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Efficacy and safety of single-agent belantamab mafodotin versus pomalidomide plus low-dose dexamethasone in patients with relapsed or refractory multiple myeloma (DREAMM-3): a phase 3, open-label, randomised study

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Abstract

Background: Multiple myeloma remains incurable, and heavily pretreated patients with relapsed or refractory disease have few good treatment options. Belantamab mafodotin showed promising results in a phase 2 study of patients with relapsed or refractory multiple myeloma at second or later relapse and a manageable adverse event profile. We aimed to assess the safety and efficacy of belantamab mafodotin in a phase 3 setting.

Methods: In the DREAMM-3 open-label phase 3 study, conducted at 108 sites across 18 countries, adult patients were enrolled who had confirmed multiple myeloma (International Myeloma Working Group criteria), ECOG performance status of 0-2, had received two or more previous lines of therapy, including two or more consecutive cycles of both lenalidomide and a proteasome inhibitor, and progressed on, or within, 60 days of completion of the previous treatment. Participants were randomly allocated using a central interactive response technology system (2:1) to receive belantamab mafodotin 2·5 mg/kg intravenously every 21 days, or oral pomalidomide 4·0 mg daily (days 1-21) and dexamethasone 40·0 mg (20·0 mg if >75 years) weekly in a 28-day cycle. Randomisation was stratified by previous anti-CD38 therapy, International Staging System stage, and number of previous therapies. The primary endpoint was progression-free survival in all patients who were randomly allocated. The safety population included all randomly allocated patients who received one or more doses of study treatment. This trial is registered with ClinicalTrials.gov, NCT04162210, and is ongoing. Data cutoff for this analysis was Sept 12, 2022.

Findings: Patients were recruited between April 2, 2020, and April 18, 2022. As of September, 2022, 325 patients were randomly allocated (218 to the belantamab mafodotin group and 107 to the pomalidomide-dexamethasone group); 184 (57%) of 325 were male and 141 (43%) of 325 were female, 246 (78%) of 316 were White. Median age was 68 years (IQR 60-74). Median follow-up was 11·5 months (5·5-17·6) for belantamab mafodotin and 10·8 months (5·6-17·1) for pomalidomide-dexamethasone. Median progression-free survival was 11·2 months (95% CI 6·4-

14·5) for belantamab mafodotin and 7·0 months (4·6-10·6) for pomalidomide-dexamethasone (hazard ratio 1·03 [0·72-1·47]; p=0·56). Most common grade 3-4 adverse events were thrombocytopenia (49 [23%] of 217) and anaemia (35 [16%]) for belantamab mafodotin, and neutropenia (34 [33%] of 102) and anaemia (18[18%]) for pomalidomide-dexamethasone. Serious adverse events occurred in 94 (43%) of 217 and 40 (39%) of 102 patients, respectively. There were no treatment-related deaths in the belantamab mafodotin group and one (1%) in the pomalidomide-dexamethasone group due to sepsis.

Interpretation: Belantamab mafodotin was not associated with statistically improved progression-free survival compared with standard-of-care, but there were no new safety signals associated with its use. Belantamab mafodotin is being tested in combination regimens for relapsed or refractory multiple myeloma.

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Comment in

Single-agent belantamab mafodotin in patients with relapsed or refractory multiple myeloma.

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