Background
• Non-small cell lung cancer (NSCLC) is by far one of the leading causes of cancer-related mortality globally. C-ros oncopGene 1 (ROS1) rearrangements define a distinct molecular subtype of NSCLC and have been validated as an actionable therapeutic target.
• Taletrectinib (AB-106/DS-6051b), a brain-penetrant, highly potent and selective ROS1 tyrosine kinase inhibitor (TKI), has shown clinically meaningful efficacy and safety profiles in ROS1+ NSCLC patients in phase 1 studies in the U.S. and Japan1,2 as well as in the ongoing phase 2 TRUST study (NCT04395677) in China3,4.
• Taletrectinib has notably demonstrated clinical activity against ROS1 G2032R resistance mutation and intracranial activity against central nervous system (CNS) metastases in the ongoing phase 2 TRUST study (NCT04395677) in China3,4.

Key study objectives
Primary Objective
• To evaluate the efficacy of taletrectinib by the objective response rate (ORR) in the patients with advanced or metastatic ROS1 positive NSCLC.
Secondary Objectives
• To evaluate the efficacy by the Duration of response (DOR); Progression-free survival (PFS); time to failure (TTF); time to response (TTR); Overall survival (OS); Intracranial activity
• To assess the safety and tolerability
• To determine pharmacokinetic profile.

Study design
This is a Phase 2, multi-country, multi-center, open-label, non-randomized study.

Treatment
• Taletrectinib 600 mg (3 capsules) once daily administered until disease progression and unacceptable toxicity

Cohorts
• 1. systematic chemotherapy naïve or ≤ one prior line and ROS1 naïve NSCLC (N=53).
• 2. one ROS1 TKI treatment and with progression, chemotherapy naïve or ≤ one line of platinum and/or pemetrexed based therapy, NSCLC (N=46).
• 3. ≤2 prior ROS1 TKI treatments and with progression, either chemotherapy naïve or ≤2 lines of platinum and/or pemetrexed based therapy, NSCLC (N=10).
• 4. ROS1 positive solid tumors other than NSCLC, naïve to systemic chemotherapy or ≤2 prior lines of chemotherapy, naïve to ROS1 TKI treatment (N=10).

Exclusion criteria
• Patient received other treatments prior to enrollment including investigational agents or anticancer therapy within 2 weeks, immuno-oncology within 12 weeks, and major surgery within 4 weeks.
• Radiation therapy with a limited field for palliation within 1 week before treatment.
• Unsolved adverse events caused by previous treatments.
• Use of food or drugs disrupting cytochrome P450 3A4/5 or p-glycoproteins.
• Administration of agents with potential QT interval prolonging effect.
• Tumor and/or cancerous meningitis caused spinal cord compression.
• Any gastrointestinal disorders that may affect absorption of oral medications.

Key inclusion criteria
• Histologically or cytologically confirmed locally advanced or metastatic tumors.
• Evidence of ROS1 fusion-positive tumor.
• At least one measurable disease per RECIST 1.1.
• ECOG Performance Status: 0 or 1.
• Adequate organ function.

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