

Elotuzumab

Aust Prescr 2022;45:138-9

<https://doi.org/10.18773/austprescr.2022.040>

First published
7 July 2022

Approved indication: multiple myeloma

Empliciti (Bristol-Myers Squibb) vials containing 300 mg or 400 mg powder for reconstitution

Multiple myeloma occurs when cancerous plasma cells accumulate in the bone marrow, outweighing healthy blood cells. The cell surface glycoprotein SLAMF7 has been shown to mediate the adhesion of cancerous plasma cells to the bone marrow in multiple myeloma and to activate natural killer cells, making it an ideal therapeutic target.

Elotuzumab is a humanised (IgG1) monoclonal antibody that targets SLAMF7. It directly enhances natural killer cell activity and antibody-dependent cytotoxicity. Early studies have shown synergistic clinical effects when it is used in combination with immunomodulatory drugs for multiple myeloma. Elotuzumab is therefore indicated in combination with lenalidomide and dexamethasone for the treatment of multiple myeloma in patients who have received at least one therapy previously.

The recommended dose of elotuzumab is 10 mg/kg body weight via slow intravenous infusion on days 1, 8, 15 and 22 for two 28-day cycles and then on days 1 and 15 for subsequent 28-day cycles until disease progression or unacceptable toxicity occurs. Patients must receive premedication with dexamethasone, diphenhydramine or an equivalent H₁ blocker, ranitidine or an equivalent H₂ blocker, and paracetamol before each dose. Elotuzumab is likely to be metabolised like other monoclonal antibodies, so adverse interactions with other drugs metabolised by the CYP450 system are not expected. It has a serum half-life of about 10 days. On discontinuing elotuzumab, concentrations will decrease to about 3% of the steady-state maximal serum concentration by three months. No dose adjustments are required for renal impairment of any severity or for mild hepatic impairment. Elotuzumab has not been studied in patients with moderate to severe hepatic impairment.

An open-label, randomised, phase III trial (ELOQUENT-2) included adults with multiple myeloma who had received one to three previous therapies and had documented disease progression after their most recent therapy.¹ The patients were randomly assigned to receive either elotuzumab plus lenalidomide and dexamethasone, or lenalidomide and dexamethasone alone (control). The median progression-free survival durations were 19.4 months with the elotuzumab regimen and 14.9 months with the control regimen.¹ A clinical response was achieved in 79% (252/321) of

the patients with the elotuzumab regimen and in 66% (213/325) of the patients with the control regimen.¹ Four years after treatment, the median overall survival durations were 48 months with the elotuzumab regimen (rate of 50%) and 40 months with the control regimen (rate of 43%).²

The most common grade 3-4 adverse events in patients receiving elotuzumab in the ELOQUENT-2 trial were lymphocytopenia (77% vs 49% with the control regimen), neutropenia (34% vs 44%), thrombocytopenia (19% vs 20%), anaemia (19% vs 21%) and fatigue (8% vs 8%).¹ Infections were reported in 81% of the patients receiving the elotuzumab regimen, compared with 74% receiving the control regimen.¹ The incidence of herpes zoster infection was 4.1 per 100 patient-years in those receiving the elotuzumab regimen (vs 2.2 with the control regimen).¹ Clinicians should continue to assess patients for the need for antiviral prophylaxis to manage infections. Infusion reactions, such as pyrexia, chills and hypertension, were reported in 10% of those receiving the elotuzumab regimen, with 70% of these reactions occurring with the first dose.¹ Treatment may be stopped or the infusion rate may be reduced to manage infusion reactions. Two patients (1%) discontinued treatment because of infusion reactions that did not resolve, and 2% of patients receiving either regimen died due to infections or other disorders.¹ At the four-year follow-up, the adverse events were similar to those observed in the first part of the ELOQUENT-2 trial.²

As with all therapeutic proteins, there is a potential for immunogenicity with elotuzumab. Of 299 patients receiving the elotuzumab regimen who were tested for the presence of neutralising antibodies, 45 (15%) tested positive at least once.¹

There are no data on the drug's effects on fertility. The safety and efficacy of elotuzumab have not been studied in children or pregnant women. As the drug is taken in combination with lenalidomide, women should avoid pregnancy during treatment, during dose interruptions and for four weeks after stopping treatment.

Clinical trial data suggest that the addition of elotuzumab to a regimen of lenalidomide and dexamethasone improves progression-free survival in patients with relapsed or refractory multiple myeloma who have received previous therapies. In a study including newly diagnosed, previously untreated patients, no significant clinical benefits were observed on adding elotuzumab to lenalidomide and dexamethasone.³ Elotuzumab has also been studied with other drug combination regimens, such as pomalidomide and bortezomib.^{4,5} In previously

treated patients, the addition of elotuzumab to immunomodulatory drugs results in improved clinical benefit with an increase in adverse events, which should be managed accordingly. The benefits of elotuzumab plus lenalidomide and dexamethasone appear favourable for four years in patients with multiple myeloma.

T manufacturer provided relevant information

REFERENCES

1. Lonial S, Dimopoulos MA, Palumbo A, White D, Grosicki S, Spicka I, et al. Elotuzumab therapy for relapsed or refractory multiple myeloma. *New Engl J Med* 2015;373:621-31. <https://doi.org/10.1056/nejmoa1505654>
2. Dimopoulos MA, Lonial S, Betts KA, Chen C, Zichlin ML, Brun A, et al. Elotuzumab plus lenalidomide and dexamethasone in relapsed/refractory multiple myeloma: extended 4-year follow-up and analysis of relative progression-free survival from the randomized ELOQUENT-2 trial. *Cancer* 2018;124:4032-3. <https://doi.org/10.1002/cncr.31680>
3. Dimopoulos MA, Richardson PG, Bahlis NJ, Grosicki S, Cavo M, Beksaç M, et al. Addition of elotuzumab to lenalidomide and dexamethasone for patients with newly diagnosed, transplantation ineligible multiple myeloma (ELOQUENT-1): an open-label, multicentre, randomised, phase 3 trial. *Lancet Haematol* 2022 [Online] [https://doi.org/10.1016/S2352-3026\(22\)00103-X](https://doi.org/10.1016/S2352-3026(22)00103-X)
4. Dimopoulos MA, Dytfeld D, Grosicki S, Moreau P, Takezako N, Hori M, et al. Elotuzumab plus pomalidomide and dexamethasone for multiple myeloma. *N Engl J Med* 2018;379:1811-2. <https://doi.org/10.1056/NEJMoa1805762>
5. Jakubowiak A, Offidani M, Pégourie B, de la Rubia J, Garderet L, Laribi K, et al. Randomized phase 2 study: elotuzumab plus bortezomib/dexamethasone vs bortezomib/dexamethasone for relapsed/refractory MM. *Blood* 2016;127:2833-40. <https://doi.org/10.1182/blood-2016-01-694604>

The Transparency Score is explained in [New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.](#)

At the time the comment was prepared, information about this drug was available on the websites of the [Food and Drug Administration](#) in the USA, the [European Medicines Agency](#) and the [Therapeutic Goods Administration](#).