**Safety and efficacy results of a phase 1 study of the novel BCL2 inhibitor sonrotoclax (sonro; BGB-11417) for relapsed/refractory (R/R) Waldenström macroglobulinemia (WM)**

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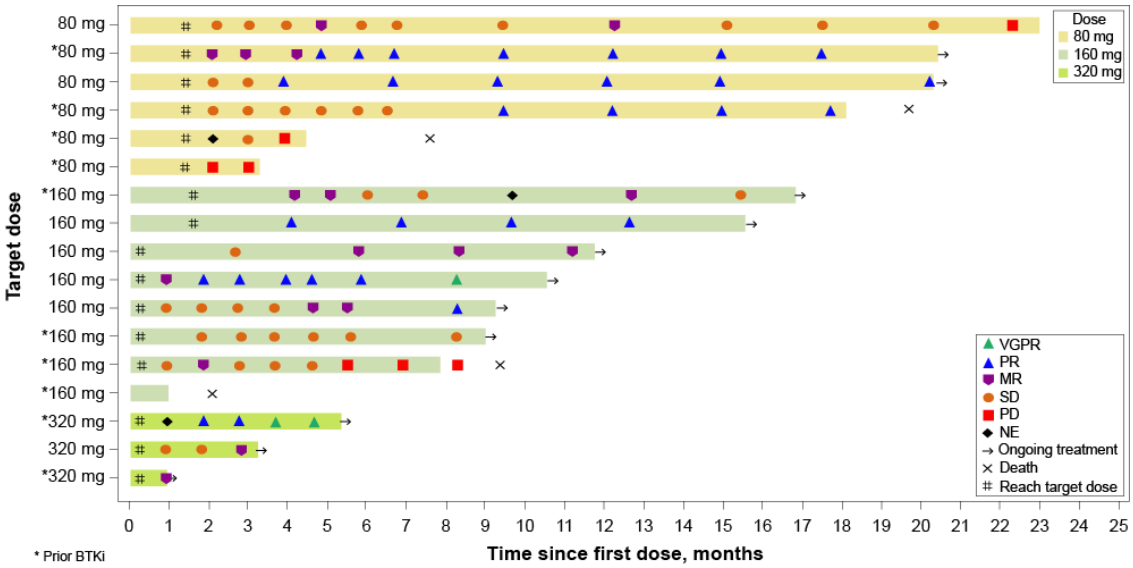
**ABSTRACT**

**Introduction:** Sonro (BGB-11417), a novel BCL2 inhibitor, is a more selective and pharmacologically potent inhibitor of BCL2 than venetoclax. Updated safety and efficacy of sonro in patients (pts) with R/R WM from the BGB-11417-101 (NCT04277637) study are presented.

**Methods:** Pts with R/R WM (≥1 prior therapy) received sonro (planned dose escalation: 80, 160, 320, or 640 mg QD) with dose ramp-up to mitigate TLS risk. The primary endpoint was safety per CTCAE v5.0. The secondary endpoint was ORR (minor response [MR] or better per modified Owens 2013 criteria). TLS was assessed per Howard 2011 criteria.

**Results:** As of Oct 31, 2023, 17 pts with R/R WM were enrolled (80 mg, n=6; 160 mg, n=8; 320 mg, n=3). Pts had a median age of 68 (range, 48-87) years and a median of 2 (range, 2-9) prior treatments (tx). Ten pts had a prior BTK inhibitor (noncovalent, n=1; covalent, n=9) and 14 had prior anti-CD20. Median follow-up was 10.6 (range, 1-24) mo. Six pts discontinued tx (progressive disease [PD], n=4; AEs, n=2 [multifocal neurological syndrome and COVID-19]), and 4 pts died on study (PD, n=2; COVID-19 pneumonia, n=1; pneumonia, n=1). TEAEs occurring in ≥20% of pts were anemia (n=6; 35%), COVID-19 (n=6; 35%), pyrexia (n=5; 29%), neutropenia (n=4; 24%), and pruritus (n=4; 24%). Anemia was the most common grade ≥3 TEAE (n=4; 24%). No DLTs or TLS occurred up to the highest dose tested (320 mg). No atrial or ventricular fibrillation occurred. No deaths or AEs leading to tx discontinuation were determined by the investigator to be tx related. In 17 response-evaluable pts, overall, major, and very good partial response (VGPR) rates were 76% (13/17), 41% (7/17), and 12% (2/17), respectively (**Figure**). In 7 pts who had a BTK inhibitor as their last tx, the ORR was 70% (MR, n=2; PR, n=1; VGPR, n=2). In the 320-mg cohort, the median follow-up was 3.3 (range, 1-5) mo and ORR was 100% (n=3), with 1 VGPR.

**Conclusions:** Sonro monotherapy was well tolerated and had encouraging preliminary antitumor activity in this heavily pretreated R/R WM population. Based on these findings, further evaluation of sonro monotherapy in pts with R/R WM is ongoing in a potentially pivotal phase 2 study.


Target dose
80 mg
*80 mg
80 mg
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160 mg
160 mg
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160 mg
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*160 mg
*320 mg
320 mg
*320 mg
Dose
80 mg
160 mg
320 mg
VGPR
PR
MR
SD
PD
NE
Ongoing treatment
Death
Reach target dose
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Time since first dose, months
* Prior BTKi