in the KarMMa and KarMMa-3 studies, infections (all grades) occurred in 61% of patients. Grade 3 or 4 infections occurred in 21% of patients. Grade 3 or 4 infections with an unspecified pathogen occurred in 12%, viral infections in 7%, bacterial infections in 4.3%, and fungal infections in 1.4% of patients. Overall, 15 patients had Grade 5 infections (4.3%); 8 patients (2.3%) with infections of pathogen unspecified, 3 patients (0.9%) with fungal infections, 3 patients (0.9%) with viral infections, and 1 patient (0.3%) with bacterial infection.

Monitor patients for signs and symptoms of infection before and after ABECMA infusion and treat appropriately. Administer prophylactic, pre-emptive, and/or therapeutic antimicrobials according to standard institutional guidelines.

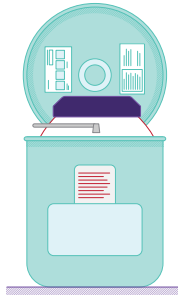
Please see Important Safety Information throughout and [click here for full Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

General Guidelines for Safe Handling (cont'd)

Always work in a well-ventilated area



Always keep the outer container and LN₂ dry vapor shipper in an upright position



ABECMA must be handled according to institutional procedures for cellular products, which may contain infectious materials¹

- ABECMA contains human blood cells that are genetically modified with replication incompetent, self-inactivating lentiviral vector
- Follow universal precautions and local biosafety guidelines for handling and disposal to avoid potential transmission of infectious diseases

IMPORTANT SAFETY INFORMATION (cont'd)

Infections (cont'd): Febrile neutropenia was observed in 38% (133/349) 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. Consider antiviral therapy to prevent viral reactivation per local institutional guidelines/clinical practice.

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LN₂ Dry Vapor Shipper Contents

ABECMA[®] is stored within a temperature-controlled LN₂ dry vapor shipper that is placed inside an outer container⁶

Affixed to the outside of the outer container are:

- The waybill and shipper receipt documentation
- FedEx[®] return label
- A label containing the shipper expiry and anonymized patient identifiers, including JOIN*
- Warning labels

Attached to the inside lid of the outer container are:

- The RFI certificate
- ABECMA Prescribing Information and Medication Guide
- A temperature control monitor lies within the outer shipper container and remotely tracks the internal temperature of the LN₂ dry vapor shipper until removal of the drug product



*The JOIN is a unique identification code that is assigned to the patient's specific cellular material and is the link between the patient and their cells throughout the manufacturing process.

IMPORTANT SAFETY INFORMATION (cont'd)

Prolonged Cytopenias: In patients receiving ABECMA in the KarMMa and KarMMa-3 studies, 40% of patients (139/349) experienced prolonged Grade 3 or 4 neutropenia and 42% (145/349) experienced prolonged Grade 3 or 4 thrombocytopenia that had not resolved by Month 1 following ABECMA infusion. In 89% (123/139) 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 76% (110/145) of patients who recovered from Grade 3 or 4 thrombocytopenia, the median time to recovery was 1.9 months. Five patients underwent stem cell therapy for hematopoietic reconstitution due to prolonged cytopenia. The rate of Grade 3 or 4 thrombocytopenia was 62% (44/71) and 56% (135/241) for patients treated in dose range of 460 to 510 x 10⁶ CAR-positive T cells and 300 to 460 x 10⁶ CAR-positive T cells, respectively.

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LN₂ Dry Vapor Shipper Contents (cont'd)

Inside the LN₂ dry vapor shipper is^{1,6}:

- The ABECMA drug product, which will be packaged in 1 or more infusion bags containing a total of 300 to 510 x 10⁶ CAR-positive T cells
 - Each infusion bag is contained within a metal cassette, which is stored in a rack within the LN₂ dry vapor shipper

ABECMA components^{1,6}

- The ABECMA formulation contains Plasma-Lyte A and CryoStor® CS10, resulting in a final DMSO concentration of 5%
- ABECMA is cryopreserved and supplied in 1 or more infusion bag(s). The full contents of each infusion bag supplied should be administered
- Each infusion bag of ABECMA is individually packed in a metal cassette. ABECMA is stored in the vapor phase of LN₂ and supplied in an LN₂ dry vapor shipper

The LN₂ dry vapor shipper will be monitored remotely by Bristol Myers Squibb for temperature deviations until the product is received at the site.

In the event that the temperature goes above -130 °C, DO NOT initiate ABECMA infusion, and call Bristol Myers Squibb at 1-888-805-4555 to determine next steps.

IMPORTANT SAFETY INFORMATION (cont'd)

Prolonged Cytopenias (cont'd): Monitor blood counts prior to and after ABECMA infusion. Manage cytopenia with myeloid growth factor and blood product transfusion support according to local institutional guidelines.

Hypogammaglobulinemia: In all patients receiving ABECMA in the KarMMa and KarMMa-3 studies, hypogammaglobulinemia was reported as an adverse event in 13% (46/349) of patients; laboratory IgG levels fell below 500 mg/dL after infusion in 37% (130/349) of patients treated with ABECMA.

Hypogammaglobulinemia either as an adverse reaction or laboratory IgG level below 500 mg/dL after infusion occurred in 45% (158/349) of patients treated with ABECMA. Forty-one percent of patients received intravenous immunoglobulin (IVIG) post-ABECMA for serum IgG <400 mg/dL.

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

Use of Live Vaccines: The safety of immunization with live viral vaccines during or after 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.

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ABECMA[®] Storage

The method of storage will depend on individual site capabilities^{1,6}

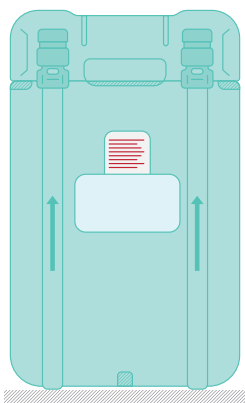
There are 2 delivery/storage options for ABECMA:

Method 1: Just-in-time delivery

ABECMA arrives on or near the date of infusion and remains in the LN₂ dry vapor shipper until the product is thawed for patient administration.

NOTE: The LN₂ dry vapor shipper will arrive the day of intended infusion or earlier, pending delivery logistics and agreement with the infusion site.

- The LN₂ dry vapor shipper should be stored upright in a LOCKED, WELL-VENTILATED room upon arrival at the site and until time of infusion of ABECMA
- If ABECMA is received earlier than the intended infusion day, it can be kept temporarily in the LN₂ dry vapor shipper until the time of infusion, as long as it does not exceed the maximum allowable LN₂ dry vapor shipper storage duration
- Storage of the LN₂ dry vapor shipper should not exceed the shipper expiration date; planned date of administration should be before this expiration date for just-in-time delivery
- If the patient is not expected to be ready for same-day administration before the shipper expires and the infusion site is not qualified for on-site storage, contact Bristol Myers Squibb at 1-888-805-4555 to arrange for return shipment



IMPORTANT SAFETY INFORMATION (cont'd)

Secondary Malignancies: Patients treated with ABECMA may develop secondary malignancies. In KarMMa-3, myeloid neoplasms (four cases of myelodysplastic syndrome and one case of acute myeloid leukemia) occurred in 2.2% (5/222) of patients following treatment with ABECMA compared to none in the standard regimens arm at the time of the safety update. The median time to onset of myeloid neoplasm from ide-cel infusion was 338 days (Range: 277 to 794 days). Three of these five patients have died following the development of myeloid neoplasm. One out of the five cases of myeloid neoplasm occurred after initiation of subsequent antimyeloma therapy.

Please see Important Safety Information throughout and [click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.](#)

ABECMA[®]

Storage (cont'd)

Method 2: On-site storage (by preapproval process)^{6*}

ABECMA is transferred to on-site vapor-phase LN₂ storage.

- Preparation for transfer
 - The transfer should be completed by 2 qualified site staff who can ensure it is done in less than 2 minutes
 - Prepare for the upcoming COI checks by locating the RFI certificate and identifying the location of the data points required for COI check #2
- On-site institutional temperature monitoring: Store ABECMA frozen in the vapor phase of LN₂ (-130 °C or colder)
 - In the event that the temperature goes above -130 °C, **DO NOT** initiate ABECMA infusion, and call Bristol Myers Squibb at 1-888-805-4555
- Upon arrival, ABECMA should be transferred to on-site vapor-phase LN₂ storage. Complete the transfer to on-site storage within 2 minutes
 - Remove the metal cassettes within the LN₂ dry vapor shipper
 - Transfer the metal cassettes to your site's storage rack immediately
 - During transfer, keep the metal cassette over the vapor phase of the shipper to prevent thawing
 - Complete COI check #2 outlined in the purple box below

2. After transferring ABECMA to on-site storage⁶

STOP AND CONFIRM PATIENT ID

Two site staff are required to verify the patient information listed on the product RFI certificate matches the information listed on the cassette labels[†]:

- Patient's first and last name
- Patient's date of birth
- JOIN[‡]

NOTE: This COI check only occurs if storing ABECMA in on-site vapor-phase LN₂ storage.

*Applies to institutions that have demonstrated capacity and have been prequalified for on-site storage.

[†]ABECMA infusion bags will arrive in a labeled cassette.

[‡]The JOIN is a unique identification code that is assigned to the patient's specific cellular material and is the link between the patient and their cells throughout the manufacturing process.

IMPORTANT SAFETY INFORMATION (cont'd)

Secondary Malignancies (cont'd): T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA. Mature T cell malignancies, including CAR-positive tumors, may present as soon as weeks following infusion, and may include fatal outcomes.

Monitor life-long for secondary malignancies. In the event that a secondary malignancy occurs, contact Bristol-Myers Squibb at 1-888-805-4555 for reporting and to obtain instructions on collection of patient samples for testing of secondary malignancy.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

Lymphodepleting Chemotherapy

Begin administration of low-dose lymphodepleting chemotherapy 5 days before ABECMA[®] infusion^{1,7}

- ✓ Confirm the availability of ABECMA before starting the lymphodepleting chemotherapy regimen
- ✓ Administer lymphodepleting chemotherapy regimen: fludarabine 30 mg/m²/day IV and cyclophosphamide 300 mg/m²/day IV for 3 days*
- ✓ Administer ABECMA 2 days after completion of lymphodepleting chemotherapy

Delay the infusion of ABECMA for up to 7 days if a patient has any of the following conditions:

- Unresolved serious adverse events (especially pulmonary events, cardiac events, or hypotension), including those after preceding chemotherapies
- Active infections or inflammatory disorders

*See the prescribing information of cyclophosphamide and fludarabine for information on dose adjustment in renal impairment.

IV=intravenously.

IMPORTANT SAFETY INFORMATION (cont'd)

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 pyrexia, CRS, hypogammaglobulinemia, infections – pathogen unspecified, musculoskeletal pain, fatigue, febrile neutropenia, hypotension, tachycardia, diarrhea, nausea, headache, chills, upper respiratory tract infection, encephalopathy, edema, dyspnea and viral infections.

Please see Important Safety Information throughout and [click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.](#)

Considerations Before Lymphodepleting Chemotherapy



Washout periods before lymphodepleting chemotherapy in the KarMMa-3 trial^{1,3}

MM bridging therapies (following leukapheresis)	Stopped ≥ 14 days prior to lymphodepleting chemotherapy
---	--

- Some patients may have an urgent need for treatment, and you may not consider them candidates for ABECMA
- However, an effective bridging therapy can be administered to maintain disease control during the ABECMA manufacturing process
 - This may make ABECMA accessible to more patients

IMPORTANT SAFETY INFORMATION

Warnings and Precautions:

Early Death: In KarMMa-3, a randomized (2:1), controlled trial, a higher proportion of patients experienced death within 9 months after randomization in the ABECMA arm (45/254; 18%) compared to the standard regimens arm (15/132; 11%). Early deaths occurred in 8% (20/254) and 0% prior to ABECMA infusion and standard regimen administration, respectively, and 10% (25/254) and 11% (15/132) after ABECMA infusion and standard regimen administration, respectively. Out of the 20 deaths that occurred prior to ABECMA infusion, 15 occurred from disease progression, 3 occurred from adverse events and 2 occurred from unknown causes. Out of the 25 deaths that occurred after ABECMA infusion, 10 occurred from disease progression, 11 occurred from adverse events, and 4 occurred from unknown causes.

Cytokine Release Syndrome (CRS): CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA. Among patients receiving ABECMA for relapsed refractory multiple myeloma in the KarMMa and KarMMa-3 studies (N=349), CRS occurred in 89% (310/349), including \geq Grade 3 CRS (Lee grading system) in 7% (23/349) of patients and Grade 5 CRS in 0.9% (3/349) of patients. The median time-to-onset of CRS, any grade, was 1 day (range: 1 to 27 days), and the median duration of CRS was 5 days (range: 1 to 63 days). In the pooled studies, the rate of \geq Grade 3 CRS was 10% (7/71) for patients treated in dose range of 460 to 510 x 10⁶ CAR-positive T cells and 5.4% (13/241) for patients treated in dose range of 300 to 460 x 10⁶ CAR-positive T cells.

The most common manifestations of CRS (greater than or equal to 10%) included pyrexia (87%), hypotension (30%), tachycardia (26%), chills (19%), hypoxia (16%). Grade 3 or higher events that may be associated with CRS include hypotension, hypoxia, hyperbilirubinemia, hypofibrinogenemia, ARDS, atrial fibrillation, hepatocellular injury, metabolic acidosis, pulmonary edema, coagulopathy, renal failure, multiple organ dysfunction syndrome and HLH/MAS.

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.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

Preparing for the Infusion

Before beginning treatment with ABECMA^{®1}

- ✔ Ensure that a minimum of 2 doses of tocilizumab per patient and emergency equipment are available prior to infusion and during the recovery period
- ✔ Monitor patients for signs and symptoms of infection before and after ABECMA infusion and treat appropriately. ABECMA should not be administered to patients with active infections or inflammatory disorders
- ✔ Monitor complete blood counts prior to and after ABECMA infusion

ABECMA may cause a false-positive HIV test result by some commercial tests.

Premedication on infusion day¹

30-60 minutes before ABECMA infusion:

- ✔ Administer acetaminophen (650 mg orally) and diphenhydramine (12.5 mg IV or 25 to 50 mg orally, or another H₁-antihistamine)

Avoid prophylactic use of dexamethasone or other systemic corticosteroids, as they may interfere with the activity of ABECMA.

IMPORTANT SAFETY INFORMATION (cont'd)

Cytokine Release Syndrome (CRS) (cont'd): Of the 349 patients who received ABECMA in clinical trials, 226 (65%) patients received tocilizumab; 39% (135/349) received a single dose, while 26% (91/349) received more than 1 dose of tocilizumab. Overall, 24% (82/349) of patients received at least 1 dose of corticosteroids for treatment of CRS. Almost all patients who received corticosteroids for CRS also received tocilizumab. For patients treated in dose range of 460 to 510 x 10⁶ CAR-positive T cells, 76% (54/71) of patients received tocilizumab and 35% (25/71) received at least 1 dose of corticosteroids for treatment of CRS. For patients treated in dose range of 300 to 460 x 10⁶ CAR-positive T cells, 63% (152/241) of patients received tocilizumab and 20% (49/241) received at least 1 dose of corticosteroid for treatment of CRS.

Monitor patients at least daily for 7 days following ABECMA infusion at the REMS-certified healthcare facility for signs or symptoms of CRS and monitor patients for signs or symptoms of CRS for at least 4 weeks after ABECMA infusion. At the first sign of CRS, institute treatment with supportive care, tocilizumab and/or corticosteroids as indicated. Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of ABECMA. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

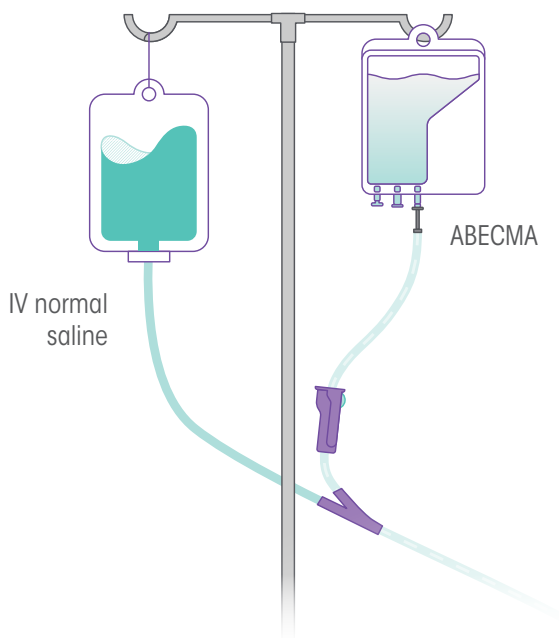
Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

Preparing for the Infusion (cont'd)

Setup^{1,6}

A Y-type administration set is recommended to accommodate the infusion bag on one arm and a bag of normal saline on the second arm.

- ABECMA can be administered via peripheral or central venous access. Central venous access is encouraged in patients with poor peripheral access



DO NOT use a leukodepleting filter.

IMPORTANT SAFETY INFORMATION (cont'd)

Neurologic Toxicities: Neurologic toxicities, including immune-effector cell-associated neurotoxicity (ICANS), which may be severe or life-threatening, occurred concurrently with CRS, after CRS resolution, or in the absence of CRS following treatment with ABECMA.

In patients receiving ABECMA in the KarMMa and KarMMa-3 studies, CAR T cell-associated neurotoxicity occurred in 40% (139/349), including Grade 3 in 4% (14/349) and Grade 4 in 0.6% (2/349) of patients. The median time to onset of neurotoxicity was 2 days (range: 1 to 148 days). The median duration of CAR T cell-associated neurotoxicity was 8 days (range: 1 to 720 days) in all patients including those with ongoing neurologic events at the time of death or data cut off. CAR T cell-associated neurotoxicity resolved in 123 of 139 (88%) patients and median time to resolution was 5 days (range: 1 to 245 days). One-hundred and thirty four out of 349 (38%) patients with neurotoxicity had CRS. The onset of neurotoxicity during CRS was observed in 93 patients, before the onset of CRS in 12 patients, and after the CRS event in 29 patients. The rate of Grade 3 or 4 CAR T cell-associated neurotoxicity was 5.6% (4/71) and 3.7% (9/241) for patients treated in dose range of 460 to 510 x 10⁶ CAR-positive T cells and 300 to 460 x 10⁶ CAR-positive T cells, respectively. The most frequent (greater than or equal to 5%) manifestations of CAR T cell-associated neurotoxicity include encephalopathy (21%), headache (15%), dizziness (8%), delirium (6%), and tremor (6%).

Please see Important Safety Information throughout and [click here for full Prescribing Information](#), including **Boxed WARNINGS** and **Medication Guide**.

Preparing to Thaw ABECMA[®]

Ensure that the following steps are completed prior to thawing ABECMA^{1,6}:

When removing ABECMA from vapor-phase LN₂ storage, proper PPE should be worn. Ensure that personnel are trained on the handling of LN₂ according to institutional practices.

- ✓ Have the RFI certificate ready
- ✓ Confirm with site staff that the patient is ready for infusion and has been appropriately premedicated
- ✓ Confirm the infusion start time in advance and adjust the start time of the thaw so that ABECMA is available for infusion when the patient is ready
- ✓ Preheat approved thaw device or water bath to 37 °C
- ✓ Verify that the number of infusion bags and label information match the ABECMA RFI certificate

IMPORTANT SAFETY INFORMATION (cont'd)

Neurologic Toxicities (cont'd): At the safety update for KarMMa-3 study, one patient developed fatal neurotoxicity 43 days after ABECMA. In KarMMa, 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.

Cerebral edema has been associated with ABECMA in a patient in another study in multiple myeloma. Grade 3 myelitis and Grade 3 parkinsonism have occurred 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 or symptoms of neurologic toxicities and monitor patients for signs or symptoms of neurologic toxicities for at least 4 weeks after ABECMA infusion and treat promptly. Rule out other causes of neurologic symptoms. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed. Counsel patients to seek immediate medical attention should signs or symptoms occur at any time.

Hemophagocytic Lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS): In patients receiving ABECMA in the KarMMa and KarMMa-3 studies, HLH/MAS occurred in 2.9% (10/349) of patients. All events of HLH/MAS had onset within 10 days of receiving ABECMA, with a median onset of 6.5 days (range: 4 to 10 days) and occurred in the setting of ongoing or worsening CRS. Five patients with HLH/MAS had overlapping neurotoxicity. The manifestations of HLH/MAS include hypotension, hypoxia, multiple organ dysfunction, renal dysfunction and cytopenia.

In KarMMa-3, one patient had Grade 5, two patients had Grade 4 and two patients had Grade 3 HLH/MAS. The patient with Grade 5 HLH/MAS also had Grade 5 candida sepsis and Grade 5 CRS. In another patient who died due to stroke, the Grade 4 HLH/MAS had resolved prior to death. Two cases of Grade 3 and one case of Grade 4 HLH/MAS had resolved.

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 guidelines.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

Preparing to Thaw ABECMA® (cont'd)

3. Prior to thawing ABECMA^{1,6}

STOP AND CONFIRM PATIENT ID

Two site staff are required to verify the patient information on the ABECMA RFI certificate matches the cassette labels and bag labels:

- Patient's first and last name
- Patient's date of birth
- JOIN*

NOTE: Do not remove the ABECMA infusion bag from the cassette if the information on the patient-specific label does not match the intended patient. Contact Bristol Myers Squibb at 1-888-805-4555 if there are any discrepancies between the labels and the patient identifiers.

*The JOIN is a unique identification code that is assigned to the patient's specific cellular material and is the link between the patient and their cells throughout the manufacturing process.

IMPORTANT SAFETY INFORMATION (cont'd)

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 contact Bristol-Myers Squibb at 1-866-340-7332.

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.

In all patients receiving ABECMA in the KarMMa and KarMMa-3 studies, infections (all grades) occurred in 61% of patients. Grade 3 or 4 infections occurred in 21% of patients. Grade 3 or 4 infections with an unspecified pathogen occurred in 12%, viral infections in 7%, bacterial infections in 4.3%, and fungal infections in 1.4% of patients. Overall, 15 patients had Grade 5 infections (4.3%); 8 patients (2.3%) with infections of pathogen unspecified, 3 patients (0.9%) with fungal infections, 3 patients (0.9%) with viral infections, and 1 patient (0.3%) with bacterial infection.

Monitor patients for signs and symptoms of infection before and after ABECMA infusion and treat appropriately. Administer prophylactic, pre-emptive, and/or therapeutic antimicrobials according to standard institutional guidelines.

Febrile neutropenia was observed in 38% (133/349) 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.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

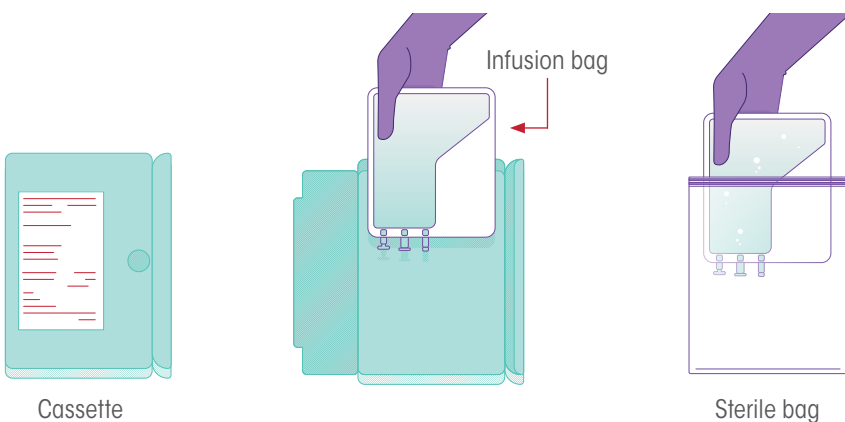
ABECMA® Thawing^{1,6}

NOTE: The ABECMA infusion bags should be administered in series. If more than 1 infusion bag is required for administration, **keep the remaining bag(s) in LN₂ storage until prior bag has been infused and patient is ready; proceed to the subsequent infusion bag based on clinical judgment.** Each infusion bag must be infused within 1 hour of the start of its thaw.*

Step 1

Open the cassette for the first infusion bag, gently remove from cassette, and immediately place the infusion bag inside a second sterile bag per local guidelines.

- **DO NOT** unfold the label flap
- Inspect the infusion bag for any breaches of integrity such as breaks or cracks before thawing. If the bag is compromised, contact Bristol Myers Squibb at 1-888-805-4555
- Recommend recording the start time of the thaw and expiry for the thaw bag on the ABECMA RFI certificate or product label. Thaw begins when the infusion bag is removed from LN₂ storage



*ABECMA is stable for 2 hours at room temperature once thawed.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

ABECMA[®] Thawing^{1,6} (cont'd)

Step 2

Thaw ABECMA at approximately 37 °C using an approved thaw device or water bath until there is no visible ice in the infusion bag.

- Gently mix the contents of the bag to disperse clumps of cellular material. If visible cell clumps remain, continue to gently mix the contents of the bag. Small clumps of cellular material should disperse with gentle manual mixing
- **DO NOT** walk away from the thawing product
- **DO NOT** wash, spin down, and/or resuspend ABECMA in new media prior to infusion

If more than 1 infusion bag has been received for treatment, thaw each infusion bag 1 at a time.

Step 3

If thawing in a cell therapy lab, transport ABECMA to bedside in an insulated room temperature carrier. Note: thaw begins at time ABECMA is removed from frozen storage.

Provide the RFI certificate to the staff performing product administration.

Repeat

Follow the same procedure for all subsequent infusion bags for the identified patient.

IMPORTANT SAFETY INFORMATION (cont'd)

Infections (cont'd): *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. Consider antiviral therapy to prevent viral reactivation per local institutional guidelines/clinical practice.

Prolonged Cytopenias: In patients receiving ABECMA in the KarMMA and KarMMA-3 studies, 40% of patients (139/349) experienced prolonged Grade 3 or 4 neutropenia and 42% (145/349) experienced prolonged Grade 3 or 4 thrombocytopenia that had not resolved by Month 1 following ABECMA infusion. In 89% (123/139) 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 76% (110/145) of patients who recovered from Grade 3 or 4 thrombocytopenia, the median time to recovery was 1.9 months. Five patients underwent stem cell therapy for hematopoietic reconstitution due to prolonged cytopenia. The rate of Grade 3 or 4 thrombocytopenia was 62% (44/71) and 56% (135/241) for patients treated in dose range of 460 to 510 x 10⁶ CAR-positive T cells and 300 to 460 x 10⁶ CAR-positive T cells, respectively.

Monitor blood counts prior to and after ABECMA infusion. Manage cytopenia with myeloid growth factor and blood product transfusion support according to local institutional guidelines.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

ABECMA[®] Infusion Process

After obtaining the RFI certificate, ensure that the following steps are completed immediately before administering ABECMA^{1,2,6}:

- ✔ Conduct a general nursing assessment
- ✔ Check for fever or infection, monitor complete blood counts, and confirm the patient can appropriately receive ABECMA
- ✔ Confirm that the patient has been appropriately premedicated
- ✔ Determine peripheral or central venous access
- ✔ Confirm 1 hour after thaw has not passed
- ✔ Tubing of the infusion set has been primed with normal saline
- ✔ Gently massage the thawed infusion bag and attach it to the administration set

NOTE: The ABECMA infusion bags should be administered in series. If more than 1 infusion bag is required for administration, **keep the remaining bag(s) in LN₂ storage until prior bag has been infused and patient is ready; proceed to the subsequent infusion bag based on clinical judgment.** Each infusion bag should be infused within 1 hour of the start of its thaw.*

*ABECMA is stable for 2 hours at room temperature once thawed.

IMPORTANT SAFETY INFORMATION (cont'd)

Hypogammaglobulinemia: In all patients receiving ABECMA in the KarMMa and KarMMa-3 studies, hypogammaglobulinemia was reported as an adverse event in 13% (46/349) of patients; laboratory IgG levels fell below 500 mg/dL after infusion in 37% (130/349) of patients treated with ABECMA.

Hypogammaglobulinemia either as an adverse reaction or laboratory IgG level below 500 mg/dL after infusion occurred in 45% (158/349) of patients treated with ABECMA. Forty-one percent of patients received intravenous immunoglobulin (IVIG) post-ABECMA for serum IgG <400 mg/dL.

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

Use of Live Vaccines: The safety of immunization with live viral vaccines during or after 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.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

ABECMA® Infusion Process (cont'd)

4. Prior to ABECMA administration⁶

STOP AND CONFIRM PATIENT ID

Two site staff are required to verify the patient information on the ABECMA RFI certificate matches the cassette labels and bag labels:

- Patient's first and last name
- Patient's date of birth
- JOIN[†]

Site staff must verify patient information on product labels against the patient's medical records, as well as verbally with the patient prior to infusion.

Each infusion bag should be infused within 1 hour from start of thaw^{1,6}

Step 1

Infuse the contents of the infusion bag by gravity flow

Step 2

After the entire contents of the infusion bag have been infused, flush the tubing with 30 to 60 mL of normal saline at the same infusion rate to ensure all of the cells are delivered

Step 3

If more than 1 infusion bag is being administered, repeat the procedure (thawing through saline flush) to administer subsequent infusion bags of ABECMA in series

[†]The JOIN is a unique identification code that is assigned to the patient's specific cellular material and is the link between the patient and their cells throughout the manufacturing process.

IMPORTANT SAFETY INFORMATION (cont'd)

Secondary Malignancies: Patients treated with ABECMA may develop secondary malignancies. In KarMMa-3, myeloid neoplasms (four cases of myelodysplastic syndrome and one case of acute myeloid leukemia) occurred in 2.2% (5/222) of patients following treatment with ABECMA compared to none in the standard regimens arm at the time of the safety update. The median time to onset of myeloid neoplasm from ide-cel infusion was 338 days (Range: 277 to 794 days). Three of these five patients have died following the development of myeloid neoplasm. One out of the five cases of myeloid neoplasm occurred after initiation of subsequent antimyeloma therapy.

T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA. Mature T cell malignancies, including CAR-positive tumors, may present as soon as weeks following infusion, and may include fatal outcomes.

Monitor life-long for secondary malignancies. In the event that a secondary malignancy occurs, contact Bristol-Myers Squibb at 1-888-805-4555 for reporting and to obtain instructions on collection of patient samples for testing of secondary malignancy.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.



Early death:

- In KarMMa-3, a randomized (2:1), controlled trial, a higher proportion of patients experienced death within 9 months after randomization in the ABECMA arm (45/254; 18%) compared with the standard regimens arm (15/132; 11%)
- Early deaths occurred in 8% (20/254) and 0% prior to patients to ABECMA infusion and standard regimen administration infusion, respectively, and 10% (25/254) and 11% (15/132) after ABECMA infusion and standard regimen administration, respectively
- Of the 20 deaths that occurred prior to ABECMA infusion, 15 occurred from disease progression, 3 occurred from adverse events and 2 occurred from unknown causes. Of the 25 deaths that occurred after ABECMA infusion, 10 occurred from disease progression, 11 occurred from adverse events, and 4 occurred from unknown causes

Before selecting ABECMA, please consider the elements of KarMMa-3 trial design, such as patient inclusion criteria and treatment approach.

Cytokine Release Syndrome

During administration and at least daily for the first 7 days following ABECMA[®] infusion, monitor your patients at the certified healthcare facility for adverse reactions¹

These reactions can include CRS and neurologic toxicity:

- Refer to the CRS and neurologic toxicity tables on pages 28-29 and 32-33 for grading and management
- Accurate grading is imperative for appropriate management

CRS across registrational studies (N=349)^{1*}

Median time to onset

1 day

Range: 1 to 27 days

Median time to resolution

5 days

Range: 1 to 63 days

All grades

89%

(n=310)

Grades ≥ 3

7%

(n=23)

Grade 5: 0.9%

(n=3)

CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA.

*Pooled registrational studies included KarMMa-3 and KarMMa (5L+).

[†]Lee criteria for grading CRS (Lee et al, 2014).

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

Cytokine Release Syndrome (cont'd)

Monitoring and management of CRS¹

- **Counsel** patients to seek immediate medical attention should signs or symptoms of CRS occur at any time
 - Symptoms of CRS include fever, difficulty breathing, dizziness or light-headedness, nausea, headache, fast heartbeat, low blood pressure, or fatigue
- **Instruct** patients to remain within proximity of the certified healthcare facility for at least 4 weeks following infusion
- **Monitor** patients for signs and symptoms of CRS
 - At least daily for 7 days at the certified healthcare facility following ABECMA infusion
 - For at least 4 weeks after ABECMA infusion
- **Treat** at the first sign of CRS with supportive care, tocilizumab, and/or corticosteroids as needed based on the grading and management guidelines
 - If CRS is suspected, manage according to the recommendations in the full Prescribing Information
 - If concurrent CRS is suspected during an NT event, manage CRS according to the recommendations in the full Prescribing Information
- **Ensure** that a minimum of 2 doses of tocilizumab per patient are available prior to infusion of ABECMA

CRS Treatment

- **Treat** at the first sign of CRS with supportive care, tocilizumab, and/or corticosteroids as indicated
- 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
 - In patients with progressive symptoms of CRS or refractory CRS despite treatment, evaluate for evidence of HLH/MAS
 - 65% (226/349) of patients received tocilizumab
 - 39% (135/349) received a single dose
 - 26% (91/349) received more than 1 dose
- Overall, 24% (82/349) of patients received at least 1 dose of corticosteroids for treatment of CRS
 - All patients who received corticosteroids for CRS also received tocilizumab

If CRS is suspected, manage according to the recommendations in the tables on pages 28-29.

HLH/MAS=hemophagocytic lymphohistiocytosis/macrophage activation syndrome.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

Cytokine Release Syndrome (cont'd)

CRS grading from the ABECMA® Prescribing Information^{1*}

Grade 1	Symptoms require symptomatic treatment only (eg, fever, nausea, fatigue, headache, myalgia, malaise).
Grade 2	Symptoms require and respond to moderate intervention. Oxygen requirement <40% FiO ₂ or hypotension responsive to fluids, or low dose of 1 vasopressor, or Grade 2 organ toxicity.
Grade 3	Symptoms require and respond to aggressive intervention. Fever, oxygen requirement ≥40% FiO ₂ , or hypotension requiring high-dose or multiple vasopressors, or Grade 3 organ toxicity or Grade 4 transaminitis.
Grade 4	Life-threatening symptoms. Requirements for ventilator support, continuous veno-venous hemodialysis (CVVHD), or Grade 4 organ toxicity (excluding transaminitis).



The ASTCT Consensus Grading system is another guideline for evaluating cell therapy-associated CRS.⁸ Please refer to these guidelines for additional information.

ASTCT=American Society for Transplantation and Cellular Therapy.

Please see Important Safety Information throughout and click here for full Prescribing Information, including **Boxed WARNINGS** and Medication Guide.

Cytokine Release Syndrome (cont'd)

CRS management guidance from the ABECMA Prescribing Information^{1*}

Tocilizumab [†]	Corticosteroids [‡]
Grade 1	
<p>If onset ≥72 hours after infusion, treat symptomatically.</p> <p>If onset <72 hours after infusion, consider tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg).</p>	<p>Consider dexamethasone 10 mg IV every 24 hours.</p>
Grade 2	
<p>Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg).</p> <p>Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen.</p> <p>Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.</p>	<p>Consider dexamethasone 10 mg IV every 12-24 hours.</p>
<p>If no improvement within 24 hours or rapid progression, repeat tocilizumab and escalate dose and frequency of dexamethasone (20 mg IV every 6 to 12 hours).</p> <p>If no improvement within 24 hours or continued rapid progression, switch to methylprednisolone 2 mg/kg followed by 2 mg/kg divided 4 times per day. After 2 doses of tocilizumab, consider alternative anticytokine agents. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.</p>	
Grade 3	
<p>Per Grade 2.</p>	<p>Administer dexamethasone 10 mg IV every 12 hours.</p>
<p>If no improvement within 24 hours or rapid progression, repeat tocilizumab and escalate dose and frequency of dexamethasone (20 mg IV every 6 to 12 hours).</p> <p>If no improvement within 24 hours or continued rapid progression, switch to methylprednisolone 2 mg/kg followed by 2 mg/kg divided 4 times per day. After 2 doses of tocilizumab, consider alternative anticytokine agents. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.</p>	
Grade 4	
<p>Per Grade 2.</p>	<p>Administer dexamethasone 20 mg IV every 6 hours.</p>
<p>After 2 doses of tocilizumab, consider alternative anticytokine agents. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total. If no improvement within 24 hours, consider methylprednisolone (1-2 g, repeat every 24 hours if needed; taper as clinically indicated) or other anti-T cell therapies.</p>	

^{*}Lee criteria for grading CRS (Lee et al 2014).

[†]Refer to tocilizumab Prescribing Information for details.

[‡]If corticosteroids are initiated, continue corticosteroids for at least 3 doses, and taper over a maximum of 7 days.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

Neurologic Toxicity

Neurologic toxicity across registrational studies (N=349)^{1*}

Median time to onset

2 days

Range: 1 to 148 days

All grades

40%

(n=139)

Median time to resolution

5 days[†]

Range: 1 to 245 days

In 123 of 139 patients who had resolved neurologic toxicity

Grades 3-4

4.6%

(n=16)

1 Grade 5 neurologic toxicity event was observed

- Cerebral edema has been associated with ABECMA[®] in a patient in another study in multiple myeloma
- Neurologic toxicities, which may be severe or life-threatening, including immune-effector cell-associated neurotoxicity (ICANS), occurred following treatment with ABECMA, including concurrently with CRS, after CRS resolution, or in the absence of CRS

No cases of parkinsonism or Guillain-Barré syndrome were observed across registrational studies^{8†}

Through September 2023, BMS safety reporting analysis notes that out of 3243 cases seen with ABECMA, there were^{9-11§}:

- 5 cases of parkinsonism
- 0 cases of Guillain-Barré syndrome

*Pooled registrational studies included KarMMa-3 and KarMMa (5L+).

[†]The median duration of CAR T cell-associated neurotoxicity was 8 days (range: 1 to 720 days) in all patients including those with ongoing neurologic events at the time of death or data cutoff.

[‡]Grade 3 myelitis and grade 3 parkinsonism have occurred after treatment with ABECMA in another study in multiple myeloma. National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) criteria (version 4.03) utilized for grading neurologic toxicities.

[§]Of the 3243, patients span clinical trials (744) and real-world safety reporting on commercial product (2622). Identification of adverse events in real-world setting is dependent on physician reporting and grading perspectives. Post-marketing surveillance is voluntary.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

Neurologic Toxicity (cont'd)

Monitoring and management of neurologic toxicity¹

- **Counsel** patients to seek immediate medical attention should signs or symptoms of neurologic toxicity occur at any time
- **Instruct** patients to remain within proximity of the certified healthcare facility for at least 4 weeks following infusion
- **Monitor** patients for signs and symptoms of neurologic toxicity
 - At least daily for 7 days at the certified healthcare facility following ABECMA infusion
 - For at least 4 weeks after ABECMA infusion
- **Exclude** other causes of neurologic signs or symptoms
- **Treat** promptly with supportive care and/or corticosteroids as needed based on the grading and management guidelines
 - If neurologic toxicity is suspected, manage according to the recommendations in the full Prescribing Information
 - If concurrent CRS is suspected during the neurologic toxicity event, manage CRS according to the recommendations in the full Prescribing Information
 - Patients with any-grade neurologic toxicity should be treated with non-sedating antiseizure medicine for seizure prophylaxis

If neurologic toxicity is suspected, manage according to the recommendations in the table on pages 32-33.

Management recommendations from the Prescribing Information for each grade of CRS and neurologic toxicity are outlined in the tables on pages 28-29 and 32-33, respectively.

Neurologic Toxicity (cont'd)

Neurologic toxicity management guidance from the ABECMA® Prescribing Information¹

Grade*	Corticosteroids and antiseizure medicines
Grade 1	<p>Start non-sedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis.</p> <p>If ≥72 hours after infusion, observe patient.</p> <p>If <72 hours after infusion, consider dexamethasone 10 mg IV every 12 to 24 hours for 2 to 3 days.</p>
Grade 2	<p>Start non-sedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis.</p> <p>Start dexamethasone 10 mg IV every 12 hours for 2 to 3 days, or longer for persistent symptoms. Consider taper for a total steroid exposure of >3 days. Steroids are not recommended for isolated Grade 2 headaches.</p> <p>If no improvement after 24 hours or worsening of NT, increase the dose and/or frequency of dexamethasone up to a maximum of 20 mg IV every 6 hours.</p>

*NCI CTCAE criteria was used for grading neurologic toxicities.

Please see Important Safety Information throughout and click here for full Prescribing Information, including **Boxed WARNINGS** and Medication Guide.

Neurologic Toxicity (cont'd)

Grade*	Corticosteroids and antiseizure medicines
Grade 3	<p>Start non-sedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis.</p> <p>Start dexamethasone 10 to 20 mg IV every 6 to 12 hours. Steroids are not recommended for isolated Grade 3 headaches.</p> <p>If no improvement after 24 hours or worsening of NT, escalate to methylprednisolone (2 mg/kg loading dose, followed by 2 mg/kg divided into 4 times a day; taper within 7 days).</p> <p>If cerebral edema is suspected, consider hyperventilation and hyperosmolar therapy. Give high-dose methylprednisolone (1 to 2 g, repeat every 24 hours if needed; taper as clinically indicated) and cyclophosphamide 1.5 g/m².</p>
Grade 4	<p>Start non-sedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis.</p> <p>Start dexamethasone 20 mg IV every 6 hours.</p> <p>If no improvement after 24 hours or worsening of NT, escalate to high-dose methylprednisolone (1 to 2 g, repeated every 24 hours if needed; taper as clinically indicated).</p> <p>If cerebral edema is suspected, consider hyperventilation and hyperosmolar therapy. Give high-dose methylprednisolone (1 to 2 g, repeat every 24 hours if needed; taper as clinically indicated), and cyclophosphamide 1.5 g/m².</p>

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HLH/MAS and Prolonged Cytopenias

HLH/MAS across registrational studies (N=349)^{1*}

- HLH/MAS occurred in 2.9% (10/349) of patients
- All events of HLH/MAS had onset within 10 days of receiving ABECMA[®] and occurred in the setting of ongoing or worsening CRS
- Median time to onset was 6.5 days (range: 4 to 10 days)
- Five patients had overlapping neurotoxicity

Prolonged cytopenias¹

Patients received ABECMA across a dose range of 175 to 529 x 10⁶ CAR-positive T cells (median dose: 445 x 10⁶ CAR-positive T cells)

Across registrational studies (N=349):

- Prolonged neutropenia rates: 40% grade ≥3 (n=139)
 - Median time to recovery was 1.9 months in 89% (n=123) of patients who recovered from grade 3 or 4 neutropenia after Month 1
- Prolonged thrombocytopenia rates: 42% grade ≥3 (n=145)
 - Median time to recovery was 1.9 months in 76% (n=110/145) of patients who recovered from grade 3 or 4 thrombocytopenia

Secondary Malignancies

- In KarMMa-3, myeloid neoplasms (4 cases of myelodysplastic syndrome and 1 case of acute myeloid leukemia) occurred in 2.2% (5/222) of patients following treatment with ABECMA compared to none in the control arm at the time of the safety update
- Median time to onset of myeloid neoplasm from ABECMA infusion was 338 days (range: 277 to 794 days); 3 out of 5 of these patients died following the development of myeloid neoplasm

T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA. Monitor life-long for secondary malignancies.

¹Not resolved by Month 1 following ABECMA infusion.

HLH/MAS=hemophagocytic lymphohistiocytosis/macrophage activation syndrome.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.



ABECMA Safety Profile

Most common adverse reactions¹

- The most common nonlaboratory adverse reactions (incidence $\geq 20\%$) included pyrexia, CRS, hypogammaglobulinemia, infections–pathogen unspecified, musculoskeletal pain, fatigue, febrile neutropenia, hypotension, tachycardia, diarrhea, nausea, headache, chills, upper respiratory tract infection, encephalopathy, edema, dyspnea, and viral infections
- The most common grade 3 or 4 laboratory adverse reactions (incidence $\geq 50\%$) included leukocyte count decreased, neutrophil count decreased, lymphocyte count decreased, platelet count decreased, and hemoglobin decreased

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ABECMA[®] Safety Profile (cont'd)

Adverse reactions observed in at least 10% of patients treated with ABECMA in the KarMMa-3 study (N=222)¹

	Any Grade (%)	Grade 3 or Higher (%)
Cardiac disorders		
Tachycardia ^a	32	0
Gastrointestinal disorders		
Diarrhea ^b	31	2.3
Nausea	27	0.9
Constipation	17	0
Vomiting ^c	14	0
General disorders and administration site conditions		
Pyrexia	91	9
Fatigue ^d	33	1.4
Edema ^e	20	0.5
Immune system disorders		
Cytokine release syndrome	91	4.1
Hypogammaglobulinemia	48	0.9
Infections and infestations		
Infections—Pathogen unspecified ^f	35	9
Infections—Viral ^f	18	5
Infections—Bacterial ^f	15	4.5

^aTachycardia includes heart rate increased, sinus tachycardia, tachycardia.

^bDiarrhea includes colitis, colitis microscopic, diarrhea, enterocolitis.

^cVomiting includes retching, vomiting.

^dFatigue includes asthenia, fatigue, malaise, muscle fatigue.

^eEdema includes edema, edema peripheral, generalized edema, peripheral swelling, swelling, eyelid edema, face edema, fluid retention, hypervolemia, localized edema, mouth swelling, periorbital edema, periorbital swelling, swelling face.

^fInfections and infestations System Organ Class Adverse Events are grouped by high level grouped term (HLGT) pathogen type.

Please see Important Safety Information throughout and click here for full Prescribing Information, including **Boxed WARNINGS** and **Medication Guide**.

ABECMA® Safety Profile (cont'd)

	Any Grade (%)	Grade 3 or Higher (%)
Metabolism and nutrition disorders		
Decreased appetite	17	1.8
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain ^g	36	1.8
Nervous system disorders		
Headache ^h	24	0
Encephalopathy ⁱ	22	3.6
Dizziness ^j	14	1.8
Psychiatric disorders		
Sleep disorder ^k	11	0

^gMusculoskeletal pain includes arthralgia, back pain, bone pain, joint stiffness, muscle strain, musculoskeletal chest pain, musculoskeletal discomfort, musculoskeletal pain, musculoskeletal stiffness, myalgia, neck pain, non-cardiac chest pain.

^hHeadache includes headache, head discomfort.

ⁱEncephalopathy includes amnesia, cognitive disorder, confusional state, depressed level of consciousness, disturbance in attention, dysgraphia, encephalopathy, Immune effector cell-associated neurotoxicity syndrome incoherent, lethargy, memory impairment, mental status changes, metabolic encephalopathy, somnolence, stupor, toxic encephalopathy.

^jDizziness includes dizziness, presyncope, syncope, vertigo, vertigo positional, vestibular disorder.

^kSleep disorder includes hypersomnia, insomnia, sleep disorder.

Please see Important Safety Information throughout and click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.

ABECMA[®] Safety Profile (cont'd)

Adverse reactions observed in at least 10% of patients treated with ABECMA in the KarMMa-3 study (N=222)¹

	Any Grade (%)	Grade 3 or Higher (%)
Renal and urinary disorders		
Renal failure ^l	11	4.1
Respiratory, thoracic, and mediastinal disorders		
Dyspnea ^m	21	1.8
Cough ⁿ	14	0
Vascular disorders		
Hypotension ^o	36	2.3
Hypertension	14	7

^lRenal failure includes acute kidney injury, blood creatinine increased, chronic kidney disease, creatinine renal clearance decreased, glomerular filtration rate decreased, nephropathy toxic, oliguria, renal failure, renal impairment, urine output decreased.

^mDyspnea includes dyspnea, dyspnea exertional, dyspnea paroxysmal nocturnal, tachypnea.

ⁿCough includes cough, productive cough, upper-airway cough syndrome.

^oHypotension includes hemodynamic instability, hypotension, orthostatic hypotension.

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ABECMA® Safety Profile (cont'd)

Grade 3 or 4 laboratory abnormalities worsening from baseline in $\geq 10\%$ of patients treated with ABECMA in the KarMMa-3 study¹

	170-529 x 10 ⁶ CAR-Positive T Cells (N=222)
	Grade 3 or 4 (%)
Lymphocyte decreased	98
Leukocyte decreased	96
Neutrophil decreased	96
Platelet decreased	59
Hemoglobin decreased	52
Phosphate decreased	45
Triglyceride increased	21
Alanine aminotransferase increased	13
Sodium decreased	11
Gamma-glutamyltransferase increased	10

Laboratory tests were graded according to NCI CTCAE Version 4.03. Laboratory abnormalities are sorted by decreasing frequency.

Please see Important Safety Information throughout and [click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.](#)

Returning the LN₂ Dry Vapor Shipper⁶

1. Load the cassette rack into the inner chamber of the outer container and replace the inner chamber lid
2. Remove shipping pouch from the pocket inside the outer container. The shipping pouch contains the FedEx[®] return label and an “EMPTY” label
3. Remove the “EMPTY” label from the shipping pouch and place “EMPTY” label on one of the metal plates on the outer container
4. Seal the shipping pouch containing the FedEx[®] return label, remove sticker backing, and place FedEx[®] return label on the other metal plate on the outer container
5. Close the outer container lid and lock the latch by turning the key to the right
6. Place LN₂ dry vapor shipper in scheduled pickup location or contact Bristol Myers Squibb at 1-888-805-4555 to schedule a pickup

NOTE: Cassettes should be disposed of on site after administration of ABECMA[®].

IMPORTANT SAFETY INFORMATION (cont'd)

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 pyrexia, CRS, hypogammaglobulinemia, infections – pathogen unspecified, musculoskeletal pain, fatigue, febrile neutropenia, hypotension, tachycardia, diarrhea, nausea, headache, chills, upper respiratory tract infection, encephalopathy, edema, dyspnea and viral infections.

Please see Important Safety Information throughout and [click here for full Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

Transition Back to Primary Oncologist

Considerations^{1,12}

After at least 4 weeks of monitoring by the certified healthcare facility, the patient may return to the primary oncologist for continued monitoring and routine care appointments. Consider the following before returning your patients to home care:

- **Before transitioning care**, regularly meet with your patients to discuss the treatment they received, side effects, medications, infection prevention, and immunization recommendations
- **Provide** updated medical records and confirm home care is appropriate
- **Transition care** back to the primary oncologist or hematologist within 7 days



IMPORTANT SAFETY INFORMATION (cont'd)

Early Death: In KarMMa-3, a randomized (2:1), controlled trial, a higher proportion of patients experienced death within 9 months after randomization in the ABECMA arm (45/254; 18%) compared to the standard regimens arm (15/132; 11%). Early deaths occurred in 8% (20/254) and 0% prior to ABECMA infusion and standard regimen administration, respectively, and 10% (25/254) and 11% (15/132) after ABECMA infusion and standard regimen administration, respectively. Out of the 20 deaths that occurred prior to ABECMA infusion, 15 occurred from disease progression, 3 occurred from adverse events and 2 occurred from unknown causes. Out of the 25 deaths that occurred after ABECMA infusion, 10 occurred from disease progression, 11 occurred from adverse events, and 4 occurred from unknown causes.

Cytokine Release Syndrome (CRS): CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA. Among patients receiving ABECMA for relapsed refractory multiple myeloma in the KarMMa and KarMMa-3 studies (N=349), CRS occurred in 89% (310/349), including \geq Grade 3 CRS (Lee grading system) in 7% (23/349) of patients and Grade 5 CRS in 0.9% (3/349) of patients. The median time-to-onset of CRS, any grade, was 1 day (range: 1 to 27 days), and the median duration of CRS was 5 days (range: 1 to 63 days). In the pooled studies, the rate of \geq Grade 3 CRS was 10% (7/71) for patients treated in dose range of 460 to 510 x 10⁶ CAR-positive T cells and 5.4% (13/241) for patients treated in dose range of 300 to 460 x 10⁶ CAR-positive T cells.

Please see Important Safety Information throughout and [click here for full Prescribing Information, including Boxed WARNINGS and Medication Guide.](#)

Long-Term Monitoring

Warnings and precautions include¹:

- **CRS:** 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
- **NT:** NT, 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
- **HLH/MAS:** HLH/MAS, including fatal and life-threatening reactions, occurred in patients following treatment with ABECMA. HLH/MAS can occur with CRS or NT
- **Prolonged cytopenias:** Prolonged cytopenia with bleeding and infection, including fatal outcomes, occurred following treatment with ABECMA. Patients may exhibit Grade 3 or higher cytopenias for several weeks following pretreatment and ABECMA infusion. Monitor complete blood counts prior to and after ABECMA infusion

IMPORTANT SAFETY INFORMATION (cont'd)

Cytokine Release Syndrome (CRS) (cont'd): The most common manifestations of CRS (greater than or equal to 10%) included pyrexia (87%), hypotension (30%), tachycardia (26%), chills (19%), hypoxia (16%). Grade 3 or higher events that may be associated with CRS include hypotension, hypoxia, hyperbilirubinemia, hypofibrinogenemia, ARDS, atrial fibrillation, hepatocellular injury, metabolic acidosis, pulmonary edema, coagulopathy, renal failure, multiple organ dysfunction syndrome and HLH/MAS.

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.

Of the 349 patients who received ABECMA in clinical trials, 226 (65%) patients received tocilizumab; 39% (135/349) received a single dose, while 26% (91/349) received more than 1 dose of tocilizumab. Overall, 24% (82/349) of patients received at least 1 dose of corticosteroids for treatment of CRS. Almost all patients who received corticosteroids for CRS also received tocilizumab. For patients treated in dose range of 460 to 510 x 10⁶ CAR-positive T cells, 76% (54/71) of patients received tocilizumab and 35% (25/71) received at least 1 dose of corticosteroids for treatment of CRS. For patients treated in dose range of 300 to 460 x 10⁶ CAR-positive T cells, 63% (152/241) of patients received tocilizumab and 20% (49/241) received at least 1 dose of corticosteroid for treatment of CRS.

Monitor patients at least daily for 7 days following ABECMA infusion at the REMS-certified healthcare facility for signs or symptoms of CRS and monitor patients for signs or symptoms of CRS for at least 4 weeks after ABECMA infusion. At the first sign of CRS, institute treatment with supportive care, tocilizumab and/or corticosteroids as indicated. Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of ABECMA. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

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Long-Term Monitoring (cont'd)

- **Hypersensitivity reactions:** Monitor for hypersensitivity reactions during infusion
- **Infections:** Monitor patients for signs and symptoms of infection; treat appropriately
- **Hypogammaglobulinemia:** Monitor immunoglobulin levels after treatment. Manage using infection precautions, antibiotic or antiviral prophylaxis, and immunoglobulin replacement
- **Use of live vaccines:** Not recommended for at least 6 weeks prior to lymphodepleting chemotherapy, during treatment with ABECMA, and until immune recovery following treatment
- **Secondary malignancies:** Monitor life-long. In the event that 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 use machines:** Advise patients to refrain from driving or operating heavy or potentially dangerous machines for at least 8 weeks after ABECMA administration

IMPORTANT SAFETY INFORMATION (cont'd)

Neurologic Toxicities: Neurologic toxicities, including immune-effector cell-associated neurotoxicity (ICANS), which may be severe or life-threatening, occurred concurrently with CRS, after CRS resolution, or in the absence of CRS following treatment with ABECMA.

In patients receiving ABECMA in the KarMMa and KarMMa-3 studies, CAR T cell-associated neurotoxicity occurred in 40% (139/349), including Grade 3 in 4% (14/349) and Grade 4 in 0.6% (2/349) of patients. The median time to onset of neurotoxicity was 2 days (range: 1 to 148 days). The median duration of CAR T cell-associated neurotoxicity was 8 days (range: 1 to 720 days) in all patients including those with ongoing neurologic events at the time of death or data cut off. CAR T cell-associated neurotoxicity resolved in 123 of 139 (88%) patients and median time to resolution was 5 days (range: 1 to 245 days). One-hundred and thirty four out of 349 (38%) patients with neurotoxicity had CRS. The onset of neurotoxicity during CRS was observed in 93 patients, before the onset of CRS in 12 patients, and after the CRS event in 29 patients. The rate of Grade 3 or 4 CAR T cell-associated neurotoxicity was 5.6% (4/71) and 3.7% (9/241) for patients treated in dose range of 460 to 510 x 10⁶ CAR-positive T cells and 300 to 460 x 10⁶ CAR-positive T cells, respectively. The most frequent (greater than or equal to 5%) manifestations of CAR T cell-associated neurotoxicity include encephalopathy (21%), headache (15%), dizziness (8%), delirium (6%), and tremor (6%).

At the safety update for KarMMa-3 study, one patient developed fatal neurotoxicity 43 days after ABECMA. In KarMMa, 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.

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INDICATION

ABECMA (idecabtagene vicleuce) 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 two or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAS, PROLONGED CYTOPENIA and SECONDARY HEMATOLOGICAL MALIGNANCIES

- 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.
- T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA
- ABECMA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS.

Please see Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

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