(PS1726) EFFICACY AND SAFETY OF ISATUXIMAB SUBCUTANEOUS (SC) PLUS CARFILZOMIB AND DEXAMETHASONE (ISA-KD) IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM): RESULTS OF THE PHASE 2 STUDY IZALCO

Topic: 14. Myeloma and other monoclonal gammopathies – Clinical

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Abstract

Background:

IV isatuximab (Isa) can provide benefit to patients (pts) in multiple combinations across the therapeutic spectrum for MM. SC administration would offer a more convenient treatment option for pts and caregivers. Results of a Phase 1b study demonstrated safety and efficacy of Isa SC administration via an on-body delivery system (OBDS; an investigational wearable injector), plus pomalidomide and dexamethasone in RRMM pts.

Aims:

In the Phase 2 IZALCO study (NCT05704049), we evaluated efficacy (primary objective), safety, pharmacokinetics (PK), and pt preference for Isa SC administration by manual injection or OBDS, in combination with carfilzomib and dexamethasone (Kd), in RRMM pts.

Methods:

Isa SC 1400 mg was given weekly in cycle (C)1 then biweekly. In Part 1 of the study, pts received Isa injected SC manually. In Part 2, pts were randomized to Isa administered SC via OBDS (C1–C3) followed by manual injection (C4–C6), or to manual injection (C1–C3) followed by OBDS administration (C4–C6); from C7, pts could choose either treatment modality. All pts received treatment with carfilzomib (20 mg/m2 on D1–2 then 56 mg/m2 biweekly) and dexamethasone (20 mg). Primary study endpoint (EP) was overall response rate (ORR); pt preference for Isa SC administration modality was the key secondary EP.

Results:

Overall, 74 RRMM pts were enrolled: 8 in Part 1 and 66 in the randomized cohort (Part 2). At study entry, pts had a median age of 65 (44–85) yrs and a median of 1 prior therapy line (1–5); 56.8%, 32.4% and 10.8% had ISS stage I, II or III, respectively. The ORR rate was 79.7% (median follow-up 10.1 mo). After treatment with both modalities for Isa SC delivery, 74.5% of pts expressed a preference for the OBDS rather than manual injection (p = 0.0004); 8.5% had no preference. Other key efficacy and safety results are shown in table. Treatment with Isa SC plus Kd was well tolerated. A single infusion reaction event (1 of Grade [G]1, 1 of G2) occurred in 2 pts (2.7%, both with manual injection at first dose). Six (8.1%) pts had 18 injection site reactions (17 of G1, 1 of G2) in 1297 (1.1%) manual or OBDS injections. Comparable PK exposure was observed between OBDS and manual administration.

Table

Isatuximab SC + Kd	**All N=74**
Efficacy, %	
ORR	79.7
≥VGPR	62.2
≥CR	21.6
Safety, %	
≥G3 TEAE	54.1
Serious TEAE	40.5
G5 TEAE	5.4
Treatment-related ≥G3 TEAE	35.1

G, grade; TEAE, treatment-emergent adverse event; VGPR, very good partial response.

Summary/Conclusion:

The study met its primary endpoint, demonstrating efficacy and safety of Isa SC administration in combination with Kd, either by manual injection or OBDS. Our study findings are comparable to those reported in the Phase 3 study IKEMA with Isa IV. Pts expressed a clear preference for receiving Isa SC by an OBDS.