Updated Safety of Isatuximab Subcutaneous At-Home Administration by On-Body Injector in Relapsed/Refractory Multiple Myeloma in the Phase 3 IRAKLIA Study

609

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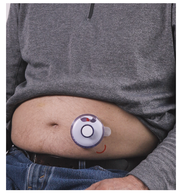
Introduction

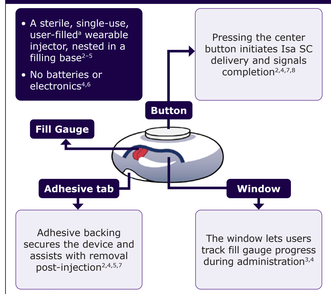
- At-home administration of anti-cancer therapies may help address:[1]
  - Health disparities
  - Treatment adherence barriers
  - Flexibility and convenience
- A subcutaneous (SC) formulation of isatuximab (Isa) administered via an innovative on-body injector (OBI) has been investigated in relapsed/refractory multiple myeloma (RRMM) patients[1] (**Figures 1 & 2**)
- Isa SC OBI administration adapted for at-home use has the potential to improve accessibility for patients and remove common barriers to patient retention and adherence, such as frequency of visits and distance to clinical and outpatient sites, which result in patient and caregiver travel burden[1]
- The safety and feasibility of at-home SC administration of Isa via OBI has previously been shown in IRAKLIA[1]

Figure 1. Isa SC OBI



Device pictured on a model.

Figure 2. Key attributes of Isa SC OBI administration



- Flat dose[b]: No adjustments for body weight[9,10]
- Hands-free administration[6,11-14]
- Hidden ~30-gauge needle: User does not see needle before, during, or after administration[4,7-9]
- Sharps injury prevention feature[8]
- No hyaluronidase[2,4]
- 10 mL injection volume[10,11]
- Individualized and controlled flow rate based on SC interstitial pressure[14]
- Potential at-home administration[3,11,15]
- Median injection time is 13 minutes[1]

[a]During clinical studies, the OBI is filled using a disposable Luer lock syringe. Future iterations of the filling mechanism are under development.
[b]Flat dose investigated in TCD15484 study.

- IRAKLIA (NCT05405166) is an ongoing, global, non-inferiority Phase 3 trial investigating Isa SC administration plus pomalidomide and dexamethasone (Pd) vs intravenous (IV) administration plus Pd in patients with RRMM:
  - At-home administration was studied in a subset of patients in IRAKLIA, with Isa SC administered using OBI
  - Isa SC OBI showed non-inferiority to Isa IV in efficacy and pharmacokinetics, with higher patient satisfaction for the delivery method and a lower incidence of infusion reactions (IRs)

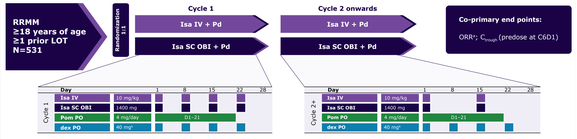
Aim

To present updated results of at-home Isa SC OBI administration in IRAKLIA with data from 148 at-home injections at a median follow-up of 21.75 months

Methods

- In IRAKLIA, patients with RRMM aged ≥18 years with ≥1 prior line of therapy were randomly assigned 1:1 to Isa SC OBI (1400 mg; n=263) or Isa IV (10 mg/kg; n=268) weekly in Cycle (C)1, then every 2 weeks, + P (4 mg/day, Day [D]1–21) + d (40 mg [20 mg if aged ≥75 years] weekly) in 4-week cycles (**Figure 3**)
- After 5 cycles, at-home administration by a healthcare professional (HCP) was optional for Isa SC OBI patients on D15 from C6 onward (D1 visits from C6 remained clinic based)
- At-home eligibility depended on an absence of IRs at C4 and C5, hematology test results at D1 of each cycle, investigator judgment, and patient willingness
- During at-home visits, HCPs prepared and administered the Isa SC OBI device and then safely disposed of the device upon completion, evaluated the injection site and vital signs, and completed documentation
- For the first Isa injection performed at home, an additional assessment was to be performed 30 min after the end of the injection
- Thereafter, local tolerability was assessed at end of injection

Figure 3. IRAKLIA Study Design

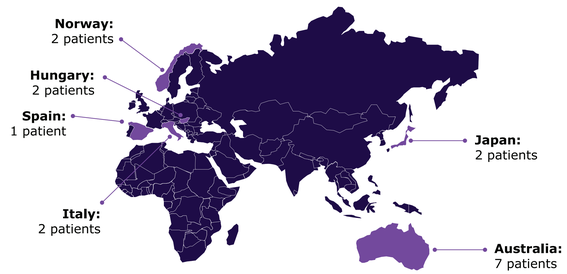


[a]Defined according to 2016 International Myeloma Working Group criteria.[1] [b]20 mg for patients aged ≥75 years.
C, Cycle; d, dexamethasone; D, Day; Isa, isatuximab; LOT, line of therapy; OBI, on-body injector; ORR, overall response rate; P, pomalidomide; PO, oral; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneous. Kumar S, et al. *Lancet Oncol* 2016;17:e328–46.

Results

- In the ongoing IRAKLIA trial, at-home administration was not allowed in some countries due to local regulations
- Out of a total of 263 patients treated with Isa SC OBI in IRAKLIA, 202 patients resided in countries where at-home administration was permissible
  - Some sites did not want to participate in at-home administration
  - Other sites were willing to participate, but implementation was ongoing at the time of the database lock
- A total of 16 (6.1%) patients participated in at-home administration at the cut-off date of August 29, 2025 and median follow-up period of 21.75 months (**Figure 4**)
  - A total of 148 injections were performed at home so far
- Baseline characteristics were generally well balanced between patients who received Isa SC OBI regardless of participation in home administration (**Table 1**)

Figure 4. Number of participants with at least one at-home administration by country[a]



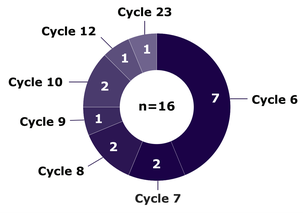
[a]Cut-off date: August 29, 2025; median follow-up period: 21.75 months.

Table 1. Baseline characteristics in participants who received Isa SC OBI with at-home administration and all participants who received Isa SC OBI

	Isa SC OBI + Pd with home administration (N=16)	Isa SC OBI + Pd, all patients (N=263)
Age in years, median (range)	66 (55–83)	66 (36–86)
Race, %		
White	75	70
Black or African American	0	3
Asian	18.8	20.2
Sex, %		
Male	62.5	52.1
Female	37.5	47.9
ECOG performance status, %		
0	62.5	53.2
1	31.3	41.4
2	6.3	5.3
Baseline weight by category, %		
≤65 kg	18.8	31.6
>65 kg to ≤85 kg	56.3	44.9
>85 kg	25	23.6

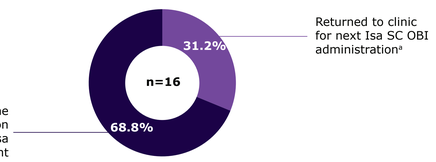
- 7 patients started on Cycle 6, the first cycle available for home administration and 9 patients started Cycle 7 or beyond (**Figure 5**)

Figure 5. Treatment cycle at which home administration was started



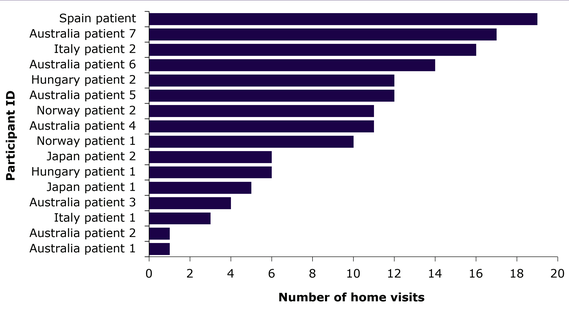
- The majority of patients who switched to at-home administration continued with the at-home administration (**Figure 6**)
  - Of the 16 patients who switched to at-home administration, 11 (68.8%) have not returned to hospital for the D15 visit of their next cycle
- The number of at-home Isa OBI administration visits per patient is shown in **Figure 7**

Figure 6. At-home administration continuation



[a]Includes participants who returned to clinic for next Isa SC OBI administration and resumed home administration thereafter

Figure 7. Number of at-home administration visits by participant



- Reliability of Isa SC OBI injections was observed with the high completion rate without interruption and a median injection time comparable to the overall IRAKLIA population (**Figure 8**)

Figure 8. Isa SC OBI device performance during home administration

Injection completion rate

100%

148 of 148 administrations with the Isa SC OBI completed without interruption

Median injection duration

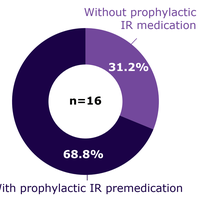
13 min overall IRAKLIA population

12 min at-home administration

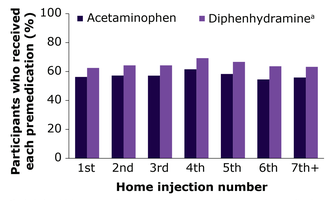
- At-home administration was well-tolerated:
  - No new safety signals
  - No systemic IRs linked to at-home visits were reported
  - Out of 16 participants who received at-home administration of Isa SC OBI, 11 participants received prophylactic IR premedication (**Figure 9a**)
  - Of 148 Isa SC OBI injections, 52 (35.1%) were completed without any IR premedication and 96 (64.9%) were completed with IR premedication
  - At each home injection, participants received prophylactic acetaminophen and/or, diphenhydramine (or equivalent) with no participants requiring steroids, montelukast, or other premedications (**Figure 9b**)
  - Low rate of injection-site reactions (ISR; n=1):
    - The single grade 1 ISR consisted of injection-site swelling
    - Resolved within the same day with no treatment
    - The majority of subsequent day 15 administrations were performed at home for this patient
  - No other adverse events, systemic IRs, or device events were associated with at-home administration

Figure 9. IR premedications

a. Premedication use in patients who received at-home Isa SC OBI administration



b. Type of IR medication given for prophylaxis at each home injection



[a]Included cetirizine, promethazine, dexchlorpheniramine or any other medication according to local approval and availability.

Key Conclusions

- IRAKLIA is the first MM phase 3 study to incorporate the use of an innovative hands-free OBI, designed to maximize patient convenience and practice efficiency
- Updated data from the ongoing IRAKLIA trial demonstrate that at-home administration of Isa SC OBI by an HCP is feasible and well tolerated for the treatment of patients with RRMM
- Median injection time and success rate are consistent with in-clinic use
- Home administration was well-tolerated with no new safety concerns
- **These data support the safety of Isa SC OBI at-home administration by an HCP in addition to in-clinic administration, enabling more flexible, accessible, and comfortable care for patients with MM**
- **Isa SC OBI at-home administration has the potential to reduce common barriers to patient retention and therapy compliance**

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Abbreviations
C, Cycle; C_{trough}, trough concentration; D, Day; dex, dexamethasone; ECOG, Eastern Cooperative Oncology Group; HCP, healthcare professional; IR, infusion reaction; Isa, isatuximab; ISR, injection-site reaction; IV, intravenous; LOT, line of therapy; MM, multiple myeloma; OBI, on-body injector; ORR, overall response rate; Pd, pomalidomide and dexamethasone; PO, oral; Pom, pomalidomide; RRMM, relapsed/refractory MM; SC, subcutaneous.

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