BGB-11417-302, a phase 3, randomized, double-blind study of sonrotoclax (BGB-11417) + zanubrutinib vs placebo + zanubrutinib in relapsed/refractory mantle cell lymphoma

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ABSTRACT

Introduction: Mantle cell lymphoma (MCL) is an uncommon subtype of B-cell non-Hodgkin lymphoma that is typically aggressive. Despite treatment with approved therapies, most patients with MCL experience relapsed or refractory disease and require novel therapy options. Inhibition of B-cell lymphoma 2 (BCL2) and Bruton tyrosine kinase (BTK) with venetoclax + ibrutinib, respectively, has demonstrated efficacy in patients with relapsed or refractory MCL; however, use of this regimen can be limited by toxicity and development of treatment resistance. Sonrotoclax (BGB-11417), a next-generation BCL2 inhibitor, is a more selective and pharmacologically potent inhibitor of BCL2 than venetoclax. Zanubrutinib, a next-generation covalent BTK inhibitor, is approved as monotherapy for relapsed or refractory MCL in the US and China. In an ongoing phase 1 trial (NCT04277637), combination treatment with sonrotoclax + zanubrutinib has been generally well tolerated and has shown anti-lymphoma activity in patients with relapsed or refractory MCL. Based on these encouraging results, additional studies to evaluate sonrotoclax + zanubrutinib combination therapy in patients with relapsed or refractory MCL have been designed. Here, an ongoing phase 3 study that will compare the efficacy and safety of sonrotoclax + zanubrutinib vs sonrotoclax-matched placebo + zanubrutinib in adult patients with previously treated, BTK inhibitor–naive/intolerant, relapsed or refractory MCL is described.

Methods: BGB-11417-302 (NCT06742996) is a global, randomized, double-blind, phase 3 clinical study performed across 145 sites in 16 countries. Eligible patients are ≥18 years of age with a confirmed diagnosis of MCL who have received 1–5 prior lines of therapy and have relapsed or refractory disease after the last line of therapy. Patients who have had prior treatment with a BCL2 or BTK inhibitor are ineligible, except for those with intolerance to a BTK inhibitor other than zanubrutinib. Approximately 300 patients will be enrolled and randomized 1:1 to receive orally administered sonrotoclax for a fixed duration plus zanubrutinib until progression/intolerance or sonrotoclax-matched placebo for a fixed duration plus zanubrutinib until progression/intolerance. No crossover will be allowed between arms. The primary endpoint is progression-free survival (PFS), as determined by blinded independent review committee per Lugano classification (Cheson et al. J Clin Oncol. 2014). Secondary endpoints include overall survival, PFS (assessed by investigator), overall response rate, complete response rate, duration of response, and safety/tolerability. Recruitment is ongoing.