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POSTER ABSTRACTS

653.MULTIPLE MYELOMA: PROSPECTIVE THERAPEUTIC TRIALS

Patterns of Response to 200 Mg Linvoseltamab in Patients with Relapsed/Refractory Multiple Myeloma: Longer Follow-Up of the Linker-MM1 Study

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Background
Linvoseltamab, a B-cell maturation antigen (BCMA)×CD3 bispecific antibody, demonstrated promising efficacy and generally manageable safety as therapy for relapsed/refractory multiple myeloma (RRMM; Lee et al. ASCO 2023). Here we report additional analysis of efficacy, including response pattern over time, and safety.

Methods
To enroll into LINKER-MM1 (NCT03761108) patients (pts) had to have multiple myeloma (MM) that either progressed on/after ≥3 lines of therapy including a proteasome inhibitor (PI), an immunomodulatory drug (IMiD), and an anti-CD38 antibody; or that was ≥triple-class (PI/IMiD/anti-CD38 antibody) refractory. Pts received intravenous linvoseltamab once a week through week 14, then once every two weeks. In the 200 mg phase 2 expansion cohort, pts achieving very good partial response (VGPR) or better received linvoseltamab once every four weeks after week 24. Primary endpoint was objective response rate (ORR). Key secondary endpoints included progression free survival (PFS) and overall survival. Treatment-emergent adverse events (TEAEs) reported are those that occurred from first dose until 30 days after the end of study treatment.

Results

As of February 28, 2023, 117 MM pts enrolled into the 200 mg cohort; median age was 70 (range: 37-91) with 26% ≥75, 26% were non-white, 14% had extramedullary (excluding paramedullary) plasmacytomas ≥2 cm, 36% had a high-risk cytogenetics, 22% had bone marrow plasma cells ≥50%, and 74% were ≥triple-class refractory. Median duration of follow-up was 5.6 months (interquartile range [Q1-Q3]: 3.02-8.34) ORR was 71% with ≥complete response (CR) rate of 30%. Responses deepen over time: median time to ≥partial response (PR) was 0.95 months (Q1-Q3: 0.76-1.87); median time to ≥VGPR was 1.87 months (0.79-3.55); and median time to ≥CR was 5.32 months (3.71-7.69). Moreover, high ORR and high rates of ≥CR were observed in many subgroups of difficult-to-treat MM pts. Specifically, ORR and ≥CR rates were: 70% and 29% in pts with ≥triple-class refractory disease; 68% and 26% in pts ≥75 years old; 62% and 26% in pts with high cytogenetic risk; and 47% and 18% in pts with International Staging System stage III. High rates of overall response and ≥CR were also observed in patients with high tumor burden as determined by various measures including bone marrow plasmacytosis ≥50% (50% and 31%) and soluble BCMA at baseline ≥ 0.4mg/L (55% and 25%). Kaplan-Meier (KM) estimated median duration of response was not reached (NR) (95% confidence interval [CI] non-evaluable [NE], NE), and probability of response at 12 months was 79% (95% CI 63, 89). KM estimated median PFS was NR (95% CI NE, NE) and probability of PFS at 12 months was 66% (95% CI 52, 77).

TEAEs occurred in all patients with Grade [Gr] ≥3 in 79%. The most common TEAE was cytokine release syndrome (any grade: 45%, Gr3-4: 1%, Gr5: 0; tocilizumab was utilized to treat these symptoms in 16 [13.7%] pts). Other common TEAEs were cough (33%, 0, and 0), neutropenia (32%, 31%, and 0), diarrhea (32%, 2%, and 0), and fatigue (32%, 0, and 0). Rate of infections of any grade was 59.8% with ≥Gr3 in 36.8%. The most common infections were pneumonia (any grade 17.1%, ≥Gr3 13.7%), upper respiratory tract infection (12.0%, and 2.6%), and COVID-19 (12.0%, 5.1%). Opportunistic infections (any grade) were observed in 9 (7.7%) pts including 7 (6.0%) pts ≥Gr3. Twenty-six of 117 (22%) pts were treated with intravenous immunoglobulin.

Conclusions

Linvoseltamab 200 mg induced deep responses in patients with RRMM including those with high-risk myeloma and high tumor burden, and deepened responses over time while maintaining a generally manageable safety profile. More mature data with longer follow-up will be reported at the meeting.

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