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

Abstract TPS7590

MAHOGANY
Phase 3 Relapsed/Refractory FL/MZL

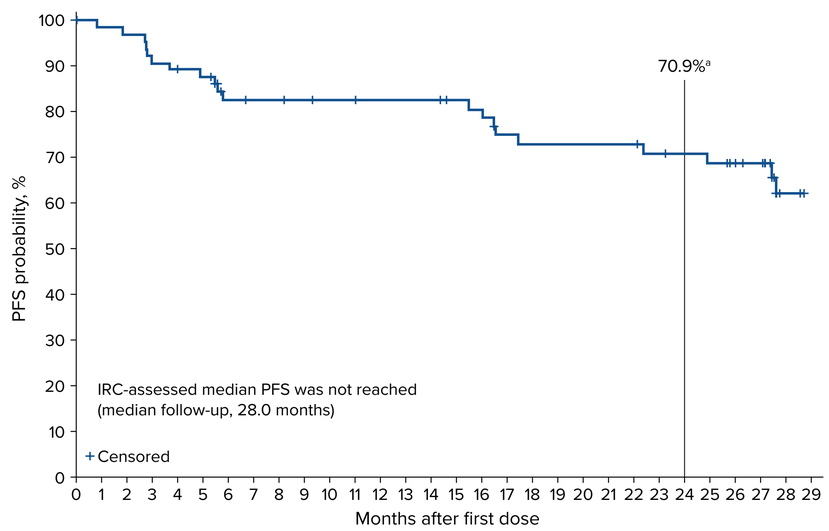
Loretta J. Nastoupil,[1] Yuqin Song,[2] Laurie H. Sehn,[3] Clémentine Sarkozy,[4] Pier Luigi Zinzani,[5] Antonio Salar,[6] Jun Zhang,[7] Sha Huang,[7] Julie Wang,[7] Richard Delarue,[7] Judith Trotman[8]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Peking University Cancer Hospital and Institute, Beijing, China; [3]BC Cancer and the University of British Columbia, Vancouver, BC, Canada; [4]Institut Curie, Saint Cloud, Paris, France; [5]University of Bologna, Bologna, Italy; [6]Hospital del Mar, Barcelona, Spain; [7]BeiGene (Shanghai) Co, Ltd, Shanghai, China, and BeiGene USA, Inc, San Mateo, CA, USA; [8]Concord Repatriation General Hospital, University of Sydney, Concord, NSW, Australia

BACKGROUND

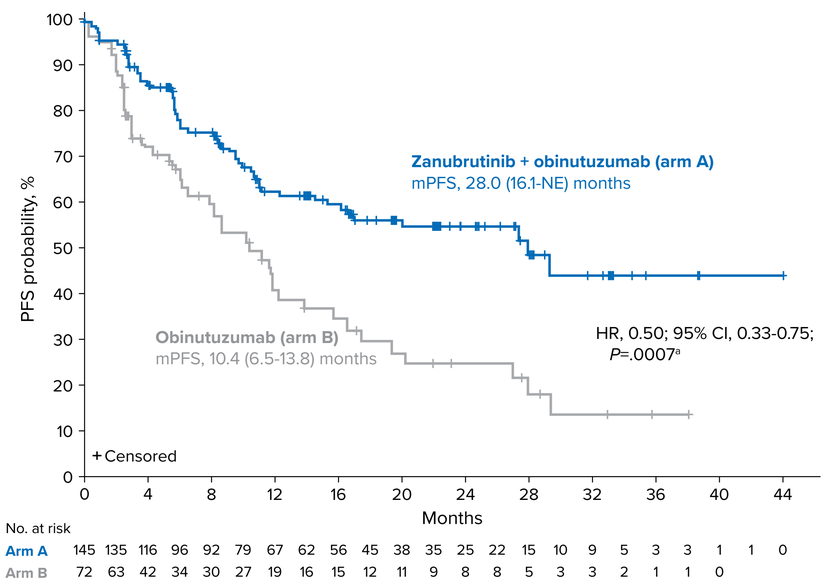
- Relapsed/refractory (R/R) disease is common in patients with follicular lymphoma (FL) and marginal zone lymphoma (MZL)
- Zanubrutinib is a second-generation, potent, specific Bruton tyrosine kinase (BTK) inhibitor approved in the US for the treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), Waldenström macroglobulinemia (WM), MZL, and mantle cell lymphoma[1]
  - In patients with CLL/SLL[2] and WM,[3] zanubrutinib was shown to be more effective and better tolerated than ibrutinib, a first-generation BTK inhibitor
- Previous findings have suggested that zanubrutinib may lead to improved responses in R/R MZL and FL
  - In the phase 2 MAGNOLIA study in R/R MZL (NCT03846427), zanubrutinib led to an overall response rate (ORR) of 68.2% (complete response [CR] rate, 25.8%) as assessed by an independent review committee (IRC); median progression-free survival (PFS) was not reached (**Figure 1**)[4]
  - In the randomized phase 2 ROSEWOOD study in R/R FL (NCT03332017), zanubrutinib + obinutuzumab led to an IRC-assessed ORR of 69.0% (CR rate, 39.3%) and prolonged PFS (**Figure 2**)[5]

Figure 1. PFS by IRC in the Phase 2 MAGNOLIA R/R MZL Trial[4]



Adapted from Opat S, et al. *Blood.* 2022;140(suppl 1). Abstract 623. Data cutoff: May 4, 2022.
IRC, independent review committee.
[a] By PET and/or CT.

Figure 2. PFS by IRC in the Phase 2 ROSEWOOD R/R FL Trial[5]

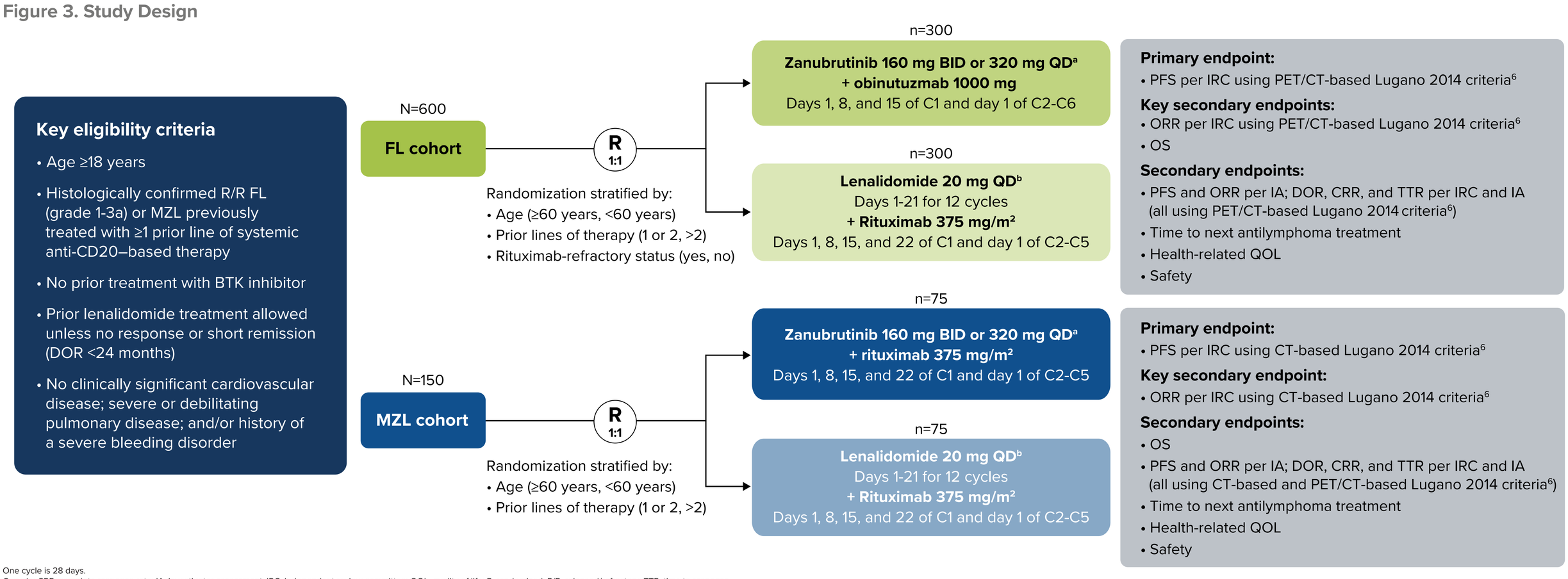


IRC, independent review committee.
[a] Descriptive 2-sided *P* value.

METHODS

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

Figure 3. Study Design

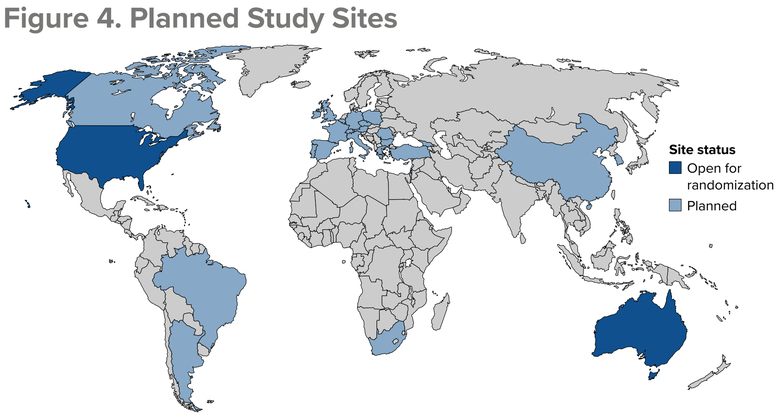


One cycle is 28 days.
C, cycle; CRR, complete response rate; IA, investigator assessment; IRC, independent review committee; QOL, quality of life; R, randomized; R/R, relapsed/refractory; TTR, time to response.
[a] After completion of combination treatment, patients will receive zanubrutinib monotherapy 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 to 21 of a 28-day cycle at the discretion of the treating physician from C3 to C12.

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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CORRESPONDENCE

Loretta J. Nastoupil, MD
The University of Texas MD Anderson Cancer Center
Houston, TX
LNastoupil@mdanderson.org