Updated Results From the Phase 2 IZALCO Study: Efficacy and Safety of Isatuximab Subcutaneous Plus Carfilzomib and Dexamethasone in Relapsed/Refractory Multiple Myeloma Patients

780

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Introduction

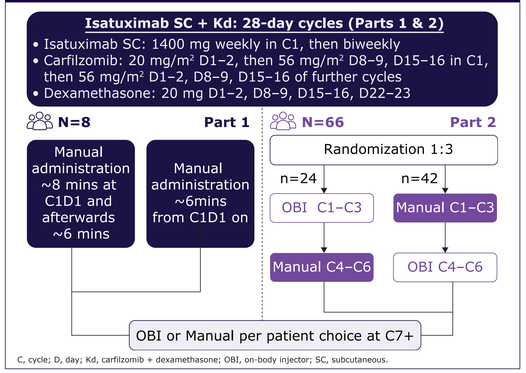
- Isatuximab (Isa) is an anti-CD38 monoclonal antibody approved for intravenous (IV) administration in combination with other therapies for relapsed/refractory multiple myeloma (RRMM), transplant-ineligible newly diagnosed multiple myeloma (NDMM), and in the EU, transplant-eligible NDMM patients.[1,2]
- The Phase 3 IRAKLIA (NCT05405166) trial demonstrated non-inferiority in efficacy and pharmacokinetics of Isa subcutaneously (SC) delivered via a wearable on-body injector (OBI) vs Isa IV, in combination with pomalidomide and dexamethasone (Pd) in RRMM patients.[1]
- The OBI is an innovative wearable device with a small, hidden, retractable needle featuring hands-free administration and constant pressure delivery.[1]
- At the data cutoff of November 8, 2024, the Phase 2 IZALCO study (NCT05704049) showed efficacy and safety of Isa SC delivered via manual injection or OBI, plus carfilzomib and dexamethasone (Kd), in patients with RRMM.[3]
  - Following exposure to both methods, 74.5% of patients showed higher preference for Isa SC OBI compared with 17% who preferred manual SC injection.[3]
  - In Part 2, 90.4% of patients opted to receive Isa SC via OBI from cycle (C)7 onwards.[4]

Here we present updated efficacy and safety results from IZALCO.

Methods

- RRMM patients with 1–3 prior lines of therapy received 1400 mg flat dose Isa SC weekly in C1 then biweekly, plus Kd. The study design is shown in **Figure 1**.
- The primary endpoint was **overall response rate (ORR)** evaluated by an independent review committee (IRC). **Patients' preference for the injection delivery method** at C6D15 was the key secondary endpoint.
- Other secondary endpoints evaluated included patient experience/satisfaction with Isa, safety, incidence of infusion reactions (IRs), incidence of injection site reactions (ISRs), isatuximab pharmacokinetics (PK) and immunogenicity.
- Patients' satisfaction with and preference for the injection method was evaluated using the Patient Experience and Satisfaction Questionnaire (PESQ).

Figure 1. Study design



C, cycle; D, day; Kd, carfilzomib + dexamethasone; OBI, on-body injector; SC, subcutaneous.

Results

Baseline characteristics

- A total of 74 RRMM patients were enrolled (8 in Part 1; 66 in the randomized cohort, Part 2, **Figure 1**).
- At the data cutoff of November 10, 2025, **59** pts remained in the study, and the median follow up duration was 21.9 months.
- At study entry, patients had a median age of **65.0 years (range: 44–85 years)**, median weight of **75.9 kg (range: 40.0–129.0 kg)**, and median of 1 prior line of therapy (1–5), and **56.8%** had ISS stage I disease (**Table 1**).

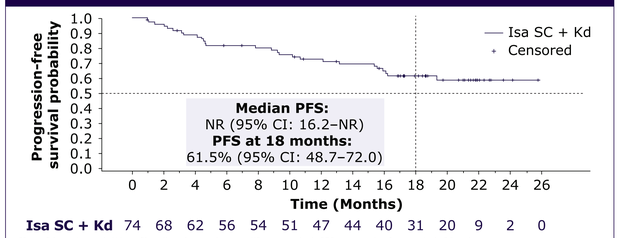
Table 1. Baseline characteristics[3]

	All patients Isa SC + Kd N=74
Age in years, median (range)	65.0 (44–85)
Weight in kg, median (range)	75.9 (40.0–129.0)
ISS stage at study entry, n (%)	
I	42 (56.8)
II	24 (32.4)
III	8 (10.8)
MM subtype at study entry, n (%)	
Ig G	47 (63.5)
Ig A	15 (20.3)
Ig M	1 (1.4)
Kappa light chain only	7 (9.5)
Lambda light chain only	4 (5.4)
Bone marrow plasma cells (%) at baseline, median (range)	13.5 (0.0–88.0)
Beta 2-microglobulin (mg/L), median (range)	3 (1.3–26.3)
eGFR <60ml/min/1.73 m²	15 (20.3)
Cytogenetic risk, n (%)	
High risk	12 (16.2)
Standard risk	39 (52.7)
Unknown	23 (31.1)
Bone lesions, n (%)	58 (78.4)
Number of prior lines of therapy, median (range)	1 (1–5)
Soft tissue plasmacytoma, n (%)	12 (16.2)
Number of patients with ≥1 transplant, n (%)	41 (55.4)
Refractory to, n (%)	
Immunomodulatory imide drug (IMiD)	34 (45.9)
Protease inhibitor (PI)	31 (41.9)
IMiD & PI	14 (18.9)

Efficacy

- Median time to best response was 5.3 months (95% CI: 3.3–6.2).
- Progression-free survival (PFS) at 18 months was 61.5% (95% CI: 48.7–72.0). Median PFS was not reached (NR) (95% CI: 16.2–NR) (**Figure 2**).
- Overall survival (OS) at 18 months was 80.8% (95% CI: 69.8–88.2); median OS was not reached (95% CI: NR–NR).

Figure 2. Progression-free survival



CI, confidence interval; Kd, carfilzomib + dexamethasone; NR, not reached; PFS, progression free survival; SC. subcutaneous.

Safety Summary

- Overall, grade ≥3 TEAEs occurred in **66.2% of patients** and serious TEAEs in **51.4%** patients (**Table 2 & 3**).
- IRs on C1D1 occurred in **2 patients (2.7%)** with manual SC injections; no IRs occurred with Isa SC OBI.
- Six (**8.1%**) patients had **14 (0.58%) ISRs, 13** were grade 1 and related to isatuximab, out of **2425** Isa SC Manual or Isa SC OBI injections.
- Only **1** ISR was deemed related to Isa SC OBI.

Table 2. Safety Summary

n (%)	All patients Isa SC + Kd N=74
Total number of patients	74 (100.0)
Any TEAE	71 (95.9)
Grade ≥3 TEAE	49 (66.2)
Treatment-related Grade ≥3 TEAE	35 (47.3)
Any TEAE leading to permanent full discontinuation	9 (12.2)
Any TEAE leading to permanent partial discontinuation of	
Isatuximab	0 (0.0)
Carfilzomib	10 (13.5)
Dexamethasone	5 (6.8)
Any injector device related TEAE	1 (1.4)
Any serious TEAE	38 (51.4)
Any serious treatment-related TEAE	21 (28.4)
Grade 5 TEAE	5 (6.8)

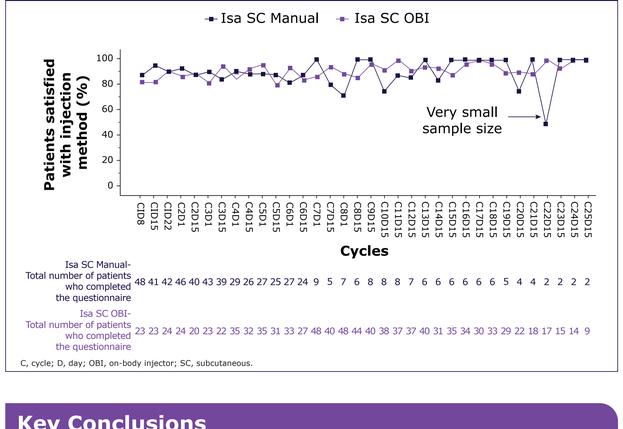
Table 3. TEAEs with an incidence of ≥10% by preferred term

n (%)	All patients Isa SC + Kd N=74	
	All grades	Grade ≥3
Any event	71 (95.9)	49 (66.2)
Upper respiratory tract infection	34 (45.9)	3 (4.1)
Pneumonia	20 (27.0)	15 (20.3)
Hypertension	19 (25.7)	5 (6.8)
Diarrhea	16 (21.6)	1 (1.4)
Headache	12 (16.2)	1 (1.4)
COVID-19	10 (13.5)	0
Insomnia	10 (13.5)	3 (4.1)
Neutropenia	10 (13.5)	9 (12.2)
Nausea	9 (12.2)	0
Back pain	8 (10.8)	1 (1.4)
Bone pain	8 (10.8)	1 (1.4)
Dyspnea	8 (10.8)	2 (2.7)
Muscular weakness	8 (10.8)	0
Nasopharyngitis	8 (10.8)	0
Oedema peripheral	8 (10.8)	0
Pyrexia	8 (10.8)	1 (1.4)

Patient satisfaction & duration of injection

- Patient satisfaction, as indicated through patients reporting they were "satisfied" or "very satisfied" with their method of injection, remained consistently high with Isa SC OBI up to C25D15 (**Figure 3**).
- The median duration of injection was **12 minutes** for **Isa SC OBI** and **6 minutes** for **Isa SC Manual**.

Figure 3. Patient experience and satisfaction



C, cycle; D, day; OBI, on-body injector; SC, subcutaneous.

Key Conclusions

- Updated results of the IZALCO study continue to show the efficacy and safety of Isa SC delivered either by manual injection or OBI, plus Kd.
- **Patient satisfaction with Isa SC OBI remained consistently high after patient choice of injection method at C7D1.**
- These safety and efficacy findings are consistent with those reported in the Phase 3 IKEMA study (Isa IV plus Kd).[5]
- Overall, these results support the efficacy, safety and feasibility of Isa delivered subcutaneously via OBI in patients with RRMM.

References
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Abbreviations
CI, confidence interval; C, cycle; D, day; ImiD, immunomodulatory imide drug; Isa, isatuximab; ISR, injection site reaction; ISS, international staging system; IR, injection reaction; IRC, independent review commitee; IV, intravenous; Kd, carfilzomib + dexamethasone; LOT, line of therapy; NR, not reached; OBI, on-body injector; ORR, overall response rate; OS, overall survival; Pd, pomalidomide + dexamethasone; NR, not reached; PESQ, patient experience and satisfaction questionnaire; PI, protease inhibitor; PK, pharmacokinetics; PFS, progression free survival; RRMM, relapsed/refractory multiple myeloma; SAE, serious adverse event; SC, subcutaneous; TEAE, treatment-emergent adverse event.

Disclosures
Marcelo Capra: Speaker's bureau for Amgen, Janssen, and Sanofi; **Gurdeep Parmar:** Consulting/advisory role for Janssen and Sanofi. Honoraria from Bristol Myers Squibb and Sanofi; **Fernanda Seguro:** No competing interests; **Vania Hungria:** Honoraria from Abbvie, Amgen, Bristol Myers Squibb/Celgene, Janssen, Sanofi, and Takeda. Support for attending meetings and/or travel from Amgen, Bristol Myers Squibb/Celgene, Janssen, and Sanofi. Participation on a data safety monitoring board or advisory board for Amgen, Bristol Myers Squibb/Celgene, Janssen, and Sanofi. Participation on a data safety monitoring board or advisory board for Amgen, BeiGene, Bristol Myers Squibb, GlaxoSmithKline, Janssen, Menarini-Stemline, Regeneron, Sanofi, and Takeda; **Sosana Delimpasi:** Honoraria for advisory boards and satellite symposia Amgen, AOP Pharma, Bristol Myers Squibb, GlaxoSmithKline, Johnson & Johnson, Sanofi; **Junichiro Yuda:** Research funding from AbbVie, Amgen, AstraZeneca, BrightPath Bio, Bristol Myers Squibb, Celaid Therapeutics, Chugai, Daiichi Sankyo, Genmab, Incyte, Janssen, Mitsubishi Tanabe, MSD, Novartis, Sanofi, Sumitomo Pharma, and Takeda; **Ivan Špička:** Consulting fees from Amgen, Bristol Myers Squibb, GlaxoSmithKline, Janssen-Cilag, Sanofi, and Takeda. Honoraria for lectures, presentations, and speaker bureaus from Amgen, Bristol Myers Squibb, Janssen-Cilag, Sanofi, and Takeda. Support for attending meetings and/or travel from Janssen-Cilag, Sanofi, and Takeda. Participation on a data safety monitoring board or advisory board for Amgen, Janssen-Cilag, Sanofi, and Takeda; **Roman Hájek:** Grants or contracts from Amgen, Bristol Myers Squibb, Celgene, Janssen, Novartis, and Takeda. Consulting fees from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Novartis, PharmaMar, and Takeda. Honoraria for lectures, presentations, and speaker bureaus from Amgen, Bristol Myers Squibb, Celgene, Janssen, PharmaMar, and Takeda. Support for attending meetings and/or travel from Amgen, Celgene, Janssen, and Takeda. Participation on a data safety monitoring board or advisory board for Amgen, Bristol Myers Squibb, GlaxoSmithKline, Janssen, Oncopeptides, Sanofi, and Takeda; **Christine Soufflet, Disa Yu, and Florence Suzan:** Employed by Sanofi; may hold stock and/or stock options in the company; **Victorine Koch:** Employed by Excelya on behalf of Sanofi; may hold stock and/or stock options in the company; **Jiří Minařík:** Consulting fees from Amgen, Bristol Myers Squibb, Celgene, GlaxoSmithKline, Janssen, and Sanofi. Honoraria for lectures, presentations, and speaker bureaus from Amgen, Bristol Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Pfizer, and Sanofi. Participation on a data safety monitoring board or advisory board for Amgen, Bristol Myers Squibb, Celgene, GlaxoSmithKline, Janssen, and Sanofi; **Hang Quach:** Research funding from Bristol Myers Squibb, GlaxoSmithKline, Karyopharm, and Sanofi. Consulting/advisory role for Antengene, Beigene, Bristol Myers Squibb, GlaxoSmithKline, Janssen Cilag, Karyopharm, Regeneron, and Sanofi.

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