Abecma™
(idecabtagene vicleucel) SUSPENSION FOR IV INFUSION

# ABECMA® Monitoring and Management Guide

## Explore presentation, monitoring, and management information for adverse events following ABECMA infusion

### Indication

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

### IMPORTANT SAFETY INFORMATION

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

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

Please see additional Important Safety Information on pages **21-25,** and click here for full **Prescribing Information,** including **Boxed WARNINGS**.

This guide is interactive, with navigation buttons available in the Table of Contents below and at the top of each content page for quick access to select adverse event information

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# ABECMA® Monitoring Timeline Post-Infusion[1]

During administration and at least daily for 7 days following ABECMA infusion, monitor your patients at the certified healthcare facility for adverse reactions

**ABECMA Infusion**

**Short-term monitoring**

- Administer ABECMA **2 days** after the completion of lymphodepleting chemotherapy* at a REMS-certified healthcare facility
- Monitor patients at least daily for **7 days** following ABECMA infusion at the certified healthcare facility for signs and symptoms of CRS and NTs

**Long-term monitoring**

- Instruct patients to remain within proximity (2 hours) of the certified healthcare facility for at least **4 weeks** following infusion. A dedicated caregiver is encouraged for post-infusion support
- Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery for at least **8 weeks** following infusion

**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 of T cell origin

CRS=cytokine release syndrome; IV=intravenous; NT=neurologic toxicity; REMS=Risk Evaluation and Mitigation Strategy.
*Lymphodepleting chemotherapy regimen: fludarabine 30 mg/m$^2$/day IV and cyclophosphamide 300 mg/m$^2$/day IV for 3 days. See the prescribing information of cyclophosphamide and fludarabine for information on dose adjustment in renal impairment.

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# Cytokine Release Syndrome[1,2]

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Overview | Management Table

## Incidence* in the KarMMa Trial

150-450 x $10^6$ CAR-positive T cells (N=127)

**Median time to onset**

1 DAY

Range: 1-23 days

**Median duration**

7 DAYS

Range: 1-63 days

**9% Grade ≥3 (n=12)**

**85% All grades (n=108)**

46% Grade 1 (n=58) / 30% Grade 2 (n=38)

Grade 5 CRS was reported in one (0.8%) patient

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

### Most common manifestations of CRS (N=127)

| | | | |
|---|---|---|---|
| PYREXIA | 98% | HYPOXIA | 20% |
| HYPOTENSION | 41% | FATIGUE | 12% |
| TACHYCARDIA | 35% | HEADACHE | 10% |
| CHILLS | 31% | | |

## Monitoring and Management

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

**Ensure** that a minimum of 2 doses of tocilizumab per patient are available prior to infusion of ABECMA

**Treat** at the first sign of CRS with supportive care, tocilizumab, and/or corticosteroids as needed based on the **grading and management guidelines**

- If concurrent NT is suspected during CRS, manage NT and CRS according to the recommendations in the full Prescribing Information

**Patients in the KarMMa trial received tocilizumab and corticosteroids for management of CRS**

**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**

Patients who experience CRS should be closely monitored for cardiac and organ function until resolution of symptoms

- For severe or life-threatening CRS, consider intensive care unit level monitoring and supportive therapy
- Patients who experience Grade 2 or higher CRS should be monitored with continuous cardiac telemetry and pulse oximetry

HLH/MAS=Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome.
*Lee criteria for grading CRS (Lee et al, 2014).

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# Cytokine Release Syndrome[1,2]

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Overview | Management Table

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**Treat** at the first sign of CRS with supportive care, tocilizumab, and/or corticosteroids as needed based on the grading and management guidelines

- If concurrent … dations in the full Prescribing Inf…

Patients in th… of CRS

**Identify** CRS … fever, hypoxia, and hypotens…

- CRS has been … syndromes may overlap. In patients with progressive symptoms of CRS or refractory CRS despite treatment, **evaluate for evidence of HLH/MAS**

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- Patients who experience Grade 2 or higher CRS should be monitored with continuous cardiac telemetry and pulse oximetry

**CRS management in the KarMMa trial**

- 54% (68/127) of patients received tocilizumab
  - 35% (45/127) received a single dose
  - 18% (23/127) received more than 1 dose
- Overall, 15% (19/127) of patients received at least 1 dose of corticosteroids for treatment of CRS
  - All patients that received corticosteroids for CRS also received tocilizumab

HLH/MAS=Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome.
*Lee criteria for grading CRS (Lee et al, 2014).

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# Cytokine Release Syndrome[1,2]

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After 2 doses of tocilizumab, consider alternative anticytokine agents; do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses total

| CRS Grade (Lee criteria, 2014)[3] | When to Use Tocilizumab* | When to Use Corticosteroids† |
|---|---|---|
| Grade 1 | • If onset ≥72 hours after infusion, treat symptomatically<br>• If onset <72 hours after infusion, consider tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg) | Consider dexamethasone 10 mg IV every 24 hours |
| Grade 2 | • Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg)<br>• Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen | Consider dexamethasone 10 mg IV every 12-24 hours |
| | • 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)<br>• 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 | |
| Grade 3 | • Per Grade 2 | Administer dexamethasone 10 mg IV every 12 hours |
| | • 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)<br>• 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 | |
| Grade 4 | • Per Grade 2 | Administer dexamethasone 20 mg IV every 6 hours |
| | • 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 | |

There are other guidelines that exist for evaluating cell therapy-associated CRS. Please refer to your institutional guidelines.

CVVHD=continuous veno-venous hemodialysis; $FiO_2$=fraction of inspired oxygen.
*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.

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# Cytokine Release Syndrome[1,2]

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After 2 doses of tocilizumab, consider alternative anticytokine agents; do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses total

| CRS Grade (Lee criteria, 2014)[3] | When to Use Tocilizumab* | When to Use Corticosteroids† |
|---|---|---|
| Grade | over 1 hour (not to exceed 800 mg) | Consider dexamethasone 10 mg IV every 24 hours |
| Grade | 0 mg)<br>intravenous fluids or increasing | Consider dexamethasone 10 mg IV every 12-24 hours |
| | cilizumab and escalate dose and frequency of dexamethasone (20 mg IV every 6 to 12 hours)<br>, switch to methylprednisolone 2 mg/kg followed by 2 mg/kg divided 4 times per day | |
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| | cilizumab and escalate dose and frequency of dexamethasone (20 mg IV every 6 to 12 hours)<br>, switch to methylprednisolone 2 mg/kg followed by 2 mg/kg divided 4 times per day | |
| Grade | | Administer dexamethasone 20 mg IV every 6 hours |
| | -2 g, repeat every 24 hours if needed; taper as clinically indicated) or other anti-T cell therapies | |

**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 vasopresor, 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 or CVVHD, OR
- Grade 4 organ toxicity (excluding transaminitis)

There are other guidelines that exist for evaluating cell therapy-associated CRS. Please refer to your institutional guidelines.

CVVHD=continuous veno-venous hemodialysis; $FiO_2$=fraction of inspired oxygen.
*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.

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# Neurologic Toxicity[1,2]

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## Incidence in the KarMMa Trial

150-450 x $10^6$ CAR-positive T cells (N=127)

**Median time to onset**

2 DAY

Range: 1-42 days

**Median duration**

5* DAYS

Range: 1-61 days
in 33 of 36 patients who had resolved NT

**4%** Grade 3 (n=5)

**28%** All grades (n=36)

17% Grade 1 (n=21)/ 8% Grade 2 (n=10)

There were no grade 4 or 5 NT events in KarMMa

NT events, which may be severe or life-threatening, occurred following treatment with ABECMA, including concurrently with CRS (n=34), with onset during CRS (n=29), before CRS (n=3), after CRS resolution (n=2), or in the absence of CRS

### Most common (≥5%) manifestations of NT (N=127)

| | | | |
|---|---|---|---|
| ENCEPHALOPATHY | 20% | APHASIA | 7% |
| TREMOR | 9% | DELIRIUM | 6% |

## Monitoring and Management

**Counsel** patients and caregivers to seek immediate medical attention should signs or symptoms of NT occur at any time

**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

In KarMMa, no grade 3 or higher Parkinsonian or motor symptoms were observed[1,4†]

**If concurrent NT is suspected during CRS, or if concurrent CRS is suspected during the NT event, administer:**

- Corticosteroids according to the more aggressive intervention based on the CRS and NT grades
- Tocilizumab according to the CRS grade
- Antiseizure medication according to the NT grade

*For patients who experienced NT, including 3 patients with ongoing NT, the median duration of CAR T cell-associated NT was 6 days (range: 1 to 578 days).
†NCI CTCAE criteria for grading neurologic toxicities version 4.03.

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# Neurologic Toxicity[1,2]

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**NT Grade** (NCI CTCAE criteria v4.03)

| When to Use Corticosteroids | | When to Use Antiseizure Medications |
|---|---|---|
| Grade 1 | • If onset ≥72 hours after infusion, observe patient<br>• If onset <72 hours after infusion, consider dexamethasone 10 mg IV every 12 to 24 hours for 2-3 days | Start non-sedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis |
| Grade 2 | • Start dexamethasone 10 mg IV every 12 hours for 2-3 days, or longer for persistent symptoms<br>– Consider taper for a total corticosteroid exposure of >3 days. Corticosteroids are not recommended for isolated Grade 2 headaches<br>• 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 | |
| Grade 3 | • Start dexamethasone 10 to 20 mg IV every 6-12 hours<br>– Corticosteroids are not recommended for isolated Grade 3 headaches<br>• 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)<br>• If cerebral edema is suspected:<br>– Consider hyperventilation and hyperosmolar therapy<br>– Give high-dose methylprednisolone (1 to 2 g, repeat every 24 hours if needed; taper as clinically indicated), and cyclophosphamide 1.5 g/m$^2$ | |
| Grade 4 | • Start dexamethasone 20 mg IV every 6 hours<br>• If no improvement after 24 hours or worsening of NT:<br>– Escalate to high-dose methylprednisolone (1-2 g, repeated every 24 hours if needed; taper as clinically indicated)<br>– Consider cyclophosphamide 1.5 g/m$^2$<br>• If cerebral edema is suspected:<br>– Consider hyperventilation and hyperosmolar therapy<br>– Give high-dose methylprednisolone (1 to 2 g, repeat every 24 hours if needed; taper as clinically indicated), and cyclophosphamide 1.5 g/m$^2$ | |

CTCAE criteria are updated on a periodic basis. **Please refer to their website** to access new and archived versions of CTCAE.

There are other guidelines that exist for evaluating cell therapy-associated NT. Please refer to your institutional guidelines.

ADL=activities of daily living; AE=adverse event; CTCAE=Common Terminology Criteria for Adverse Events; NCI=National Cancer Institute.

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# Neurologic Toxicity[1,2]

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## NT Grade

(NCI CTCAE criteria v4.03)

## When to Use Corticosteroids

## When to Use Antiseizure Medications

**CTCAE v4.03 grading for most common NT manifestations in the KarMMa trial[5]**

| AE Term | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|---|
| **Encephalopathy** A disorder characterized by a pathologic process involving the brain. | Mild symptoms | Moderate symptoms; limiting instrumental ADL | Severe symptoms; limiting self-care ADL | Life-threatening consequences; urgent intervention indicated | Death |
| **Tremor** A disorder characterized by the uncontrolled shaking movement of the whole body or individual parts. | Mild symptoms | Moderate symptoms; limiting instrumental ADL | Severe symptoms; limiting self-care ADL | – | – |
| **Dysphasia*** A disorder characterized by impairment of verbal communication skills, often resulting from brain damage. | Awareness of receptive or expressive characteristics; not impairing ability to communicate | Moderate receptive or expressive characteristics; impairing ability to communicate spontaneously | Severe receptive or expressive characteristics; impairing ability to read, write, communicate intelligibly | – | – |
| **Delirium** A disorder characterized by the acute and sudden development of confusion, illusions, movement changes, inattentiveness, agitation, and hallucinations. Usually, it is a reversible condition. | Mild acute confusional state | Moderate and acute confusional state; limiting instrumental ADL | Severe and acute confusional state; limiting self care ADL; hospitalization indicated | Life-threatening consequences, threats of harm to self or others; hospitalization indicated | Death |

*The ABECMA® Prescribing Information uses the term "aphasia" while NCI CTCAE criteria uses the term "dysphasia."

CTCAE criteria are updated on a periodic basis. **Please refer to their website** to access new and archived versions of CTCAE.

There are other guidelines that exist for evaluating cell therapy-associated NT. Please refer to your institutional guidelines.

ADL=activities of daily living; AE=adverse event; CTCAE=Common Terminology Criteria for Adverse Events; NCI=National Cancer Institute.

# HLH/MAS Presentation, Monitoring, and Management[1]

## Incidence in the KarMMa Trial

150-450 x $10^6$ CAR-positive T cells (N=127)

**Median time to onset**


Range: 4-9 days

**4%** **All grades (n=5)**

One Grade 5 HLH/MAS was observed. In another patient with fatal bronchopulmonary aspergillosis, HLH/MAS was contributory to the fatal outcome

- All events of HLH/MAS occurred in the setting of ongoing or worsening CRS
- Two patients with HLH/MAS had overlapping NT

## Monitoring and Management

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

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

## Manifestations of HLH/MAS include

- HYPOTENSION
- HYPOXIA
- MULTIPLE ORGAN DYSFUNCTION
- RENAL DYSFUNCTION
- CYTOPENIA

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# Prolonged Cytopenias* Presentation, Monitoring, and Management[1]

## Incidence in the KarMMa Trial

150-450 x $10^6$ CAR-positive T cells (N=127)

### Prolonged Neutropenia

Median time to recovery

**1.9** MONTHS

in 83% (n=43/52) of patients who recovered from grade 3 or 4 neutropenia after 1 month

**41%** Grade ≥3 (n=52)

### Prolonged Thrombocytopenia

Median time to recovery

**2.1** MONTHS

in 65% (n=40/62) of patients who recovered from grade 3 or 4 thrombocytopenia after 1 month

**49%** Grade ≥3 (n=62)

2 of 3 patients who underwent hematopoietic reconstitution due to prolonged cytopenia died

## Monitoring and Management

**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

*Not resolved by month 1 following ABECMA infusion.

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# Hypersensitivity Reactions Monitoring and Management[1,4]

## Allergic reactions may occur with infusion of ABECMA®

Serious hypersensitivity reactions, including anaphylaxis, may be due to DMSO in ABECMA

ABECMA has a final DMSO concentration of 5%

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

## Monitoring and Management

**Monitor** for hypersensitivity reactions during infusion

**Administer** the following medications approximately 30-60 minutes prior to ABECMA infusion to minimize the risk of infusion reactions

- Acetaminophen (650 mg orally)
- Diphenhydramine (12.5 mg IV or 25 to 50 mg orally, or another $H_1$-antihistamine)

**Treat** infusion reactions as needed per institutional guidelines

DMSO=dimethyl sulfoxide.



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# Infections Monitoring and Management[1]

## Incidence in the KarMMa Trial

Severe, life-threatening, or fatal infections occurred in patients after ABECMA® infusion

150-450 x $10^6$ CAR-positive T cells (N=127)

**23%** Grade 3 or 4 (n=29)

**70%** All grades (n=89)

4 patients (3%) had Grade 5 infections

ABECMA should not be administered to patients with active infections or inflammatory disorders

## Monitoring and Management

**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

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

**Consider antiviral therapy** to prevent viral reactivation per local institutional guidelines/clinical practice

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# Hypogammaglobulinemia Monitoring and Management[1]

## Incidence in the KarMMa Trial

Plasma cell aplasia and hypogammaglobulinemia can occur in patients receiving treatment with ABECMA®

**150-450 x $10^6$ CAR-positive T cells (N=127)**

**21%** **Reported as an AE (n=27)**

Laboratory IgG levels fell below 500 mg/dL after infusion in 25% (32/127) of patients

Hypogammaglobulinemia either as an adverse reaction or laboratory IgG level below 500 mg/dL after infusion occurred in 41% (52/127) of patients

61% of patients in the KarMMa study received IVIG post-ABECMA for serum IgG <400 mg/dL

## Monitoring and Management

**Monitor** immunoglobulin levels after treatment with ABECMA and administer IVIG for IgG <400 mg/dL

**Manage** per local institutional guidelines, including infection precautions and antibiotic or antiviral prophylaxis

## Use of Live Vaccines

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

AE=adverse event; IgG=immunoglobulin G; IVIG=intravenous immunoglobulin.

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# Follow-up Care[1,7]

**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

## Considerations for Transitioning 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**

## Long-term Monitoring

Advise patients to **refrain from driving and engaging in hazardous occupations or activities,** such as operating heavy or potentially dangerous machinery, for **at least 8 weeks** following ABECMA® infusion

**Monitor** for signs and symptoms of **CRS and NT**

**Monitor CBC. Watch for signs and symptoms** of serious infections, febrile neutropenia, cytopenias, and hypogammaglobulinemia

Monitor life-long for secondary malignancies. 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

CBC=complete blood count.



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# ABECMA® Safety Profile[1]

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## Adverse Reactions

- The most common nonlaboratory adverse reactions (incidence ≥20%) in the clinical trials experience included CRS, infections—pathogen unspecified, fatigue, musculoskeletal pain, hypogammaglobulinemia, diarrhea, upper respiratory tract infection, nausea, viral infections, encephalopathy, edema, pyrexia, cough, headache, and decreased appetite
- Serious adverse reactions occurred in 67% of patients. The most common nonlaboratory (≥5%) serious adverse reactions included CRS (18%), general physical health deterioration (10%), pneumonia (12%), infections—pathogen unspecified (19%), viral infections (9%), sepsis (7%), and febrile neutropenia (6%). Fatal adverse reactions occurred in 6%
- The most common (≥10%) grade 3 or 4 nonlaboratory adverse reactions were febrile neutropenia (16%) and infections—pathogen unspecified (15%)

**Click here** to view a summary of adverse reactions observed in at least 10% of patients treated with ABECMA in the KarMMa study

**Click here** to view grade 3 or 4 laboratory abnormalities worsening from baseline in at least 10% of patients treated with ABECMA in the KarMMa study

**Click here** to view ABECMA Important Safety Information

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# Summary of Adverse Reactions

## Summary of adverse reactions observed in at least 10% of patients treated with ABECMA® in the KarMMa study[1]

150-450 x $10^6$ CAR-positive T cells (N=127)

| | Any Grade, % | Grade 3 or Higher, % |
|---|---|---|
| **BLOOD AND LYMPHATIC SYSTEM DISORDERS** | | |
| Febrile neutropenia | 16 | 16 |
| **CARDIAC DISORDERS** | | |
| Tachycardia* | 19 | 0 |
| **GASTROINTESTINAL DISORDERS** | | |
| Diarrhea | 35 | 1.6 |
| Nausea | 29 | 0 |
| Constipation | 16 | 0 |
| Vomiting | 15 | 0 |
| Oral Pain† | 12 | 0 |
| **GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS** | | |
| Fatigue‡ | 45 | 3.1 |
| Pyrexia | 25 | 1.6 |
| General physical health deterioration | 11 | 10 |
| Edema§ | 25 | 0 |
| Chills | 11 | 0 |
| **IMMUNE SYSTEM DISORDERS** | | |
| Cytokine release syndrome | 85 | 9 |
| Hypogammglobulinemia‖ | 41 | 0.8 |

*Tachycardia includes sinus tachycardia, tachycardia.
†Oral pain includes oral pain, oropharyngeal pain, toothache.
‡Fatigue includes asthenia, fatigue, malaise.
§Edema includes edema, face edema, fluid overload, fluid retention, generalized edema, peripheral edema, peripheral swelling, scrotal swelling, swelling.
‖Hypogammaglobulinemia includes patients with adverse events (21%) of blood immunoglobulin G decreased, hypogammaglobulinemia, hypoglobulinemia; and/or patients with laboratory IgG levels below 500 mg/dL following ABECMA infusion (25%).

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# Summary of Adverse Reactions

## Summary of adverse reactions observed in at least 10% of patients treated with ABECMA® in the KarMMa study[1]

150-450 x $10^6$ CAR-positive T cells (N=127)

| | Any Grade, % | Grade 3 or Higher, % |
|---|---|---|
| **INFECTIONS AND INFESTATIONS*** | | |
| Infections – Pathogen unspecified | 51 | 15 |
| Viral Infections | 27 | 9 |
| Bacterial infections | 15 | 3.9 |
| Pneumonia† | 17 | 9 |
| Upper respiratory tract infections‡ | 34 | 1.6 |
| **INVESTIGATIONS** | | |
| Weight decreased | 13 | 1.6 |
| **METABOLISM AND NUTRITION DISORDERS** | | |
| Decreased appetite§ | 22 | 0.8 |
| **MUSCULOSKELETAL AND CONECTIVE TISSUE DISORDERS** | | |
| Musculoskeletal pain‖ | 45 | 3.1 |
| Motor dysfunction¶ | 11 | 0 |
| **NERVOUS SYSTEM DISORDERS** | | |
| Encephalopathy# | 26 | 6 |
| Headache** | 23 | 0 |
| Dizziness†† | 17 | 0.8 |
| Neuropathy peripheral‡‡ | 17 | 0.8 |
| Tremor§§ | 10 | 0 |

*Infections and infestations System Organ Class Adverse Events are grouped by pathogen type and selected clinical syndromes.
†Pneumonia includes bronchopulmonary aspergillosis, lung infection, pneumonia, pneumonia aspiration, pneumonia cytomegaloviral, pneumonia pneumococcal, pneumonia pseudomonal. Pneumonias may also be included under pathogen categories.
‡Upper respiratory tract infection includes laryngitis, nasopharyngitis, pharyngeal erythema, pharyngitis, respiratory tract congestion, respiratory tract infection, rhinitis, rhinovirus infection, sinusitis, upper respiratory tract infection, upper respiratory tract infection bacterial. Upper respiratory tract infections may also be included under pathogen categories.
§Decreased appetite includes decreased appetite, hypophagia.
‖Musculoskeletal pain includes arthralgia, back pain, bone pain, musculoskeletal chest pain, musculoskeletal discomfort, musculoskeletal pain, musculoskeletal stiffness, myalgia, neck pain, spinal pain.
¶Motor dysfunction includes dysphonia, eyelid ptosis, hypotonia, motor dysfunction, muscle spasms, muscular weakness, restless legs syndrome.
#Encephalopathy includes amnesia, bradyphrenia, cognitive disorder, confusional state, depressed level of consciousness, disturbance in attention, dyscalculia, dysgraphia, encephalopathy, lethargy, memory impairment, mental status changes, metabolic encephalopathy, somnolence, toxic encephalopathy.
**Headache includes headache, head discomfort, sinus headache.
††Dizziness includes dizziness, presyncope, syncope, vertigo.
‡‡Neuropathy peripheral includes carpal tunnel syndrome, hypoesthesia, hypoesthesia oral, neuralgia, neuropathy peripheral, paresthesia, peripheral sensorimotor neuropathy, peripheral sensory neuropathy, sciatica.
§§Tremor includes asterixis, tremor.

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# Summary of Adverse Reactions

## Summary of adverse reactions observed in at least 10% of patients treated with ABECMA® in the KarMMa study[1]

150-450 x $10^6$ CAR-positive T cells (N=127)

| | Any Grade, % | Grade 3 or Higher, % |
|---|---|---|
| **PSYCHIATRIC DISORDERS** | | |
| Insomnia* | 13 | 0 |
| Anxiety† | 12 | 0.8 |
| **RENAL AND URINARY DISORDERS** | | |
| Renal failure‡ | 10 | 2.4 |
| **RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS** | | |
| Cough§ | 23 | 0 |
| Dyspnea‖ | 13 | 2.4 |
| **SKIN AND SUBCUTANEOUS TISSUE DISORDERS** | | |
| Rash¶ | 14 | 0.8 |
| Xerosis# | 11 | 0 |
| **VASCULAR DISORDER** | | |
| Hypotension** | 17 | 0 |
| Hypertension | 11 | 3.1 |

*Insomnia includes insomnia, sleep deficit, sleep disorder.
†Anxiety includes anxiety, feeling jittery, nervousness.
‡Renal failure includes acute kidney injury, blood creatinine increased, chronic kidney disease, renal failure, renal impairment.
§Cough includes cough, productive cough, upper-airway cough syndrome.
‖Dyspnea includes acute respiratory failure, dyspnea, dyspnea exertional, respiratory failure.
¶Rash includes acne, dermatitis, dermatitis bullous, erythema, rash, rash macular, rash papular, urticaria.
#Xerosis includes dry eye, dry mouth, dry skin, lip dry, xerosis.
**Hypotension includes hypotension, orthostatic hypotension.

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# Summary of Adverse Reactions

## Grade 3 or 4* laboratory abnormalities worsening from baseline in at least 10% of patients treated with ABECMA® in the KarMMa study[1]

| | 150-450 × $10^6$ (N=127) % |
|---|---|
| Neutropenia | 96 |
| Leukopenia | 96 |
| Lymphopenia | 92 |
| Thrombocytopenia | 63 |
| Anemia | 63 |
| Hypophosphatemia | 45 |
| Hyponatremia | 10 |
| aPTT Increased (seconds) | 10 |

aPTT=activated partial thromboplastin time.
*Laboratory tests were graded according to NCI CTCAE Version 4.03. Laboratory abnormalities are sorted by decreasing frequency in the 150 to 450 x $10^6$ column.

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# Important Safety Information

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

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

Abecma™ (idecabtagene vicleucel) SUSPENSION FOR IV INFUSION

# Important Safety Information (cont'd)

## Warnings and Precautions:

### Cytokine Release Syndrome (CRS):

- CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA in 85% (108/127) of patients.
  - Grade 3 or higher CRS occurred in 9% (12/127) of patients, with Grade 5 CRS reported in one (0.8%) patient.
  - The median time to onset of CRS, any grade, was 1 day (range: 1 - 23 days) and the median duration of CRS was 7 days (range: 1 - 63 days).
  - The most common manifestations included pyrexia, hypotension, tachycardia, chills, hypoxia, fatigue, and headache.
  - Grade 3 or higher events that may be associated with CRS include hypotension, hypoxia, hyperbilirubinemia, hypofibrinogenemia, acute respiratory distress syndrome (ARDS), atrial fibrillation, hepatocellular injury, metabolic acidosis, pulmonary edema, multiple organ dysfunction syndrome, and HLH/MAS.
- 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.
- Fifty four percent (68/127) of patients received tocilizumab (single dose: 35%; more than one dose: 18%).
- Overall, 15% (19/127) of patients received at least 1 dose of corticosteroids for treatment of CRS. All patients that received corticosteroids for CRS received tocilizumab.
- Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of ABECMA.
- Monitor patients at least daily for 7 days following ABECMA infusion at the REMS-certified healthcare facility for signs 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.
- Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

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# Important Safety Information (cont'd)

## Neurologic Toxicities:

- Neurologic toxicities, which may be severe or life-threatening, occurred following treatment with ABECMA in 28% (36/127) of patients receiving ABECMA, including Grade 3 in 4% (5/127) of patients.
  - One patient had ongoing Grade 2 neurotoxicity at the time of death.
  - Two patients had ongoing Grade 1 tremor at the time of data cutoff.
  - The median time to onset of neurotoxicity was 2 days (range: 1 - 42 days). CAR T cell-associated neurotoxicity resolved in 92% (33/36) of patients with a median time to resolution of 5 days (range: 1 - 61 days).
  - The median duration of neurotoxicity was 6 days (range: 1 - 578) in all patients including 3 patients with ongoing neurotoxicity.
  - Thirty-four patients with neurotoxicity had CRS with onset in 3 patients before, 29 patients during, and 2 patients after CRS.
  - The most frequently reported manifestations of CAR T cell-associated neurotoxicity include encephalopathy, tremor, aphasia, and delirium. Grade 4 neurotoxicity and edema in 1 patient, Grade 3 myelitis, and Grade 3 parkinsonism have been reported 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):

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

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# 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 1-888-423-5436.

## Hypersensitivity Reactions:

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

## Infections:

- ABECMA should not be administered to patients with active infections or inflammatory disorders. Severe, life-threatening, or fatal infections occurred in patients after ABECMA infusion. Infections (all grades) occurred in 70% of patients. Grade 3 or 4 infections occurred in 23% of patients. Overall, 4 patients had Grade 5 infections (3%); 2 patients (1.6%) had Grade 5 events of pneumonia, 1 patient (0.8%) had Grade 5 bronchopulmonary aspergillosis, and 1 patient (0.8%) had cytomegalovirus (CMV) pneumonia associated with Pneumocystis jirovecii. Monitor patients for signs and symptoms of infection before and after ABECMA infusion and treat appropriately. Administer prophylactic, pre-emptive, and/or therapeutic antimicrobials according to standard institutional guidelines.
- Febrile neutropenia was observed in 16% (20/127) of patients after ABECMA infusion and may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad-spectrum antibiotics, fluids, and other supportive care.
- Viral Reactivation: CMV infection resulting in pneumonia and death has occurred following ABECMA administration. Monitor and treat for CMV reactivation in accordance with clinical guidelines. Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, can occur in patients treated with drugs directed against plasma cells. Perform screening for CMV, HBV, hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in accordance with clinical guidelines before collection of cells for manufacturing.

## Prolonged Cytopenias:

- In the clinical study, 41% of patients (52/127) experienced prolonged Grade 3 or 4 neutropenia and 49% (62/127) experienced prolonged Grade 3 or 4 thrombocytopenia that had not resolved by Month 1 following ABECMA infusion. In 83% (43/52) of patients who recovered from Grade 3 or 4 neutropenia after Month 1, the median time to recovery from ABECMA infusion was 1.9 months. In 65% (40/62) of patients who recovered from Grade 3 or 4 thrombocytopenia, the median time to recovery was 2.1 months.
- Three patients underwent stem cell therapy for hematopoietic reconstitution due to prolonged cytopenia. Two of the three patients died from complications of prolonged cytopenia. Monitor blood counts prior to and after ABECMA infusion. Manage cytopenia with myeloid growth factor and blood product transfusion support.

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# Important Safety Information (cont'd)

## Hypogammaglobulinemia:

- Hypogammaglobulinemia was reported as an adverse event in 21% (27/127) of patients; laboratory IgG levels fell below 500 mg/dl after infusion in 25% (32/127) of patients treated with ABECMA.
- Monitor immunoglobulin levels after treatment with ABECMA and administer IVIG for IgG <400 mg/dl. Manage appropriately per local institutional guidelines, including infection precautions and antibiotic or antiviral prophylaxis.
- 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.

## Secondary Malignancies:

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

## Effects on Ability to Drive and Operate Machinery:

- Due to the potential for neurologic events, 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 include CRS, infections – pathogen unspecified, fatigue, musculoskeletal pain, hypogammaglobulinemia, diarrhea, upper respiratory tract infection, nausea, viral infections, encephalopathy, edema, pyrexia, cough, headache, and decreased appetite.

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# Support and References

Visit us at

**AbecmaHCP.com** | **ABECMA.com**

The ABECMA® professional and patient websites provide additional resources for you and your patients.

Visit us at

**celltherapy360.com**

Call us at

**1-888-805-4555**

Cell Therapy 360® provides patient support and a commercial scheduling portal.

## References

**1.** ABECMA [package insert]. Summit, NJ: Bristol-Myers Squibb Company; 2021.

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