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Teclistamab-cqyv: The First Bispecific T-Cell Engager Antibody for the Treatment of Patients With Relapsed or Refractory Multiple Myeloma

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Authors' disclosures of conflicts of interest are found at the end of this article.

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Abstract

Multiple myeloma (MM) remains an incurable malignancy originating from plasma cells. Despite significant advances in treatment, relapses remain inevitable, and novel therapies continue to be needed. Teclistamab-cqyv is a first-in-class, bispecific T-cell engager (BiTE) antibody for the treatment of MM. Teclistamab-cqyv activates the immune system by binding to the cluster of differentiation 3 (CD3) receptor expressed on the surface of T cells and to the B-cell maturation antigen (BCMA) expressed on the surface of MM cells and some healthy B-lineage cells. Teclistamab-cqyv has been shown to be effective in a pivotal trial that demonstrated an overall response rate of more than 60% in heavily pretreated patients. Compared with other BCMA-targeted agents, the side effect profile of teclistamab-cqyv suggests a more tolerable option for elderly patients. Teclistamab-cqyv is now approved by the US Food and Drug Administration (FDA) as monotherapy for the treatment of adult patients with relapsed or refractory MM.

Multiple myeloma (MM) is a plasma cell disorder characterized by the clonal proliferation of malignant plasma cells in the bone marrow with monoclonal protein in the serum and/or urine and associated organ dysfunction (Kyle & Rajkumar, 2004). Multiple myeloma is the second most common hematologic malignancy, with an incidence of around 4.5 to 6 per 100,000 per year (Dimopoulos et al., 2021). Each year, approximately 100,000 deaths from MM occur worldwide (Siegel et al., 2020). Incidence rates for MM increase with age and are higher in men, particularly African American men. Additional risk factors include obesity and exposure to radiation, such as x-rays (Sergentanis et al., 2015).

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Despite recent advancements in treatment, MM remains incurable, with a natural history characterized by remission and relapse. Although overall survival (OS) has increased dramatically with new novel agents, it is important to consider acute and delayed toxicities, the choice of active agents, and quality of life. With relapses being inevitable, innovative therapies are needed for relapsed or refractory disease. As many MM patients may now live many years with treatment, it is critical to consider the tolerability and response to treatment by focusing on the toxicity profile, as well as the therapy targets (particularly in later lines of therapy). Teclistamab-cqyv (Tecvayli) is a first-in-class bispecific T-cell engager (BiTE) therapy that binds to the cluster of differentiation 3 (CD3) receptor on T cells and B-cell maturation antigen (BCMA) expressed on MM cells. Compared with historical controls, the use of teclistamab-cqyv resulted in a high rate of deep and durable response in heavily pretreated MM patients (Moreau et al., 2022). Teclistamab-cqyv is now approved for the treatment of relapsed and refractory MM and is currently recommended in the National Comprehensive Cancer Network (NCCN) Guidelines for patients who have received four or more prior therapies, including a proteasome inhibitor (PI), immunomodulatory drug (IMiD), and anti-CD38 antibody (Janssen Biotech, Inc., 2022).

PHARMACOLOGY AND MECHANISM OF ACTION

Teclistamab-cqyv is a humanized antibody and a bispecific BCMA-directed CD3 T-cell engager. BCMA is a protein that is preferentially expressed by late-stage B cells and plasma cells (Kleber et al., 2021). BCMA represents an antigen target of interest for novel MM therapies given its role in the survival mechanism of malignant plasma cells (Einsele et al., 2020). BiTE therapies aim to connect endogenous T cells to tumor-expressed antigens. Teclistamab-cqyv engages in T-cell activation by targeting the CD3 receptor on the surface of T cells and BCMA expressed on the surface of MM cells, leading to the release of various proinflammatory cytokines, and ultimately lysis of BCMA-expressing MM cells (Moreau et al., 2022). The steady-state volume distribution of teclistamab-cqyv is 5.63 liters (Janssen Biotech, Inc., 2022). The bioavailability of teclistamab-cqyv is 72% with its subcutaneous formulation. The time to peak effect of teclistamab-cqyv is approximately 139 hours (range: 19–168 hours) after the first treatment dose and 72 hours (range: 24–168 hours) after the 13th treatment dose. The clearance of teclistamab-cqyv is expected to decrease over time, with a mean clearance of 0.472 liters per day at the 13th treatment dose (Janssen Biotech, Inc., 2022).

CLINICAL TRIALS

The approval of teclistamab-cqyv was based on the MajesTEC-1 clinical trial, a single-arm, open-label, multicenter, phase I–II study (N = 165; Moreau et al., 2022). Patients who received at least three previous lines of therapy, including triple-class exposure, were eligible. Eligible patients must be 18 years of age or older with an Eastern Cooperative Oncology Group (ECOG) Performance Status scale of 0 or 1 and a documented diagnosis of relapsed or refractory MM. The trial excluded patients who had a stroke, seizure, allogeneic stem cell transplantation within the past 6 months, previous BCMA-targeted treatment, known active central nervous system involvement or clinical signs of meningeal involvement of MM, and active or documented history of autoimmune disease (Moreau et al., 2022).

Patients received step-up doses of 0.06 mg/kg and 0.3 mg/kg, followed by 1.5 mg/kg subcutaneously once weekly until disease progression, unacceptable toxicity, withdrawal of consent, death, or end of the study (defined as 2 years after the administration of the first dose of teclistamab-cqyv in the last enrolled participant). In the MajesTEC-1 trial, hospitalization and premedication with dexamethasone, acetaminophen, and diphenhydramine were required for each step-up dose and for the first full dose of teclistamab-cqyv. The cycle duration was 21 days in phase I and 28 days in phase II (Moreau et al., 2022).

The median number of prior lines of therapy was five (range: 2–14 therapies). Around 82% of patients received prior stem cell transplantation (Moreau et al., 2022). All patients had received prior therapy with a PI, an IMiD, and an anti-CD38 monoclonal antibody, with 78% being triple-class refractory (refractory to PI, IMiD, and anti-CD38

monoclonal antibody). The primary outcome was the overall response rate (ORR), defined as a partial response (PR) or better (very good partial response [VGPR]), complete response (CR), or stringent complete response (sCR) according to the International Myeloma Working Group. Key secondary endpoints included the duration of response; a VGPR or better; a CR or better; the time until response; progression-free survival and OS; status with respect to minimal residual disease; and safety, pharmacokinetics, and immunogenicity. With a median follow-up of 14.1 months, patients in the MajesTEC-1 trial had an ORR of 63% (95% confidence interval [CI] = 55.2%–70.4%), with 39.4% of patients achieving a CR or better. The median time until the first response was 1.2 months (range: 0.2–5.5 months) while the median duration of response was 18.4 months (95% CI = 14.9–not estimable; Moreau et al., 2022).

ADVERSE EFFECTS

In the pivotal MajesTEC-1 trial, common adverse effects were hematologic, including 70.9% of patients with neutropenia, 52.1% with anemia, and 40% with thrombocytopenia (Moreau et al., 2022).

Additionally, a notable side effect of BiTE therapy that occurred in this trial was cytokine release syndrome (CRS), a form of systemic inflammatory response (Lee et al., 2019). Cytokine release syndrome is characterized by fever, tachypnea, headache, tachycardia, hypotension, rash, and/or hypoxia (Brown et al., 2021). There were 72.1% of patients who experienced CRS, with only 0.6% experiencing grade 3 severity and no grade 4 CRS observed in MajesTEC-1. Most CRS events occurred after the step-up doses and cycle 1 dose. Most notably, 3.6% experienced CRS in cycle 2 or later of grade 1 or 2 severity. The median time until the onset of CRS was 2 days (range: 1–6 days) after the most recent dose, while the median duration was 2 days (range: 1–9 days; Moreau et al., 2022).

Neurotoxic events occurred in 14.5% of patients, with most events being grades 1 or 2 (Moreau et al., 2022). Headache was the most reported neurotoxicity event in 8.5% of patients. Immune effector cell–associated neurotoxicity syndrome (ICANS), on the other hand, occurred in 3% of patients (all grade 1 or 2). This is a disorder characterized by a pathologic process involving the central nervous system (CNS) following any immunotherapy that results in the engagement of endogenous or infused T cells and/or other immune effector cells (Lee et al., 2019). Symptoms of ICANS may range from subtle inattention, aphasia, or altered mental status, and may progress to seizures or cerebral edema. In MajesTEC-1, 1.2% of patients experienced ICANS following step-up dose 1 and 0.6% of patients experienced ICANS following step-up dose 2. The median time until onset of ICANS was 4 days (range: 2–8 days) after the most recent dose with a median duration of 3 days (range: 1–20 days; Moreau et al., 2022).

A list of treatment-related adverse events occurring in more than 10% of patients from the MajesTEC-1 trial is outlined in Table 1. Significant laboratory abnormalities that were more than 30% from baseline are summarized in Table 2. Other clinically relevant adverse events occurring in fewer than 10% of patients who received teclistamab-cqyv include febrile neutropenia, sepsis, seizure, Guillain-Barré syndrome, hepatic failure, and new onset or reactivated viral infections.

DOSING AND ADMINISTRATION

Teclistamab-cqyv is administered once weekly as a subcutaneous injection at a dose of 1.5 mg/kg. Prior to starting this weekly dosing schedule, patients must complete a step-up dosing schedule, which includes 0.06 mg/kg on day 1, 0.3 mg/kg on day 4, and 1.5 mg/kg on day 7 (Janssen Biotech, Inc., 2022). Due to the risk of CRS and neurologic toxicity, it is recommended that patients be hospitalized for 48 hours after administration of all doses within the step-up dosing schedule. Pretreatment medications should be administered before each dose of the teclistamab-cqyv step-up dosing schedule. Recommended premeditations include a corticosteroid (oral or intravenous dexamethasone 16 mg), a histamine-1 (H1) receptor antagonist (oral or intravenous diphenhydramine 50 mg or equivalent), and an antipyretic (oral or intravenous acetaminophen 650 mg to 1,000 mg or equivalent). Pretreatment medications may be necessary prior to subsequent doses of teclistamab-cqyv in patients who experienced CRS with the prior dose of teclistamab-cqyv or in patients who require repeat doses within the step-up dosing schedule following a dose delay.

Table 1. Adverse Reactions Occurring in ≥ 10% of Patients

Adverse reactions		All grades, %	Grades 3–4, %
General disorders and administration site conditions	Pyrexia	76	3.0
	Injection site reaction	37	0.6
	Fatigue	33	2.4
	Chills	16	0
	Pain	15	1.8
	Edema	13	0
Immune system disorders	Cytokine release syndrome	72	0.6
	Hypogammaglobulinemia	11	1.2
Musculoskeletal and connective tissue disorders	Musculoskeletal pain	44	4.2
	Bone pain	16	3.0
Infections	Upper respiratory tract infection	26	2.4
	Pneumonia	24	15.0
	Urinary tract infection	11	5.0
Gastrointestinal disorders	Nausea	25	0.6
	Diarrhea	21	2.4
	Constipation	18	0
	Vomiting	12	0.6
Vascular disorders	Hypotension	18	1.2
	Hemorrhage	12	1.8
	Hypertension	12	4.8
Respiratory, thoracic, and mediastinal disorders	Hypoxia	18	1.8
	Cough	15	0
Cardiac disorders	Cardiac arrhythmia	16	1.8
Metabolism and nutrition disorders	Decreased appetite	11	0.6
Renal and urinary disorders	Acute kidney injury	11	3.6

Note. Information from Janssen Biotech, Inc. (2022).

There are no dosage adjustments in the prescribing information for hepatic impairment or altered kidney function. However, the release of cytokines during teclistamab-cqyv treatment may suppress the activity of cytochrome P450 (CYP) enzymes, resulting in increased exposure to CYP substrates. The greatest risk for drug-drug interactions is likely to occur within 7 days of starting the teclistamab-cqyv step-up dosing regimen, as well as during and after CRS. Thus, it is recommended to monitor for toxicity or concentrations of CYP substrates. The information regarding dosage modifications and management specific to adverse reactions can be found in the prescribing information (Janssen Biotech, Inc, 2022). Management of cytokine release is summarized in Table 3. Table 4 outlines a step-by-step approach to the management of general neurotoxicity, while Table 5 outlines the management of ICANS.

IMPLICATIONS FOR THE ADVANCED PRACTITIONER

Teclistamab-cqyv is now approved for patients with relapsed or refractory MM who have failed four prior lines of therapy. Serious adverse effects such as CRS and ICANS have occurred with teclistamab-cqyv use. However, these events have primarily been either grade 1 or 2, with most events occurring during the step-up dosing schedule. For this reason, it is important to strongly consider

Table 2. Laboratory Abnormalities (≥ 30%) That Worsened From Baseline

Laboratory abnormalities		All grades, %	Grades 3 or 4, %
Hematology	Lymphocyte count decreased	92	84.0
	White blood cell decreased	86	41.0
	Neutrophil count decreased	84	56.0
	Platelet count decreased	71	22.0
	Hemoglobin decreased	67	33.0
Chemistry	Albumin decreased	68	6.0
	Alkaline phosphatase increased	42	2.4
	Phosphorus decreased	38	13.0
	Gamma-glutamyl transferase increased	37	8.0
	Sodium decreased	35	10.0
	Aspartate aminotransferase increased	34	1.2
	Calcium (corrected) decreased	31	1.2
	Creatinine increased	30	3.0

Note. Information from Janssen Biotech, Inc. (2022).

Table 3. Management of Cytokine Release Syndrome

Grade	Presenting symptoms	Actions
Grade 1	Temperature ≥ 38°C (100.4°F) attributed to CRS	• Withhold teclistamab-cqyv until CRS resolves. • Administer premedication prior to the next teclistamab-cqyv dose.
Grade 2	Temperature ≥ 38°C (100.4°F) attributed to CRS, with: hypotension responsive to fluids and not requiring vasopressors and/or oxygen requirement of low-flow nasal cannula (≤ 6 L/minute) or blow-by	• Withhold teclistamab-cqyv until CRS resolves. • Administer premedication prior to the next dose. • Patients should be hospitalized for 48 hours following the next teclistamab-cqyv dose.
Grade 3	Temperature ≥ 38°C (100.4°F) attributed to CRS, with: hypotension requiring one vasopressor with or without vasopressin and/or oxygen requirement of high-flow nasal cannula (> 6 L/minute), face mask, nonrebreather mask, or Venturi mask	First occurrence of grade 3 CRS with duration < 48 hours: • Withhold teclistamab-cqyv until CRS resolves. • Provide supportive therapy as clinically necessary (may include intensive care). • Administer premedication prior to the next teclistamab-cqyv dose. • Patients should be hospitalized for 48 hours following the next teclistamab-cqyv dose. Recurrent grade 3 CRS or grade 3 CRS with duration ≥ 48 hours: • Permanently discontinue teclistamab-cqyv. • Provide supportive care as clinically necessary (may include intensive care).
Grade 4	Temperature ≥ 38°C (100.4°F) attributed to CRS, with: hypotension requiring multiple vasopressors (excluding vasopressin) and/or oxygen requirement of positive pressure (e.g., CPAP, BiPAP, intubation, and mechanical ventilation)	• Permanently discontinue teclistamab-cqyv. • Provide supportive care as clinically necessary (may include intensive care).

Note. CPAP = continuous positive airway pressure; BiPAP = bilevel positive airway pressure. Information from Janssen Biotech, Inc. (2022).

Table 4. Management of Neurologic Toxicity (Excluding ICANS)

Adverse reaction	Severity	Actions
Neurologic toxicity (excluding ICANS)	Grade 1	• Withhold teclistamab-cqyv until neurologic toxicity symptoms resolve or stabilize.
	Grade 2 Grade 3 (first occurrence)	• Withhold teclistamab-cqyv until neurologic toxicity symptoms improve to grade 1 or less. • Provide supportive therapy.
	Grade 3 (recurrent) Grade 4	• Permanently discontinue teclistamab-cqyv. • Provide supportive therapy, which may include intensive care.

Note. Adverse events grading according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.03). ICANS = immune effector cell–associated neurotoxicity syndrome. Information from Janssen Biotech, Inc. (2022).

hospitalization and administer premeditations before these doses. Additionally, teclistamab-cqyv is only available through a restricted program called Tecvayli Risk Evaluation and Mitigation Strategy (REMS). The advance practitioner must be enrolled in Tecvayli REMS and successfully complete the required knowledge assessment to prescribe teclistamab-cqyv. All patients treated with teclistamab-cqyv will receive a Patient Wallet Card. This card describes the signs and symptoms of CRS and neurologic toxicity. The advanced practitioner should also discuss the signs and symptoms associated with neurologic toxicity, including headache, confusion, dysgraphia, motor dysfunction, neuropathy, or encephalopathy. Patients are advised to immediately contact a health-care provider if they experience any signs or symptoms of neurologic toxicity.

Teclistamab-cqyv can cause severe, life-threatening infections, as observed in the trial. The advanced practitioner should monitor immunoglobulin levels during treatment with teclistamab-cqyv and treat according to guidelines, including infection precautions. Before starting treatment with teclistamab-cqyv, consider initiating antiviral prophylaxis to prevent herpes zoster reactivation (Janssen Biotech, Inc., 2022). Given the risk of neutropenia, monitor patients for signs and symptoms of infection prior to and during treatment. During periods of neutropenia, consider initiating antibiotic prophylaxis in patients at risk of opportunistic infection. The use of granulocyte colony-stimulating factor (G-CSF) should be considered for neutropenic patients. In MajesTEC-1, approximately 77.8% of patients who developed neutropenia received G-CSF at the physician's discretion.

There currently are no contraindications to use included in the prescribing information. Notable warnings and precautions for teclistamab-cqyv use include hepatotoxicity, infections, neutropenia, hypersensitivity or other administration reactions, and embryo-fetal toxicity. Based on the mechanism of action, teclistamab-cqyv may cause fetal harm when administered to pregnant women. Women of reproductive potential should use effective contraception during treatment and for 5 months after the last dose of teclistamab-cqyv. It is unknown if teclistamab-cqyv is present in breast milk; however, given the potential for adverse reactions in the breastfed infant, breastfeeding is not recommended during therapy and for 5 months after the last dose of teclistamab-cqyv.

Teclistamab-cqyv is currently supplied as 30 mg/3 mL (10 mg/mL) and 153 mg/1.7 ml (90 mg/mL), preservative-free, single-dose vials (Janssen Biotech, 2022). The estimated average wholesale price (AWP) for one 30 mg/3 mL vial is $2,124, and 153 mg/1.7 mL is $10,832.40 (Lexicomp, n.d.). Based on the current dosing schedule and AWP, the yearly cost of teclistamab-cqyv is estimated to exceed $500,000. A savings program is available through the manufacturer for commercially insured patients. There is no income requirement, and patients may pay as little as $5 per dose with a limit of $26,000 maximum program benefit per calendar year. Depending on the patient's insurance, savings may be applied toward a copay, coinsurance, or deductible. The program does not cover the costs of injection administration. Additionally, this program is not for patients who use any state or federal government-funded health-care program. Given the potentially high cost of

Table 5. Management of Immune Effector Cell–Associated Neurotoxicity Syndrome

Grade	Presenting symptoms	Actions
Grade 1	ICE score 7–9, or depressed level of consciousness: awakens spontaneously	• Withhold teclistamab-cqyv until ICANS resolves. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management, including consideration for starting nonsedating, antiseizure medicines for seizure prophylaxis.
Grade 2	ICE score 3–6, or depressed level of consciousness: awakens to voice	• Withhold teclistamab-cqyv until ICANS resolves. • Administer dexamethasone 10 mg intravenously every 6 hours; continue dexamethasone use until resolution to grade 1 or less then taper. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management, including consideration for starting nonsedating, antiseizure medicines for seizure prophylaxis. • Patients should be hospitalized for 48 hours following the next dose of teclistamab-cqyv.
Grade 3	ICE score 0–2, or depressed level of consciousness: awakens only to tactile stimulus, or seizures, either: • Any clinical seizure, focal or generalized, that resolves rapidly • Non-convulsive seizures on electroencephalogram (EEG) that resolve with intervention or raised intracranial pressure: focal/local edema on neuroimaging	First occurrence of grade 3 ICANS: • Withhold teclistamab-cqyv until ICANS resolves. • Administer dexamethasone 10 mg intravenously every 6 hours; continue dexamethasone use until resolution to grade 1 or less, then taper. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management, including consideration for starting nonsedating, antiseizure medicines for seizure prophylaxis. • Provide supportive therapy, which may include intensive care. • Patients should be hospitalized for 48 hours following the next dose of teclistamab-cqyv. Recurrent grade 3 ICANS: • Permanently discontinue teclistamab-cqyv. • Administer dexamethasone 10 mg intravenously and repeat dose every 6 hours; continue dexamethasone use until resolution to grade 1 or less, then taper. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management, including consideration for starting nonsedating, antiseizure medicines for seizure prophylaxis. • Provide supportive therapy, which may include intensive care.

Note. ICANS = immune effector cell-associated neurotoxicity syndrome; ICE = immune effector cell-associated encephalopathy. 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. Grading based on the American Society for Transplantation and Cellular Therapy (ASTCT) 2019 grading for ICANS. Information from Janssen Biotech, Inc. (2022).

☞ *Table continued on following page*

treatment, the advanced practitioner is encouraged to routinely screen for financial toxicity and discuss costs with patients.

With the recent withdrawal from the market of belantamab mafodotin-blmf (an antibody-drug conjugate targeting BCMA), options for targeting BCMA in relapsed or refractory MM patients now include chimeric antigen receptor (CAR) T-cell therapy or teclistamab-cqyv. As MM patients can incur significant toxicities across multiple lines of treatment, evaluating their potential tolerance of additional therapy remains crucial for

Table 5. Management of Immune Effector Cell–Associated Neurotoxicity Syndrome (cont.)

Grade	Presenting symptoms	Actions
Grade 4	ICE score 0, or depressed level of consciousness: either: • Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse • Stupor or coma or seizures, either: • Life-threatening prolonged seizure (> 5 minutes) • Repetitive clinical or electrical seizures without return to baseline in between, or motor findings: • Deep focal motor weakness such as hemiparesis or paraparesis or raised intracranial pressure/cerebral edema, with signs/ symptoms such as: • Diffuse cerebral edema on neuroimaging • Decerebrate or decorticate posturing • Cranial nerve VI palsy • Papilledema • Cushing's triad	• Permanently discontinue teclistamab-cqyv. • Administer dexamethasone 10 mg intravenously and repeat dose every 6 hours; continue dexamethasone use until resolution to grade 1 or less, then taper. • Alternatively, consider administration of methylprednisolone 1,000 mg per day intravenously and continue methylprednisolone 1,000 mg per day intravenously for 2 or more days. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management, including consideration for starting nonsedating, antiseizure medicines for seizure prophylaxis. • Provide supportive therapy, which may include intensive care.

Note. ICANS = immune effector cell-associated neurotoxicity syndrome; ICE = immune effector cell-associated encephalopathy. 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. Grading based on the American Society for Transplantation and Cellular Therapy (ASTCT) 2019 grading for ICANS. Information from Janssen Biotech, Inc. (2022).

practitioners. Teclistamab-cqyv is being studied in combination with other therapies in both the newly diagnosed and relapsed/refractory settings. For example, the MajesTEC-2 trial is characterizing the safety and tolerability of teclistamab-cqyv with daratumumab, pomalidomide, bortezomib, and nirogacestat (ClinicalTrials.gov, 2023a). The MajesTEC-3 study, on the other hand, is evaluating teclistamab-cqyv in combination with daratumumab subcutaneously (SC; Tec-Dara) vs. daratumumab SC, pomalidomide, and dexamethasone (DPd) or daratumumab SC, bortezomib, and dexamethasone (DVd; ClinicalTrials.gov, 2023b). The MajesTEC-2 study is estimated to be completed by April 10, 2024, while the MajesTEC-3 study is estimated to be completed by October 1, 2026. CAR T-cell therapy has limitations regarding patient eligibility and safety. Most notably, the grade ≥ 3 CRS rates have appeared more frequency in clinical trials involving anti-BCMA CAR T-cell therapies (Berdeja et al., 2021; Munshi et al., 2021). As lymphodepletion is an important component of CAR T-cell therapy, teclistamab-cqyv represent an alternative approach for patients who cannot undergo a conditioning lymphodepletion chemotherapy regimen (Shah et al., 2020). Furthermore, for patients without access to CAR T-cell therapy (due to geographic access to CAR T-cell therapy centers or prolonged manufacturing process of CAR T-cell products), teclistamab-cqyv offers an off-the-shelf or ready-to-use treatment option.

CONCLUSION

Teclistamab-cqyv represents a first-in-class CD3-BCMA BiTE therapy that has demonstrated efficacy and safety in relapsed or refractory MM patients. Like other cellular therapies, treatment-related adverse events have occurred, particularly CRS and ICANS. However, these events occurred less frequently and less severely with teclistamab-cqyv compared with BCMA-directed CAR T-cell therapy. Patients may benefit from teclistamab-cqyv given its safety profile. Thus, teclistamab-cqyv emerges as an attractive option for heavily treated, relapsed or refractory MM patients who face limited treatment options.

Disclosure

The authors have no conflicts of interest to disclose.

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