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642.CHRONIC LYMPHOCYTIC LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

Patient-Reported Outcomes (PROs) Among Patients with Previously Treated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) Receiving Pirtobrutinib: Analysis from the BRUIN Phase 1/2 Study

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Background
PROs including health-related quality of life (HRQoL) and symptom burden can provide helpful information to support benefit-risk assessment of a new treatment. Pirtobrutinib, a highly selective, non-covalent (reversible) Bruton tyrosine kinase inhibitor (BTKi), inhibits both wildtype and C481-mutant BTK with equal low nM potency, and has favorable oral pharmacology that enables continuous BTK inhibition throughout the dosing interval regardless of intrinsic rate of BTK turnover. Pirtobrutinib recently received regulatory approval in the US for the treatment of patients with relapsed or refractory mantle cell lymphoma after two or more lines of systemic therapy, including a covalent BTKi (cBTKi). BRUIN (NCT03740529) is an ongoing, open-label, multi-center phase 1/2 study investigating the safety and efficacy of pirtobrutinib for the treatment of B-cell malignancies, including CLL/SLL. This current analysis reports PROs among patients enrolled in the BRUIN study with relapsed or refractory (R/R) CLL/SLL treated with prior cBTKi-containing regimens.

Methods
Pretreated patients with R/R CLL/SLL in the BRUIN study completed PRO assessments at each clinic visit. The European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core-30 (QLQ-C30) was used to measure physical function (PF) and HRQoL via PF and Global Health Status/QoL subscales. Patient-reported CLL/SLL symptoms and fatigue were assessed using 13 and 6 EORTC Item Library (IL) items, respectively. All subscales are scored

0-100. Higher scores represent better PF and HRQoL; and higher scores represent worse CLL/SLL symptoms and fatigue. Prespecified clinically meaningful within patient change (MWPC) thresholds of at least 10-point changes in each PRO score were used to categorize patients based on their individual change from Cycle 1 Day 1 (i.e., baseline). Mean changes from baseline and proportions of patients with improved, stable, and worsened PROs from baseline were summarized by treatment cycle. PRO data were presented from Cycle 1 to 24 (a 28-day cycle) since the study median progression-free survival by investigator assessment was 19.6 months. The data cutoff date was 22 July 2022.

Results

There were 263 patients with CLL/SLL at the time of analysis; median (Quartile 1 and 3) age was 69 (62, 74) years and the majority were male (68%). All patients had received prior cBTKi; 21% received 2 or more prior cBTKi lines and 20% discontinued from their most recent cBTKi treatment due to toxicity. The mean overall completion rate of PRO instruments was 83% at baseline. 76% of all patients in the analysis completed at least one subsequent PRO assessment. Baseline mean (±SD [standard deviation]) score was 80.8 (±19.5) for PF, 61.6 (±23.2) for QoL, 24.8 (±18.4) for CLL/SLL symptoms, and 33.5 (±24.7) for fatigue. The majority of patients reported stable or clinically improved outcomes from baseline at each of the post-baseline visits (through Cycle 24) for PF (proportion of stable/improved ranged from 72.5% to 95.5%), QoL (range 80.4% to 95.0%), CLL/SLL symptoms (range 77.8% to 96.3%), and fatigue (range 77.3% to 89.9%).

Conclusion

Overall, consistent with the favorable safety profile of pirtobrutinib, HRQoL and symptoms were stable or improved for over 70% of patients with pretreated R/R CLL/SLL throughout the first 24 cycles of pirtobrutinib treatment. These PRO data should be interpreted with caution due to single arm trial design and small numbers of patients available for assessment in later cycles.

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OffLabel Disclosure: Pirtobrutinib is approved in the USA for the treatment of relapsed or refractory MCL after at least 2 lines of systemic therapy, including prior BTKi.

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