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TRUST-III: Phase 3 Head-to-Head Study of Taletrectinib vs Crizotinib in Patients With ROS1+ Non-Small Cell Lung Cancer (NCT06564324)

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Background & Rationale

- ROS1 gene fusions are oncogenic alterations occurring in approximately 2% of patients with NSCLC[1,2]
- Patients with ROS1+ NSCLC are typically younger (median age of 50 years at diagnosis), never-smokers, female, diagnosed at an advanced stage, and with adenocarcinoma histology[3,4]
- ROS1 TKIs are the current SOC for ROS1+ NSCLC[1]
- Crizotinib was the first TKI approved for ROS1+ NSCLC but its utility is limited by poor CNS penetration and the development of resistance mutations, such as G2032R[1]
- Taletrectinib is a next-generation, CNS-active, selective, oral ROS1 inhibitor with efficacy against the G2032R resistance mutation[2,5]
- In a pooled analysis of two Phase 2 studies, TRUST-I and TRUST-II, taletrectinib demonstrated promising efficacy, including IC activity, and a favorable safety profile in patients with TKI-naïve and TKI-pretreated ROS1+ NSCLC[5]

Pooled Data From TRUST-I and TRUST-II[5]

Efficacy	TKI-naïve (n=160)	TKI-pretreated (n=113)
cORR, %	88.8	55.8
Median DOR, months	44.2	16.6
Median PFS, months	45.6	9.7
IC Efficacy	**(n=17)**	**(n=32)**
IC-ORR, %	76.5	65.6

- The most common TEAEs with taletrectinib were elevated AST (72%), elevated ALT (68%), diarrhea (64%), nausea (46%), and vomiting (44%), most of which were Grade 1 or 2 in severity[5]
- Taletrectinib was approved by China's NMPA in January 2025 and by the US FDA in June 2025 for the treatment of adult patients with locally advanced or metastatic ROS1+ NSCLC[6,7]
- This Phase 3 TRUST-III study aims to confirm the clinical benefit of taletrectinib compared with crizotinib in patients with ROS1+ NSCLC who have not previously received ROS1 TKIs
- This study is being conducted as part of a regulatory commitment to the NMPA, to support taletrectinib approval in China

TRUST-III Study Design

- TRUST-III (NCT06564324) is a Phase 3, open-label, multicenter, randomized study evaluating the efficacy and safety of taletrectinib vs crizotinib in TKI-naïve patients with locally advanced or metastatic ROS1+ NSCLC

Screening for Eligibility

- TKI-naïve locally advanced or metastatic ROS1+ NSCLC
- Stable CNS involvement allowed
- Age ≥18 years (or ≥20 years as required by local regulations)
- ECOG PS 0–1

Estimated enrollment: N=138

Stratified by:
- Presence of baseline CNS metastases (yes vs no)
- Prior chemotherapy for advanced disease (yes vs no)

R 1:1

Arm A
Taletrectinib 600 mg QD
28-day cycles

Arm B
Crizotinib 250 mg BID
28-day cycles

Eligible patients may crossover to taletrectinib after BIRC-confirmed progression

Key Endpoints

Primary

- PFS assessed by BIRC per RECIST v1.1

Secondary

- cORR, DOR, TTR, and DCR assessed by BIRC and Investigator per RECIST v1.1
- PFS assessed by Investigator per RECIST v1.1
- IC endpoints assessed by BIRC per RECIST v1.1 (IC-ORR, IC-TTP, IC-DOR, IC-PFS)
- Overall survival
- Safety and tolerability
- Pharmacokinetics
- Patient-reported outcomes

Key Eligibility Criteria

Inclusion Criteria

- Histologically or cytologically confirmed locally advanced or metastatic ROS1+ NSCLC
- ≥1 measurable lesion(s) per Investigator assessment using RECIST v1.1
- Prior CNS metastases allowed if asymptomatic and stable (including leptomeningeal metastases)
- Age ≥18 years (or ≥20 years as required by local regulations)
- ECOG PS 0–1
- Adequate organ function

Exclusion Criteria

- Prior ROS1 TKIs
- Prior immune checkpoint inhibitors or ≥1 prior regimen(s) of systemic anticancer therapy
- Chemotherapy or radiation therapy ≤14 days prior to randomization
- Major surgery ≤28 days prior to randomization
- History or evidence of ILD or drug-related pneumonitis
- Active infection, including HBV, HCV, and HIV

Trial Progress

- TRUST-III (NCT06564324) is currently recruiting patients in China
- Estimated primary completion date: January 2029
- Estimated study completion date: September 2030

Summary

- Taletrectinib demonstrated high and durable response rates, along with a favorable safety profile, in patients with advanced or metastatic ROS1+ NSCLC,[5] and is now approved in both China and the US[6,7]
- TRUST-III (NCT06564324) is a Phase 3 study evaluating the efficacy and safety of taletrectinib vs crizotinib in TKI-naïve patients with locally advanced or metastatic ROS1+ NSCLC
- The primary endpoint is PFS, while secondary endpoints include ORR, DOR, IC efficacy, overall survival, and safety
- The study is currently recruiting patients in China with an estimated completion date of September 2030

Abbreviations

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; BIRC, Blinded Independent Review Committee; c, confirmed; CNS, central nervous system; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDA, Food and Drug Administration; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IC, intracranial; ILD, interstitial lung disease; NMPA, National Medical Products Administration; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; QD, once daily; R, randomized; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; ROS1, ROS proto-oncogene 1; SOC, standard of care; TEAE, treatment-emergent adverse event; TKI, tyrosine kinase inhibitor; TTP, time to disease progression; TTR, time to response; US, United States

References

1. Boulanger MC, et al. *Oncologist* 2024;29:943–956
2. Katayama R, et al. *Nat Commun* 2019;10:3604
3. Zhu Q, et al. *Transl Lung Cancer Res* 2015;4:300–309
4. Bergethon K, et al. *J Clin Oncol* 2012;30:863–870
5. Pérol M, et al. *J Clin Oncol* 2025;43:1920–1929
6. Nuvation Bio. Nuvation Bio Receives Approval from China's National Medical Products Administration for Taletrectinib for Patients with Advanced ROS1-positive Non-Small Cell Lung Cancer. Accessed July 09, 2025 https://investors.nuvationbio.com/news/news-details/2025/Nuvation-Bio-Receives-Approval-from-Chinas-National-Medical-Products-Administration-for-Taletrectinib-for-Patients-with-Advanced-ROS1-positive-Non-Small-Cell-Lung-Cancer
7. IBTROZI™ (taletrectinib). Prescribing Information 2025

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