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POSTER ABSTRACTS

624.HODGKIN LYMPHOMAS AND T/NK CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

A Novel PI3K γ/δ and DNA-PK Triple Inhibitor, BR101801, for r/r PTCL: A Phase 1a/b, Multi-Center, Open-Label Clinical Trial

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Background
BR101801, a triple inhibitor of PI3Kγ/δ and DNA-PK, inhibits not only the signal affecting cell growth caused by PI3Kγ/δ but also efficiently induces cell cycle arrest and apoptosis through inhibition of DNA-PK activation, with this triple target inhibition it decreases the stability of oncogenic protein, c-Myc (AACR2020 abstract #655). BR101801 is currently being evaluated in a phase 1a/b study in advanced hematologic malignancies. In phase 1a study, BR101801 exhibited evidence of clinical activity and was established at 200mg orally once daily 28-day cycle (RP2D) in patients with r/r PTCL (ASCO2023 abstract #7551).
Methods
This is a phase 1, open-label, multi-center, dose escalation (1a), and expansion (1b) study of BR101801 in adult patients with advanced hematologic malignancies (NCT04018248). In the phase 1a study, Dose was escalated at 50, 100, 200 and 325 mg QD. PTCL-NOS, AITL, FTCL and Nodal PTCL with TFH phenotype were determined as target indications for phase 1b with the RP2D.
Results
As of Jul 19, 2023, a total of 26 patients were enrolled in dose-escalation phase (n=12) and dose-expansion phase (n=14). The median age was 66 years (range of 30-83). Histological subtypes include PTCL-NOS (n=11, 42%), AITL (n=11, 42%), DLBCL (n=2, 8%), MZL (n=1, 4%) and MF (n=1, 4%). The majority of patients had stage III or IV (92%). In the phase 1a study, Dose limiting toxicity (DLT) occurred at 325 mg; thus, 200 mg QD was determined as the maximum tolerated dose (MTD) and RP2D. Of 19 evaluable patients with r/r PTCL (PTCL-NOS and AITL) in the phase 1 study. Patients' stage was III or IV (100%) with 47.4 % of patients having received three or more prior systemic therapies. The ORR was 31.6% (95% CI, 12.6-56.6) with 4 CRs (21.1%) and 2 PRs (10.5%), CBR was 47.4% (95% CI, 24.5-71.1). In median follow-up duration of 12.9 months, the median PFS was 7.5 months (95% CI, 1.7-NC), median OS and DoR (range of 1.9+-31.8+) has not reached. Currently, 5 patients still remain on treatment.
Safety analysis was conducted for the 26 patients; 23 patients (88.5%) experienced adverse events (AEs). The most common ($\geq$ 20%) AEs were Rash (23.1%), AST increased (23.1%), ALT increased (23.1%) and Cough (23.1%). Grade 3/4 ADRs occurred in 12 patients (46.2%) and those were ($\geq$ 10%, frequency) AST increased (19.2%), ALT increased (15.4%), Neutropenia (15.4%). There were no treatment related mortality observed.
Conclusion
BR101801, the triple inhibitor of PI3K γ/δ and DNA-PK, demonstrated as a promising therapeutic option for r/r PTCLs patients. Preliminary results showed the ORR of 31.6% and a CR rate of 21.1%. Phase 2 study is warranted further investigate the safety and efficacy of BR101801 in r/r PTCL and Nodal TFH cell lymphoma at 200 mg QD orally.

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