TPS8613^ General Poster Session (Board #57B), Sun, 8:00 AM-11:45 AM

A phase III study of ibrutinib in combination with bendamustine and rituximab (BR) in elderly patients with newly diagnosed mantle cell lymphoma (MCL).

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Background: MCL is a distinct subtype of B-cell non-Hodgkin lymphoma (NHL) accounting for approximately 6% of NHL diagnoses. Current immunochemotherapy followed by rituximab maintenance results in a prolonged duration of remission, but a constant relapse pattern is still observed. Ibrutinib, an oral Bruton's tyrosine kinase(BTK) inhibitor, demonstrated promising single-agent activity in 115 patients with relapsed or refractory MCL who were enrolled in the phase II study PCYC-1104. The overall response rate (ORR) was 68%, with 46% of patients achieving partial response (PR) and 22% achieving complete remission (CR) (Wang ASH 2012). Blum et al (ASH 2012) demonstrated that ibrutinib can be safely combined with BR in a phase I combination study in relapsed or refractory NHL and that it enhanced BR's clinical activity with an ORR in 5 evaluable MCL patients of 100% (80% CR, 20% PR). These data suggest that combining ibrutinib with BR will improve the outcome of these patients. **Methods:** The SHINE study, PCI-32765MCL3002, is a phase III double-blind study of ibrutinib in combination with BR versus BR for the treatment of patients with newly diagnosed MCL. The study aims to enroll 520 patients (approximately 260 patients per arm). All patients will receive BR therapy for 6 cycles; those patients achieving a CR or PR will receive R maintenance for 2 years. In addition to BR and R, all patients will receive an oral daily dose of 560 mg ibrutinib or placebo concomitant with the chemotherapy and ongoing as a single agent until disease progression or unacceptable toxicity. The primary objective is to evaluate if the addition of ibrutinib to BR will result in prolongation of progression-free survival, with secondary objectives of ORR (CR+PR), CR rate, duration of response, safety, and overall survival. The study will enroll patients aged 65 years or older who are not suitable for high-dose chemotherapy. Key exclusion criteria include diagnosis or treatment for malignancy other than MCL, requirement for treatment with warfarin or equivalent vitamin K antagonists, and treatment with strong CYP3A4/5 inhibitors. Approximately 200 sites globally will enroll patients. Enrollment began in Q1 of 2013. Clinical trial information: NCT01776840.