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

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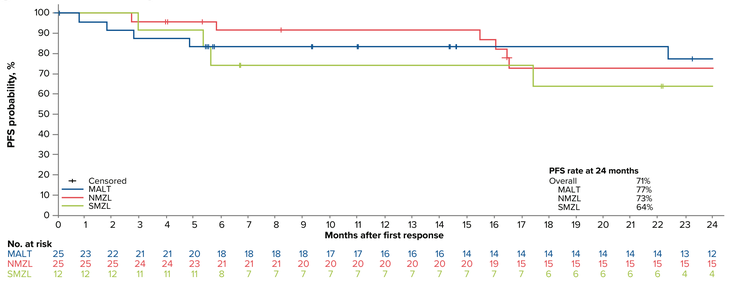
BACKGROUND

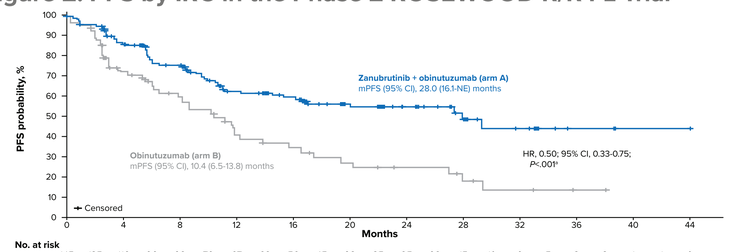
- Relapsed/refractory (R/R) disease is common in patients with follicular lymphoma (FL) and marginal zone lymphoma (MZL)
- Treatment of FL and MZL largely relies on immunochemotherapy, and additional novel therapies are greatly needed
- Zanubrutinib is a next-generation, potent, specific Bruton tyrosine 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]

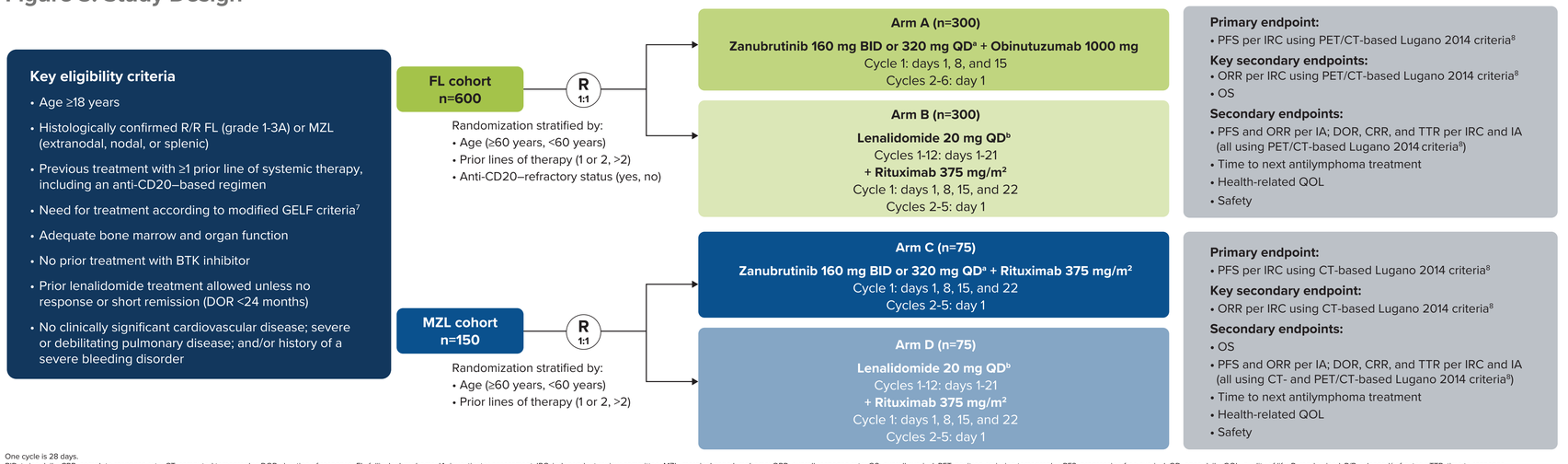


Median follow-up, 20.2 months.
HR, hazard ratio; IRC, independent review committee; mPFS, median progression-free survival; NE, not estimable.
[a] Descriptive 2-sided *P* value.

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

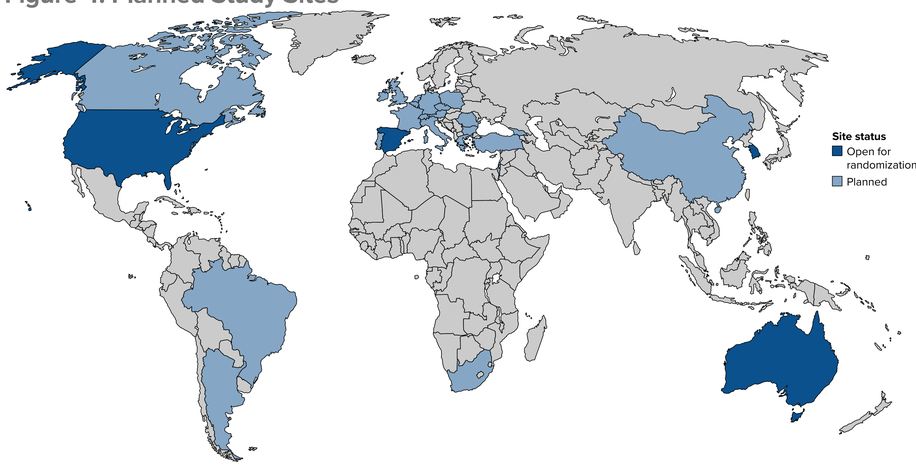


One cycle is 28 days.
BID, twice daily; CRR, complete response rate; CT, computed tomography; DOR, duration of response; FL, follicular lymphoma; IA, investigator assessment; IRC, independent review committee; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PET, positron 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

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