**BACKGROUND**

- Oprozomib (OPZ) is an orally administered proteasome inhibitor that binds selectively and irreversibly to its target, mandatory subunits of the 20S proteasome.

- In a phase 1/2 study of single-agent OPZ in patients with hematologic malignancies, OPZ has shown promising antitumor activity in patients with multiple myeloma and Waldenström macroglobulinemia.

- This multicenter, single-arm, phase 2/6 dose-escalation study is evaluating the safety and tolerability of OPZ with low-dose dexamethasone (DXM) in patients with relapsed and/or refractory multiple myeloma.

- Table 1 shows the demographics and disease characteristics of patients enrolled in the study.

**METHODS**

- The multicenter, open-label, phase 2/6 study (NC10183272) is being conducted in the United States.

- Patients with relapsed and/or refractory multiple myeloma who have received 1–5 prior lines of therapy (at least 1 regimen must have included lenalidomide and/or bortezomib) are eligible for enrollment.

- The primary objectives of the phase 2 portion of the study are to determine the maximum tolerated dose (MTD) and the recommended phase 2 dose (RP2D) of OPZ and DXM to evaluate safety and tolerability.

- Patients are receiving OPZ tablets orally on days 1, 2, 8, and 9 of a 28-day cycle (2/7 schedule) or in days 1–5 of a 28-day cycle (5/14 schedule) (Figure 1).

- The starting OPZ dose was 210 mg on both schedules.

- OPZ doses are being escalated in 30-mg increments using a standard 3+3 design.

**RESULTS**

- 12 patients were evaluated for response.

- Median number of prior regimens: 5 (range, 2–7).

- Six patients experienced grade 4 adverse events: thrombocytopenia (n=4), 2/7 schedule, neuplasia (n=1, 5/14 schedule), described platelet count (n=1, 5/14 schedule), decreased lymphocyte count (n=1, 5/14 schedule), and hypogammaglobulinemia (n=1, 5/14 schedule).

- Two grade 5 adverse events were observed: grade 5 sepsis occurred in 1 patient each in the 2/7 schedule (140 mg/d) and the 5/14 schedule (310 mg/d).

- Treatment was discontinued because of adverse events in 3 patients in the 2/7 schedule (2 patients discontinued due to gastrointestinal adverse events [nausea, vomiting, constipation], and 1 patient due to thrombocytopenia) and 5 patients in the 5/14 schedule.

- The most common adverse events experienced by patients enrolled in the study are shown in Table 2.

**REFERENCES**

1. Roccaro AM, Sacco A, Aujay M, et al. Presented at the 8th International Workshop on Multiple Myeloma: initial Results from the Dose-escalation portion of the Phase 1b/2, Multicenter, Open-Label Study.

2. Waldenström macroglobulinemia 3-6

3. Presentations at the American Society of Hematology Annual Meeting; December 6–9, 2014; San Francisco, CA

4. Neuman: Consulting, Research Funding; Amgen: Consulting, Research Funding; Millennium/Novartis: Consultancy, Research Funding; Genzyme: Research Funding; Consultant, Research Funding; Prolexys Pharmaceuticals: Research Funding; Consultant; Bristol-Myers Squibb: Research Funding, Consultancy, Support.

5. Medical writing and editorial assistance was provided by BlueMomentum, a division of Ashfield, a U.S. King-Devick Company, on behalf of Progenics Pharmaceuticals, Inc.


10. Amgen: Speaker’s Bureau, advisory board. Millenium/Novartis: Consulting, Research Funding; Bristol-Myers Squibb: Research Funding, Consultancy, Support. Onyx: Research Funding, Consultancy, Support. Pembrolizumab: Research Funding; Consultant, Research Funding.