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Belantamab Mafodotin-blmf: A Novel Antibody-Drug Conjugate for Treatment of Patients With Relapsed/Refractory Multiple Myeloma

EMILY BEHREN KETCHUM, PharmD, ANDREA CLARKE, PharmD, BCOP, and AMBER B. CLEMMONS, PharmD, BCOP

From Augusta University Medical Center, Augusta, Georgia

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Correspondence to Emily Behren Ketchum, PharmD, 914 New Bailie Street HM Bldg, Augusta, GA 30912. E-mail: eketchum@augusta.edu

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Abstract

Multiple myeloma (MM) is a hematologic malignancy characterized by proliferation of plasma cells with or without production of monoclonal immunoglobulins. Management of patients with MM begins with induction therapy, typically a proteasome inhibitor (PI) with dexamethasone and an immunomodulator (IMID), followed by autologous hematopoietic stem cell transplantation in eligible patients. Although various treatments are available, MM is considered incurable, and patients with progression after multiple treatment lines, including CD38 monoclonal antibodies, have a median overall survival of 8.6 months. Belantamab mafodotin-blmf (Blenrep) is a first-in-class antibody-drug conjugate directed against B-cell maturation antigen (BCMA) that obtained U.S. Food and Drug Administration accelerated approval in August 2020 for patients with multiply relapsed/refractory MM. This article provides information on the mechanism of action, efficacy, safety, monitoring, and current place in therapy for belantamab mafodotin-blmf.

Multiple myeloma (MM) is a hematologic malignancy characterized by proliferation of plasma cells with or without production of monoclonal immunoglobulins. The median age of diagnosis is 69 years, with a 5-year survival rate of 54% (American Society of Clinical Oncology, 2021a). Symptomatic multiple myeloma is diagnosed by ≥ 10% plasma cells in the bone marrow or extramedullary plasmacytoma plus one or more myeloma-defining event, generally referred to as the SLiM-CRAB criteria. SLiM are biomarkers of malignancy, which include 60% bone marrow involvement (S), free light chain ratio ≥ 100 mg/L (Li), or one or more non-

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osteolytic focal marrow lesion on MRI (M). CRAB is an acronym for common disease manifestations of hypercalcemia (C), renal failure (R), anemia (A), and bone lesions (B; National Comprehensive Cancer Network [NCCN], 2020).

Treatment decisions are based on risk stratification of patients, which includes assessment of cytogenetic abnormalities, and disease characteristics. The management of patients with MM begins with induction therapy, typically a proteasome inhibitor (PI) with dexamethasone and an immunomodulator (IMiD), followed by autologous hematopoietic stem cell transplantation (HCT) if eligible. Patient eligibility for HCT is a balance between chemotherapy toxicity and treatment efficacy (Atrash et al., 2020). Although older age and renal dysfunction are not absolute contraindications, ineligible patients may include advanced elderly, poor performance status, multiple comorbidities, or organ dysfunction, including hepatic, pulmonary, renal, or cardiac dysfunction. Maintenance therapy is recommended for patients who demonstrate response or stable disease after primary therapy and after HCT (NCCN, 2020). Goals of treatment include achieving a deep and durable response, which is associated with improved overall survival (OS) and longer time to relapse (van de Donk et al., 2021). Although various treatments are available, MM is considered incurable, and patients often require multiple lines of combination therapy for life (American Society of Clinical Oncology, 2021b).

Immunomodulators and PIs, introduced in the early 2000s, significantly improved remission and survival rates. More recently, CD38 monoclonal antibodies daratumumab (Darzalex) and isatuximab (Sarclisa) were integrated into standard of care for patients with refractory MM due to improved outcomes in single-agent and combination regimens (Pulte et al., 2015). However, patients with progression after multiple treatment lines, including CD38 monoclonal antibodies, have a median OS of 8.6 months (Gandhi et al., 2019). Belantamab mafodotin-blmf (Blenrep), also referred to as belamaf, obtained U.S. Food and Drug Administration (FDA) accelerated approval in August 2020 for patients with multiply relapsed/refractory MM (GlaxoSmithKline, 2020). This article provides information on the mechanism of action, efficacy, safety, monitoring, and current place in therapy for belamaf.

NOVEL TARGET AND IMMUNOCONJUGATE MECHANISM

Belamaf is a first-in-class antibody-drug conjugate (ADC) directed against B-cell maturation antigen (BCMA). BCMA, a member of the tumor necrosis factor (TNF) receptor superfamily, is a cell-surface receptor protein or messenger RNA expressed almost solely in human plasma cells. Ergo, BCMA is an ideal target due to the lack of expression in normal human tissues and upregulation in MM cells. During malignant transformation of immature plasma cells, BCMA receptor and ligand (APRIL and BAFF) overexpression activate several signal transduction pathways involved in oncogenesis, including nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB), protein kinase B (AKT), signal transducer and activator of transcription 3 (STAT3), phosphoinositide 3-kinase (PI3K), and mitogen-activated protein kinases (MAPK) cascades. Thus, BCMA overexpression promotes tumor growth, survival, and drug resistance within malignant plasma cells (Abramson, 2020). Preclinical studies indicate that blocking BCMA ligand binding and inhibiting BCMA target pathways decreases MM cell viability and colony formation (Tai et al., 2016).

Belamaf is a humanized IgG1 antibody that binds BCMA and is conjugated to a cytotoxic agent, monomethyl auristatin F (mafodotin), by a protease-resistant maleimidocaproyl linker (Trudel et al., 2018). After binding BCMA, belamaf is internalized and undergoes proteolytic cleavage, releasing mafodotin. The released mafodotin disrupts microtubular networks leading to cell cycle arrest and apoptosis. Additional anticancer effects include antibody-dependent cellular toxicity and antibody-dependent cellular phagocytosis via recruitment of the immune system from an afucosylated parent antibody (GlaskoSmithKline, 2020).

DOSING AND ADMINISTRATION

Recommended dosing for belamaf is 2.5 mg/kg using actual body weight administered once every 3 weeks and continued until disease progression or unacceptable toxicity. No dose modification is required for renal impairment if the

estimated glomerular filtration rate (eGFR) is > 30 mL/min/1.73 m^2 or for mild hepatic impairment where total bilirubin is ≤ 1.5 times upper limit of normal. However, no dosing recommendations have been established for patients with eGFR < 30 mL/min/1.73 m^2, those with end-stage renal disease either with or without dialysis, or those with moderate to severe hepatic impairment. Therefore, due to the lack of safety and efficacy data for severe renal and hepatic impairment at this time, belamaf should be considered contraindicated in these patients. Belamaf demonstrated no difference in pharmacokinetics for subjects with body weight from 42 kg to 130 kg. Dose interruption, reduction, or discontinuation may be required for adverse events such as thrombocytopenia, infusion reactions, or corneal adverse events. In general, dose reduction for the first adverse event is belamaf 1.9 mg/kg of actual body weight once every 3 weeks. If the patient is unable to tolerate this reduced dose, discontinuation of therapy is recommended (Table 1; GlaxoSmithKline, 2020).

Belamaf is administered as an intravenous infusion over 30 minutes via an infusion set made from polyolefin or PVC. Utilization of a 0.2 micron polyethersulfone-based filter is optional. For product preparation, after belamaf vials reach room temperature and are reconstituted, the calculated patient-specific dose must be further diluted into 250 mL of normal saline to final concentration of 0.2–2 mg/mL. Diluted solution may be stored refrigerated for 24 hours, and once removed from the refrigerator, the diluted solution should be allowed to equilibrate to room temperature prior to administration, which must be completed within 6 hours of removal from refrigerator (GlaxoSmithKline, 2020).

Belamaf does not require any premedication. However, if a patient experiences an infusion reaction, then premedication should be administered for all subsequent infusions (GlaxoSmithKline, 2020). Prior to administration, providers shall ensure compliance with Risk Evaluation and Mitigation Strategy (REMS) requirements, including ocular screening (see the following section). This agent does not have any known effects on transporters or drug metabolism (GlaxoSmithKline, 2020).

CLINICAL EFFICACY

The DREAMM-1 study was a phase I, open-label, multinational trial assessing dose escalation of belamaf with a maximum of 4.6 mg/kg in part 1 and 3.4 mg/kg every 3 weeks in part 2. A dose of 3.4 mg/kg was selected after part 1 due to a balance of efficacy and toxicity, although no dose-limiting toxicity was identified. Preliminary efficacy data for part 2 showed an overall response rate (ORR) of 60% (95% confidence interval [CI] = 42%–76.1%; Trudel et al., 2018).

The FDA accelerated approval for belamaf was based on results from the DREAMM-2 study, a phase II, open-label, single-arm, multinational trial for patients with relapsed or refractory MM who had an Eastern Cooperative Oncology Group (ECOG) score of 0 to 2 and progression after receiving three or more prior lines of therapy including immunomodulatory drugs and proteasome inhibitors and refractory or intolerant (or both) to an anti-CD38 monoclonal antibody and were either post-autologous stem cell transplantation or had been deemed ineligible for transplant. One hundred and ninety-six subjects were randomized to belamaf 2.5 mg/kg or 3.4 mg/kg every 3 weeks until disease progression or unacceptable toxicity. Median prior lines of therapy were 7 (range 3–21) in the 2.5 mg/kg arm and 6 (3–21) in the 3.4 mg/kg arm, demonstrating patients were heavily pretreated, with the majority (75% of the 2.5 mg/kg arm) having undergone autologous HCT.

Overall response rate, defined as confirmed partial response or better, was documented in 31% (97.5% CI = 20.8–42.6) of subjects in the 2.5 mg/kg arm and 34% (97.5% CI = 23.9–46) of subjects in the 3.4 mg/kg arm, respectively, with a median follow-up duration of 6.3 months (IQR [interquartile range] 3.7–7.7) and 6.9 months (IQR 4.8–7.9). Median progression-free survival (PFS) was 2.9 months (95% CI = 2.1–3.7) and 4.9 months (95% CI = 2.3–6.2), respectively. Dose delays and reductions were less common in the 2.5 mg/kg arm (54% and 29%) than in the 3.4 mg/kg arm (62% and 41%). The authors concluded that belamaf demonstrated efficacy and acceptable safety, with the 2.5 mg/kg dose showing similar activity and an improved safety profile in comparison with the higher dose in heavily pretreated patients (Lonial et al., 2020).

Table 1. Belantamab Mafodotin-blmf Dose Adjustments for Toxicity

Toxicity	Modification	Resume[a]
Ocular toxicity		
Grade 1: Mild superficial keratopathy or decline from baseline of 1 line on Snellen Visual Acuity	Continue	N/A
Grades 2–3: Moderate to severe superficial keratopathy or decline from baseline of 2 or 3 lines on Snellen Visual Acuity and not worse than 20/200	Withhold	At the same dose with improvement in both corneal examination findings and change in BCVA to grade 1 or better
Grade 4: Corneal epithelial defect or Snellen Visual Acuity worse than 20/200	Consider permanent discontinuation	At reduced dose (1.9 mg/kg) with improvement in both corneal examination findings and change in BCVA to grade 1 or better
Thrombocytopenia		
25,000 to 50,000 cells/μL	Consider withholding and/or dose reduction	If dose reducing, consider 1.9 mg/kg
< 25,000 cells/μL	Withhold	Consider reduced dose (1.9 mg/kg) once improved to ≤ grade 3
Infusion-related reactions		
Grades 2–3[b]: Moderate to severe indicating therapy interruption either promptly responsive to treatment or prolonged reaction not rapidly responsive to interruption or treatment, a recurrence of symptoms after initial improvement, or requiring hospitalization	Interrupt infusion and provide supportive care	Once symptoms resolve and reduce rate by ≥ 50%; administer premedications with all subsequent infusions
Grade 4[b]: Life-threatening with urgent intervention indicated	Permanently discontinue	N/A
Other adverse reactions		
Grade 3	Withhold	Consider reduced dose (1.9 mg/kg) once improved to grade 1 or better
Grade 4	Consider permanent discontinuation	At reduced dose (1.9 mg/kg) once improved to grade 1 or better

Note. BCVA = best corrected visual acuity.
[a]If unable to tolerate 1.9 mg/kg, discontinue therapy.
[b]Per Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 grading.

Thirteen-month follow-up of the 2.5 mg/kg arm of the DREAMM-2 trial reported a similar ORR and safety profile as the initial analysis with a median duration of response (DOR) of 11 months, OS of 13.7 months, and PFS of 2.8 months. Subjects received a median of 3 cycles (1–17), and median time on study was 2.1 months, with the majority discontinuing treatment due to progressive disease. Of note, the authors attribute the difference in PFS and OS to the use of salvage therapies, and subjects experiencing a very good partial response or better had a PFS of 14 months. Dose delays (54%) and reductions (35%) due to adverse effects were common. Sixteen subjects identified as belamaf responders experienced ≥ 1 prolonged dose delay (defined as missing > 3 cycles). Dose delays did not significantly affect outcomes, as 14 of the subjects (88%) demonstrated continued clinical benefit and 6 subjects (38%) deepened response. Subgroup analysis demonstrated similar safety and efficacy among subjects with high-risk cytogenetics and for those with mild or moderate renal impairment efficacy was similar with higher rates of anemia and thrombocytopenia (Lonial et al., 2021a).

Currently, ClinicalTrials.gov lists numerous trials for belamaf for the treatment of patients with MM, including in the first-line setting and in combination with various other agents. DREAMM-3, a phase III open-label randomized trial comparing

belamaf to pomalidomide (Pomalyst) plus low-dose dexamethasone in patients with relapsed/refractory MM, is ongoing. As opposed to the single-arm DREAMM-2 study, DREAMM-3 will provide a direct comparison of belamaf to standard of care. DREAMM-12 and DREAMM-13 trials will assess safety and efficacy in patients with severe renal and hepatic impairment. Additional trials are ongoing to evaluate belamaf in other disease states, including amyloidosis, plasmablastic lymphoma, and large B-cell lymphoma. Further, other interventions targeting BCMA such as autologous and allogeneic chimeric antigen receptor T-cell therapy (CAR-T), bispecific T-cell engager antibodies, and ADCs are currently in the pipeline.

ADVERSE EFFECTS

In the DREAMM-1 study, common adverse events seen in the selected 3.4 mg/kg dosing included corneal events (63%), 54% of which were grade 1 or 2. The most common grade 3 or 4 reactions were thrombocytopenia (34%) and anemia (14%; Trudel et al., 2018). The phase II DREAMM-2 study did not uncover any new safety concerns. Keratopathy (defined as corneal epithelial changes found on eye exams with or without symptoms) was the most common grade 1 or 2 adverse event, seen in 43% and 54% of patients at 2.5 mg/kg and 3.4 mg/kg doses, respectively. Keratopathy was also one of the most common grade 3 or 4 adverse events, occurring in 27% and 21% of patients, respectively (Lonial et al., 2020).

The ocular toxicity seen in the DREAMM-1 and -2 trials can be attributed to the cytotoxic mafodotin component of the ADC. This toxicity may present as severe vision loss, corneal ulceration, blurred vision, dry eye syndrome, epithelial keratopathy, or decreased visual acuity. Onset of toxicity can vary, although most events occur within the first two cycles. The exact mechanism is not well defined, but proposed mechanisms include premature cleavage of the linker in extracellular environments, linker-cytotoxin intracellular metabolism, and Fc-receptor–mediated cellular uptake. This keratopathy may be asymptomatic and only detectable on slit lamp and visual acuity exams; therefore, screening and documentation per a REMS program is required, as detailed in the following section (Wahab et al., 2021). Current management of ocular toxicity includes a multidisciplinary approach and is mainly preventative with the use of dose modifications (Table 1) and lubricating eye drops throughout treatment. Corticosteroid eye drops are not recommended due to a lack of benefit found in the DREAMM-2 study. Investigation of the mechanism and pharmacokinetics of ocular toxicity is underway, as are evaluations of various mitigation and management strategies (Lonial et al., 2021b).

Other notable adverse reactions observed in the DREAMM-2 trial include infusion-related reactions, thrombocytopenia, and anemia. Most infusion-related reactions were grade 1 or 2 (18% with 2.5 mg/kg dosing and 15% with 3.4 mg/kg dosing), and almost all reactions occurred with the first infusion. Grade 3 infusion-related reactions occurred in only 3% and 1% respectively, with one patient discontinuing treatment due to grade 3 reactions at both first and second infusions. Premedications for infusion-related reactions were not required by protocol but were administered to approximately one third of patients with no overt difference in reaction rate. Thrombocytopenia occurred in 35% of patients at the 2.5 mg/kg dose (15% grade 1–2; 20% grade 3–4) and in 58% at the 3.4 mg/kg dose (24% grade 1–2; 33% grade 3–4; 1% grade 5), with a median time to onset of 22 days. Anemia was also commonly observed, occurring in 24% (4% grade 1–2; 20% grade 3–4) and 37% (12% grade 1–2; 25% grade 3–4) of patients, respectively. Serious adverse events occurred in 40% and 47% of subjects, with two potentially treatment-related deaths from sepsis and hemophagocytic lymphohistiocytosis. The 2.5 mg/kg dose was ultimately deemed more tolerable and granted FDA accelerated approval (GlaxoSmithKline, 2020; Lonial et al., 2020).

IMPLICATIONS FOR THE ADVANCED PRACTITIONER

Many patients with MM will ultimately relapse and require additional treatment. Several new therapies, alongside belamaf, are available for patients with late relapse and triple refractory MM, including allogeneic HCT, selinexor (Xpovio) plus dexamethasone, and CAR T-cell therapy.

NCCN Guidelines recommend allogeneic HCT be completed in the context of a clinical trial due to

limited data on when and who may benefit and the best type of conditioning regimen (myeloablative or nonmyeloablative) to select (NCCN, 2020).

Selinexor, a selective inhibitor of exportin 1, in combination with dexamethasone was evaluated in patients who were refractory to at least two IMiDs, two PIs, and a CD38 antibody, and demonstrated two complete responses and a partial response or better in 26% (95% CI = 19–35) of patients with a median PFS of 3.7 months, DOR of 4.4 months, and OS of 8.6 months. Common adverse reactions were thrombocytopenia (73%), anemia (67%), fatigue (73%), and nausea (72%; Chari et al., 2019). An indirect comparison study of belamaf (DREAMM-2) vs. selinexor plus dexamethasone (STORM Part 2) suggests that while ORR was similar, belamaf may have improved OS (hazard ratio [HR] 0.53; 95% CI = 0.34–0.83) and DOR (HR 0.41; 95% CI 0.21–0.83) with a favorable safety profile due to fewer grade 3 to 4 hematologic toxicities and all-grade nonhematologic adverse events (Prawitz et al., 2021). Of note, direct comparison of these regimens has not been published to date, limiting interpretations.

At this time, one CAR T-cell product for patients with MM is available with others in the pipeline. A BCMA-targeted CAR T-cell therapy, idecabtagene vicleucel (Abecma), was approved in March 2021 for multiply relapsed MM after patients received lymphodepleting chemotherapy. This agent demonstrated ORR of 73% and complete response in 33% of patients with a median PFS of 8.8 months (95% CI = 5.6–11.6) and common toxicities of cytokine release syndrome (84%), neutropenia (91%), anemia (70%), thrombocytopenia (63%), and neurotoxicity (18%). Responses were also durable with an overall DOR of 10.6 months and 23 months for those with complete response. Follow-up data demonstrated an OS of 24.8 months (95% CI = 19.1–31.2; Munshi et al., 2021). This CAR T-cell therapy showed significant and durable responses in a heavily pretreated population (5–7 prior lines of therapy). Another CAR T-cell product, ciltacabtagene autoleucel (ciltacel), is currently under FDA review based on the phase I/IIb study CARTITUDE-1. Ciltacabtagene autoleucel demonstrated impressive and durable responses in a heavily pretreated (6 median prior lines of therapy) triple refractory population of 113 patients, but had a high rate of toxicity including six deaths due to treatment-related adverse effects (Berdeja et al., 2021). Overall, a significant advantage of CAR T-cell therapy in patients with MM is the potential for patients to remain off therapy until disease progression, in contrast to HCT, as patients often require maintenance therapy. Potential disadvantages include costs and patients committing to be in proximity of a transplant center for 30 days after the infusion and avoiding driving or operating heavy machinery for 8 weeks.

When considering the previously mentioned options for heavily pretreated patients with MM, the selection of therapy depends on patient and disease characteristics, patient desires, toxicity profile, and available resources. Selinexor-dexamethasone is an oral regimen given twice weekly, while belamaf is an intravenous and steroid-free regimen given every 3 weeks. Side effect profiles differ, with selinexor-dexamethasone showing higher rates of hematologic toxicity and no ocular adverse effects. CAR T-cell therapy likely provides a more effective and durable response but is an intense process only offered at select centers, often requiring hospitalization and close follow-up, with an increased risk of severe adverse events.

Pertinent treatment parameters to be reviewed by the provider for belamaf include ensuring eGFR is ≥ 30 mL/min/1.73 m^2, total bilirubin is ≤ 1.5 times upper limit of normal, and platelets are ≥ 50,000/μL prior to each infusion. Due to the incidence of ocular toxicity, ophthalmic exams should be completed by an ophthalmologist at baseline (within 3 weeks of the first dose), prior to each dose (at least 1 week after the previous dose and within 2 weeks of the next dose), and with any vision changes. Specific dose modifications listed in the package insert should be followed to avoid severe disease. Patients should be counseled to avoid contact lenses and use lubricating eye drops four times daily from the first infusion until the end of treatment. While the DREAMM-2 study does not specify a definition for end of treatment, continuing lubricating eye drops through the end of the last cycle is reasonable based on the 14-day half-life. Other monitoring parameters include baseline plus periodic complete blood counts to evaluate for anemia and thrombocytopenia and baseline plus periodic complete metabolic pan-

els to evaluate for renal and hepatic dysfunction and electrolyte abnormalities. The advanced practitioner should counsel patients to report signs and symptoms of ocular toxicity, such as dry eyes, changes in eyesight, or vision problems; anemia; thrombocytopenia; and infusion-reactions (GlaxoSmithKline, 2020). Guidelines for the management of belamaf-associated corneal events highlight the importance of the advanced practitioner in educating the patient, encouraging them to report ocular symptoms, making referrals to eye care specialists, and collaborating with hematologists/oncologists and ocular specialists to ensure optimal management (Lonial et al., 2021b).

To establish provider and patient education and manage risk of ocular toxicity, belamaf is available through a REMS-restricted distribution program (Table 2). Health-care settings should designate an authorized representative to oversee implementation and adherence to the program. Advanced practitioners may serve as the authorized representative. Prior to administration, health-care settings that dispense belamaf must obtain an authorization to dispense each dose in order to verify prescriber certification and patient enrollment and complete the REMS checklist available on the belamaf REMS program website. Within 5 business days of administration, health-care settings are required to submit the checklist to the REMS program. To become certified, providers must review the prescribing information and program education, then complete and submit a knowledge assessment. Providers enroll in the program by completing and submitting the prescriber enrollment form. Before treatment, providers are to counsel patients on the ocular risk and monitoring requirements, enroll patients by completing and submitting the patient enrollment form, consult an eye care specialist using the eye care professional consult request form to complete visual acuity and slit lamp examinations, and submit the patient status form after assessing results of the consult. Providers are to continue consulting an eye care specialist and submitting the consult request form and patient status form with each treatment. Patients are required to receive counseling, enroll in the program by filling out the patient enrollment form with the provider, and attend ophthalmic visits (FDA, 2020).

The average wholesale price of a 100-mg vial of belamaf is approximately $10,081 (Lexicomp, 2021). A program entitled "Together with GSK" offers a co-pay assistance program for commercially insured patients and a patient assistance

Table 2. Belantamab Mafodotin-blmf Risk Evaluation and Mitigation Strategy (REMS): Restricted Distribution Program Requirements

Party	Action	Forms for submission	How often
Health-care setting	• Designate authorized representative • Train staff • Establish processes and procedures	• Health-care setting enrollment form	Once with enrollment
	• Obtain authorization to dispense each dose	• REMS checklist	Each dispense
Providers	• Review prescribing information • Review program overview and education • Complete knowledge assessment • Enroll as prescriber • Counsel on ocular toxicity and ophthalmic evaluations • Enroll patient	• Knowledge assessment • Prescriber enrollment form • Patient enrollment form	Once with enrollment
	• Consult eye care professional • Assess consult	• Eye care professional consult request form • Patient status form	Each treatment
Patients	• Receive counseling • Enroll	• Patient enrollment form	Once with enrollment
	• Attend ophthalmic exams		Each treatment

program (PAP) for patients with Medicare or those who are uninsured. Patients receiving prescription drug insurance through Medicaid, VA, DOD, TRICARE, or through a government run program (excluding Medicare) do not qualify. Providers can download and complete the co-pay assistance form and check eligibility for PAP on the Together with GSK Oncology website (GSK Oncology, 2020).

CONCLUSION

Despite advances, new therapies are needed for patients with MM who progress through multiple lines of therapy. Belamaf is a first-in-class ADC that targets BCMA receptors expressed on the surface of MM cells, offering the advantage of a targeted therapy approach. Providers should take note the initial FDA approval was granted for the treatment of patients with multiply relapsed/refractory MM who failed four or more lines of therapy due to the heavily pretreated (84% with > 4 prior lines of therapy) population in DREAMM-2. Traditionally, MM response to treatment is thought to diminish with each subsequent line of therapy. Belamaf demonstrated impressive and durable responses in heavily pretreated subjects. Belamaf offers the advantages of targeted-therapy, steroid-free, and convenient every-3-week intravenous dosing. Important adverse reactions include ocular toxicity that must be monitored via the REMS program, as well as anemia, thrombocytopenia, and infusion reactions. Further research is forthcoming to elucidate its place in therapy and effects on patients with organ dysfunction. As the first FDA-approved BCMA-targeted agent, long-term efficacy and safety data are needed.

Disclosure

The authors have no conflicts of interest to disclose.

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