Low-dose belantamab mafodotin (belamaf) in combination with nirogacestat vs belamaf monotherapy in patients with relapsed/refractory multiple myeloma (RRMM): Phase 1/2 DREAMM-5 platform sub-study 3

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Introduction

Belantamab mafodotin (belamaf), a first-in-class truncated antibody-drug conjugate (ADC) targeting BCMA, has a multifunctional mechanism of action that promotes multiple immune effector mechanisms in a cell-context-dependent manner and results in T-cell-dependent killing of BCMA-positive cells and is an immunomodulatory agent, and an on-target (CD19) ADCC/PGR.

Belantamab mafodotin (belamaf) administered as a 2.5mg/kg Q3W GSK916 has shown promising overall response rates (ORR) in previous phase 1/2 clinical trials, with median duration of response (mDOR) of 9.4 months, 5-year RRMM survival of 42%, and progression-free survival (PFS) of 9.4 months, and has been shown to be non-myelosuppressive in patients with relapsed/refractory multiple myeloma (RRMM) when administered at doses up to 6 mg/kg.

Methods

The Phase 1/2 platform study incorporated a master protocol evaluating multiple belamaf-containing combinations in distinct RRMM subgroups (Table 1). Each cohort was designed with a single target or combination, and included 10 patients in an initial cohort. Results of interim analysis of this sub-study DE arm led to discontinuation of belamaf + niro combination CE cohort 29.5 (1–57) and belamaf monotherapy CE cohort 27.0 (1–56). Median (range) follow-up duration (weeks) was: belamaf + niro combination DE cohort 51 (5–106), belamaf monotherapy DE cohort 33.6 (2–106), belamaf monotherapy CE cohort 10 (1–56). The AE profile seen with the belamaf + niro combination appears consistent with the known safety profiles of belamaf monotherapy and nirogacestat. Safety

Results

For the CE phase combination and monotherapy cohorts, respectively, observed ORR was 39% (95% CI: 15.1, 67.7) and 18% (95% CI: 4.1, 41.2), and best response was partial response (PR) in 65% and 45%, respectively. 5-year RRMM survival was 33% and 31%, respectively. 5 and 6 year median duration of response (mDOR) was 9.4 and 10.2 months respectively. The AE profile seen with the combination was consistent with the known safety profiles of belamaf monotherapy and nirogacestat. Safety

Conclusions

While single-agent belamaf continues to demonstrate strong efficacy, low-dose belamaf + nirogacestat demonstrated an encouraging clinical effect with a substantial reduction of high-grade adverse events, consistent with the hypothesis that non-myelosuppressive belamaf benefits.

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References


Disclosures

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