Internal

Poster #
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# TRIAL IN PROGRESS: PHASE 2 SUBQSA STUDY OF SUBCUTANEOUS ISATUXIMAB, ADMINISTERED BY AN ON-BODY INJECTOR (OBI), IN COMBINATION WITH WEEKLY CARFILZOMIB AND DEXAMETHASONE IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

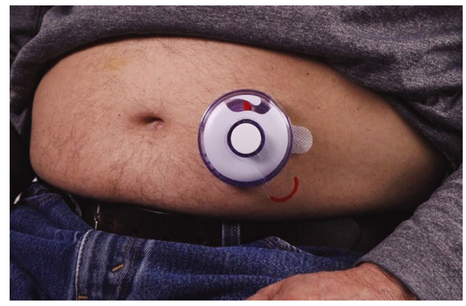
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## Introduction

- Isatuximab (Isa) is an anti-CD38 monoclonal antibody that induces myeloma cell death through multiple mechanisms.[1]
- The addition of Isa to pomalidomide/dexamethasone (Isa-Pd) and carfilzomib/dexamethasone (Isa-Kd) demonstrated improved progression-free survival and a manageable safety profile in relapsed/refractory multiple myeloma (RRMM) in phase 3 ICARIA and IKEMA clinical trials.[2-4]
- Intravenous (IV) Isa-Pd and Isa-Kd are FDA- and EMA-approved treatments for RRMM.[5,6]
  - In most countries, Isa is administered as a 250-mL fixed-volume IV infusion over 75 minutes.[7]
- To improve patient quality of life and reduce healthcare resource utilization, subcutaneous (SC) Isa administration via on-body injector (OBI) is under investigation.[7-10]
  - OBI (Enable Injections, Inc., Cincinnati, OH, USA) is a sterile, single-use, disposable, elastomeric, user-filled, wearable bolus injector applied to a single injection site in the periumbilical region that is rotated at each administration.[7,11] **(Figure 1)**
  - The median injection duration is 13 minutes.[7]
- In a phase 1b study (TCD15484, NCT04045795) in patients with RRMM, efficacy and safety of SC Isa administered by an investigational OBI plus Pd were comparable to IV Isa-Pd, with no infusion reactions (IRs).[12,13]
- Isa SC OBI is also currently being investigated in combination with Pd in a phase 3 study (IRAKLIA, NCT05405166) and with Kd in a phase 2 study (IZALCO, NCT05704049) for the treatment of RRMM.[14,15] Results show similar efficacy, safety, and pharmacokinetics (PK) with SC OBI compared to IV administration,[7] and a preference for SC OBI by both patients and healthcare providers.[16]
- **Benefits of SC Isa via OBI**[10,11]
  - A smaller fixed administration volume (10 mL)
  - Hands-free delivery
  - Smaller, hidden, retractable needle
  - Individualized flow rate
- **The efficacy and safety of SC Isa via OBI is being further investigated in combination with Kd in the phase 2 SubQSA study.**

**Figure 1.** On-body injector applied to abdomen[a]



[a]CAUTION: Investigational device. Limited by federal (or US) law to investigational use. Device pictured on a model.

## Objective

**Here, we describe the design of a phase 2 study to assess the efficacy and safety of SC Isa, administered by OBI, in combination with weekly carfilzomib and dexamethasone, in patients with RRMM.**

## Study Design and Methods

- SubQSA (NCT06356571) is a single-arm, open-label, phase 2 study of patients receiving SC Isa via OBI in combination with weekly carfilzomib (K) and dexamethasone (d).[17] **(Figure 2)**
- This is a multicenter study enrolling at 30–40 sites in the USA.
- **Isa** (10 mL) will be administered by OBI, at the recommended SC phase 2 dose of 1400 mg, on Days (D) 1, 8, 15, and 22 for Cycle (C) 1 and then on D1 and 15 for subsequent cycles. Isa may be decreased to monthly dosing after C6 at the investigator's discretion.
- **K** will be administered at 20 mg/m² on D1 of C1 and then escalated to 70 mg/m² on D8 and 15 of C1, followed by D1, 8, and 15 of subsequent cycles; administration will be IV.
  - Once-weekly dosing of K was chosen for this study because it most accurately represents real-world US practice.
- **d** will be administered at 20 mg on D1, 8, 15, and 22 of C1 and then on D1, 8, and 15 of subsequent cycles; administration will be IV on D1 of C1, and subsequently either IV or oral.
- The duration of each cycle is 28 days.
- In addition to d, patients will receive premedication for IRs with montelukast (C1 only), acetaminophen/paracetamol, and diphenhydramine (or equivalent). Methylprednisolone (or equivalent) will be administered if d is discontinued earlier than Isa.
- Patients can continue therapy until disease progression, unacceptable AEs, patient request to discontinue treatment, or any other reason. After 12 months of study treatment, patients can switch to post-trial access.
- Estimated enrollment is 64 patients, of whom 15 will participate in immunogenicity/PK analyses.
- The cutoff date for primary analysis will be 6 months after last participant in (LPI).
- Final analysis will be performed 12 months after LPI.
- This study is currently recruiting.

**Figure 2.** Study design for phase 2 SubQSA: SC Isa + Kd in RRMM with 1–3 prior LOT

**RRMM**
**N=64, estimated**

**Key inclusion criteria**
- ✓ Age ≥18 years with RRMM
- ✓ Patients with ≥1 (and no more than 3) prior LOT

**Key exclusion criteria**
- × Primary refractory MM
- × Refractory to carfilzomib
- × Prior anti-CD38 <6 months before first Isa administration
- × Intolerance to anti-CD38 previously received

**Cycle 1:** Isa SC OBI + Kd
**Cycle 2 onwards:** Isa SC OBI + Kd
**(~32 months)** 6 months after LPI

| | Day | | 1 | 8 | 15 | 22 | 28 |
|---|---|---|---|---|---|---|---|
| Cycle 1 | Isa SC OBI | 1400 mg | ■ | ■ | ■ | ■ | |
| | K IV | 20 mg/m² | ■ | | | | |
| | | 70 mg/m² | | ■ | ■ | | |
| | d IV or PO | 20 mg | ■ | ■ | ■ | ■ | |

| | Day | | 1 | 8 | 15 | 22 | 28 |
|---|---|---|---|---|---|---|---|
| Cycle 2+ | Isa SC OBI* | 1400 mg | ■ | | ■ | | |
| | K IV | 70 mg/m² | ■ | ■ | ■ | | |
| | d IV or PO | 20 mg | ■ | ■ | ■ | | |

**Baseline assessments:** Physical examination, ECOG, weight, vitals, cardiac ultrasonography, hematology, urinalysis

**Assessments throughout study:** Physical examination, weight, vitals, PRO surveys, hematology, urinalysis

**The phase 2 SubQSA study is evaluating the efficacy and safety of SC Isa administration via OBI + Kd in RRMM**

**Primary endpoint:**
- Overall response rate (ORR)

**Secondary endpoints include:**
- Safety
  - Incidence of IRs
  - Incidence of TEAEs
  - Incidence of SAEs
- Tolerability
  - Incidence of ISRs
- Efficacy
  - ≥CR and ≥VGPR rate
  - DOR
  - Time to first response
- Patient satisfaction
- Immunogenicity and PK exposure parameters

* After C6, Isa may be decreased to monthly dosing at the investigator's discretion

## Key Conclusions

- The phase 2 SubQSA study will measure the efficacy and safety of Isa administered via SC OBI in combination with weekly carfilzomib, which accurately represents real-world use, and dexamethasone.
- Together with results from other studies of Isa administered via the OBI system, the findings from this study will provide further insight on the benefit of administering SC Isa through the OBI system compared to IV Isa in the treatment of RRMM.

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## Abbreviations

AE, adverse event; C, Isa, isatuximab; cycle; CR, complete response; D, day; d, dexamethasone; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; EMA, European Medicines Agency; FDA, Food and Drug Administration; IR, infusion reaction; ISR, injection-site reaction; IV, intravenous; K, carfilzomib; Kd, carfilzomib and dexamethasone; LOT, lines of therapy; LPI, last participant in; MM, multiple myeloma; OBI, on-body injector; ORR, overall response rate; P, pomalidomide; Pd, pomalidomide and dexamethasone; PK, pharmacokinetic; PO, orally; PRO, patient-reported outcomes; RRMM, relapsed/refractory multiple myeloma; SAE, serious adverse event; SC, subcutaneous; TEAE, treatment-emergent adverse event; VGPR, very good partial response.

## Disclosures

**Buck:** Sanofi, Janssen, BMS: Honoraria. **Cutrer:** No relationships to disclose. **Gabrail:** Celgene; Chemiocare: Consultancy; Janssen Oncology; Karyopharm Therapeutics; Taiho Pharmaceutical; Tesaro/GSK: Speakers' Bureau; Amgen; Bayer; Chemiocare; Chemiocare; Kartos Therapeutics; Seagen: Research Funding; Oncology Supply: Travel, Accommodations, Expenses. **Geils:** AbbVie: Other: Investigator on trial. **Philipovskiy:** Immuneering; Arvinas; Valerio; Frontier Med; Monte Rosa Therapeutics: Research Funding; Florida Cancer Specialists and Research Institute: Current Employment. **Salib:** No relationships to disclose. **Barnes**: Sanofi: Current Employment. **Brill:** Sanofi: Current Employment. **Fukao:** Sanofi: Current Employment. **Leroy-Carita:** Sanofi: Current Employment. **Berdeja:** AstraZeneca; BMS; Caribou Biosciences; Galapagos; Janssen; K36 Therapeutics; Kite Pharma; Legend Biotech; Pfizer; Roche; Sanofi-Aventis; and Takeda: Consultancy; 2seventy bio; AbbVie; Amgen; BMS; C4 Therapeutics; Caribou Biosciences; CARsgen; Cartesian Therapeutics; Celularity; CRISPR Therapeutics; Fate Therapeutics; Genentech; GSK; Ichnos Sciences; Incyte; Janssen; Juno Therapeutics; K36 Therapeutics; Karyopharm: Research Funding; Janssen: Honoraria. **Off-Label Disclosure:** Isatuximab is currently approved in various countries for intravenous administration in patients with relapsed/refractory multiple myeloma (RRMM). The present study investigates subcutaneous administration of isatuximab in patients with RRMM.

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