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Taletrectinib in TKI-Naïve Patients With ROS1+ NSCLC: Updated Data From TRUST-I and TRUST-II

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Disclosure Information

Lyudmila Bazhenova, MD

I declare the following potential conflicts of interest:

- Independent contractor for: AbbVie, AnHeart Therapeutics, Bayer, Bristol Myers Squibb, Boehringer Ingelheim, Eli Lilly, Genentech, Johnson & Johnson, Merck, Natera, Nuvalent, Pfizer, Revolution Medicines, Summit, and Taiho Oncology

- **Taletrectinib** is a **next-generation, CNS-active, selective ROS1 TKI** approved in the US, Japan, and China for the treatment of patients with locally advanced/metastatic ROS1+ NSCLC^{1–5}
- Taletrectinib has shown **robust efficacy**, including intracranial activity, and a **manageable safety profile** in both TKI-naïve and TKI-pretreated patients with ROS1+ NSCLC in the Phase 2 TRUST-I (NCT04395677) and TRUST-II (NCT04919811) studies^{6–8}
- Here we report **updated efficacy data for taletrectinib in TKI-naïve patients from TRUST-I and TRUST-II**, along with updated data from an integrated safety analysis

CNS, central nervous system; NSCLC, non-small cell lung cancer; ROS1, ROS proto-oncogene 1; TKI, tyrosine kinase inhibitor; US, United States.

1. Katayama R, et al. *Nat Commun* 2019;10:3604. 2. Nagasaka M, et al. *Future Oncol* 2023;19:123–135. 3. IBTROZI® (taletrectinib). Prescribing Information. Nuvation Bio Inc. 2025.

4. Nippon Kayaku. IBTROZI® Capsules 200mg (taletrectinib) has been approved in Japan. Accessed February 26, 2026; https://www.nipponkayaku.co.jp/english/news/detail.php?n=20250919_6G5AI1Y7.

5. Nuvation Bio. Nuvation Bio Receives Approval from China's NMPA for Taletrectinib. Accessed February 26, 2026; <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>.

6. Pérol M, et al. *J Clin Oncol* 2025;43:1920–1929. 7. Li W, et al. *J Thorac Oncol* 2025;20(Suppl 1):S500. 8. Liu G, et al. *J Thorac Oncol* 2025;20(Suppl 1):S56.

TRUST-I and TRUST-II: Pivotal Phase 2 Trials of Talrectinib in ROS1+ NSCLC

Key Eligibility Criteria

- Locally advanced or metastatic NSCLC with ROS1 fusion
- Age ≥18 years^a
- ECOG PS 0–1
- Brain metastases were allowed if stable

TRUST-I
China Phase 2 Study
(NCT04395677)

Cohort 1:
TKI-naïve^b

Cohort 2:
TKI-pretreated^{b,c}

TRUST-II
Global Phase 2 Study
(NCT04919811)

Cohort 1:
TKI-naïve^b

Cohort 2:
TKI-pretreated^{b,c}

Taletrectinib
600 mg QD^d

Endpoints

Primary:

- IRC-assessed cORR per RECIST v1.1

Key Secondary:

- DOR
- PFS
- OS
- IC-ORR
- Safety

- The efficacy population reported here included **TKI-naïve patients** from TRUST-I and TRUST-II with ≥1 measurable baseline lesion per RECIST v1.1 by IRC who started treatment on taletrectinib 600 mg QD
- Safety was evaluated in **TKI-naïve and TKI-pretreated patients** with ROS1+ NSCLC from Phase 1 and Phase 2 trials who received ≥1 dose of taletrectinib 600 mg QD

^aOr ≥20 years in TRUST-II, as required by local regulations. ^bRegistrational cohorts. ^cPatients who received one prior TKI. ^dThree TKI-naïve patients from TRUST-I started treatment on taletrectinib 400 mg QD as part of the lead-in stage, two of whom escalated to 600 mg QD.

c, confirmed; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IC, intracranial; IRC, independent review committee; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; QD, once daily; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; ROS proto-oncogene 1; TKI, tyrosine kinase inhibitor.

Pérol M, et al. *J Clin Oncol* 2025;43:1920–1929.

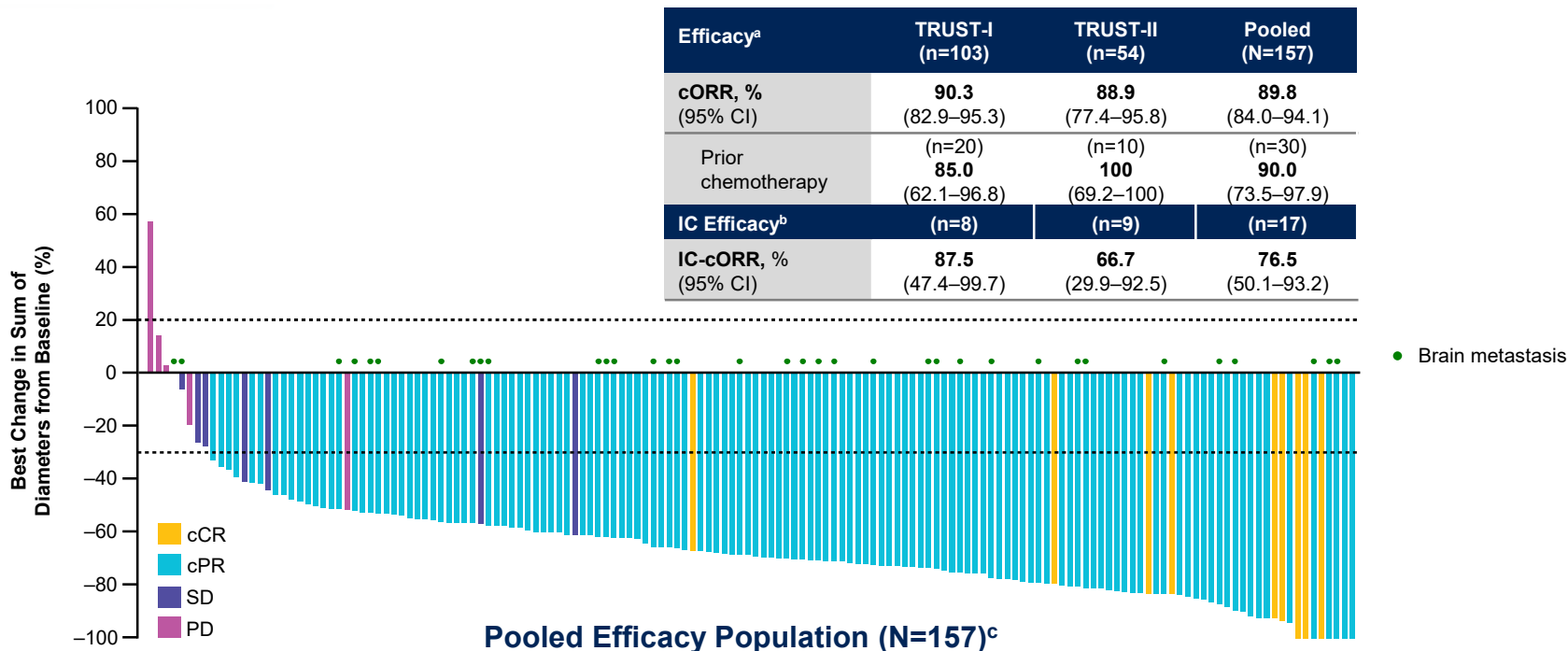
Baseline Characteristics

Baseline Characteristics	TKI-Naïve Patients			Integrated Safety Population (N=363) ^c
	TRUST-I (n=106) ^a	TRUST-II (n=55)	Pooled Efficacy Population (N=157) ^b	
Median age, years (range)	56 (26–78)	57 (27–83)	57 (26–83)	56 (26–83)
Female, n (%)	59 (55.7)	31 (56.4)	87 (55.4)	206 (56.7)
Asian, n (%)	106 (100)	36 (65.5)	138 (87.9)	263 (72.5)
Stage IV disease, n (%)	97 (91.5)	49 (89.1)	143 (91.1)	341 (93.9)
ECOG PS 1, n (%)	86 (81.1)	33 (60.0)	116 (73.9)	244 (67.2)
Never smoker, n (%)	78 (73.6)	28 (50.9)	102 (65.0)	NA
Prior chemotherapy, n (%)	22 (20.8)	11 (20.0)	30 (19.1)	NA
Brain metastases, ^d n (%)	18 (17.0)	19 (34.5)	37 (23.6)	NA

^aIncludes three patients who started treatment on taletrectinib 400 mg QD. ^bIncludes patients with ≥1 measurable baseline lesion per RECIST v1.1 by IRC who started treatment on taletrectinib 600 mg QD (103 patients from TRUST-I and 54 patients from TRUST-II). ^cIncludes TKI-naïve and TKI-pretreated patients with ROS1+ NSCLC from Phase 1 and 2 trials who received ≥1 dose of taletrectinib 600 mg QD. ^dAssessed by IRC per mRECIST v1.1.

ECOG PS, Eastern Cooperative Oncology Group performance status; IRC, independent review committee; (m)RECIST v1.1, (modified) Response Evaluation Criteria in Solid Tumors version 1.1; NA, not available; NSCLC, non-small cell lung cancer; QD, once daily; TKI, tyrosine kinase inhibitor.

Tumor Response in TKI-Naïve Patients

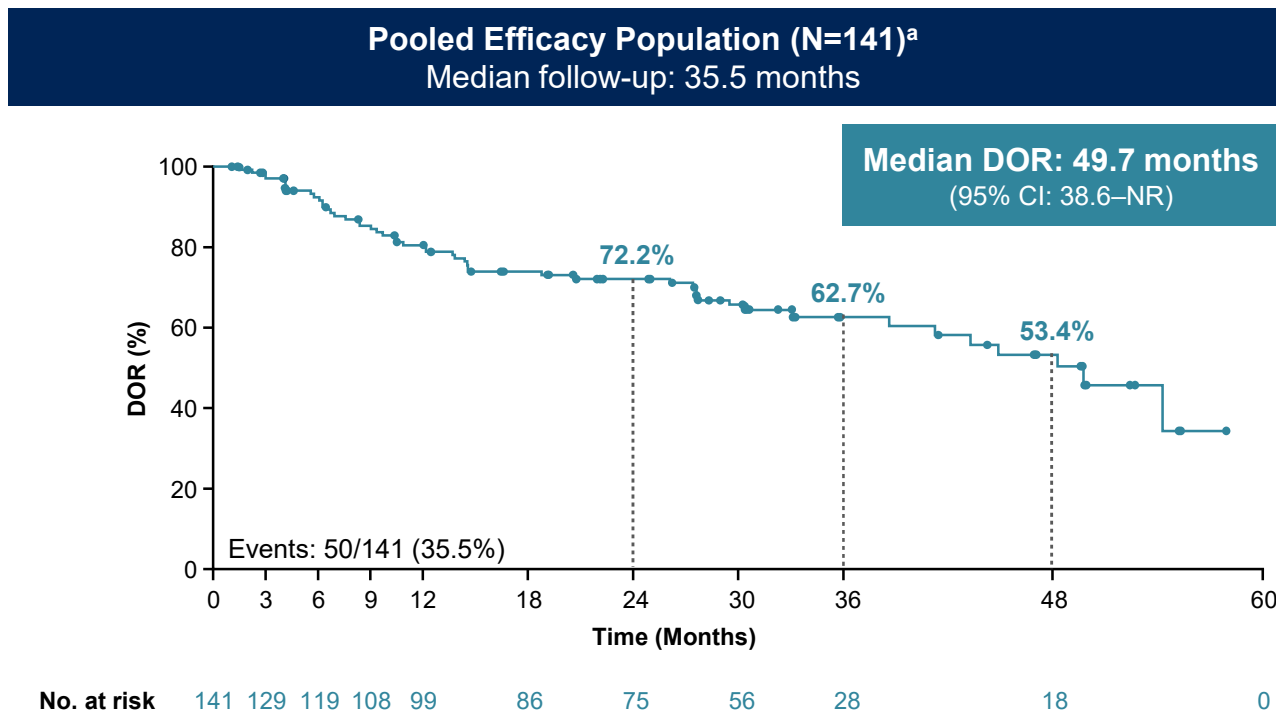


Data cutoff: August 31, 2025

^aPatients with ≥ 1 measurable baseline lesion per RECIST v1.1 by IRC who started treatment on taletrectinib 600 mg QD. ^bAssessed by IRC per mRECIST v1.1 in patients with ≥ 1 measurable baseline brain metastasis. Among these, three patients from TRUST-II had been previously treated with IC radiotherapy. ^cThree patients with cBOR of NE are not shown in the figure. One patient with cBOR of SD had a best % change of 0%.

BOR, best overall response; c, confirmed; CI, confidence interval; CR, complete response; IC, intracranial; IRC, independent review committee; (m)RECIST v1.1, (modified) Response Evaluation Criteria in Solid Tumors version 1.1; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; QD, once daily; SD, stable disease; TKI, tyrosine kinase inhibitor.

DOR in TKI-Naïve Patients From the Pooled Efficacy Analysis



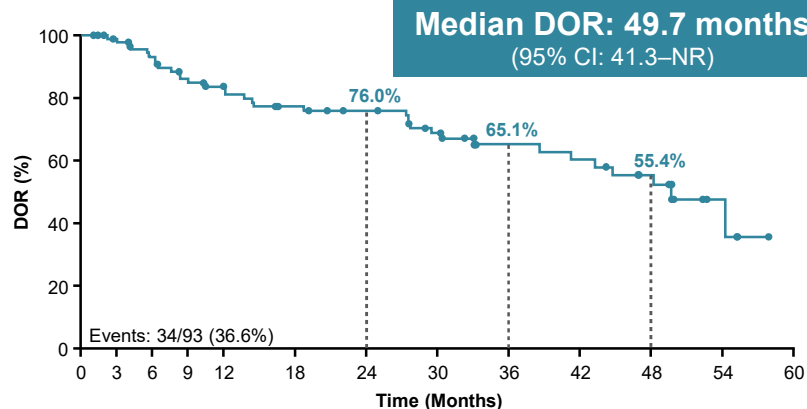
Data cutoff: August 31, 2025

^aDOR reported only for patients with a complete or partial tumor response.

CI, confidence interval; DOR, duration of response; NR, not reached; TKI, tyrosine kinase inhibitor.

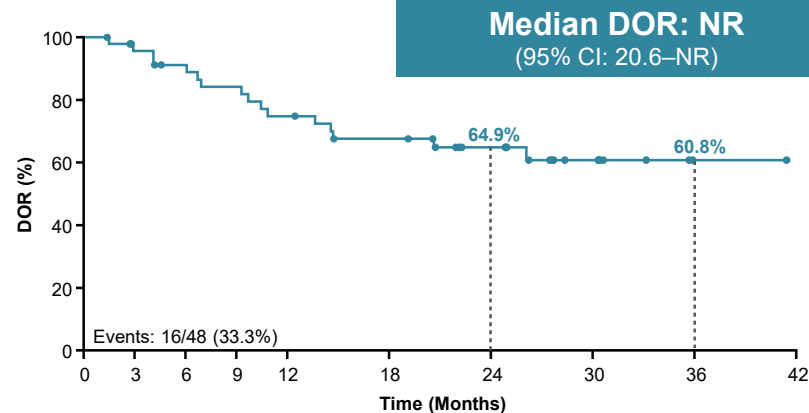
DOR in TKI-Naïve Patients From TRUST-I and TRUST-II

TRUST-I (n=93)^a Median follow-up: 51.0 months



No. at risk 93 86 80 72 67 59 55 46 27 25 18 4 0

TRUST-II (n=48)^a Median follow-up: 30.6 months



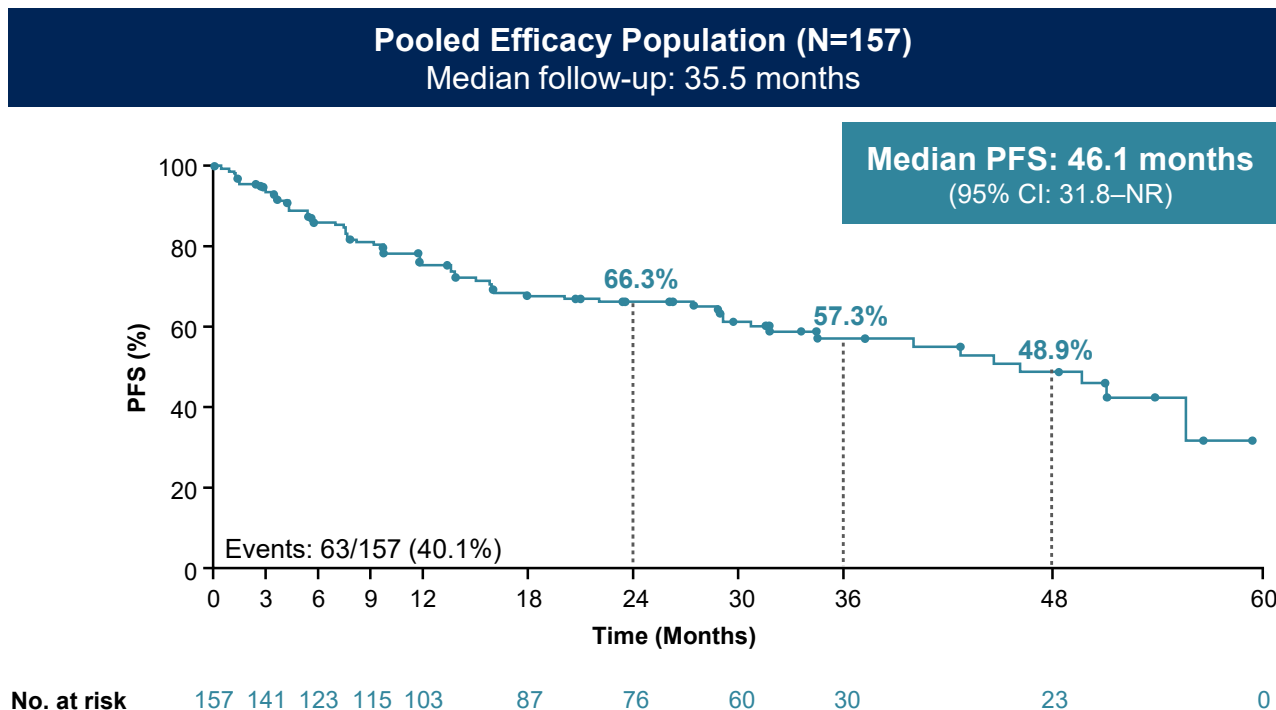
No. at risk 48 43 39 36 32 27 20 10 1 0

Data cutoff: August 31, 2025

^aDOR reported only for patients with a complete or partial tumor response.

CI, confidence interval; DOR, duration of response; NR, not reached; TKI, tyrosine kinase inhibitor.

PFS in TKI-Naïve Patients From the Pooled Efficacy Analysis



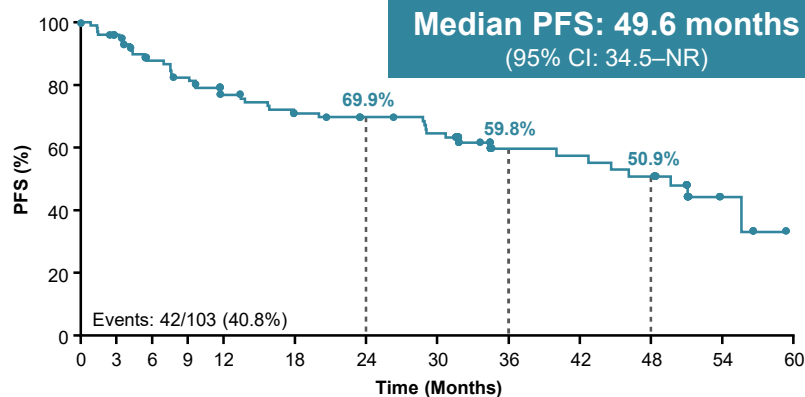
Data cutoff: August 31, 2025

CI, confidence interval; NR, not reached; PFS, progression-free survival; TKI, tyrosine kinase inhibitor.

PFS in TKI-Naïve Patients From TRUST-I and TRUST-II

TRUST-I (n=103)

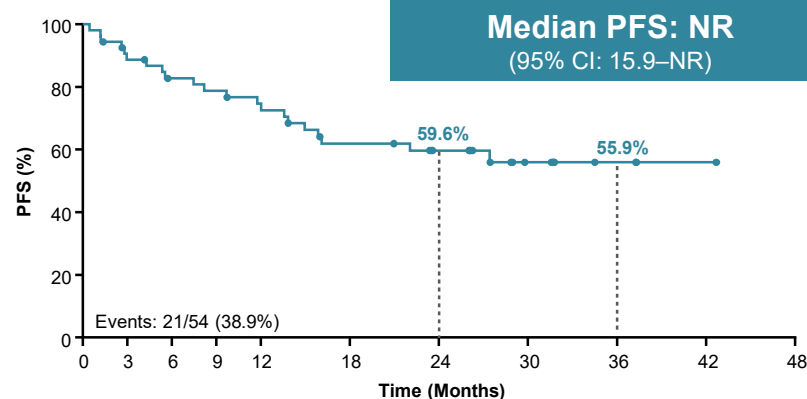
Median follow-up: 51.0 months



No. at risk 103 95 82 76 67 59 55 50 27 26 23 4 0

TRUST-II (n=54)

Median follow-up: 30.6 months

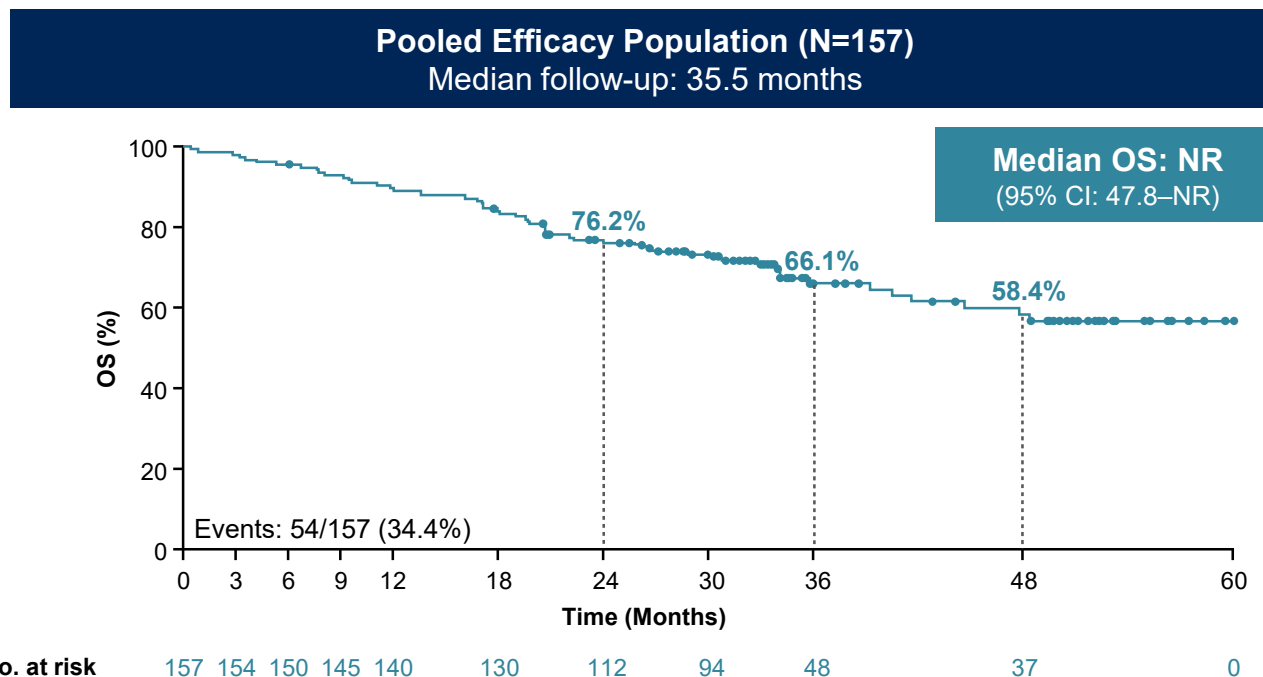


No. at risk 54 46 41 39 36 28 21 10 3 1 0

Data cutoff: August 31, 2025

CI, confidence interval; NR, not reached; PFS, progression-free survival; TKI, tyrosine kinase inhibitor.

OS in TKI-Naïve Patients



Median OS was **NR** (95% CI: 41.6–NR) for TRUST-I and **NR** (95% CI: NR–NR) for TRUST-II

Data cutoff: August 31, 2025

CI, confidence interval; NR, not reached; OS, overall survival; TKI, tyrosine kinase inhibitor.

Taletrectinib Safety Profile in the Integrated Safety Analysis (N=363)^a

Most frequent TEAEs (≥20% of patients), n (%)	Any grade	Grade 1	Grade 2	Grade ≥3
AST increased	261 (71.9)	166 (45.7)	65 (17.9)	30 (8.3)
ALT increased	248 (68.3)	143 (39.4)	65 (17.9)	40 (11.0)
Diarrhea	234 (64.5)	181 (49.9)	44 (12.1)	9 (2.5)
Nausea	174 (47.9)	131 (36.1)	38 (10.5)	5 (1.4)
Vomiting	164 (45.2)	127 (35.0)	32 (8.8)	5 (1.4)
Anemia	139 (38.3)	80 (22.0)	44 (12.1)	15 (4.1)
Dizziness	78 (21.5)	67 (18.5)	10 (2.8)	1 (0.3)
Electrocardiogram QT prolonged	76 (20.9)	52 (14.3)	11 (3.0)	13 (3.6)
Constipation	74 (20.4)	62 (17.1)	12 (3.3)	0
Blood creatinine increased	73 (20.1)	62 (17.1)	11 (3.0)	0

- With longer follow-up, no new safety signals were identified, and safety was consistent between the integrated safety population and TKI-naïve patients
- The most common (any grade) TEAEs were increased AST, increased ALT, diarrhea, nausea, and vomiting
- Rates of neurologic TEAEs were low and mostly Grade 1 or 2
 - Dizziness:** 18.5% Grade 1; 2.8% Grade 2
 - Dysgeusia:** 13.2% Grade 1; 2.2% Grade 2
- TEAEs led to dose interruptions in 42.7% of patients, dose reductions in 31.3%, and treatment discontinuations in 8.5%

Data cutoff: August 31, 2025

^aThe integrated safety population includes TKI-naïve and TKI-pretreated patients with ROS1+ NSCLC who received ≥1 dose of talrectinib 600 mg QD from Phase 2 trials (TRUST-I and TRUST-II) and a Phase 1 trial (J102).

ALT, alanine aminotransferase; AST, aspartate aminotransferase; NSCLC, non-small cell lung cancer; QD, once daily; ROS1, ROS proto-oncogene 1; TEAE, treatment-emergent adverse event, TKI, tyrosine kinase inhibitor.

Conclusions

- With ~3 years of follow-up in the pooled analysis and >4 years of follow-up in TRUST-I, taletrectinib demonstrated **high and durable response rates** in TKI-naïve patients with ROS1+ NSCLC, with a **median DOR of >4 years**
- To the best of our knowledge, these results represent the **highest ORR and longest DOR and PFS** reported to date for an FDA-approved ROS1 TKI in this patient population¹⁻³
- With 10 months of additional follow-up since the last report, taletrectinib continued to demonstrate a **manageable safety profile**, with **low rates of neurologic AEs** and no new safety signals
- These data support taletrectinib as an **effective, durable, and tolerable treatment option** for patients with advanced ROS1+ NSCLC who have not received a prior ROS1 TKI

Other presentations on taletrectinib at AACR 2026
Tuesday 21 April 2:00 PM – 5:00 PM (Poster Session)
Taletrectinib in TKI-Pretreated Patients (CT244)
Taletrectinib Preclinical Data (5864)

Journal of Clinical Oncology[®]

**Long-Term Efficacy and
Safety of Taletrectinib in
Patients With ROS1+
Non-Small Cell Lung
Cancer: Results from the
Phase II TRUST-I Study**

<https://ascopubs.org/doi/10.1200/JCO-26-00434>

Dr. Caicun Zhou



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