TPS8662 Poster Session

Phase 2 cohort-2 trial in progress: Vabametkib plus lazertinib for patients with EGFR-mutant NSCLC who developed resistance to 1st-line, 3rd-gen-EGFR TKIs via C-Met dysregulation.

Dae Ho Lee, Hye Ryun Kim, Hanlim Moon, Inyoung Kim, Nirmal Rajasekaran, Sunyhe Im, Na Young Kim, Jun Young Choi, Youngkee Shin, Se-Hoon Lee; Asan Medical Center, Seoul, South Korea; Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; MediRama, Seoul, South Korea; Medirama Inc, Seoul, South Korea; Abion Inc, Seoul, South Korea; ABION Inc., Seoul, South Korea; Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, Seoul National University, Seoul, South Korea; Samsung Medical Center, Seoul, South Korea

Background: Third-generation Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors (EGFR TKIs) have emerged as a promising first-line treatment for Non-Small-Cell Lung Cancer (NSCLC) patients with EGFR T790M mutations, as well as EGFR exon 19 deletions and exon 21 L858R mutations. Recently, lazertinib, combined with amivantamab, has been approved as a potential first-line therapy for NSCLC. Despite these advancements, there remains a significant unmet medical need for patients who develop resistance to first-line third-generation EGFR TKIs. ABN401 (vabametkib), a selective oral c-MET inhibitor, has shown anti-tumor activity in preclinical studies, both as monotherapy and in combination with other treatments. Currently in a phase 2 clinical trial, this study aims to evaluate the combination of vabametkib and lazertinib in patients who have developed resistance to 3rd generation EGFR TKIs. **Methods:** ABN401-003 phase 2 cohort-2 is a multicenter, open-label trial that evaluates the dose escalation, safety and efficacy of the combination therapy of vabametkib and lazertinib in patients resistant to first-line EGFR TKIs. Enrollment criteria include MET amplification (GCN >10 by NGS or FISH) or c-MET overexpression (IHC score ≥90). The study consists of three parts: Part 1 (safety run-in), a traditional 3+3 dose-escalation study assesses the safety of vabametkib combined with lazertinib. Up to 18 patients will be evaluated in safety run-in, with dose adjustments based on dose-limiting toxicities (DLTs). Part 2: Randomized Dose Optimization – Two combination dose levels, determined from Part 1, will be tested in 40 patients to identify the optimal dose. Part-2 may be skipped if the maximum tolerated dose (MTD) is established in Part 1. Part 3 [randomized clinical trial – The optimal dose combination will be compared to the standard of care (SOC) in 80 patients. Key secondary endpoints include objective response rate (ORR), disease control rate (DCR), progression free survival (PFS) and duration of response (DOR). Additionally, safety and patient-reported outcome will be evaluated. Clinical trial information: NCT05541822. Research Sponsor: None.