Immunotherapy in Multiple Myeloma

Charise Gleason and Donna D. Catamero

Objectives: *To review the use of monoclonal antibodies (mAbs) in the treatment of multiple myeloma (MM) and the management of most common side effects.*

Data Sources: *Review of journal articles related to mAbs in MM.*

Conclusion: *The therapeutic options for MM have improved dramatically and the development of mAbs has been associated with improvement in clinical outcomes and favorable toxicity profiles.*

Implications for Nursing Practice: *With appropriate pre-medications and nursing management, mAbs are a well-tolerated treatment option for myeloma patients.*

Key Words: *multiple myeloma, monoclonal antibodies, elotuzumab, daratumumab.*

Multiple myeloma (MM) is a malignant disorder that represents about 1.8% of all new cancer cases in the United States and accounts for approximately 30,280 new cases in 2017.[1] While there has been a substantial improvement in survival due to the development of new drug classes such as immunomodulatory agents (IMIDs) and proteasome inhibitors (PIs) along with autologous stem cell transplant (ASCT), most MM patients will still relapse at some point and require a change in therapy.[2-4] As treatment options continue to emerge, one of the most promising class of agents in development are the monoclonal antibodies (mAbs). MAbs have been used in other types of cancers for many years and are an important emerging class of agents in MM. Currently FDA approved MAbs target CD38 (Daratumumab) and SLAMF7 (Elotuzumab) to be clear as other MAbs are in development with different MOAs and targets.[5] This review will focus on elotuzumab a humanized IgG1 mAb that facilitates the destruction of MM cells by targeting the SLAMF7 protein and daratumumab (DARA), a first in class, human immunoglobulin G1 kappa (IgG1κ) anti–CD38-directed antibody.

Charise Gleason, MSN, NP-BC, AOCNP: *Advance Practice Provider Chief, Winship Cancer Institute of Emory University, Atlanta, GA*. Donna D. Catamero, ANP-BC, OCN®, CCRC: *Program Manager, Mount Sinai Medical Center, Multiple Myeloma Program, New York, NY*.

Address correspondence to Donna D. Catamero, ANP-BC, OCN®, CCRC, Mount Sinai Medical Center, Multiple Myeloma Program, One Gustave L. Levy Place, New York, NY 10029-6574. e-mail: donna.catamero@mountsinai.org

0749-2081
http://dx.doi.org/10.1016/j.soncn.2017.05.011

Elotuzumab

While elotuzumab did not demonstrate single-agent activity,[6,7] preclinical data did show synergy with the combination of elotuzumab and lenalidomide.[8] Elotuzumab in combination with

lenalidomide and dexamethasone was approved in November 2015 for MM patients who have received one to three prior lines of therapy. Elotuzumab is a humanized IgG1 mAb that facilitates the destruction of MM cells by targeting the SLAMF7 protein. SLAMF7 is a receptor present on immune cells including natural killer (NK) cells that mediates activating or inhibitory effects in NK cells. SLAMF7 is highly expressed in MM cells. Upon binding to myeloma cells, elotuzumab exerts its effects through antibody-dependent cellular cytotoxicity (ADCC); the antibody induces lysis of MM cells by activated NK cells.[6]

In the randomized phase II trial comparing elotuzumab 10 mg/kg versus 20 mg/kg with lenalidomide and dexamethasone, the overall response rate (ORR) was 92% versus 76% with a better progression-free survival (PFS) with the 10-mg dosing.[9] In the pivotal phase III clinical trial, Eloquent-2, patients who received elotuzumab in combination with lenalidomide and dexamethasone had increased response rates (79% ORR ʊ 66% in the control group) and longer PFS (68% ʊ 57% at 1 year and 41% ʊ 27% at 2 years). Median PFS was 19.4 months versus 14.9% in patients who received the combination therapy.[10]

Elotuzumab is administered intravenously (IV) at a given dose of 10 mg/kg for 8 weeks, followed by once every 2 weeks for subsequent cycles. Lenalidomide is administered as per standard recommended dosing. Dexamethasone 28 mg is given orally the day before or up until 3 hours prior to elotuzumab administration. An additional 8 mg is given IV 45–90 minutes prior to dosing of elotuzumab.

Patients will need additional premedications 45–90 minutes prior to dosing of elotuzumab of an H1 blocker (diphenhydramine 25–50 mg orally/IV or equivalent H1 blocker), an H2 blocker (ranitidine 50 mg IV or 150 mg orally or equivalent H2 blocker), and acetaminophen 650–1,000 mg orally. In patients who have received four cycles the infusion rate may be increased to a maximum of 5 mL/min (see Table 1).

Preclinical data supported the combination of elotuzumab and dexamethasone with bortezomib[11] and a randomized phase II study (CA204-009) compared elotuzumab, bortezomib, and dexamethasone (EBd) versus bortezomib and dexamethasone (Bd) alone in relapsed patients.[12] Elotuzumab 10 mg/kg was given weekly for the first two cycles and then on days 1 and 11 for cycles 3–8, and then on days 1 and 15. Bortezomib 1.3 mg/m^2 IV or subcutaneously was given on days 1, 4, 8, and 11 for cycles 1–8, then on days 1, 8, and 15. Dexamethasone 20 mg was given on non-elotuzumab days and 8 mg orally plus 8 mg IV on elotuzumab days. The 2-year PFS was 18% for EBd arm and 10% for the Bd arm. ORR was 65% in the EBd arm versus 63% in the Bd arm. Grade 3–4 adverse events (AEs) occurred in ≥15% with thrombocytopenia (7 in EBd ʊ 13 in Bd), and infections (17 in EBd ʊ 11 in Bd).[12]

Safety

Infusion reactions with elotuzumab are possible, though rare. Approximately 10% of patients in the Eloquent-2 clinical trial experienced a reaction to the infusion. Infusion reactions typically present as fever, chills, hypertension or hypotension, and bradycardia. Most infusion reactions were grade 1–2; only 1% of patients had a grade 3 reaction. No grade 4–5 reactions were reported in the clinical trial.[10] Proper premedication reduces the likelihood and severity of an infusion reaction.

If a grade 2 infusion reaction does occur, interrupt the infusion and administer appropriate medical management. Upon resolution to a grade 1 or less, restart the infusion at 0.5 mL/min and gradually increase the rate every 30 minutes as tolerated until the rate at which the infusion reaction occurred is reached. The infusion rate resumes as per standard protocol. Vital signs should be monitored every 30 minutes for 2 hours and then once more at the end of the infusion. If the infusion

TABLE 1.
Infusion Rates for Elotuzumab

Cycle 1, day 1	Cycle 1, day 8	Cycle 3, day 15 and subsequent cycles
Time/Rate	Time/Rate	Time/Rate
0–30 min 0.5 mL/min	0–30 min 1 mL/min	2 mL/min
30–60 min 1 mL/min	30 min or more 2 mL/min	
60 min or more 2 mL/min		