MAHOGANY: A Phase 3 Trial of Zanubrutinib Plus Anti-CD20 Antibodies vs Lenalidomide Plus Rituximab in Patients With Relapsed or Refractory Follicular or Marginal Zone Lymphoma

Poster P1083

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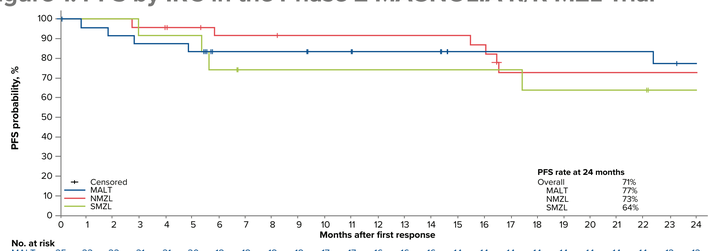
BACKGROUND

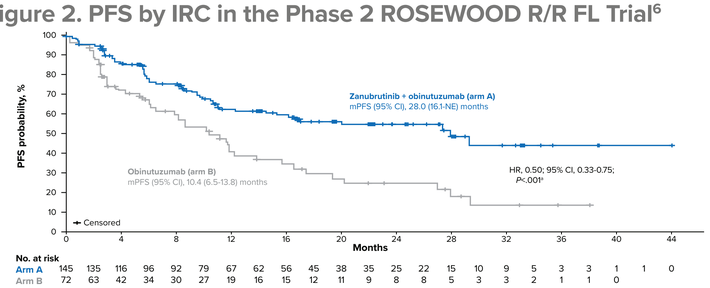
- Relapsed/refractory (R/R) disease is common in patients with follicular lymphoma (FL) and marginal zone lymphoma (MZL)
- Treatment of FL and MZL largely relies on immunochemotherapy, and additional novel therapies are greatly needed
- Zanubrutinib is a next-generation, potent, specific Bruton tyrosine kinase (BTK) inhibitor approved in the EU and US for the treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), Waldenström macroglobulinemia (WM), and MZL[1,2] and in the US for previously treated mantle cell lymphoma[1]
  - Zanubrutinib demonstrated clinically meaningful benefit in patients with WM[3] and superior efficacy over ibrutinib in patients with R/R CLL/SLL[4]
  - In both WM[3] and CLL/SLL,[4] zanubrutinib was better tolerated than ibrutinib
- Previous findings have suggested that zanubrutinib may lead to high response rates and durable responses in R/R MZL and FL[5,6]
  - In the phase 2 MAGNOLIA study in R/R MZL (NCT03846427), zanubrutinib led to an overall response rate (ORR) of 68% (complete response [CR] rate, 26%) as assessed by an independent review committee (IRC); the progression-free survival (PFS) rate at 24 months was 71% (**Figure 1**)[5]
  - In the randomized phase 2 ROSEWOOD study in R/R FL (NCT03332017), zanubrutinib + obinutuzumab led to an IRC-assessed ORR of 69% (CR rate, 39%); the PFS rate at 24 months was 55% (**Figure 2**)[6]

Figure 1. PFS by IRC in the Phase 2 MAGNOLIA R/R MZL Trial[5]



MALT, mucosa-associated lymphoid tissue; NMZL, nodal marginal zone lymphoma; PFS, progression-free survival; SMZL, splenic marginal zone lymphoma.

Figure 2. PFS by IRC in the Phase 2 ROSEWOOD R/R FL Trial[6]

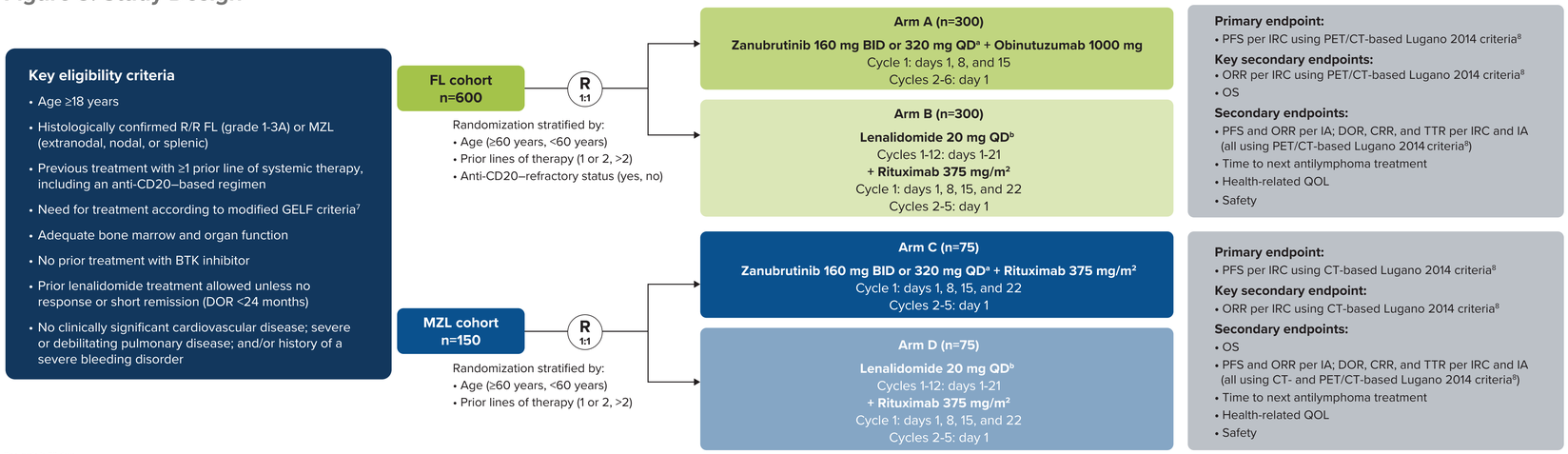


Median follow-up, 20.2 months.
HR, hazard ratio; IRC, independent review committee; mPFS, median progression-free survival; NE, not estimable.
[a] Descriptive 2-sided *P* value.

METHODS

- MAHOGANY (BGB-3111-308; NCT05100862) is a randomized (1:1), open-label, multicenter phase 3 trial evaluating zanubrutinib combined with the anti-CD20 antibody obinutuzumab in patients with R/R FL or rituximab in patients with R/R MZL vs lenalidomide combined with rituximab (**Figure 3**)

Figure 3. Study Design

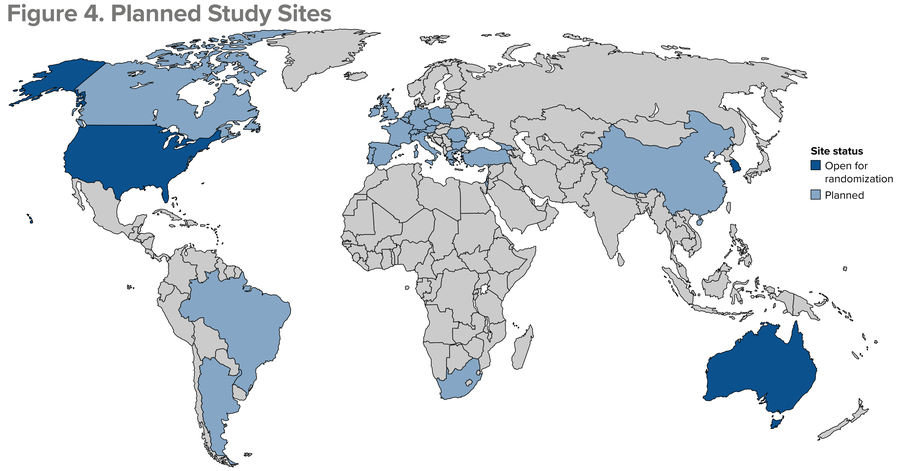


One cycle is 28 days.
BID, twice daily; CRR, complete response rate; CT, computed tomography; DOR, duration of response; FL, follicular lymphoma; IA, investigator assessment; IRC, independent review committee; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; QD, once daily; QOL, quality of life; R, randomized; R/R, relapsed/refractory; TTR, time to response.
[a] After completion of combination treatment, patients will receive zanubrutinib monotherapy until confirmed disease progression, unacceptable toxicity, withdrawal of consent, or study termination, whichever comes first. [b] Patients with creatinine clearance ≥30 mL/min but <60 mL/min will receive 10 mg QD. If the patient remains free of lenalidomide-related grade 3 or 4 toxicities for ≥2 cycles, the dose may be increased to 15 mg QD on days 1-21 of a 28-day cycle at the discretion of the treating physician from cycles 3-12.

Study status

- Enrollment for MAHOGANY began in March 2022, and the study is currently recruiting
- Approximately 300 study sites in 25 countries are planned (**Figure 4**), with an estimated enrollment of 750 patients

Figure 4. Planned Study Sites



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DISCLOSURES

CB received research funding from Roche/Genentech, Janssen, Celltrion, MSD, Pfizer, and Amgen; honoraria from Roche/Genentech, Janssen, BeiGene, Novartis, Pfizer, Incyte, AbbVie, Gilead Sciences, Celltrion, MorphoSys, Regeneron, Sobi, and Lilly; participated in speakers bureaus for Roche/Genentech, Janssen, BeiGene, Novartis, Pfizer, Incyte, AbbVie, Gilead Sciences, Celltrion, MorphoSys, Regeneron, Sobi, and Lilly; and had a consulting or advisory role with Gilead Sciences, Janssen, Roche, Pfizer, BeiGene, Celltrion, AbbVie, Incyte, Regeneron, MorphoSys, Novartis, Sobi, and Lilly. **LJN** received research funding from Janssen Biotech, Genentech/Roche, Epizyme, IGM Biosciences, Novartis, Caribou Biosciences, Gilead Sciences, Allogene Therapeutics, Bristol Myers Squibb/Celgene, and Takeda; honoraria from Gilead/Kite, Novartis, Janssen Oncology, TG Therapeutics, Bristol Myers Squibb, ADC Therapeutics, MorphoSys, Epizyme, Genmab, Takeda, Genentech/Roche, Caribou Biosciences, Medscape, Neil Love, and PeerView; and travel support from Roche/Genentech; and had a consulting or advisory role with LRF Scientific, SIRPant, Interius Bio, ADC Therapeutics, AbbVie, Genentech, MEI, Denovo, Takeda, Caribou Biosciences, Incyte, and Janssen. **YS** has nothing to disclose. **LHS** had a consulting or advisory role with AbbVie, Seagen, Janssen, Amgen, Roche/Genentech, Gilead Sciences, Kite, Merck, Teva, TG Therapeutics, AstraZeneca, Incyte, Sandoz-Novartis, Genmab, Celgene/Bristol Myers Squibb, and BeiGene; honoraria from Amgen, AbbVie, Gilead Sciences, Janssen-Ortho, Kite, Merck, Roche/Genentech, Seagen, Teva, AstraZeneca, Incyte, Sandoz-Novartis, Genmab, Celgene/Bristol Myers Squibb, and BeiGene; and research funding from Roche/Genentech and Teva paid to their institution. **CS** received honoraria from AbbVie; research funding from Roche; and travel support from Roche and Incyte; provided expert testimony on behalf of Incyte; and had a consulting or advisory role with Janssen, GSK, Incyte, and Bristol Myers Squibb. **PLZ** received honoraria from BeiGene, Bristol Myers Squibb, Gilead, Incyte, Kyowa Kirin, MSD, Novartis, Roche, and Takeda; and participated in speakers bureaus for BeiGene, Bristol Myers Squibb, Gilead, Incyte, Kyowa Kirin, MSD, Novartis, Roche, and Takeda. **AS** received research funding from AbbVie and Roche; participated in speakers bureaus for BeiGene and Roche; and received travel funds from Kite and Janssen. **JZ** and **WZ** are employees of BeiGene and own stock in BeiGene. **PF** is an employee of BeiGene and owns stock in BeiGene and Bristol Myers Squibb. **RD** has been an employee of Celgene/Bristol Myers Squibb, is an employee of BeiGene, and owns stock in Celgene/Bristol Myers Squibb and BeiGene. **JT** has received research funding from BeiGene, Janssen, Pharmacyclics, Roche, Celgene/Bristol Myers Squibb, and Selectar and has served on an advisory board for BeiGene.

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