7017 Poster Discussion Session (Board #9), Sat, 8:00 AM-12:00 PM and 12:00 PM-1:00 PM

Update on a phase I study of the selective PI3Kδ inhibitor idelalisib (GS-1101) in combination with rituximab and/or bendamustine in patients with relapsed or refractory CLL.

Jacqueline Claudia Barrientos, Richard R. Furman, John Leonard, Ian Flinn, Kanti Roop Rai, Sven De Vos, Marshall T. Schreeder, Nina D. Wagner-Johnston, Jeff Porter Sharman, Thomas E. Boyd, Nathan Hale Fowler, Leanne Holes, David Michael Johnson, Daniel Li, Roger D. Dansey, Thomas Michael Jahn, Steven E. Coutre; Hofstra North Shore-LIJ School of Medicine, Hyde Park, NY; Weill Cornell Medical College, New York, NY; Sarah Cannon Research Institute, Nashville, TN; University of California, Los Angeles Medical Center, Los Angeles, CA; Clearview Cancer Institute, Huntsville, AL; Washington University School of Medicine in St. Louis, St. Louis, MO; Willamette Valley Cancer Institute/US Oncology Research, Springfield, OR; Yakima Valley Memorial Hospital/North Star Lodge Cancer Center, Yakima, WA; The University of Texas MD Anderson Cancer Center, Houston, TX; Gilead Sciences, Inc., Seattle, WA; Stanford Cancer Institute, Stanford, CA

Background: PI3K-delta signaling is critical for proliferation, survival, homing and tissue retention of malignant B cells. Idelalisib is a first-in-class, selective, oral inhibitor of PI3Kδ that has shown considerable monotherapy activity in pts with heavily pretreated CLL. **Methods:** This phase I study evaluated idelalisib continuously given at 150 mg BID in combination with rituximab (R, 375 mg/m^2 every wk x 8), bendamustine (B, 70 or 90 mg/m^2 x 2, every 4 wks x 6) or BR (every 4 wks x 6) for relapsed/refractory CLL. Pts still on treatment after 48 weeks were eligible to continue idelalisib on an extension study. Clinical response was evaluated according to published criteria (Hallek 2008; Cheson 2012). **Results:** 52 pts (23F/29M) with a median (range) age of 64 (41-87) years were enrolled. Adverse disease characteristics included bulky lymphadenopathy (62%), refractory disease (50%), multiple prior therapies (median 3, range: 1-14) with 96% receiving prior R and 44% receiving prior B. As of 14 Jan 2013, the median (range) treatment duration was 18 (1-33) months. 31/52 (60%) pts enrolled into the extension study; of those, 24/52 (46%) pts are continuing idelalisib treatment on the extension study. The ORR was 81%, with 1 CR, and a median (range) time to response of 1.9 (1.5-8.3) months. The 2-year PFS and OS were 62% and 85%, respectively. At 2 years follow up, 71% of responses were still enduring. There was no difference in outcomes for pts with <3 prior treatments (n=21) vs ≥ 3 prior treatments (n=31). The most common TEAEs (any Grade/$\geq$Gr 3, independent of causality) included pyrexia (44%/6%), diarrhea (40%/14%), cough (31%/2%), fatigue (29%/2%), nausea (29%/0%). Pneumonia (any Gr/$\geq$Gr 3) occurred in 15%/12% and rash was seen in 15%/0%. 10% of patients experienced $\geq$Gr 3 ALT/AST elevation based on laboratory values. **Conclusions:** A lack of overlapping toxicities allowed idelalisib to be co-administered with R, B, or BR, and all 3 combination regimens were highly active, resulting in durable tumor control in pts with heavily pretreated relapsed/refractory CLL. Phase III trials evaluating the efficacy of idelalisib in combination with R or BR are ongoing. Clinical trial information: NCT01088048.