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BGB-11417-203, an Ongoing, Phase 2 Study of Sonrotoclax (BGB-11417), a Next-Generation BCL2 Inhibitor, in Patients With Waldenström Macroglobulinemia

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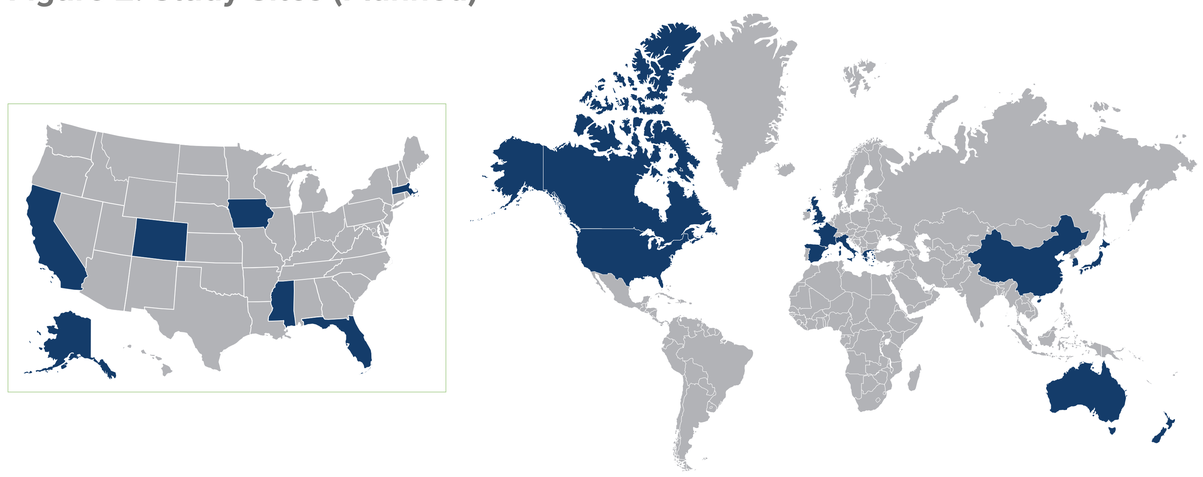
INTRODUCTION

- Waldenström macroglobulinemia (WM) is a rare, incurable, B-cell malignancy for which BTK inhibitors and anti-CD20 antibody–based therapies are preferred treatment options[1]
  - To date, no treatments have been approved for patients with WM that is refractory to both BTK inhibitors and anti-CD20 antibody–based therapy
- Venetoclax, the first-generation BCL2 inhibitor, has demonstrated clinical activity in patients with relapsed/refractory (R/R) WM but is not currently approved for WM[2]
- Sonrotoclax (BGB-11417), a next-generation BCL2 inhibitor, is more selective and a more pharmacologically potent inhibitor of BCL2 than venetoclax[3]
- In the ongoing phase 1 BGB-11417-101 (NCT04277637) study, sonrotoclax monotherapy has been well tolerated at doses up to 640 mg and has shown preliminary antitumor activity in patients with R/R WM[4]
- Based on these encouraging phase 1 data, a phase 2 study of sonrotoclax in WM was designed and is currently enrolling patients

STUDY STATUS

- Enrollment for BGB-11417-203 began in September 2023, and the study is currently recruiting
- Approximately 73 study sites in Australia, China, Europe (Italy, Spain, France, Greece), the UK, Canada, and the US are planned (**Figure 2**)

Figure 2. Study Sites (Planned)



METHODS

- BGB-11417-203 (NCT05952037) is an open-label, multicenter, international, phase 2 study to evaluate the efficacy and safety of sonrotoclax in patients with R/R WM (**Figure 1**)
- Approximately 85 patients will be enrolled to receive 320 mg sonrotoclax once daily

Figure 1. Study Design

Key Eligibility Criteria

- Age ≥18 years
- Histologically confirmed WM
- R/R disease or intolerant of most recent therapy
- Adequate bone marrow and organ function
- ECOG PS of 0-2
- No prior BCL2 inhibitor
- No CNS involvement by WM
- No transformation to aggressive lymphoma

Study Design

Cohort 1
R/R to BTKi and anti-CD20–based therapy combined with chemotherapy or PI
(n≈65)

Cohort 2
R/R to anti-CD20–based therapy combined with chemotherapy or PI and intolerant of BTKi
(n≈10)

Cohort 3
R/R to BTKi and unsuitable for chemoimmunotherapy
(n≈10)

→ **Sonrotoclax 320 mg QD[a]**
Until PD, unacceptable toxicity, withdrawal of consent, loss to follow-up, or study termination

Endpoints

Primary
- MRR[b] (IRC) for cohort 1

Secondary
- MRR[b] (INV) for cohort 1
- MRR[b] (IRC and INV) for cohort 2 and cohort 3
- DOR, CR and VGPR rate, ORR, PFS, and time to major response (IRC and INV)
- OS
- Safety and tolerability
- HRQOL

[a] To monitor and mitigate TLS risk, TLS prophylaxis and laboratory monitoring are used, and clinical visits are required on ramp-up days. [b] Proportion of patients achieving PR or better per IWWM-11 response criteria.
BTKi, BTK inhibitor; CNS, central nervous system; DOR, duration of response; HRQOL, health-related quality of life; INV, assessed by investigator; IRC, assessed by independent review committee; MRR, major response rate; PI, proteasome inhibitor; R/R, relapsed/refractory; TLS, tumor lysis syndrome; VGPR, very good partial response; WM, Waldenström macroglobulinemia.

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DISCLOSURES

H-PL: Consulting fees: BeiGene; Stock or other ownership: CSL Behring; Honoraria: Takeda. **SO:** Consulting fees: AbbVie, AstraZeneca, BeiGene, Ipsen, Gilead, Merck, Janssen, Takeda; Research funding: AbbVie, AstraZeneca, BeiGene, Ipsen, Gilead, Janssen, Merck, Novartis, Roche, Takeda; Honoraria: AbbVie, AstraZeneca, BeiGene, Ipsen, Gilead, Janssen, Merck, Sanofi. **PM:** Consulting fees: AbbVie, AstraZeneca, Astellas, BeiGene, Janssen, Jazz, Menarini, Otsuka, Pfizer, Gilead, MSD, Servier, Novartis; Speakers' Bureau: AbbVie. **CD, AL, JZ, HG:** Employment and may hold stock: BeiGene. **SPT:** Research funding and/or honoraria: AbbVie/Pharmacyclics, BeiGene, BMS, Eli Lilly, Janssen, Ono, Parexel, X4. **JH, DK, PL:** Nothing to disclose.

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