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High MRD negativity rates and prolonged PFS with belantamab mafodotin plus daratumumab, lenalidomide, and dexamethasone in transplant ineligible newly-diagnosed myeloma: Results of the Bela-DRd study

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Background

Belantamab mafodotin (belamaf) have shown high efficacy in relapsed/refractory myeloma. The aim of this study was to assess the efficacy and safety of Bela-DRd in transplant ineligible newly diagnosed myeloma patients.

Methods

BelaDRd is a phase 1/2, open-label study (EUCT-2021-006792-42). Part 1 established belamaf 1.9 mg/kg Q8W, extended to Q12W as the recommended phase 2 dose (RP2D). Part 2 (dose-expansion phase) evaluates the safety and efficacy of the RP2D in two cohorts Groups A and B, guided by an ophthalmologist and hematologist (using Vision-Related Anamnestic, VRA tool), respectively.

Results

In Part 1, 24 patients (median age: 73 years; male: 54.2%) entered the study. At a median follow-up of 34.3 months, the overall response rate (ORR) was 91.7%; 70% of patients achieved $\geq$ CR. MRD negativity was achieved in 13/16 (81.3%). Of 380 planned belamaf doses, 105 (27.6%) doses were skipped due to OAEs. In Part 2 (n=12 patients; median age: 74 years). At a median follow-up of 17.9 months, ORR was 91.7% (11/12 patients), while MRD negativity was achieved in 5/7 (71.4%). Of 113 planned belamaf doses 13 (11.5%) doses were skipped due to OAEs. The median time to $\geq$ PR was 1.1 months. At 18 months, PFS was 91.7% (95% CI 76.4-97.2) and 87.5% (95% CI 66.1-95.8) in the overall and RP2D populations, respectively. Fatal TEAEs occurred in 3 pts of cohort 1 and none observed in part 2. Fatigue was the most common Gr $\geq$ 3 non-ocular AE in parts 1 and 2 (13 pts [54.2%] and 6 pts [50.0%], respectively); mainly attributed to lenalidomide. Grade $\geq$ 3 BCVA decline was observed in 74 (10.4%) of ocular assessments in part 1 and 4 (3.9%) and 5 (5.3%) in part 2 groups A and B, respectively. Grade $\geq$ 2/ $\geq$ 3 keratopathy occurred in 20.2%/0.6% of assessments in Part 1; in Part 2, respective rates were 6.7%/0% (Group A) and 10.6%/0% (Group B). Median $\geq$ Grade 2 BCVA OAE/keratopathy resolution time was 1.1/1.0 months (Part 1) and 1.9/1.0 months (Part 2).

Conclusions

BelaDRd, with belamaf administered every 2 to 3 months, demonstrated robust clinical activity, with rapid and deep responses and high MRD negativity rates with manageable toxicity.

Clinical trial identification

NCT05280275.

Legal entity responsible for the study

The authors.

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GSK.

Disclosure

M.A.C. Dimopoulos: Financial Interests, Personal, Other, Honoraria: AbbVie, Amgen, Bristol-Myers Squibb, GSK, Janssen, Karyopharm, Pharmacocyclics, Pfizer, Sanofi, Takeda. M. Gavriatopoulou: Financial Interests, Personal, Other, Honoraria: GSK, Janssen, Sanofi, AbbVie, Amgen, Takeda. I. Ntanasis-Stathopoulos: Financial Interests, Personal, Other, Honoraria: Janssen. E. Kastritis: Financial Interests, Personal, Other, Honoraria and Research Funding: Janssen, Amgen, GSK, Pfizer. E. Terpos: Financial Interests, Personal, Advisory Board, Advisory board or lecture: Amgen, AstraZeneca, Bristol-Myers Squibb, EUSA Pharma, Integris Pharma, Janssen, Pfizer, Sanofi, Takeda; Financial Interests, Institutional, Research Funding: Amgen, GSK, Janssen, Sanofi, Takeda; Financial Interests, Personal and Institutional, Other, Travel grant: Amgen, EUSA Pharma, Takeda. All other authors have declared no conflicts of interest.

