(S203) ISATUXIMAB SUBCUTANEOUS VIA AN ON-BODY DELIVERY SYSTEM VERSUS ISATUXIMAB INTRAVENOUS, PLUS POMALIDOMIDE AND DEXAMETHASONE, IN RELAPSED/REFRACTORY MULTIPLE MYELOMA: THE RANDOMIZED PHASE 3 IRAKLIA STUDY

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Abstract

Background:

Intravenous (IV) isatuximab (Isa) in combination with pomalidomide and dexamethasone (Isa-Pd) is approved to treat patients with relapsed/refractory multiple myeloma (RRMM) based on the Phase 3 ICARIA-MM study. A Phase 1b study showed the safety and efficacy of Isa subcutaneous (SC) via an on-body delivery system (OBDS), an investigational wearable bolus injector, in combination with Pd, in patients with RRMM. Isa SC offers shorter duration of administration, a fixed dose, and smaller administration volume.

Aims:

To report the results of the IRAKLIA trial (NCT05405166), which compared Isa SC OBDS versus Isa IV plus Pd in patients with RRMM, and to report the first use of an OBDS in a Phase 3 myeloma trial.

Methods:

This multicenter, open-label study enrolled patients aged ≥18 years who had received ≥1 prior line of therapy (LOT). Patients were randomized 1:1 to receive Isa SC OBDS (1400 mg) or Isa IV (10 mg/kg) weekly in Cycle (C)1, then every 2 weeks, plus pomalidomide (4 mg/day, Day [D]1–21) and dexamethasone (40 mg [20 mg if age ≥75 years] weekly). Patients received 4-week cycles until disease progression, unacceptable toxicity, or patient request to discontinue treatment. Co-primary endpoints were overall response rate (ORR; non-inferiority concluded if lower limit of 95% confidence interval [CI] of relative risk ≥ non-inferiority [NI] margin of 0.839) and Isa trough level (C_{trough}) at steady state (predose at C6D1; noninferiority concluded if lower limit of 90% CI of geometric mean ratio ≥0.8).

Results:

531 patients (SC OBDS arm, n=263; IV arm, n=268 [4 not treated]) were randomized. Baseline demographic and disease characteristics were balanced between arms (median age 66 years; median 2 prior LOT). After a median follow-up of 12 months, ORR was 71.1% in the SC OBDS arm and 70.5% in the IV arm (relative risk [95% CI] = 1.008 [0.903–1.126]; lower CI was above the NI margin). Mean (standard deviation) C_{trough} at C6D1 predose was 499 (259) µg/mL in the SC OBDS arm and 340 (169) µg/mL in the IV arm. The geometric mean ratio (90% CI) for Ctrough at C6D1 predose was 1.532 (1.316–1.784); lower CI was above the NI margin. Results for the co-primary endpoints and all four key secondary endpoints including patient experience are summarized in the Table. Grade ≥3 treatment-emergent adverse events occurred in 81.7% of patients in the SC OBDS arm and 76.1% of patients in the IV arm; with treatment discontinuation rates of 8.4% and 8.7%, respectively. Injection site reactions (ISRs) occurred in 4.2% (11/263) of patients in the SC arm and in 19 (0.4%) of 5145 SC injections; all were of Grade 1–2 severity. 99.9% of OBDS injections were completed without interruption.

Summary/Conclusion:

IRAKLIA met its co-primary endpoints, showing efficacy and pharmacokinetic non-inferiority of Isa SC OBDS compared with Isa IV, plus Pd. No new safety signal besides a low ISR incidence was observed, showing excellent tolerability of Isa SC OBDS. Far fewer infusion reactions and a higher patient satisfaction were also noted for Isa SC OBDS compared with Isa IV. The efficacy and safety findings from this study are comparable to those reported for Isa IV in ICARIA-MM. These results from IRAKLIA support the potential use of Isa SC delivered via the OBDS, designed to improve patient experience and practice efficiency.

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Table. Co-primary and key secondary endpoints

	Isa SC OBDS + Pd	**Isa IV + Pd**
Efficacy, %	**N=263**	**N=268**
ORR	71.1	70.5
≥VGPR	46.4	45.9
PK*, µg/mL	**N=131/121**	**N=126/121**
Geometric mean Isa C_{trough} at C2D1 / C6D1	360/426	277/278
Safety, %	**N=263**	**N=264**
All grade IR	1.5	25.0
Patient satisfaction with injection method at C5D15, %	70.0	53.4

*PK was analyzed at C6D1 in the PP PK population and at C2D1 in the PP CT4W population.

C, cycle; CT4W, C_{trough} at 4 weeks; d, dexamethasone; D, day; IR, infusion reaction; Isa, isatuximab; IV, intravenous; OBDS, on-body delivery system; ORR, overall response rate; P, pomalidomide; PK, pharmacokinetics; PP, per protocol; SC, subcutaneous; VGPR, very good partial response.