Real-World Experience With Isatuximab in Patients With Relapsed and/or Refractory Multiple Myeloma (RRMM): IONA-MM First Interim Analysis

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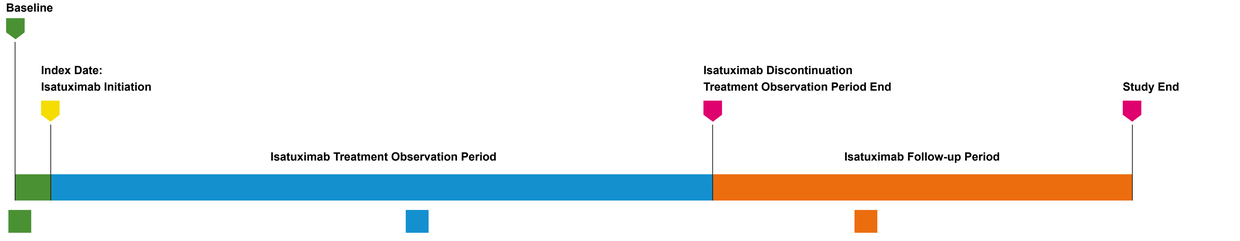
INTRODUCTION

- Multiple myeloma (MM) accounts for approximately 1% of all cancers worldwide and is the second most common hematologic malignancy[1,2]
- Isatuximab (Isa) is an anti-CD38 monoclonal antibody that targets a specific CD38 epitope and induces myeloma cell death via multiple mechanisms[3-5]
- The Phase 3 ICARIA-MM (NCT02990338) study reported that Isa in combination with pomalidomide and dexamethasone (Pd) significantly improved progression-free survival (PFS) compared with Pd alone (median PFS 11.5 vs 6.5 months; hazard ratio [HR], 0.60; 95% confidence interval [CI], 0.44–0.81; p=0.001) in patients with relapsed and/or refractory MM (RRMM)[7]
- Based on the results of the ICARIA-MM study, Isa is approved in several countries in combination with Pd for the treatment of adult patients with RRMM who have received ≥2 prior therapies, including lenalidomide and a proteasome inhibitor[7,8]
- The Phase 3 IKEMA study (NCT03275285) demonstrated that Isa plus carfilzomib-dexamethasone (Kd) significantly improved PFS compared with Kd (median PFS 35.7 vs 19.2 months; HR, 0.58; 95% CI, 0.42–0.79) in patients with relapsed MM[9,10]
- Based on the IKEMA study, to date, Isa plus Kd is approved in the United States for patients with RRMM who have received 1–3 previous lines of therapy and in the European Union for patients with MM who have received ≥1 prior therapy[8,11]
- Currently, there is limited real-world evidence available for patients treated with Isa-Pd/Isa-Kd
- The IONA-MM registry study aims to investigate the effectiveness, safety, and quality of life in patients with RRMM treated with Isa-based regimens in routine clinical practice
- This first interim analysis of the IONA-MM study details baseline characteristics, treatment exposure, and safety for patients with RRMM treated with Isa in the real-world setting

METHODS

- The IONA-MM (NCT04458831) study is an ongoing, non-interventional, multinational, observational study of patients with RRMM treated with Isa in the real-world setting.[12] The study design is shown in **Figure 1**
- Patients aged ≥18 years with RRMM who received ≥1 prior treatment line were included
- Patients were enrolled prospectively and retrospectively (exposure to Isa ≤3 months prior to enrollment)
- The treating physician determined Isa treatment, and treatment decision was established prior to and independent of enrollment; treatment duration was in accordance with local prescribing regulations
- Treatment-emergent adverse events (TEAEs) and laboratory abnormalities were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0

Figure 1. IONA-MM study design



Baseline Assessments:

Up to 4 weeks prior to isatuximab intiation

Assessments collected:

- Patients demographics
- Medical and surgical history and comorbidities
- Prior anti-myeloma treatment history
- Baseline disease assessments
- Concomitant medications
- Patient-reported outcome assessments

Treatment Observation Period:

Begins at isatuximab initiation. Routine clinical assessments collected at 4 weeks after treatment initiation and every 3 months up to 30 days after discontinuation of isatuximab treatment

Assessments collected:

- Disease monitoring assessments
- Study treatment details
- Response assessments
- Concomitant medications
- Patient-reported outcome assessments
- Safety assessments
- Progression-free survival assessment

Follow-up Period:

Follow-up assessments collected for each patient for a maximum of 6 months beginning 30 days after isatuximab discontinuation until loss to follow-up, withdrawal of consent, death, or study end, whichever comes first

Assessments collected:

- Progression-free survival data if progressive disease did not occur
- First subsequent line of anti-myeloma treatment
- Safety assessments
- Survival status

RESULTS

Patients and treatment exposure

- The IONA-MM study is ongoing and currently enrolling patients. This first interim analysis included 112 patients who received ≥1 dose of Isa-Pd (n=81), Isa-Kd (n=26), or other Isa regimens (n=5) between 13 August 2020 and 22 February 2022 from 38 study sites across 6 countries
- Treatment duration of the study drugs at data cut-off are shown in **Table 1**
- At data cut-off, the median (min–max) duration of Isa exposure was 5.4 (0–18.8) months for Isa-Pd and 6.2 (0–10.6) months for Isa-Kd
  - 79.0% and 74.1% of patients were still receiving Isa-Pd and Isa-Kd, respectively

Table 1. Exposure to study treatments

Treatment duration (months)	Isa-Pd (n=81)	Isa-Kd (n=26)
Isatuximab, median (min–max)	5.4 (0–18.8)	6.2 (0–10.6)
Pomalidomide, median (min–max)	4.7 (0–18.8)	NA
Carfilzomib, median (min–max)	NA	7.0 (0–10.6)
Dexamethasone, median (min–max)	5.5 (0–15.7)	6.7 (0–10.6)

Isa-Pd, isatuximab, pomalidomide, and dexamethasone; Isa-Kd, isatuximab, carfilzomib, and dexamethasone; NA, not applicable

Baseline characteristics

- **Table 2** shows a comparison of the baseline characteristics among patients in the IONA-MM study with those in the corresponding Phase 3 Isa studies (ICARIA-MM and IKEMA)
- Compared with the baseline characteristics of the patients in the corresponding treatment arms of ICARIA-MM or IKEMA, in the IONA-MM study:
  - Higher proportions of patients aged ≥75 years received Isa-Pd (39.5%)/Isa-Kd (30.8%)
  - Higher proportions of patients were International Staging System (ISS) stage III in the Isa-Pd (37.8%)/Isa-Kd (26.7%) arms
  - A lower proportion of patients reported high-risk cytogenetics in the Isa-Kd (12.5%) arm
  - Median prior lines of therapy was 3.0 in both Isa-Pd and Isa-Kd arms
  - A higher proportion of patients in the Isa-Kd arm (23.1%) received ≥4 prior lines of therapy
  - Higher proportions of daratumumab-exposed patients received Isa-Pd (18.5%)/Isa-Kd (23.1%)
  - A lower proportion of patients were lenalidomide-refractory in the Isa-Pd arm (50.6%) and a higher proportion were lenalidomide-refractory in the Isa-Kd arm (61.5%)
- Among the patients in the IONA-MM study, 90.1% of patients in the Isa-Pd arm and all patients in the Isa-Kd arm received prior medications for MM

Table 2. Patient demographic and baseline characteristics

Patient characteristic	Isa-Pd		Isa-Kd	
	IONA-MM (n=81)	ICARIA-MM (n=154)	IONA-MM (n=26)	IKEMA (n=179)
Median age, years (min–max)	71.0 (41–89)	68.0 (36–83)	70.0 (47–85)	65.0 (37–86)
Age in years by category				
<65	24 (29.6)	54 (35.1)	8 (30.8)	88 (49.2)
≥65 to <75	25 (30.9)	68 (44.2)	10 (38.5)	74 (41.3)
≥75	32 (39.5)	32 (20.8)	8 (30.8)	17 (9.5)
ISS stage				
Stage I	17/45 (37.8)	64 (41.6)	1/15 (6.7)	89 (49.7)
Stage II	11/45 (24.4)	53 (34.4)	10/15 (66.7)	63 (35.2)
Stage III	17/45 (37.8)	34 (22.1)	4/15 (26.7)	26 (14.5)
Unknown	0	3 (1.9)	0	1 (0.6)
Cytogenetic risk				
High*	6/54 (11.1)	24 (15.6)	2/16 (12.5)	42 (23.5)
Standard	44/54 (81.5)	103 (66.9)	14/16 (87.5)	114 (63.7)
Missing	4/54 (7.4)	27 (17.5)	0/16 (0)	23 (12.8)
1q21 abnormalities				
Present	12/12 (100.0)	76 (49.4)	5/5 (100)	75 (41.9)
Absent	-	38 (24.7)	-	84 (46.9)
Unknown/missing	-	40 (26.0)	-	20 (11.2)
ECOG				
0	11/46 (23.9)	55 (35.7)	5/16 (31.3)	95 (53.1)
1	26/46 (56.5)	83 (53.9)	9/16 (56.3)	73 (40.8)
2	7/46 (15.2)	16 (10.4)	1/16 (6.3)	10 (5.6)
3	2/46 (4.3)	0	0/16 (0)	1 (0.6)
4	0/46 (0)	0	1/16 (6.3)	0
Abnormal creatinine clearance†	14/52 (26.9)	55/142 (39)	3/16 (18.8)	43/165 (26)
Prior lines of therapy				
Median (min–max)	3.0 (1–9)	3.0 (2–11)	3.0 (1–8)	2.0 (1–4)
1	7/73 (9.6)	0	8/26 (30.8)	79 (44.1)
2	22/73 (30.1)	45 (29.2)	3/26 (11.5)	64 (35.8)
3	15/73 (20.5)	52 (33.8)	7/26 (26.9)	33 (18.4)
≥4	23/73 (31.5)	57 (37.0)	6/26 (23.1)	3 (1.7)
Main anti-myeloma therapies by class and agent				
Alkylating agents	26 (32.1)	139 (90.3)	8 (30.8)	169 (94.4)
Proteasome inhibitors	64 (79.0)	154 (100.0)	16 (61.5)	166 (92.7)
Immunomodulators	61 (75.3)	154 (100.0)	20 (76.9)	136 (76.0)
Lenalidomide	58 (71.6)	154 (100.0)	20 (76.9)	72 (40.2)
Corticosteroids	66 (81.5)	154 (100.0)	18 (69.2)	179 (100.0)
Monoclonal antibodies	19 (23.5)	2 (1.3)	12 (46.2)	5 (2.8)
Daratumumab	15 (18.5)	1 (0.6)	6 (23.1)	1 (0.6)
Refractory status				
Immunomodulatory drug	48 (59.3)	147 (95.5)	16 (61.5)	78 (43.6)
Lenalidomide	41 (50.6)	144 (93.5)	16 (61.5)	57 (31.8)
Lenalidomide in last regimen	13 (16.0)	93 (60.4)	6 (23.1)	36 (20.1)
Proteasome inhibitor	37 (45.7)	118 (76.6)	11 (42.3)	56 (31.3)
Immunomodulatory drug and proteasome inhibitor	11 (13.6)	113 (73.4)	4 (15.4)	35 (19.6)
Last regimen	47 (58.0)	150 (97.4)	19 (73.1)	89 (49.7)

Data are n (%) unless otherwise indicated
*High-risk was defined as del(17p), or t(4;14), or t(14;16) by fluorescence in-situ hybridization. Cytogenetic status was assessed by a central laboratory with cut-offs of 50% for del(17p) and 30% for t(4;14) and t(14;16)
†Defined as <60 mL/min per 1.73 m² eGFR (MDRD) in ICARIA-MM and IKEMA
ECOG, Eastern Cooperative Oncology Group; eGFR, estimated glomerular filtration rate; Isa-Pd, isatuximab, pomalidomide, and dexamethasone; Isa-Kd, isatuximab, carfilzomib, and dexamethasone; ISS, International Staging System; MDRD, modification of diet in renal disease

Safety

- In the IONA-MM safety population, all-grade, Grade 3–4, and serious TEAEs with Isa-Pd or Isa-Kd treatment were lower than those reported in the corresponding Phase 3 studies (**Table 3**)
- In IONA-MM, fatal (Grade 5) TEAEs during study treatment occurred in 4 (4.9%) patients in the Isa-Pd arm and 1 (3.8%) patient in the Isa-Kd arm
  - Fatal TEAEs in the Isa-Pd arm included sepsis in 2 patients, septic shock in 1 patient, and failure to thrive in 1 patient
  - 1 patient in the Isa-Kd arm had a fatal TEAE due to pneumonia
- TEAEs leading to Isa discontinuation occurred in 6 (7.4%) and 3 (11.5%) patients with Isa-Pd and Isa-Kd, respectively
- The most common TEAEs occurring in ≥5% of patients in either of the Isa treatment arms in IONA-MM study are shown in **Table 4**
- The most common all-grade TEAE was neutropenia in the Isa-Pd arm and diarrhea in the Isa-Kd arm

Table 3. Treatment-emergent adverse events

n (%)	Isa-Pd		Isa-Kd	
	IONA-MM (n=81)	ICARIA-MM (n=152)	IONA-MM (n=26)	IKEMA (n=177)
Any TEAE	52 (64.2)	151 (99.3)	16 (61.5)	172 (97.2)
Any Grade 3–4 TEAE	36 (44.4)	135 (88.8)	10 (38.5)	134 (75.7)
Any Grade 5* TEAE	4 (4.9)	14 (9.2)	1 (3.8)	6 (3.4)
Serious TEAE	21 (25.9)	111 (73.0)	8 (30.8)	105 (59.3)
Any TEAE leading to definitive isatuximab discontinuation	6 (7.4)	4 (2.6)	3 (11.5)	1 (0.6)

*TEAE with fatal outcome during the treatment period
Isa-Pd, isatuximab, pomalidomide, and dexamethasone; Isa-Kd, isatuximab, carfilzomib, and dexamethasone; TEAE, treatment-emergent adverse event

Table 4. Most common (≥5%) TEAEs in IONA-MM

TEAE, n (%)	Isa-Pd (n=81)		Isa-Kd (n=26)	
	All grades	Grade ≥3	All grades	Grade ≥3
Any TEAE	52 (64.2)	36 (44.4)	16 (61.5)	10 (38.5)
Neutropenia	18 (22.2)	17 (21.0)	2 (7.7)	2 (7.7)
Diarrhea	5 (6.2)	3 (3.7)	4 (15.4)	0
Infusion-related reaction	5 (6.2)	1 (1.2)	0	0
Fatigue	4 (4.9)	2 (2.5)	3 (11.5)	0
Pneumonia	2 (2.5)	2 (2.5)	2 (7.7)	2 (7.7)
Bronchitis	2 (2.5)	0	2 (7.7)	1 (3.8)
Acute kidney injury	1 (1.2)	0	2 (7.7)	2 (7.7)
Decreased weight	1 (1.2)	0	2 (7.7)	0
Thrombocytopenia	0	0	2 (7.7)	0
Nausea	0	0	3 (11.5)	0
Vomiting	0	0	2 (7.7)	0
Peripheral edema	0	0	2 (7.7)	0
Increased blood creatinine	0	0	2 (7.7)	0
Decreased appetite	0	0	2 (7.7)	0

Isa-Pd, isatuximab, pomalidomide, and dexamethasone; Isa-Kd, isatuximab, carfilzomib, and dexamethasone; TEAE, treatment-emergent adverse event

CONCLUSIONS

- Despite significant advances in the therapeutic landscape of MM, the identification of the optimal therapeutic approach in a real-world setting remains a major challenge
- The IONA-MM study provides real-world evidence to inform the use of isatuximab in patients with RRMM outside of clinical trials and in wider populations
- In this first interim analysis of the IONA-MM study, baseline characteristics of patients in the Isa-Pd and Isa-Kd arms were comparable to those seen in the corresponding Phase 3 Isa studies, with a few differences in the proportion of patients aged ≥75 years old, ISS stage III, high-risk cytogenetics, and prior lines of therapy
- Both Isa-Pd and Isa-Kd had an expected safety profile with a low rate of discontinuation due to an adverse event in routine clinical practice
- Response data are forthcoming. The study is recruiting patients and enrollment will continue until the sample size of 1100 patients is reached

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REFERENCES:
1. Kazandjian D. *Semin Oncol*. 2016;43(6):676-681.
2. Sung H, Ferlay J, Siegel RL, et al. *CA Cancer J Clin*. 2021;71(3):209-249.
3. Deckert J, Wetzel MC, Bartle LM, et al. *Clin Cancer Res*. 2014;20(17):4574-4583.
4. Martin TG, Corzo K, Chiron M, et al. *Cells*. 2019;8(12):1522.
5. Moreno L, Perez C, Zabaleta A, et al. *Clin Cancer Res*. 2019;25(10):3176-3187.
6. Zhu C, Song Z, Wang A, et al. *Front Immunol*. 2020;11:1771.
7. Attal M, Richardson PG, Rajkumar SV, et al. *Lancet*. 2019;394(10214):2096-2107.
8. Sanofi. Sarclisa (isatuximab-irfc) [package insert]. In. Bridgewater, NJ: Sanofi-Aventis U.S. LLC; 2021.
9. Moreau P, Dimopoulos M, Mikhael J, et al. *Ann Oncol*. 2022;33(6):664-665.
10. Moreau P, Dimopoulos MA, Mikhael J, et al. *Lancet*. 2021;397(10292):2361-2371.
11. Sanofi. Sarclisa (isatuximab). https://www.ema.europa.eu/en/medicines/human/EPAR/sarclisa. Published 2022. Accessed July 06, 2022.
12. NCT04458831. A non-interventional, multinational, observational study with isatuximab in patients with relapsed and/or refractory multiple myeloma (RRMM) (IONA-MM). 2020. https://www.clinicaltrials.gov/ct2/show/NCT04458831.

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