Abstract: S212

Title: LINVOSELTAMAB IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA IN THE LINKER-MM1 STUDY: DEPTH AND DURABILITY OF RESPONSE AT 14-MONTH MEDIAN FOLLOW-UP

Abstract Type: Oral Presentation

Session Title: Novel agents in RRMM

Background:

We report durability and depth of response for 200 mg linvoseltamab, a B-cell maturation antigen × CD3 bispecific antibody, in the LINKER-MM1 (NCT03761108) clinical trial. Previous results have shown encouraging efficacy and a generally manageable safety profile for linvoseltamab (Jagannath *et al.*, ASH 2023).

Aims:

LINKER-MM1 is a Phase 1/2, first-in-human, open-label study to evaluate the safety, tolerability, and anti-tumor activity of linvoseltamab monotherapy as treatment for relapsed/refractory multiple myeloma (RRMM).

Methods:

Eligible Phase 2 patients had RRMM that was either triple-class exposed or triple-class refractory to a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 monoclonal antibody. Phase 2 patients received intravenous linvoseltamab once weekly through Week 14, then once every 2 weeks. Phase 2 patients receiving the 200 mg dose who achieved very good partial response or better (≥VGPR) and received treatment for ≥24 weeks were transitioned to administration once every 4 weeks (Q4W). The primary endpoint was objective response rate (ORR) per Independent Review Committee. Secondary endpoints included safety, duration of response (DOR), progression free survival (PFS), and overall survival (OS). Informed consent was obtained for all participants.

Results:

As of September 8, 2023, the median duration of follow-up for the 117 patients enrolled into the 200 mg dosing cohorts (Phase 1+2) was 11.1 months. All patients were at least triple-class exposed, and 82% were at least triple-class refractory. Linvoseltamab treatment was highly effective, with an ORR of 71%, including ≥VGPR rate of 62% and a complete response or better (≥CR) rate of 46%. We present new data examining DOR, PFS, and OS in patients with ≥CR. Kaplan-Meier (KM) estimated median DOR was not reached (NR) for all responders and for patients with ≥CR; probability of maintaining response at 12 months was 78% (95% confidence interval [CI] 65–86) for all responders and 92% (95% CI 77–97) for patients with ≥CR. KM estimated median PFS and OS were NR for all patients receiving 200 mg and for patients with ≥CR; probability of PFS and OS at 12 months for all patients receiving 200 mg were 69% (95% CI 58–77) and 75% (65–82), respectively; versus 95% (95% CI 81–99) and 100% (100–100), respectively, for patients with ≥CR. These data demonstrate remarkable efficacy among patients with the deepest clinical response. High ORR and deep responses were observed across prespecified high-risk subgroups, including patients with plasmacytomas (including extramedullary and paramedullary plasmacytomas; ORR: 58%; ≥CR: 25%) and with high cytogenetic risk (ORR: 67%; ≥CR: 44%). In patients aged ≥75 years, ORR was 71%, with 52% ≥CR. In patients identifying as Black or African American, ORR was 85%, with 35% ≥CR.

Cytokine release syndrome was the most common treatment-emergent adverse event, reported in 46% of patients (Grade [Gr] 2: 10%; Gr 3: 1%; Gr ≥4: 0%), followed by neutropenia (any Gr: 41%; Gr 3–4: 40%) and anemia (any Gr: 39%; Gr 3–4: 31%). Infections were reported in 73% of patients (Gr 3–4: 34%). A clinically meaningful reduction in infection frequency and severity occurred after 6 months coincident with Q4W dosing, and patients with ≥CR had no Gr 5 infections.

Summary/Conclusion:

Linvoseltamab induced high rates of deep and durable responses in patients with RRMM, including those in high-risk subgroups. Long-term data are critical to establish the value of linvoseltamab; 14-month median follow-up data, including durability across subgroups, will be presented at the meeting.

Keywords: Clinical trial, Multiple myeloma, Bispecific, Plasma cells