FINAL RESULTS OF A PHASE IB STUDY OF ISATUXIMAB PLUS POMALIDOMIDE AND DEXAMETHASONE IN RELAPSED/REFRACTORY MULTIPLE MYELOMA.

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Abstract: S850

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Background

Isatuximab (ISA) is a monoclonal antibody targeting CD38-expressing tumor cells via several modes of action. We report final data from a Phase Ib dose-escalation/expansion study of ISA in combination with pomalidomide (Pom)/dexamethasone (dex) in patients (pts) with relapsed/refractory multiple myeloma (RRMM) (NCT02283775).

Aims

To evaluate combination therapy with ISA plus Pom/dex in pts with RRMM.

Methods

Pts with RRMM (≥2 prior MM therapies; includes lenalidomide and a proteasome inhibitor [PI]) received 5, 10, or 20 mg/kg ISA (4 weekly [QW] doses, then every 2 weeks until disease progression/intolerable toxicity), Pom 4 mg (Days 1–21), and dex 40 mg (QW; 20 mg if ≥75 yrs old) in 28-day cycles. All pts provided written informed consent to participate in the study. The primary objective was to determine the recommended dose of ISA plus Pom/dex. Secondary objectives included efficacy (International Myeloma Working Group criteria), safety, and pharmacokinetics (PK).

Results

Forty-five pts received ISA at 5 (n=8), 10 (n=31), or 20 (n=6) mg/kg. Median age was 67 (42–82) yrs. Median 3 (2–10) prior lines; 41 (91%), 37 (82%), and 38 (84%) pts were refractory to their last regimen, immunomodulatory drugs (IMiDs), or PIs, respectively. Six pts had high-risk (HR) cytogenetics. Median time on treatment was 9.6 mos; 19 (42%) pts remain on treatment. Two pts (10 mg/kg) discontinued due to an adverse event (AE) (grade [Gr] 5 intestinal perforation [due to underlying MM]; Gr 3 infusion-associated reaction [IAR]). One pt at each dose reported a dose-limiting toxicity; the maximum tolerated dose was not reached. The expansion cohort was initiated at 10 mg/kg based on efficacy, safety, and PK data. The most common treatment-emergent AEs besides IARs/hematologic abnormalities were fatigue (62%), upper respiratory tract infection (42%), and dyspnea (40%). Gr ≥3 neutropenia was observed in 83% of pts (Gr 4, 56%); all cases proved manageable with dose modification (dose delay in 16 [35.6%] pts and dose reduction in 22 [48.9%] pts) and/or granulocyte colony stimulating factor support. IARs occurred in 19 (42%) pts (Gr ≥3, 1 pt): 18 (40%) pts during the first infusion, 3 (7%) pts at later infusions. Overall response rate (ORR) was 62%; ORR in HR cytogenetics: 33%; IMiD refractory: 57%; PI refractory: 63%. Twelve (27%) pts achieved ≥ very good partial response (1 complete response; 1 stringent complete response). Median time to first response was 0.95 mos and median duration of response was 18.7 mos (95% confidence interval [CI] 12.5–not calculable). Median progression-free survival was 17.6 mos (95% CI 6.8–20.5). ISA PK is unaffected by co-administration with Pom/dex.

Conclusion

These final results confirm the promising clinical activity and manageable safety profile of ISA in combination with Pom/dex in heavily pretreated RRMM. A Phase III confirmatory trial is ongoing with results expected later in 2018.

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