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Randomized, Double-Blind, Phase 3 TRUST-IV Study of Adjuvant Taletrectinib vs Placebo in Patients With Stage IB–IIIA ROS1+ Non-Small Cell Lung Cancer (NSCLC)

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Background & Rationale

- Taletrectinib is a next-generation, CNS-active, selective ROS1 TKI approved in the US, Japan, and China for the treatment of adult patients with locally advanced or metastatic ROS1+ NSCLC[1–5]
  - A marketing authorization application for taletrectinib has been submitted to the European Medicines Agency and is currently under review[6]
- Taletrectinib has demonstrated durable and robust efficacy in both TKI-naïve and TKI-pretreated patients with advanced ROS1+ NSCLC;[7,8] in TKI-naïve patients, cORR was 90%, with median DOR and median PFS exceeding 4 years after >4 years of follow-up[9]
- Taletrectinib has demonstrated a manageable safety profile, with AEs of clinical interest being mostly low grade and transient, and with a low rate of treatment discontinuations[7–10]
- Treatment for resectable stage IB–IIIA NSCLC typically includes complete surgical resection with perioperative platinum-based chemotherapy (neoadjuvant and/or adjuvant), with or without ICI therapy; however, disease recurrence is still common[11]
- Phase 3 trials have shown that, with some oncogenic drivers in early-stage NSCLC (e.g., EGFR mutations, ALK fusions), adjuvant targeted therapy can significantly improve DFS vs standard-of-care treatment[12,13]
  - However, no adjuvant targeted therapies are currently approved for ROS1+ NSCLC, representing a clear unmet clinical need
- Given the demonstrated efficacy of taletrectinib in advanced ROS1+ NSCLC, evaluation in the adjuvant setting following complete resection is warranted

TRUST-IV Study Design

- TRUST-IV (NCT07154706) is a randomized, double-blind, multicenter, Phase 3 study evaluating the efficacy and safety of adjuvant taletrectinib in patients with completely resected stage IB–IIIA ROS1+ NSCLC

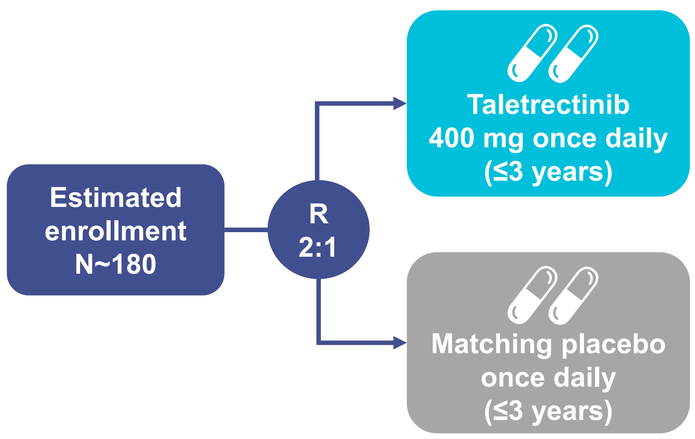
Key Eligibility Criteria → **Treatment** → **Assessment**

Key Inclusion Criteria

- Histologically confirmed stage IB, II, or IIIA NSCLC according to AJCC 9th edition based on pathological staging
- Documented ROS1 rearrangement in primary tumor by validated local assay
- Age ≥18 years (or ≥20 years as required by local regulations)
- ECOG PS 0 or 1
- Received definitive locoregional curative surgery for stage IB, II, or IIIA NSCLC; all surgical margins of resection must be negative
- Complete recovery from surgery performed[a]

Key Exclusion Criteria

- Post-operative or planned radiation therapy for current lung cancer
- Concurrent EGFR mutations or ALK fusions
- Any investigational therapy for any condition other than NSCLC within 6 months of randomization
- Prior adjuvant therapy other than standard platinum-doublet chemotherapy[b]



Randomization stratified based on:
- Use of adjuvant chemotherapy (Yes vs No)
- Stage (IB vs II vs IIIA)

Endpoints

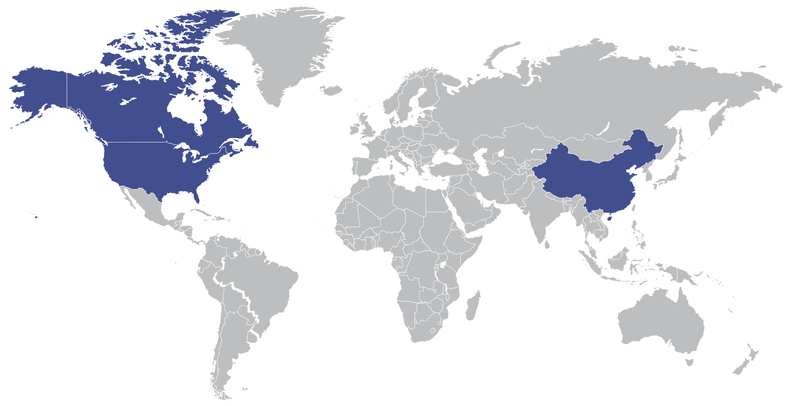
Primary:
- DFS by INV assessment

Key Secondary:
- DFS rates by INV at 2, 3, 4, and 5 years
- OS
- DFS by BICR
- CNS-DFS by INV and BICR
- PK
- AEs

[a]Surgery performed ≥4 or ≤16 weeks before randomization if no adjuvant chemotherapy was given; ≥4 or ≤30 weeks if adjuvant chemotherapy was given. [b]Adjuvant ICI therapy is allowed, but patients should have received no more than four cycles of ICI, and at the time of randomization, have at least 12 weeks of washout from the last dose of ICI.

Trial Progress[14]

- TRUST-IV (NCT07154706) is currently recruiting patients in the US, Canada, and China, with additional sites planned in other countries in 2026
- In the US, this study is included in the Tempus TIME program for rapid site activation
- First patient enrolled: September 30, 2025[15]
- Estimated primary completion date: August 2030
- Estimated study completion date: August 2033



Summary

- TRUST-IV is a randomized, double-blind, multicenter, Phase 3 study evaluating the efficacy and safety of taletrectinib compared with placebo in patients with stage IB, II, or IIIA ROS1+ NSCLC following complete tumor resection
- The study is currently recruiting in the US, Canada, and China, with further global expansion in 2026

For more information, please contact Dr Alexander Spira: Alexander.Spira@USOncology.com

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Abbreviations

AE, adverse event; AJCC, American Joint Committee on Cancer; ALK, anaplastic lymphoma kinase; BICR, blinded independent central review; c, confirmed; CNS, central nervous system; DFS, disease-free survival; DOR; duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; ICI, immune checkpoint inhibitor; INV, investigator; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; R, randomized; ROS1, ROS proto-oncogene 1; TKI, tyrosine kinase inhibitor; US, United States

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