STOMP ARM 12: A Phase 1b/2 Study of Selinexor in Combination With Mezigdomide for Relapsed/ Refractory Multiple Myeloma (NCT02343042)

BACKGROUND

- Emerging clinical data demonstrates that certain chemotherapy (e.g., alkylating) and proteasome inhibitors (PIs) may promote T-cell exhaustion and inferior T-cell therapy outcomes.[1]
- The increasing use of 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.[2]
- 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.[2,3]

STUDY DESIGN

- Phase 1b/2 open-label, multicenter trial with dose evaluation (Phase 1b) and expansion (Phase 2) to independently evaluate the MTD, efficacy, and safety of selinexor combination therapies[4,5]

SELECT STUDY OBJECTIVES

- Arm 12: To evaluate the safety, tolerability and efficacy of selinexor in combination with mezigdomide and dexamethasone in patients with relapsed/refractory multiple myeloma (RRMM) who have relapsed on T-cell redirecting therapy or were not eligible for such treatments[4,5]

CONTACT

clinicaltrials@karyopharm.com

STOMP ARM 12 DESIGN

PRIMARY ENDPOINTS

- Ph 1b: MTD, RP2D
- Ph 2: ORR, DOR, CBR

SECONDARY ENDPOINTS

- Ph 1b & 2: Population PK and exploratory exposure-response analyses, safety and tolerability
- Ph 2: TTP, PFS and OS, safety, tolerability and incidence of AEs, QOL†

SEL PO QW on Days 1, 8 and 15, Q28D; DEX PO or IV QW on Days 1, 8, 15 and 22, Q28D; MEZ PO QD on Days 1–21, Q28D

SEL dosing will be formally escalated from 40 mg QW to 60 mg QW in combination with MEZ 0.6 mg QD. MEZ dosing may be de-escalated as per 3+3 criteria to 0.3 mg or escalated to 1.0 mg.

*The dose level that passes DLT evaluation (defined as the highest dose that has < 3 out of 6 cohort patients reporting a DLT) will be considered the MTD for the cohort.

†QOL measured by EORTC-QLQ-C30 and EORTC-QLQ-MY20 instruments

SELECT INCLUSION CRITERIA[4,5]

- Age ≥ 18 years at the time of signing informed consent
- Histologically confirmed RRMM with measurable disease
- ECOG PS 0–2
- Resolution of any clinically significant non-hematological toxicities (except peripheral neuropathy) from previous treatments to Grade ≤ 2 by C1D1
- Adequate hepatic, renal, and hematopoietic function within 28 days prior to C1D1
- Must have received at least two prior lines of therapy, including an IMiD, a PI and an anti-CD38 mAb
- Must have failed a T-cell redirecting treatment (e.g., CAR-T or bispecific antibody) or cannot receive such therapy due to either medical or logistic reasons

SELECT EXCLUSION CRITERIA[4,5]

- Smoldering MM or active plasma cell leukemia
- MM that does not express M-protein or FLC (i.e., non-secretory MM)
- Documented active systemic amyloid light chain amyloidosis
- RBC and platelet transfusions and blood growth factors within 7 days of C1D1
- Platelet transfusion or G-CSF within 7 days or pegfilgastrim within 14 days prior to the CBC
- Radiation, chemotherapy, or immunotherapy or any other anticancer therapy ≤ 2 weeks prior to C1D1, and radio-immunotherapy within 6 weeks prior to C1D1
- Patients with history of spinal cord compression with residual paraplegia (Dose Evaluation only)
- Treatment with an investigational anti-cancer therapy within 3 weeks prior to C1D1
- Prior autologous stem cell transplantation < 1 month prior to C1D1 or history of allogeneic stem cell or solid organ transplant at any time

AEs, adverse events; C1D1, cycle 1 day 1; CAR-T, chimeric antigen receptor T-cell therapy; CBC, complete blood count; CBR, clinical benefit rate; CD38, cluster of differentiation 38; DEX, dexamethasone; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FLC, free light-chain; G-CSF, granulocyte colony-stimulating factor; IMiD, immunomodulatory drug; IV, intravenous; mAb, monoclonal antibody; MEZ, mezigdomide; MM, multiple myeloma; MTD, maximum tolerated dose; ORR, objective response rate; OS, overall survival; PI, proteasome inhibitor; PK, pharmacokinetic; PO, by mouth; PFS, progression-free survival; Q28D, every 28 days; QD, once daily; QOL, quality of life; QW, once weekly; RBC, red blood cell; RP2D, recommended phase 2 dose; RRMM, relapsed/refractory multiple myeloma; SEL, selinexor; TTP, time to progression.

1. Binder AF, et al. *Front Immunol*. 2023;14:1275329. **2.** Stalker ME, et al. *Curr Oncol*. 2022;29(7):4464–77. **3.** Nathwani N. *Am Soc Clin Oncol Educ Book*. 2021;41:358–75. **4.** Karyopharm Therapeutics Inc. Clinical Study Protocol Version 12.0. KCP-330-017 (STOMP). **5.** ClinicalTrials.gov identifier: NCT02343042 https://clinicaltrials.gov/ct2/show/NCT02343042. Accessed April 2, 2024.

Scan here for more information on ClinicalTrials.gov

ALL-PIPE-03/24-00001