TPS7133 General Poster Session (Board #46E), Sun, 8:00 AM-11:45 AM

A phase III, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of idelalisib (GS-1101) in combination with bendamustine and rituximab for previously treated chronic lymphocytic leukemia (CLL).

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Background: PI3K-delta is critical for the activation, proliferation and survival of B cells and plays a role in homing and retention of B cells in lymphoid tissues. PI3Kδ signaling is hyperactive in many B-cell malignancies. Idelalisib is a first-in-class, selective, oral inhibitor of PI3Kδ that reduces proliferation, enhances apoptosis, and alters trafficking of malignant B cells in lymphoid tissues (Lannutti, 2011). Phase 1 trials demonstrated that idelalisib is highly active in heavily pretreated pts with CLL as a single agent or in combination with rituximab (R), bendamustine (B), or BR: pts experienced reductions in disease-associated chemokines, profound and rapid reductions in lymphadenopathy, and durable clinical benefit with an acceptable safety profile (Coutre et al, 2012; Sharman et al, 2011). **Methods:** Study will enroll 390 pts with previously treated CLL who have measurable lymphadenopathy, have received prior therapy containing a purine analog or B and an anti-CD20 monoclonal antibody, are not refractory to B, have experienced CLL progression within 36 months from the completion of the last prior therapy, and are currently sufficiently fit to receive cytotoxic therapy. Pts are randomized in a 1:1 ratio to Arm A or B. On Arm A, subjects receive idelalisib continuously at 150 mg BID + R at 375 mg/m^2 (1st dose) and then 500 mg/m^2 every 4 weeks for 6 cycles + B at 70 mg/m^2 on Days 1 and 2 of each 4-week cycle for 6 cycles. On Arm B, subjects receive placebo instead of idelalisib. Stratification factors address IGHV mutational status, del(17p)/p53 mutation status, and refractory vs relapsed disease. The primary endpoint is PFS and key secondary endpoints include ORR, lymph node response rate, CR rate, and OS. This is an event-driven trial and primary endpoint evaluation will be based on independent central review. For the primary efficacy analysis, the difference in PFS between the treatment arms will be assessed in the ITT analysis set. The study was initiated in June 2012 and a data monitoring committee has begun regular review of data. Clinical trial information: NCT01569295.