TPS8661 Poster Session

A multicenter, open-label, single-arm phase I/II study to assess the efficacy and safety of WSD0922-FU in patients with EGFR C797Sm+ advanced non-small cell lung cancer (NSCLC) in China (NCT06631989).

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Background: Although 3rd-generation EGFR TKIs, such as Osimertinib, Almonertinib, Furmonertinib, Befotertinib etc. are highly effective in front-line metastatic *EGFR*-mutated (*EGFR*m) NSCLC, treatment resistance ultimately occurs, including the emergence of the on-target C797S mutation for which there are no approved TKIs. WSD0922-FU is an oral, central nervous system (CNS)-penetrant, wildtype-sparing, ATP non-competitive, reversible EGFR inhibitor targeting EGFR aberrations in NSCLC and High-Grade Astrocytoma. It has shown promising preclinical and clinical data, including antitumor CNS activity that may improve patient outcomes. Additionally, combining WSD0922-FU with standard therapies may provide enhanced disease control across multiple lines of treatment, including against heterogenous tumors, in patients with *EGFR*m+ NSCLC. WSD0922-102 (NCT06631989) is an ongoing phase 1/2, open-label, multicenter trial evaluating the efficacy and safety of WSD0922-FU in patients with EGFR C797Sm+ NSCLC in China. **Methods:** Adult patients with EGFR C797Sm+ NSCLC were initially treated with oral WSD0922-FU, with three doses selected from phase I dose escalation (MC1914, NCT04197934) as a bridging PK study in China. After DLT evaluation, expansion was initiated for each dose followed by extension for the dose selected as the recommended phase 2 dose (RP2D). Key inclusion criteria include patients ≥18 years of age with metastatic *EGFR* C797Sm+ NSCLC; Eastern Cooperative Oncology Group performance status 0–1; and failed in the previous 3rd generation EGFR-targeted TKI treatment for bridging PK study, with only one 3rd generation EGFR TKI for expansion and with only one first-line 3rd generation EGFR TKI for extension. All patients must harbor an EGFR C797S resistance mutation (locally assessed for tissue/liquid samples). Key exclusion criteria are tumors harboring EGFR T790M mutations, EGFR exon 20 insertions, or MET aberrations. Dose escalation primary endpoints are maximum tolerated dose, RP2D and safety. The expansion and extension primary endpoints are overall response rate (ORR) by RECIST 1.1. Secondary endpoints include ORR (dose escalation), duration of response, disease control rate, progression-free survival, overall survival, antitumor CNS activity (iORR) by RANO-BM, and safety (dose expansion and extension). The phase 1 dose escalation adopts a 3+3 design. Patients will be enrolled into 3 treatment cohorts: dose escalation (n≈12-15), dose expansion (n≈20), and dose extension (n≈70). Patients may receive treatment until disease progression, unacceptable toxicity, or other discontinuation criteria are met. Enrollment in this study for dose expansion cohorts is ongoing and 15 sites are open across China. Clinical trial information: NCT06631989. Research Sponsor: None.