P3.277

Taletrectinib Across Key Subgroups in Patients With ROS1+ Non-Small Cell Lung Cancer: Results From TRUST-I and TRUST-II

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Background

- Taletrectinib is a next-generation, CNS-active, selective ROS1 TKI approved in the United States, Japan, and China for patients with locally advanced or metastatic ROS1+ NSCLC[1–5]
- In the Phase 2 TRUST-I (NCT04395677) and TRUST-II (NCT04919811) studies, taletrectinib demonstrated robust and durable efficacy and a manageable safety profile in both TKI-naïve and TKI-pretreated patients with ROS1+ NSCLC[6–8]
- Additionally, taletrectinib has shown IC activity and efficacy against the acquired G2032R resistance mutation[6–8]
- Here we report updated data from TRUST-I and TRUST-II, including efficacy across key subgroups

Abbreviations

ALT, alanine aminotransferase; AST, aspartate aminotransferase; c, confirmed; CI, confidence interval; CNS, central nervous system; DOR, duration of response; ECG, electrocardiogram; ECOG PS, Eastern Cooperative Oncology Group performance status; IC, intracranial; IRC, independent review committee; (m)RECIST v1.1, (modified) Response Evaluation Criteria in Solid Tumors version 1.1; mo, months; NA, not available; NGS, next-generation sequencing; NR, not reached; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; ROS1, ROS1 proto-oncogene 1; TEAE, treatment-emergent adverse event; TKI, tyrosine kinase inhibitor.

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Methods

- Study designs for TRUST-I and TRUST-II have been previously reported[9]
- The efficacy population included patients from TRUST-I and TRUST-II who started treatment on taletrectinib 600 mg QD and had ≥1 measurable baseline lesion per RECIST v1.1 by IRC
- Safety was evaluated in patients with ROS1+ NSCLC enrolled in Phase 1 and Phase 2 studies who received ≥1 dose of taletrectinib 600 mg QD

Efficacy Analyses

Patient Demographics and Baseline Characteristics

Baseline Characteristics	TKI-Naïve (n=157)[6,a]	TKI-Pretreated (n=113)[7,a]	Integrated Safety Population (N=363)[6,7]
Median age, years (range)	57.0 (26–83)	53.0 (27–79)	56 (26–83)
Female, n (%)	87 (55.4)	67 (59.3)	206 (56.7)
Asian, n (%)	138 (87.9)	88 (77.9)	263 (72.5)
Stage IV disease, n (%)	143 (91.1)	110 (97.3)	341 (93.9)
ECOG PS 1, n (%)	116 (73.9)	73 (64.6)	244 (67.2)
Never smoker, n (%)	102 (65.0)	78 (69.0)	NA
Prior chemotherapy, n (%)	30 (19.1)	42 (37.2)	NA
Brain metastases,[b] n (%)	37 (23.6)	55 (48.7)	NA
Prior crizotinib / entrectinib, n (%)	–	103 (91.2) / 10 (8.8)[c]	NA

[a]TKI-naïve patients included 103 patients from TRUST-I and 54 patients from TRUST-II; TKI-pretreated patients included 66 patients from TRUST-I and 47 from the registrational cohort 2 of TRUST-II who received one prior TKI. [b]Assessed by IRC per mRECIST v1.1. [c]Two patients were enrolled following crizotinib intolerance and 111 patients were enrolled following disease progression on a prior TKI.

Taletrectinib Demonstrated Robust and Durable Efficacy in TKI-Naïve and TKI-Pretreated Patients With ROS1+ NSCLC

Efficacy[a]	TKI-Naïve (n=157)[6]	TKI-Pretreated (n=113)[7]
Median follow-up, mo	**35.5**	**35.8**
cORR, % (95% CI)	**89.8** (84.0–94.1)	**55.8** (46.1–65.1)[b]
Median DOR,[c] mo (95% CI)	**49.7** (38.6–NR)	**16.6** (10.7–24.9)
Median PFS, mo (95% CI)	**46.1** (31.8–NR)	**9.7** (7.6–12.0)
IC Efficacy[d]	**(n=17)**	**(n=32)**
IC-cORR, % (95% CI)	**76.5** (50.1–93.2)	**65.6** (46.8–81.4)

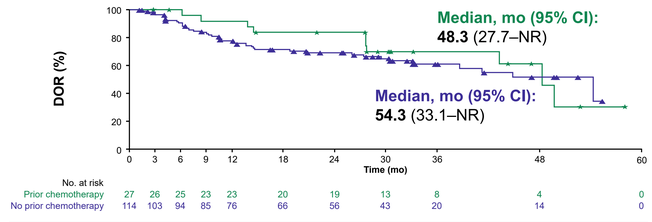
Data cutoff: August 31, 2025. [a]Assessed in patients with ≥1 measurable baseline lesion per RECIST v1.1 by IRC. [b]Responses were observed in 8/12 patients from TRUST-I with G2032R mutations (ORR 66.7% [95% CI 34.9–90.1]). [c]DOR reported only for patients with a complete or partial tumor response. [d]Assessed by IRC per mRECIST v1.1 in patients with ≥1 measurable baseline brain metastasis. Among these, three TKI-naïve patients from TRUST-II and 20 TKI-pretreated patients (eight from TRUST-I and 12 from TRUST-II) had previously received IC radiotherapy.

Efficacy Was Similar Regardless of Prior Chemotherapy

	Prior Chemotherapy	No Prior Chemotherapy
TKI-naïve	**(n=30)**	**(n=127)**
Median follow-up, mo	44.4	35.3
cORR, % (95% CI)	**90.0** (73.5–97.9)	**89.8** (83.1–94.4)
TKI-pretreated	**(n=42)**	**(n=71)**
Median follow-up, mo	36.1	35.8
cORR, % (95% CI)	**59.5** (43.3–74.4)	**53.5** (41.3–65.5)

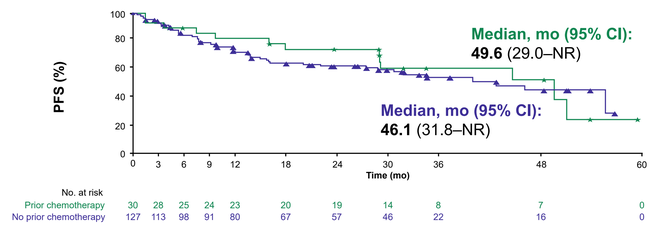
TKI-naïve

TKI-Naïve[a]	Prior Chemotherapy (n=27)	No Prior Chemotherapy (n=114)
Events, n (%)	10 (37.0)	40 (35.1)



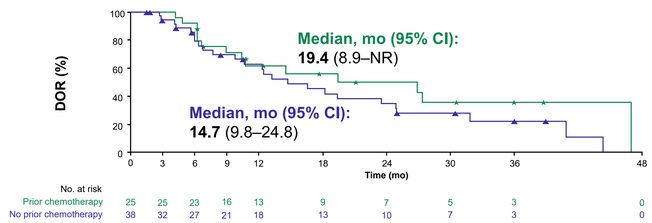
TKI-naïve

TKI-Naïve	Prior Chemotherapy (n=30)	No Prior Chemotherapy (n=127)
Events, n (%)	13 (43.3)	50 (39.4)



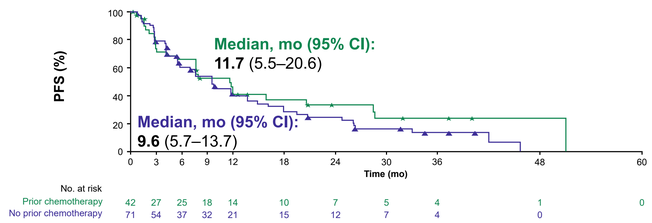
TKI-pretreated

TKI-Pretreated[a]	Prior Chemotherapy (n=25)	No Prior Chemotherapy (n=38)
Events, n (%)	14 (56.0)	25 (65.8)



TKI-pretreated

TKI-Pretreated	Prior Chemotherapy (n=42)	No Prior Chemotherapy (n=71)
Events, n (%)	27 (64.3)	54 (76.1)



Data cutoff: August 31, 2025. [a]DOR reported only for patients with a complete or partial tumor response.

Efficacy Was Similar Regardless of ROS1 Fusion Partner[a]

	CD74 Fusion Partner	Non-CD74 Fusion Partner
TKI-naïve	**(n=19)**	**(n=18)**
Median follow-up, mo	33.1	32.3
cORR, % (95% CI)	**89.5** (66.9–98.7)	**88.9** (65.3–98.6)
Median DOR,[b] mo (95% CI)	**44.8** (26.1–NR)	**43.3** (27.4–NR)
Median PFS, mo (95% CI)	**46.1** (27.4–NR)	**44.6** (15.7–NR)
TKI-pretreated	**(n=20)**	**(n=13)**
Median follow-up, mo	35.1	33.1
cORR, % (95% CI)	**55.0** (31.5–76.9)	**46.2** (19.2–74.9)
Median DOR,[b] mo (95% CI)	**10.7** (2.6–16.6)	**26.8** (4.8–NR)
Median PFS, mo (95% CI)	**7.6** (2.7–13.8)	**7.6** (2.7–NR)

Data cutoff: August 31, 2025. [a]ROS1 fusion partners were assessed by tissue-based NGS where available. [b]DOR reported only for patients with a complete or partial tumor response.

Integrated Safety Analysis (N=363)[6,7]

- As of August 31, 2025, the integrated safety population included 363 TKI-naïve and TKI-pretreated patients with ROS1+ NSCLC from Phase 1 and Phase 2 studies who received ≥1 dose of taletrectinib 600 mg QD
- With longer follow-up, taletrectinib demonstrated a manageable safety profile consistent with prior reports, with no new safety signals identified
- The most common (any-grade) TEAEs were increased AST, increased ALT, diarrhea, nausea, and vomiting, which were mostly low grade
- TEAEs led to dose interruptions in 42.7% of patients, dose reductions in 31.3%, and treatment discontinuations in 8.5%

Common TEAEs With Taletrectinib

Most Common 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)
ECG 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

Data cutoff: August 31, 2025.

Conclusions

- With almost 3 years of follow-up, taletrectinib demonstrated high and durable response rates in both TKI-naïve and TKI-pretreated patients with ROS1+ NSCLC
- Subgroup analyses indicated similar efficacy regardless of prior chemotherapy exposure or ROS1 fusion partners
- With longer follow-up, taletrectinib continued to show a manageable safety profile, with no new safety signals identified

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