XPORT-MM-031 (EMN29): A Phase 3 Randomized, Open-label Trial of Selinexor, Pomalidomide, and Dexamethasone (SPd) Versus Elotuzumab, Pomalidomide, and Dexamethasone (EloPd) in Patients With Relapsed or Refractory Multiple Myeloma (RRMM) (NCT05028348)

BACKGROUND

- The increasing use of proteasome inhibitors (PIs), immunomodulatory drugs (IMiDs), and anti-CD38 mAbs in earlier lines of therapy for patients with multiple myeloma (MM) has resulted in an increasing number of patients who become triple-class refractory early in treatment[1]
- Pomalidomide and dexamethasone (Pd) are commonly used in triplet combinations for patients with RRMM.[2] However, the early use of anti-CD38 mAbs and PIs may limit the efficacy of their subsequent use in combination with Pd.[3]
- For MM patients who have been previously treated with an IMiD, a PI, and an anti-CD38 mAb, there is an unmet medical need to introduce a different mechanism of action[2-4]

STUDY DESIGN

- Phase 3 randomized, open-label multicenter trial to evaluate the safety, tolerability, and efficacy of SPd vs EloPd in patients with RRMM who have been previously treated with an IMiD, a PI, and an anti-CD38 mAb[3,5]
- Patients will be randomized in a 1:1 manner between SPd and EloPd arms[3,5]
- All patients must have received anti-CD38 mAb therapy as part of their immediate last line of therapy prior to study entry[3,5]

KEY STUDY OBJECTIVES

- To compare the efficacy, safety, and the impact on HR-QoL of SPd versus EloPd in patients with MM who have received 1–4 prior anti-MM lines of therapy, never received pomalidomide, but have been treated with an IMiD (lenalidomide), PI, and an anti-CD38 mAb[3,5]

DISCLOSURE

This study is sponsored by the European Myeloma Network (EMA), funded by Karyopharm Therapeutics Inc.

CONTACT

clinicaltrials@karyopharm.com

Scan here for more information on ClinicalTrials.gov

PART 2†

EXPECTED ENROLLMENT (N ≈ 222)

Patients with pomalidomide-naïve and elotuzumab-naïve RRMM

- 1–4 prior lines of therapy including:
  - A PI
  - Lenalidomide
  - An anti-CD38 as part of the immediate prior line of therapy

R 1:1

SPd (n=111)

- Selinexor 40 mg QW PO on days 1, 8, 15, 22
- Pomalidomide 4 mg QD PO on days 1–21
- Dexamethasone* 40 mg PO on days 1, 8, 15, 22
- 28-day cycle

EloPd (n=111)

- Elotuzumab
  - 10 mg/kg IV on days 1, 8, 15, 22 of cycles 1–2
  - 20 mg/kg IV on day 1 for cycles ≥ 3
- Pomalidomide 4 mg QD PO on days 1–21
- Dexamethasone* 40 mg QW PO on non-Elo dosing weeks, 28 mg PO + 8 mg IV on days of Elo dosing
- 28-day cycle

Randomization stratified by:

- Number of prior anti-MM lines of therapy (1–2 versus 3–4)
- R-ISS stage III vs stage I or II
- Triple-class refractory (yes or no)

PRIMARY ENDPOINT

- PFS

KEY SECONDARY ENDPOINTS

- ORR
- OS

OTHER SECONDARY ENDPOINTS

- Safety and tolerability
- Patient-reported QoL

†Part 1 (closed) was designed to evaluate the optimal dose of selinexor (in the SPd combination) to be used in Part 2. In Part 2, patients randomized to the SPd arm will receive SPd-40.

*Dexamethasone 20 mg QW PO on Days 1, 8, 15, and 22 in SPd or on non-elotuzumab dosing weeks in EloPd administered to patients > 75 years of age. Dexamethasone dose may be divided over 2 days at the Investigator's discretion in SPd or non-elotuzumab dosing weeks in EloPd for patients ≤ 75 and > 75 years of age. On days of elotuzumab dosing, the dose of dexamethasone is 8 mg PO + 8 mg IV for patients > 75 years of age

SELECT INCLUSION CRITERIA[3,5]

- RRMM with measurable disease per IMWG guidelines
- ECOG PS 0–2
- Age ≥ 18 years at the time of signing informed consent
- Received at least 1 and no more than 4 lines of prior anti-MM therapy*
- Prior therapy that includes ≥ 2 consecutive cycles of lenalidomide and a PI given alone or in combination
- Prior therapy with an anti-CD38 mAb as part of their immediate last line of therapy prior to study entry
- Resolution of any clinically significant non-hematological toxicities (if any) from previous treatments to Grade ≤ 1 by C1D1. Patients with Grade 2 non-hematological toxicities may be included following approval from the Medical Monitor.
- Adequate hematological and hepatic function, renal function (eGFR ≥ 15 mL/min)

SELECT EXCLUSION CRITERIA[3,5]

- Smoldering MM , plasma cell leukemia, or history of CNS MM
- Documented active systemic amyloid light chain amyloidosis
- Prior treatment with:
  - A SINE compound, including selinexor
  - Pomalidomide or elotuzumab
- Uncontrolled active infection requiring parenteral antibiotics, antivirals, or antifungals within 1 week prior to C1D1
- Radiation, chemotherapy, or immunotherapy or any other anticancer therapy including investigational therapies and high dose dexamethasone (i.e., 40 mg daily for 4 days per week) ≤ 2 weeks prior to C1D1
- Prior autologous stem cell transplantation < 100 days or allogeneic stem cell transplantation < 4 months prior to C1D1

*Induction therapy followed by stem cell transplant and consolidation/maintenance therapy is considered as 1 line of therapy

C1D1, cycle 1 day 1; CD38, cluster of differentiation 38; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; Elo, elotuzumab; EloPd, elotuzumab+pomalidomide+dexamethasone; EMN, European Myeloma Network; HR-QoL, health-related quality of life; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; IV, intravenous; mAb, monoclonal antibody; MM, multiple myeloma; ORR, objective response rate; OS, overall survival; Pd, pomalidomide+dexamethasone; PFS, progression-free survival; PI, proteosome inhibitor; PO, by mouth; QoL, quality of life; QD, once daily; QW, once weekly; R, randomization; R-ISS, Revised Multiple Myeloma International Staging System; RRMM, relapsed/refractory multiple myeloma; SINE, selective inhibitors of nuclear export; SPd, selinexor+pomalidomide+dexamethasone.

1. Stalker ME, et al. *Curr Oncol*. 2022;29(7):4464–4477. **2.** Fotiou D, et al. *Ther Adv Hematol*. 2022;13: 20406207221090089. **3.** Karyopharm Therapeutics Inc. Clinical Study Protocol. Version 2.0. Dated January 23, 2022. XPORT-MM-031. **4.** Nathwani N. *Am Soc Clin Oncol Educ Book*. 2021;41:358–375. **5.** ClinicalTrials.gov identifier: NCT05028348 https://clinicaltrials.gov/ct2/show/NCT05028348. Accessed May 8, 2023.