Abstract #308

Long-Term Efficacy and Safety of Single-Agent Ibrutinib at 3 Years Follow-up in Patients With Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia (CLL/SLL)

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Context: Ibrutinib, a first-in-class, oral, covalent inhibitor of Bruton’s tyrosine kinase is FDA approved for patients with CLL who have received ≥1 prior therapy, and for patients with del(17p) CLL. Previous reports demonstrated activity with acceptable safety in treatment-naïve (TN) and previously-treated CLL/SLL (O’Brien, Lancet Oncol 2013; Byrd, NEJM 2013).

Objective: Assess ibrutinib efficacy, safety in CLL/SLL at 3-year follow-up

Design: Phase 2, open-label, multi-institutional study

Patients/Intervention: ECOG performance status ≤2 patients with TN or relapsed/refractory (R/R) CLL/SLL received 420 or 840 mg oral ibrutinib daily

Main Outcome Measures: Safety per frequency and severity of adverse events (AEs); overall response rate (ORR), progression-free survival (PFS) as secondary outcome measures. Analyses based on patients treated from first dose until long-term follow-up data cut-off.

Results: 132 patients with CLL/SLL (31 TN, 101 R/R) treated. Median age 68 years; 43% ≥70 years; 57% Rai stage III/IV; 46% bulky disease; median 4 prior therapies in R/R patients. High-risk cytogenetic abnormalities included del(17p) in 27% (2 TN, 34 R/R), del(11q) in 27% (1 TN, 35 R/R) patients. Investigator-assessed best ORR (iwCLL criteria): TN 81%, R/R 86%, R/R del(17p) 68%. Additionally, 6% TN and 4% R/R patients achieved partial response with lymphocytosis. Concordance rate 90% between responses assessed by independent review committee and investigators. At median time on study of 29 months, median duration of response not reached for TN, R/R, or del(17p) populations. Median PFS in TN and R/R, and median OS in TN, R/R, and del(17p) not reached. Median PFS in relapsed del(17p) subgroup: 28.1 months. Investigator-assessed estimated 30-month PFS rate: TN patients 96%, R/R patients 68%; estimated 30-month OS rates of 97% and 80%, respectively. Patients with R/R disease experienced grade ≥3 hematologic AEs and infections more frequently than TN patients. With continued time on ibrutinib treatment, discontinuations due to AEs decreased. At median time on treatment of 25 months, 64% of patients remain on therapy.

Conclusions: Three-year follow-up confirms durable responses with single-agent ibrutinib in patients with TN or previously-treated CLL/SLL, including those with del(17p). Ibrutinib therapy was well tolerated with manageable toxicities, allowing for extended dosing in the majority of patients.