TRUST-II: A Global Phase 2 Study of Taletrectinib in ROS1 Fusion-Positive Lung Cancer and Other Solid Tumors

Abstract# TPS8601

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Background

- ROS1 oncogenic fusions are observed in 1-2% NSCLC patients[1] as well as in cholangiocarcinoma, glioblastoma, ovarian, gastric, and colorectal cancers.
- CNS metastasis occurs in 20-30% ROS1 TKI-naïve and in up to 50% crizotinib-pretreated ROS1-positive NSCLC patients[2].
- Resistance to first-generation ROS1 inhibitors often occur with secondary mutations such as ROS1 G2032R solvent front mutation[3].
- Taletrectinib (AB-106), a next-generation, potent, selective ROS1 tyrosine kinase inhibitor, is developed to:
  - overcome resistance to first-generation ROS1 inhibitors,
  - address CNS metastasis,
  - improve efficacy and safety profile in ROS1-positive NSCLC patients, and
  - confer less TRKB-related CNS adverse events by selectively inhibiting ROS1 over TRKB[4].
- Efficacy and safety data of taletrectinib from a separate phase 2 study (TRUST, NCT04395677) are presented in ASCO 2022 poster (Abstract# 8572).

Key study objectives

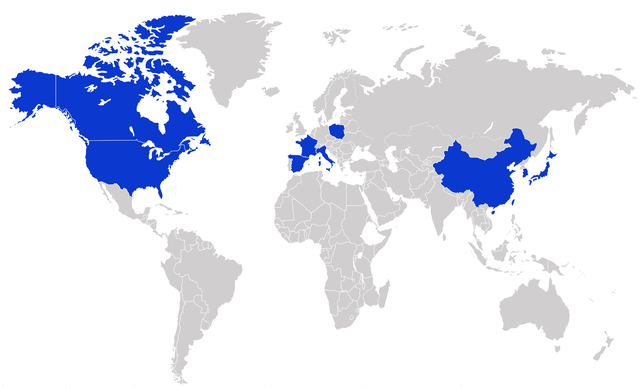
Primary Objective

- To evaluate the efficacy of taletrectinib by objective response rate (ORR) in patients with advanced or metastatic ROS1 positive NSCLC.

Secondary Objectives

- To evaluate the efficacy by 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.

TRUST II is a global study



Total of ~ 80 study sites in 9 countries.

- North America: ~ 25 sites
- Europe: ~ 30 sites
- Asia: ~ 25 sites

Trial information

Clinicaltrials.gov identifier: NCT04919811
Protocol number: AB-106-G208
Status: Recruiting
Timeline: Started in September 2021, expected to complete in September 2024

Key inclusion criteria

- Histologically or cytologically confirmed diagnosis of locally advanced or metastatic NSCLC (cohorts 1-3) or other solid tumors (cohort 4).
- Evidence of ROS1 fusion in tumor tissue determined by a validated assay as performed in Clinical Laboratory Improvement Amendments (CLIA)-certified or locally equivalent diagnostic laboratories.
- Sufficient tumor tissue is required for performing confirmatory ROS1 fusion testing at the designated central laboratories post-enrollment.
- At least one measurable disease per RECIST 1.1 assessed by investigator.
- ECOG Performance Status: 0 or 1.
- Patient with a life expectancy ≥12 weeks based on the judgement of investigator.
- Patients with adequate organ functions.

Key exclusion criteria

- Treatment with other investigational agents or anticancer therapy within 2 weeks (or 5 half-lives of the compound, whichever is longer) prior to study enrollment. In addition, no concurrent anticancer therapy is permitted.
- Previously treated with immuno-oncology (IO) including immune checkpoint inhibitors within 12 weeks before enrollment.
- Major surgery within 4 weeks prior to enrollment.
- Adverse events due to prior therapy are unresolved to ≤ CTCAE Grade 1.
- History or evidence of interstitial fibrosis, interstitial lung disease or TKI-induced pneumonitis.
- Active and clinically significant bacterial, fungal, or viral infection.

References

1. Lin, et al., J Thoracic Oncology 2017; 12(11):1611
2. Ou, et al., Lung Cancer 2019; 130:201
3. Gainor, et al., JCO Precision Oncology 2017;1:1
4. Katayama, et al., Nature Communications 2019; 10(1):3604

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/or unacceptable toxicity

Cohorts

- Cohort 1: Systemic chemotherapy naïve or pretreated with one prior line of chemotherapy, but never treated with any ROS1 TKI in ROS1 positive NSCLC;
- Cohort 2: Prior treatment with one ROS1 TKI (crizotinib or entrectinib) and disease progression. The subject could be either chemotherapy naïve or has received one line of platinum and/or pemetrexed-based chemotherapy for the locally advanced or metastatic NSCLC;
- Cohort 3: Prior treatment with ≤ 2 prior ROS1 TKIs and disease progression. The patient could be either chemotherapy naïve or has received ≤ 2 lines of platinum and/or pemetrexed based chemotherapy for the locally advanced or metastatic NSCLC;
- Cohort 4: Systemic chemotherapy naïve or pretreated with ≤ 2 prior lines of chemotherapy, but never treated with any ROS1 TKI. ROS1 positive solid tumor types other than NSCLC will be enrolled.

Acknowledgment

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