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).
- 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), and mantle cell lymphoma.
- In patients with CLL/SLL and WM, zanubrutinib was shown to be more effective and better tolerated thanibrutinib, 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).
- 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).

METHODS
- MAHOGANY (BBG-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).

Key eligibility criteria
- Age ≥18 years
- Histologically confirmed R/R FL (grade 1-3a or MZL, previously treated with ≥1 prior line of systemic anti-CD20–based therapy)
- No prior treatment with BTK inhibitor
- No prior lenalidomide treatment allowed unless no response or short remission (DOR < 24 months)
- No clinically significant cardiovascular disease, severe or debilitating pulmonary disease, and/or history of a severe bleeding disorder

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

REFERENCES

DISCLOSURES
- Author disclosures are available in the online version of the article.

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- Written informed consent was provided by all participants.

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