TPS8618 General Poster Session (Board #58B), 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 indolent non-Hodgkin lymphomas (iNHL).

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Background: PI3K-delta is critical for activation, proliferation and survival of B cells and plays a role in homing and retention 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 inhibits homing and retention of malignant B cells in lymphoid tissues (Lannutti et al, 2011). Phase I trials demonstrated that idelalisib is highly active in pts with heavily pretreated iNHL: pts experienced reductions in disease-associated chemokines, profound and rapid reductions in lymphadenopathy, and durable clinical benefit with an acceptable safety profile (de Vos et al, 2011). **Methods:** 450 pts with previously treated iNHL, who have measurable lymphadenopathy, require therapy for iNHL, have received prior anti-CD20-antibody-containing therapy and chemotherapy, and who have iNHL that is not refractory to bendamustine (B) are randomized in a 2:1 ratio into Arm A or B. In Arm A, pts receive idelalisib at 150 mg BID continuously + rituximab (R) at 375 mg/m^2 every 28 days for 6 cycles + B at 90 mg/m^2 on days 1 and 2 of each 28-d cycle. In Arm B, pts receive placebo BID instead of idelalisib. Stratification factors include tumor type (follicular lymphoma vs others), tumor burden (high vs low), and time since completion of last prior therapy for iNHL ($<$18 months vs $\geq$18 months). The primary endpoint is PFS, and key secondary endpoints include CR rate, ORR, lymph node response 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 using Kaplan-Meier methods and the stratified log-rank test. The study opened for enrollment in Dec 2012 (NCT01732926). Clinical trial information: NCT01732926.