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POSTER ABSTRACTS

802.CHEMICAL BIOLOGY AND EXPERIMENTAL THERAPEUTICS

Pirtobrutinib, a Non-Covalent (reversible) BTK Inhibitor, in Mantle Cell Lymphoma Patients Previously Treated with a Covalent BTK Inhibitor: Results from a China Phase 2 Study

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Background
Pirtobrutinib, a highly selective, non-covalent (reversible) Bruton tyrosine kinase inhibitor (BTKi), inhibits both wildtype and C481-mutant BTK and has favorable oral pharmacology that enables continuous BTK inhibition throughout the dosing interval regardless of protein turnover, and shows promising efficacy and favorable safety profile in patients with pre-treated B-cell malignancies including a covalent BTKi (cBTKi). This study (NCT04849416) was a China only phase 2, open-label, multi-center trial aiming to evaluate the safety and efficacy of oral pirtobrutinib as a monotherapy for patients with B-cell malignancies. This abstract summarizes the findings on the efficacy in a cBTKi pre-treated mantle cell lymphoma (MCL) population and safety outcomes among all enrolled patients.

Methods
Eligible Chinese patients with relapsed/refractory B-cell malignancies were enrolled and assigned to one of three cohorts based on tumor histology and prior treatment history. All enrolled patients received pirtobrutinib monotherapy at a daily dose of 200 mg, until disease progression (PD), unacceptable side effects, or other reasons for discontinuation. The primary analysis set (PAS) comprised patients with centrally confirmed non-blastoid MCL, who received a prior cBTKi, and with measurable lesion(s) at baseline. The efficacy analysis set (EAS) was extended into all MCL patients treated with a prior cBTKi. The safety population included all patients who received at least one dose of pirtobrutinib. The primary objective was to evaluate the effectiveness by assessing the overall response rate (ORR) based on Lugano criteria and was conducted by an independent review committee (IRC). Secondary objectives included duration of response (DOR), progression-free survival (PFS), overall survival (OS) and safety profile.

Results
As of April 10, 2023, of 39 enrolled MCL patients, 28 were in the PAS and 35 were in the EAS for efficacy analysis. The safety analysis included a total of 87 enrolled patients and the median duration of therapy was 4.2 months. In the PAS popula-

tion (N=28) with cBTKi pre-treated non-blastoid MCL, patients had a median of 3.0 prior lines of therapy (range, 1-8). The majority received prior chemotherapy (96.4%) and an anti-CD20 antibody (85.7%). The most common reason for discontinuation from the prior cBTKi was PD (85.7%). The IRC-assessed ORR was 71.4% (95% CI, 51.3-86.8), with 4 patients (14.3%) achieving complete responses (CR) and 16 patients (57.1%) achieving partial responses (PR). The median DOR assessed by IRC was not reached at the cut-off date with a 6-month DOR rate of 66.02% (95% CI, 39.29-83.14). The median IRC-assessed PFS was 9.43 months (95% CI: 5.32-not evaluable [NE]), and the median OS was 15.47 months (95% CI, 8.67-NE). The EAS (N=35), demonstrated similar efficacy results with IRC-assessed ORR 62.9% (95% CI, 44.9-78.5) and the 6-month DOR rate was 64.45%. In the safety population (N=87) of all enrolled B-cell malignancy patients, common treatment-emergent adverse events (TEAEs) of any grade included decreased neutrophil count (40.2%*), anemia (31%), and increased bilirubin (23.0%, with 2.3% grade ≥3 and none led to dose modification). The most frequent grade ≥3 TEAE was decreased neutrophil count (25.3%*). All grade hemorrhage was observed in 19.5% patient (n=17, with 2.3% grade ≥3), while all grade hypertension was 5.7% (n=5, with 2.3% grade ≥3), and no patient developed atrial fibrillation/flutter. Three patients (3.4%) stopped treatment due to treatment-related TEAEs, and 2 patients (2.3%) experienced treatment related fatal TEAEs (one infection and one patient with reported tumor lysis syndrome, tumor necrosis, and hemorrhage).

Conclusion

Pirtobrutinib demonstrated clinically meaningful and durable antitumor activity in a cBTKi pre-treated MCL Chinese population and showed a well-tolerated safety profile in patients with B-cell malignancies.

* Aggregate of neutropenia and neutrophil count decreased

Disclosures No relevant conflicts of interest to declare.

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