Updated clinical results show experimental agent ibrutinib as highly active in CLL patients

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Updated results from a Phase Ib/II clinical trial indicates that a novel therapeutic agent for chronic lymphocytic leukemia (CLL) is highly active and well tolerated in patients who have relapsed and are resistant to other therapy.

The agent, ibrutinib (PCI-32765), is the first drug designed to target Bruton's tyrosine kinase (BTK), a protein essential for CLL-cell survival and proliferation. CLL is the most common form of leukemia, with about 15,000 new cases annually in the U.S. About 4,400 Americans die of the disease each year.

Study co-leader Dr. John C. Byrd, director of the division of hematology at Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) presented these findings today (12/8) at the 54th Annual Meeting of the American Society of Hematology (ASH) Annual Meeting in Atlanta, GA.

The study found that response to therapy was high across cohorts, with 71 percent of previously untreated older patients experiencing a complete or partial response at either treatment dose (420mg and 840mg). The same response was observed in 67 percent of the relapsed patients and half (50%) of the high-risk patient cohort. After 22 months of follow-up, the disease had not progressed in 96 percent of previously

untreated patients and 76 percent of relapsed and high-risk patients.

"These findings are truly exciting because they demonstrate ibrutinib's potential as a highly active, well-tolerated first-line therapy for CLL that produces a high rate of durable remissions – the remissions last months on end," Byrd says. "The drug is effective in part because patients are willing to stay on treatment since the side effects are very tolerable," he states.

Only non-severe side effects, including diarrhea, fatigue, chest infection, rash, nausea, joint pain and infrequent and transient low blood counts were observed. Investigators found no evidence of cumulative toxicity or long-term safety concerns with a median follow-up of 16 months for treated patients.

Study Methodology and Results

116 CLL patients were enrolled in the study in a series of treatment cohorts, which included patients who were never treated (treatment-naïve); those who had received two or more prior therapies (relapsed/refractory); those who had relapsed within two years of treatment (high-risk); and those over age 65. Two oral dosing regimens (420 mg or 840 mg) of ibrutinib were used daily. The primary goal of the study was to determine the safety of the low and high doses. Secondary objectives included efficacy, measures of the intensity of the drug's effect in the body and the long-term safety of administering continuously until relapse.

The majority of adverse effects were diarrhea (54%), fatigue (29%), upper respiratory tract infection (29%), rash (28%), nausea (26%) and arthralgias (25%). Hematologic toxicity ≥ Gr 3 was relatively infrequent. There was no evidence of cumulative toxicity or long-term safety concerns with a median follow-up of 16 months. Estimated 22 month

progression free survival for the 85 relapsed or refractory and high-risk patients was 76 percent and 96 percent for treatment-naïve patients. Estimated 22 month overall survival for the 85 relapsed or refractory patients and high-risk patients was 85 percent and 96 percent for treatment-naïve patients. Funding from Pharmacyclics, Inc., supports this clinical trial.

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