Safety and Reliability of Isatuximab Subcutaneous On-Body Injector: Results Across the Phase 3 IRAKLIA, Phase 2 IZALCO and Phase 1b TCD15484 Trials

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Introduction

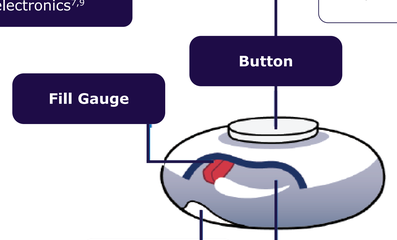
- Subcutaneous (SC) drug delivery options have become more widely available in multiple myeloma (MM), benefiting both patients and healthcare providers.[1]
- SC delivery of isatuximab (Isa), an anti-CD38 monoclonal antibody, has been investigated across clinical trials via a novel hands-free on-body injector (OBI).[2–4]
- Isa SC OBI features a small, hidden, retractable needle, establishing the first device-enabled delivery of an oncologic treatment (**Figure 1**).[4]
- Similar efficacy and safety of Isa SC OBI was demonstrated in the Phase 3 IRAKLIA (NCT05405166) and Phase 1b (TCD15484; NCT04045795) trials vs Isa IV and in the Phase 2 IZALCO (NCT05704049) trial vs Isa SC Manual in patients with relapsed/refractory MM (RRMM).[2–4]

Here, we present a pooled analysis exploring safety and reliability of Isa SC OBI in patients with RRMM.

Figure 1. Key features of the on-body injector device

- A sterile, single-use, user-filled[a] wearable injector, nested in a filling base[5–8]
- No batteries or electronics[7,9]

Pressing the center button initiates Isa SC delivery and signals completion[5,7,10,11]



Adhesive backing secures the device and assists with removal post-injection[5,7,8,10]

The window lets users track fill gauge progress during administration[6,12]

[a]During clinical studies, the OBI is filled using a disposable Luer lock syringe. Future iterations of the filling mechanism are under development.

Methods

- Patients with RRMM in IRAKLIA (N=263) and the Phase 1b expansion cohort (N=22) received 1400 mg of Isa SC OBI plus pomalidomide and dexamethasone. In IZALCO, patients with RRMM (N=64) received 1400 mg of Isa SC OBI plus carfilzomib and dexamethasone.
- The pooled population included data from all 3 trials with 349 total patients.
- Patients were monitored for 4 hours (IRAKLIA) or 1–2 hours (IZALCO) following the start of administration on cycle (C)1 day 1, for 1 hour after the end of injection for the following C1 administrations, and at the end of injection from C2 onwards to assess local tolerability.
- Pre-infusion medications included montelukast (C1 only), steroids, acetaminophen and H1 antihistamines.
- Patients without systemic infusion-related reactions (IRRs) after 4 consecutive administrations of Isa SC OBI had subsequent pre-medication reassessed at investigator's discretion.
- Safety and device performance explored in this pooled analysis of company-sponsored studies were assessed in the Isa SC OBI cohorts by the duration of injection, IRRs, local injection-site reactions (ISRs), and injections completed without interruption, which were defined similarly across all trials.

Results

- A total of 349 patients from Isa SC OBI cohorts in the IRAKLIA, IZALCO and Phase 1b studies were included in this formal pooled analysis.
- **Patients had a median age of 66.0 years (36.0–86.0), median weight of 73.7 kg (36.6–139.0) with the majority of patients having an ECOG performance status of 0 (55.9%) and ISS stage I disease (55.3%) at study entry (Table 1).**

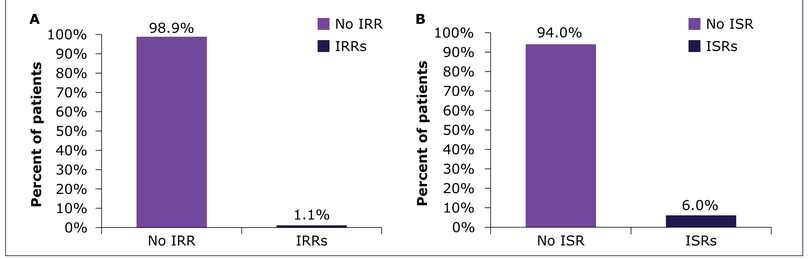
Table 1. Patient baseline demographics and disease characteristics

n (%)	Isa SC OBI (N=349)
Age in years, median (range)	66.0 (36.0–86.0)
<75 years, n (%)	282 (80.8)
≥75 years, n (%)	67 (19.2)
Weight in kg, median (range)	73.7 (36.6–139.0)
ECOG performance status, n (%)	
0	195 (55.9)
1	137 (39.3)
2	17 (4.9)
Time from initial MM diagnosis to randomization in years, median (range)	4.3 (0.3–21.0)
ISS stage at study entry, n (%)	
Stage I	193 (55.3)
Stage II	105 (30.1)
Stage III	45 (12.9)
Unknown	6 (1.7)
MM subtype at study entry, n (%)	
Ig G	210 (60.2)
Ig A	70 (20.1)
Ig M	2 (0.6)
Ig D	6 (1.7)
Ig E	0
Kappa light chain only	39 (11.2)
Lambda light chain only	21 (6.0)
Unknown/undetectable	1 (0.3)

ECOG, Eastern Cooperative Oncology Group; ISS, International Staging System; MM, multiple myeloma; SC, subcutaneous; OBI, on body injector.

- There were **6426** injections in total across all trials. IRRs across trials occurred in **4/349 (1.15%)** patients (**Figure 2A**).
- IRRs were mostly **grade 1 (5/6426, 0.08%)** with **1 grade 3 (0.02%)** and none leading to discontinuation.
- The single grade 3 IRR occurred in a patient with prior history of infusion reaction.
- ISRs occurred in **34/6426 (0.53%)** injections in **21/349 (6.02%)** patients (**Figure 2B**).
- Most ISRs were **grade 1 (33/6426, 0.51%)**, the remaining were **grade 2 (1/6426, 0.02%)** and generally occurred on the day of injection.

Figure 2. A. Infusion related reactions (IRRs) and B. Injection site reactions (ISRs) across trials



- The **median duration** of **Isa SC OBI** injections was **12.0 minutes** (**Figure 3**).
- **99.9% (6419/6426)** of injections in **98.0% (342/349)** of patients were completed without interruption across all trials (**Figure 3**).
- Prior to the **first injection, 343 (98.3%) patients** received **premedications** including acetaminophen/paracetamol **(340, 97.4%)**, diphenhydramine (**323, 92.6%**; according to local approval and availability), montelukast **(305, 87.4%)**, steroids **(1, 0.3%)**, and others **(29, 8.3%)**. Overall, **1061/6426 (16.5%) injections** were administered without premedication and led to no IRRs.
- There were **no** significant safety concerns and **no** serious adverse events (SAEs) related to the OBI.
- OBI-related treatment emergent adverse events (TEAEs) occurred in **9 (2.6%) patients**. OBI-related TEAEs included injection site reaction **(5, 1.4%)**; erythema, injection site erythema, injection site induration, injection site pain, injection site pruritus, and rash were each experienced in **1 (0.3%)** patient. [a]None of these events were grade ≥3.

[a]In IRAKLIA, 1 grade 4 platelet count decrease was erroneously reported as device-related although it was assessed by the Investigator as not related to the OBI. It is therefore not included above.

Figure 3. Total number of injections and injection duration

Total number of injections completed without interruption

6419/6426 (99.9%)

Median duration of injections

12.0 minutes

Key Conclusions

- These findings support overall low rates of IRRs and ISRs across trials, with >6000 (99.9%) Isa SC OBI injections completed without interruption.
- **Isa SC OBI shows reproducible safety and reliability in IRAKLIA, IZALCO and Phase 1b trials, supporting it as a novel administration option with the potential to improve practice efficiency and the overall patient and clinic experience.**

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Disclosures

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