ABECMA®

(IDECABTAGENE VICLEUCEL)

ISRAEL
HEALTHCARE PROFESSIONAL
GUIDE

Bristol Myers Squibb®

This Healthcare Professional Guide was approved according to the guidelines of the ministry of health in July 2025

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LIST OF ABBREVIATIONS

Term	Definition
AE	adverse event
ASTCT	American Society for Transplantation and Cellular Therapy
BCMA	B-cell maturation antigen
CAR	chimeric antigen receptor
CD	cluster of differentiation
CRS	cytokine release syndrome
CTCAE	Common Terminology Criteria for Adverse Events
CVVHD	continuous veno-venous haemodialysis
EBMT	European Society for Blood and Marrow Transplantation
EEG	electroencephalogram
EMA	European Medicines Agency
FiO2	fraction of inspired oxygen
HCP	healthcare professional
ICANS	immune effector cell-associated neurotoxicity syndrome
ICE	immune effector cell-associated encephalopathy
ICP	intracranial pressure
iiNT	investigator-identified neurotoxicity
IV	intravenous
NCI	National Cancer Institute
NT	neurologic toxicity
PI	Prescribing Information

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1. INTRODUCTION

Abecma (idecabtagene vicleucel) is a genetically modified autologous cell-based product containing T cells transduced ex-vivo using a replication incompetent lentiviral vector encoding a chimeric antigen receptor (CAR) that recognises B-cell maturation antigen (BCMA), comprising a murine-derived, anti-human BCMA single chain variable fragment (scFv) linked to a 4-1BB costimulatory domain and a cluster of differentiation (CD) 3-zeta signalling domain.

Each patient-specific infusion bag of Abecma contains idecabtagene vicleucel at a batch-dependent concentration of autologous T cells genetically modified to express an anti-BCMA CAR (CAR-positive viable T cells). The medicinal product is packaged in 1 or more infusion bags overall containing a cell dispersion of 260 to 500 x 10^6 CAR-positive viable T cells suspended in a cryopreservative solution.

The treatment consists of a single dose for infusion containing a dispersion of CAR-positive viable T cells in 1 or more infusion bags. The target dose is 420 x 10^6 CAR-positive viable T cells within a range of 260 to 500 x 10^6 CAR-positive viable T cells.

Abecma is indicated for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least 2 prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

Please see full Prescribing Information (PI) for further details.

2. ADDITIONAL RISK MINIMISATION MEASURES

This educational guide is part of the additional risk minimisation measures for Abecma and contains information regarding selected Abecma-associated adverse reactions of cytokine release syndrome (CRS), neurologic toxicities, including immune effector cell-associated neurotoxicity syndrome (ICANS) and secondary malignancy of T-cell origin. These are not all the adverse reactions associated with Abecma. Please refer to the Abecma PI for more information.

Abecma is only available to hospitals and associated centres that are qualified in accordance with the agreed controlled distribution programme by:

- Ensuring immediate, on-site access to 1 dose of tocilizumab per patient prior to Abecma infusion. The treatment centre must have access to an additional dose of tocilizumab within 8 hours of each previous dose. In the exceptional case where tocilizumab is not available, suitable alternative measures to treat CRS instead of tocilizumab must be available prior to infusion.
- Ensuring that healthcare professionals (HCPs) involved in the treatment of a patient have completed the educational programme.

HCPs that are expected to prescribe, dispense and administer Abecma must complete the educational programme by being provided with information in accordance with the agreed HCP Educational Programme.

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3. IMPORTANT POINTS TO CONSIDER BEFORE ADMINISTERING ABECMA

To mitigate the safety risks associated with Abecma treatment, hospitals and associated clinics must comply with the risk minimisation measures, as outlined in this HCP guide, prior to ordering Abecma.

Abecma must be administered in a qualified treatment centre.

Hospitals and associated centres must ensure that 1 dose of tocilizumab (for use in the event of CRS) must be available for immediate on-site use prior to infusion of Abecma. The treatment centre must have access to an additional dose of tocilizumab within 8 hours of each previous dose. In the exceptional case where tocilizumab is not available, suitable alternative measures to treat CRS instead of tocilizumab must be available prior to infusion.

The treatment centre is responsible for ensuring that this guide is provided to all relevant personnel.

4. PREPARATION FOR ABECMA ADMINISTRATION

Abecma should be transported within the treatment centre in closed, break-proof, leak-proof containers.

This medicinal product contains human blood cells. Healthcare professionals handling Abecma should take appropriate precautions (wearing gloves and glasses) to avoid potential transmission of infectious diseases.

Prior to Abecma infusion, it must be confirmed that the patient's identity matches the patient identifiers on the Abecma cassette(s), the infusion bag(s), and the release for infusion certificate (RfIC). The Abecma infusion bag must not be removed from the cassette if the information on the patient-specific label does not match the intended patient. The company must be contacted immediately at 1809-388054 (A Toll-free number) if there are any discrepancies between the labels and the patient identifiers.

If more than 1 infusion bag has been received for treatment, thaw each infusion bag 1 at a time. The timing of thaw of Abecma and infusion should be coordinated. The infusion start time should be confirmed in advance and adjusted for thaw so that Abecma is available for infusion when the patient is ready.

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4.1 Thawing Instructions

- Remove the Abecma infusion bag from the cassette and inspect the infusion bag for any breaches of container integrity such as breaks or cracks before thawing. If the infusion bag appears to have been damaged or to be leaking, it should not be infused and should be disposed of according to local guidelines on handling of waste of human-derived material.
- Place the infusion bag inside a second sterile bag.
- 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 visible clumps of cellular material. Small clumps of cellular material are expected in Abecma.
- Do not wash, spin down and/or resuspend Abecma in new media prior to infusion.
- Each bag must be infused within 1 hour from start of thaw. After thawing, the volume of the product intended for infusion should be kept at room temperature (20°C to 25°C).
- Product must NOT be refrozen following thaw.

For complete instructions on how to administer Abecma after thawing, please see the full PI.

5. PATIENT MONITORING FOLLOWING ABECMA ADMINISTRATION

Patients should be monitored for the first 10 days following infusion at the qualified treatment centre for signs and symptoms of potential CRS, neurologic events, and other toxicities.

After the first 10 days following infusion, the patient should be monitored at the physician's discretion.

Patients should be instructed to remain within proximity (within 2 hours of travel) of the qualified treatment centre for at least 4 weeks following infusion.

Patients should be monitored life-long for secondary malignancies.

Patients are expected to be enrolled in a registry in order to better understand the long-term safety and efficacy of Abecma.

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6. SAFETY RISKS ASSOCIATED WITH ABECMA

CRS, including fatal or life-threatening reactions occurred following Abecma infusion. Nearly all patients experienced some degree of CRS. At the first sign of CRS, treatment with supportive care, tocilizumab or tocilizumab and corticosteroids, should be instituted. Patients who experience CRS should be closely monitored for cardiac and organ functioning until resolution of symptoms. For severe or life-threatening CRS, intensive care unit level monitoring and supportive therapy should be considered.

Neurologic toxicities, such as aphasia, encephalopathy, and ICANS, which may be severe, or life-threatening, occurred following treatment with Abecma. Neurologic toxicities may occur 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. Intensive care supportive therapy should be provided for severe or life-threatening neurologic toxicities.

Patients treated with Abecma may develop secondary malignancies. T cell malignancies have been reported following treatment of haematological malignancies with a BCMA- or CD19-directed CAR T cell therapy, including Abecma. T cell malignancies, including CAR-positive malignancies, have been reported within weeks and up to several years following administration of a CD19- or BCMA-, directed CAR T cell therapy. There have been fatal outcomes. Patients should be monitored life-long for secondary malignancies. In the event that a secondary malignancy of T cell origin occurs, the company should be contacted to obtain instructions on the collection of patient tumour samples for testing.

Patients may exhibit prolonged cytopenias for several weeks following lymphodepleting chemotherapy and Abecma infusion (see PI section 4.8).

Plasma cell aplasia and Hypogammaglobulinaemia can occur in patients receiving treatment with Abecma (see PI section 4.8).

Severe infections, including life-threatening or fatal infections, have occurred in patients after receiving Abecma (see PI section 4.8).

Due to the risks associated with Abecma treatment, infusion should be delayed up to 7 days if a patient has any of the following conditions:

- Unresolved serious adverse events (AEs) (especially pulmonary events, cardiac events, or hypotension), including those after preceding chemotherapies
- Active infections or inflammatory disorders (including pneumonitis, myocarditis, or hepatitis)
- Active graft-versus-host disease

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7. CYTOKINE RELEASE SYNDROME

7.1 Clinical Presentation of Cytokine Release Syndrome

CRS, including fatal or life-threatening reactions, occurred in patients following Abecma infusion.

The information in this section is based on pooled data from the KarMMa, CRB-401, and KarMMa-3 studies, in which 409 patients with relapsed and refractory multiple myeloma received Abecma within the allowed dose range of 150 to 540× 10^6 CAR-positive T cells:

- Overall, across the target dose range, CRS occurred in 84.6% of patients receiving Abecma.
- Grade 3 or higher CRS (Lee grading system[1]) occurred in 5.1% of patients, with fatal outcome of CRS reported in 0.7% of patients.
- The median time to onset was 1 day.
- The median duration of CRS was 4 days.
- 59.7% of patients received tocilizumab; 37.2% received a single dose while 22.5% received more than 1 dose of tocilizumab.
- Overall, 22.7% of patients received at least 1 dose of corticosteroids for treatment of CRS. Of the 92 patients in KarMMa and CRB-401 who received the target dose of 450 × 10^6 CAR-positive T cells, 54.3% of patients received tocilizumab and 22.8% received at least 1 dose of corticosteroids for treatment of CRS. Of the 225 patients in KarMMa-3 who received Abecma infusion, 71.6% of patients received tocilizumab and 28.4% received at least 1 dose of corticosteroids for the treatment of CRS.

7.2 Signs and Symptoms of Cytokine Release Syndrome

CRS is a non–antigen specific toxicity that occurs as a result of high-level immune activation due to the mechanism of action of Abecma[1].

Clinical symptoms and severity of CRS are highly variable, ranging from mild flu-like symptoms to multiorgan failure. Fever is a hallmark of CRS.

Management can be complicated by concurrent conditions.

For severe or life-threatening CRS, intensive care unit level monitoring and supportive therapy should be considered.

The most common manifestations of CRS are based on data from 409 patients receiving Abecma in the KarMMa, CRB-401, and KarMMa-3 studies to treat relapsed or refractory multiple myeloma after at least 2 prior therapies including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody (Table 1).

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Table 1: Common Manifestations of Cytokine Release Syndrome (≥ 10%) Observed in KarMMa-3, KarMMa and CRB-401 Studies

Pyrexia	82.6%	Hypoxia	15.9%
Hypotension	29.1%	Headache	11.2%
Tachycardia	24.7%	C-reactive protein increased	10.5%
Chills	18.8%		

7.3 Management of Cytokine Release Syndrome

- Monitor patients for signs and symptoms of CRS for the first 10 days following infusion. After the first 10 days following infusion, the patient should be monitored at the physician's discretion.
- Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.
- Identify CRS based on clinical presentation. Evaluate and treat other causes of fever, hypoxia, and hypotension.
- At the first signs of CRS, initiate treatment with supportive care, tocilizumab or tocilizumab and corticosteroids, according to the recommendations outlined in Table 2. In the exceptional case where tocilizumab is not available, suitable alternative measures instead of tocilizumab to treat CRS may be used.
- Abecma can continue to expand and persist following administration of tocilizumab and corticosteroids.
- Patients who experience CRS should be closely monitored for cardiac and organ functioning until resolution of symptoms.
- For severe or life-threatening CRS, intensive care unit level monitoring and supportive therapy should be considered.
- If concurrent neurologic toxicity is suspected during CRS, the neurologic toxicity should be managed according to the recommendations in Table 3 and use the more aggressive intervention of the 2 reactions specified in Table 2 and Table 3.
- Earlier escalation (i.e., higher corticosteroid dose, alternative anticytokine agents, anti-T cell therapies) is recommended in patients with refractory CRS within 72 hours post Abecma infusion, characterised by persistent fever, end organ toxicity (e.g., hypoxia, hypotension) and/or haemophagocytic lymphohistiocytosis/macrophage activation syndrome not improving in grade within 12 hours of first line interventions.

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Table 2: Abecma CRS Grading and Management Guidance

CRS Grade[1]	Tocilizumab	Corticosteroids
Grade 1:		
Symptoms require symptomatic treatment only (e.g. fever, nausea, fatigue, headache, myalgia, malaise).	If onset 72 hours or more after infusion, treat symptomatically. If onset less than 72 hours after infusion and symptoms not controlled by supportive care alone, consider tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg).	
Grade 2:		
Symptoms require and respond to moderate intervention. Oxygen requirement less than 40% FiO_2 or hypotension responsive to fluids, or low dose of one vasopressor, or Grade 2 organ toxicity.	Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg).	Consider dexamethasone 10 mg IV every 12 to 24 hours.
Grade 3:		
Symptoms require and respond to aggressive intervention. Fever, oxygen requirement greater than or equal to 40% FiO_2, or hypotension requiring high-dose or multiple vasopressors, or Grade 3 organ toxicity or Grade 4 transaminitis.	Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg).	Administer dexamethasone (e.g. 10 mg IV every 12 hours).
For Grade 2 and 3:		
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). 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. If steroids are initiated, continue steroids for at least 3 doses, and taper over a maximum of 7 days. After 2 doses of tocilizumab, consider alternative anticytokine agents. Do not exceed 3 doses tocilizumab in 24 hours, or 4 doses in total.		
Grade 4:		
Life-threatening symptoms. Requirements for ventilator support, CVVHD, or Grade 4 organ toxicity (excluding transaminitis).	Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg).	Administer dexamethasone 20 mg IV every 6 hours.
For Grade 4:		
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 to 2 g, repeat every 24 hours if needed; taper as clinically indicated) or anti-T cell therapies such as cyclophosphamide 1.5 g/m^2 or others.		

Abbreviations: CRS, cytokine release syndrome; CVVHD, continuous veno-venous haemodialysis; FiO_2, fraction of inspired oxygen; IV, intravenous.

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8. NEUROLOGIC TOXICITY, INCLUDING ICANS

8.1 Clinical Presentation of Neurologic Toxicity

Neurologic toxicities, such as aphasia, encephalopathy, and ICANS, which may be severe or life-threatening, occurred following treatment with Abecma. Grade 3 parkinsonism with delayed onset has also been reported. Neurologic toxicities may occur concurrently with CRS, after CRS resolution, or in the absence of CRS.

In the pooled studies (KarMMa, CRB-401 and KarMMa-3) of 409 patients:

- The most frequent (≥ 5%) neurologic or psychiatric adverse reactions (independent of investigator attribution of neurotoxicity) included headache (22.5%), dizziness (12.5%), confusional state (11.0%), insomnia (10.3%), anxiety (5.9%), tremor (5.6%), and somnolence (5.6%).
- Other neurological adverse reactions occurring at a lower frequency and considered clinically important include encephalopathy (3.4%) and aphasia (2.9%).

Neurotoxicity identified by the investigators, which was the primary method of assessing CAR T cell-associated neurotoxicity in the KarMMa and KarMMa-3 studies, occurred in 16.1% of the 353 patients receiving Abecma, including Grade 3 or 4 in 3.1% of patients (with no Grade 5 events):

- The median time to onset of the first event of investigator-identified neurotoxicity (iiNT) was 3 days.
- The median duration was 3 days.
- Overall, 7.1% of patients received at least 1 dose of corticosteroid for treatment of CAR T cell-associated neurotoxicity.
- In KarMMa, across the target dose levels, 7.8% of patients received at least 1 dose of corticosteroids for treatment of CAR T cell-associated neurotoxicity, while at the target dose of 450× 10^6 CAR-positive T cells, 14.8% of patients received at least 1 dose of corticosteroids.
- In KarMMa-3, across all patients who received Abecma infusion at the target dose range, 6.7% of patients received at least 1 dose of corticosteroid for treatment of CAR T cell-associated neurotoxicity.
- Of the 353 patients in the KarMMa and KarMMa-3 studies, the most common manifestations of iiNT (≥ 2%) included confusional state (8.5%), encephalopathy (3.4%), somnolence (2.8%), aphasia (2.5%), tremor (2.3%), disturbance in attention (2.0%), and dysgraphia (2.0%).

8.2 Management of Neurologic Toxicity, Including ICANS

- Monitor patients for signs and symptoms of neurologic toxicity for the first 10 days following infusion, as discussed previously. After the first 10 days following infusion, the patient should be monitored at the physician's discretion.
- Counsel patients to seek immediate medical attention should signs and symptoms of neurologic toxicity occur at any time.
- Provide intensive care supportive therapy for severe or life-threatening neurologic toxicities.
- If neurologic toxicity is suspected, manage according to the recommendations in Table 3.
- If concurrent CRS is suspected during the neurologic toxicity reaction, it should be managed according to the recommendations in Table 2 and the more aggressive intervention used for CRS and neurologic toxicity including ICANS, as specified in Table 2 and Table 3.

Table 3: Neurologic Toxicity Including ICANS Grading and Management Guidance

Neurologic Toxicity Grade[d] Including Presenting Symptoms[a]	Corticosteroids and Antiseizure Medications
Grade 1	
Mild or asymptomatic ICE score 7-9[b] or Depressed level of consciousness:[c] awakens spontaneously.	Start non-sedating, antiseizure medicines (e.g. levetiracetam) for seizure prophylaxis. If 72 hours or more after infusion, observe patient. If less than 72 hours after infusion, and symptoms not controlled by supportive care alone, consider dexamethasone 10 mg IV every 12 to 24 hours for 2 to 3 days.
Grade 2	
Moderate ICE score 3-6[b] or Depressed level of consciousness:[c] awakens to voice.	Start non-sedating, antiseizure medicines (e.g. levetiracetam) for seizure prophylaxis. 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 greater than 3 days. Steroids are not recommended for isolated Grade 2 headaches. If no improvement after 24 hours or worsening of neurologic toxicity, increase the dose and/or frequency of dexamethasone up to a maximum of 20 mg IV every 6 hours.

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Grade 3	
Severe or Medically Significant but not Immediately Life-threatening; Hospitalisation or Prolongation Indicated; Disabling ICE score 0-2[b] *if ICE score is 0, but the patient is arousable (e.g. awake with global aphasia) and able to perform assessment.* or Depressed level of consciousness:[c] awakens only to tactile stimulus, Or seizures,[c] either: • any clinical seizure, focal or generalised, that resolves rapidly, or • non-convulsive seizures on EEG that resolve with intervention, Or raised ICP:[c] focal/local oedema on neuroimaging.	Start non-sedating, antiseizure medicines (e.g. levetiracetam) for seizure prophylaxis. Start dexamethasone 10 to 20 mg IV every 8 to 12 hours. Steroids are not recommended for isolated Grade 3 headaches. If no improvement after 24 hours or worsening of neurologic toxicity, escalate to methylprednisolone (2 mg/kg loading dose, followed by 2 mg/kg divided into 4 times a day; taper within 7 days). If cerebral oedema 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/m^2.
Grade 4	
Life threatening ICE score 0[b] or Depressed level of consciousness,[c] either: • patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse, or • stupor or coma, Or seizures,[c] either: • life-threatening prolonged seizure (> 5 min), or • repetitive clinical or electrical seizures without return to baseline in between, Or motor findings:[c] • deep focal motor weakness such as hemiparesis or paraparesis, Or raised ICP/cerebral oedema,[c] with signs/symptoms such as: • diffuse cerebral oedema on neuroimaging, or • decerebrate or decorticate posturing, or • cranial nerve VI palsy, or • papilledema, or • Cushing's triad	Start non-sedating, antiseizure medicines (e.g. levetiracetam) for seizure prophylaxis. Start dexamethasone 20 mg IV every 6 hours. If no improvement after 24 hours or worsening of neurologic toxicity, escalate to high-dose methylprednisolone (1 to 2 g, repeated every 24 hours if needed; taper as clinically indicated). Consider cyclophosphamide 1.5 g/m^2. If cerebral oedema 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/m^2.

[a] Management is determined by the most severe event, not attributable to any other cause.

[b] If patient is arousable and able to perform ICE Assessment, assess: Orientation (oriented to year, month, city, hospital = 4 points); Naming (name 3 objects, e.g., point to clock, pen, button = 3 points); Following Commands (e.g., "show me 2 fingers" or "close your eyes and stick out your tongue" = 1 point); Writing (ability to write a standard sentence = 1 point); and Attention (count backwards from 100 by ten = 1 point). If patient is unarousable and unable to perform ICE Assessment (Grade 4 ICANS) = 0 points.

[c] Attributable to no other cause.

[d] Grading per NCI CTCAE or ASTCT/ICANS.

Abbreviations EEG, electroencephalogram; ICE, immune effector cell-associated encephalopathy; ICP, intracranial pressure; IV, intravenous.

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9. Prolonged Cytopenia (including Febrile Neutropenia)

9.1 Clinical Presentation of Prolonged Cytopenia and Febrile Neutropenia

Patients may exhibit prolonged cytopenias following lymphodepleting chemotherapy and Abecma infusion.

Febrile neutropenia was observed in patients after Abecma infusion and may be concurrent with CRS.

- In the pooled studies, 38.2% of the 395 patients who had Grade 3 or 4 neutropenia and 71.3% of the 230 patients who had Grade 3 or 4 thrombocytopenia during the first month following Abecma infusion had not resolved by last assessment during the first month.
- Among the 151 patients with neutropenia not resolved by month 1, 88.7% recovered from Grade 3 or 4 neutropenia with a median time to recovery from Abecma infusion of 1.9 months.
- Of the 164 patients with thrombocytopenia not resolved by month 1, 79.9% recovered from Grade 3 or 4 thrombocytopenia with the median time to recovery of 2.0 months.

9.2 Management of Prolonged Cytopenia and Febrile Neutropenia

Blood counts should be monitored prior to and after Abecma infusion.

Cytopenias should be managed with myeloid growth factor and blood transfusion support according to institutional guidelines.

In the event of febrile neutropenia, infection should be evaluated and managed with broad spectrum antibiotics, fluids and other supportive care as medically indicated.

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10. Hypogammaglobulinaemia

10.1 Clinical Presentation of Hypogammaglobulinaemia

Plasma cell aplasia and Hypogammaglobulinaemia can occur in patients receiving treatment with Abecma (see section 4.8 in PI). Hypogammaglobulinaemia was reported in 13.7% of patients treated with Abecma in the pooled studies with a median time to onset of 90 days. See section 4.4 in Prescribing Information.

10.2 Management of Hypogammaglobulinaemia

Immunoglobulin levels should be monitored after treatment with Abecma and managed per institutional guidelines including infection precautions, antibiotic or antiviral prophylaxis and immunoglobulin replacement.

11 Pregnancy

It is not known if idecabtagene vicleucel has the potential to be transferred to the foetus. Based on the mechanism of action, if the transduced cells cross the placenta, they may cause foetal toxicity, including plasma cell aplasia or Hypogammaglobulinaemia. Therefore, Abecma is not recommended for women who are pregnant or for women of childbearing potential not using contraception.
Assessment of immunoglobulin levels in newborn infants of mothers treated with Abecma should be considered.

12 Infections

12.1 Clinical Presentation of Infections

Severe infections, including life-threatening or fatal infections, have occurred in patients after receiving Abecma.

- In the pooled studies, infections occurred in 62.8% of patients.
- Grade 3 or 4 infections occurred in 23.2% of patients.
- Grade 3 or 4 infections with an unspecified pathogen occurred in 15.2%, viral infections in 7.6%, bacterial infections in 4.6% and fungal infections in 1.2% of patients.

Fatal infections of unspecified pathogen were reported in 2.0% of patients, 0.7% of patients had fatal fungal or viral infection and 0.2% of patients had fatal bacterial infection.

12.2 Management of Infections

- Patients should be monitored and treated appropriately for signs and symptoms of infection before and after Abecma infusion.
- Prophylactic, pre-emptive and/or therapeutic antimicrobials should be administered according to institutional guidelines.

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13. TRANSGENE ASSAY SERVICE TESTING OF SECONDARY MALIGNANCIES

Patients treated with Abecma may develop secondary malignancies. Patients should be monitored life-long for secondary malignancies.

If a secondary malignancy is identified to be of T cell origin, or if it is suspected to be causally related to Abecma, Bristol-Myers Squibb will assist HCPs upon their request in coordinating transfer of tumour tissue samples from patients for Abecma transgene testing. HCPs should inform their patients about the importance of consenting transferring their samples to BMS for transgene testing.

A sample of the tumour tissue with confirmed active disease involvement will be requested to test for the presence of Abecma transgene. The most appropriate specimen for testing is the original diagnostic tumour sample previously collected and used for the diagnosis of the secondary malignancy. If the original diagnostic tumour sample is not available, a tumour sample collected after diagnosis and confirmed to have involvement with the secondary malignancy is acceptable. In the case of a secondary malignancy with bone marrow involvement, bone marrow aspirate is the preferred specimen over bone marrow biopsy for testing, if available. In addition to tumour samples, peripheral blood collected during the diagnosis of the secondary malignancy may also be requested for testing.

If Abecma transgene levels are detected at qualifying levels in the tumour specimen, insertion site analysis will be performed to assess the clonality of the transduced cell population by identifying the frequency and location of insertion sites to ascertain if insertional mutagenesis is suspected in the development of the malignancy. If insertional mutagenesis is suspected, further testing may be conducted to investigate the involvement of the GMCT with the secondary malignancy.

Details for the types and amounts of tumour and blood samples acceptable for testing, and information about the tests that will be performed can be found in the Observational Protocol CA082085 Transgene Assay Service on clinicaltrials.gov website under the study NCT06357754.

Results of testing can be provided to the reporting HCP upon request.

If a secondary malignancy occurs after treatment with Abecma, HCPs are asked to contact the company directly via the following:
Telephone: 1809-388054 (A Toll-free number)
Email: medinfo.Israel@bms.com

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14. PATIENT COUNSELLING

- Advise the patient to read the patient information leaflet.
- Talk to the patient about the risks of CRS, neurologic toxicity, including ICANS, secondary malignancy of T-cell origin and infections. Advise them to seek immediate medical care for any of the following:
  - Fever, chills, difficulty breathing, dizziness or light-headedness, nausea, headache, fast heartbeat, low blood pressure or fatigue, which may be symptoms of CRS, a serious and potentially fatal condition.
  - Any signs of an infection, which may include fever, chills or shivering, cough, shortness of breath, rapid breathing and rapid pulse.
  - Confusion, difficulty with memory, difficulty speaking or slowed speech, difficulty understanding speech, loss of balance or coordination, disorientation, being less alert (decreased consciousness) or excessive sleepiness, loss of consciousness, delirious, fits (seizures), which may be symptoms of a condition called ICANS.
  - Shaking or weakness with loss of movement on 1 side of the body, tremor, slow movements, or stiffness, which may be symptoms of parkinsonism.
  - Advise patients to talk to their doctor if they experience new swelling of the glands (lymph nodes) or changes in their skin, such as new rashes or lumps, which may be signs of a new type of cancer.
- Prior to infusion and latest at discharge, provide the patient with the Patient Card, and inform them:
  - The symptoms to look for are also provided on the Patient Card.
  - They need to carry the Patient Card at all times.
  - The batch number and contact details will be filled in by their Abecma -treating physician on the Patient Card.
- Advise patients of the need to:
  - Remain within proximity (within 2 hours of travel) of the qualified treatment centre for at least 4 weeks following infusion.
  - Refrain from driving or operating heavy or potentially dangerous machines for at least 8 weeks after Abecma infusion or until resolution of neurologic adverse reactions.

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15. REPORTING ADVERSE REACTIONS

Reporting suspected adverse reactions after administration of Abecma is important and allows continued monitoring of the benefit-risk balance of therapy.

Healthcare professionals are asked to adequately and appropriately report adverse reactions that have occurred during the use of Abecma.

You can report side effects to the Israeli Ministry of Health by using the on-line form for reporting adverse events on the Home page of the Ministry of health website: www.health.gov.il or by entering the following link: https://sideeffects.health.gov.il

You can also report side effects to BMS by phone: 1809-388-054 or email: MedInfo.Israel@BMS.com

16. COMPANY CONTACT DETAILS

For information on HCP educational material, Prescribing Information and patient information or if you have any questions, please contact BMS at:

Telephone: 1809-388054 (A Toll-free number)
Email: medinfo.Israel@bms.com

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17. REFERENCES

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