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: Inhibition of Bruton tyrosine kinase (BTK) has emerged as a strategy for treatment of patients (pts) with B-cell malignancies including indolent non-Hodgkin lymphomas. Zanubrutinib is a second-generation, potent, and specific BTK inhibitor and has shown to be more effective and better tolerated than first-generation BTK inhibitors in several diseases including chronic lymphocytic leukemia/small lymphocytic lymphoma and Waldenström macroglobulinemia. Zanubrutinib is approved in >15 countries, including the United States and European Union, for pts with relapsed or refractory (R/R) marginal zone lymphoma (MZL) who received ≥1 anti-CD20–based regimen, based on the single-arm MAGNOLIA trial (Opat et al. Clin Cancer Res 2021). In R/R follicular lymphoma (FL), ROSEWOOD, a phase 2 randomized study of zanubrutinib plus obinutuzumab (ZO) vs obinutuzumab, met its primary endpoint of increased overall response rate (ORR) at primary analysis (Zinzani et al. J Clin Oncol 2022). In this trial, ZO in pts with R/R FL demonstrated deep and durable responses with a favorable safety profile.

Methods: MAHOGANY (BGB-3111-308, NCT05100862) is a phase 3 randomized, open-label trial that compares efficacy and safety of a combination of zanubrutinib plus anti-CD20 monoclonal antibody vs lenalidomide plus rituximab in 2 independent cohorts, for pts with either R/R FL or MZL. Key eligibility criteria include histologically confirmed FL (grades 1-3A) or MZL, previously treated with ≥1 anti-CD20–based regimen, based on the single-arm MAGNOLIA trial (Opat et al. Clin Cancer Res 2021). In R/R follicular lymphoma (FL), ROSEWOOD, a phase 2 randomized study of zanubrutinib plus obinutuzumab (ZO) vs obinutuzumab, met its primary endpoint of increased overall response rate (ORR) at primary analysis (Zinzani et al. J Clin Oncol 2022). In this trial, ZO in pts with R/R FL demonstrated deep and durable responses with a favorable safety profile.
according to investigator, until progression or unacceptable toxicity. Obinutuzumab or rituximab are given for up to 8 infusions. Lenalidomide is given according to approved label for up to 12 cycles. Recruitment is ongoing.