Waldenström macroglobulinemia (WM) is a rare, incurable, B-cell lymphoma, and more tolerable and effective treatments are needed for patients who experience progression on standard treatments.  

- Inhibition of BCL2 has demonstrated antitumor activity in patients with WM, however, no BCL2 inhibitors are currently approved.
- Sonrotoclax (BGB-11417), a next-generation BCL2 inhibitor, is a more selective and pharmacologically potent inhibitor of BCL2 than venetoclax with a shorter half-life and no anticoagulation.
- Here, updated safety and efficacy data are presented for patients with relapsed/refractory (R/R) WM treated with sonrotoclax monotherapy in the ongoing BGB-11417-101 study.

**RESULTS**

- As of February 4, 2024, a total of 20 patients with R/R WM had received sonrotoclax (80, 160, 320, or 640 mg), and 14 remained on treatment (Figure 2).
- Six patients (31%) had discontinued treatment due to progressive disease (PD), ORR in four and AEs of multicellular neurological syndrome (n=2) and COVID-19 (n=2); neither AE was considered related to sonrotoclax by the investigator.

**CONCLUSIONS**

- Sonrotoclax monotherapy was well tolerated in patients with R/R WM, the MTD was not reached
- Preliminary antitumor activity was encouraging in this heavily pretreated population, with high and durable responses across all tested dose levels
- Further evaluation of sonrotoclax monotherapy in patients with R/R WM is ongoing in a pivotal study (BGB-11417-203)

**METHODS**

- BGB-11417-101 (NCT04277637) is a first-in-human, phase 1, open-label, multicenter, dose-escalation and -expansion study in patients with B-cell malignancies (Figure 1).
- Eligible patients had R/R WM (disease that relapsed after or was refractory to prior systemic therapy) and required treatment per NCCN guidelines.
- The primary objectives of the study were to assess safety/tolerability, evaluate the ramp-up and hold schedule of the MTD, and determine the BPD of sonrotoclax monotherapy in patients with B-cell malignancies, including R/R WM.
- Responses were assessed per modified Cheson 2013 criteria.
- Sonrotoclax was administered orally with a ramp-up schedule to mitigate potential risk of TILs.

**INTRODUCTION**

- Waldenström macroglobulinemia (WM) is a rare, incurable, B-cell lymphoma, and more tolerable and effective treatments are needed for patients who experience progression on standard treatments.
- Inhibition of BCL2 has demonstrated antitumor activity in patients with WM, however, no BCL2 inhibitors are currently approved.
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