Updated Efficacy and Safety of Taletrectinib in Patients With ROS1+ Non-Small Cell Lung Cancer: The Global TRUST-II Study

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TRUST-II[a]: Phase 2 Trial of Taletrectinib in ROS1+ NSCLC

Key Eligibility Criteria

- Locally advanced or metastatic NSCLC with ROS1 fusion
- Age ≥18 years[b]
- ECOG PS 0–1

Cohort 1
TKI-naïve[c]

Cohort 2
TKI-pretreated[c]

Taletrectinib
600 mg QD

Endpoints

Primary:
- IRC-assessed cORR per RECIST v1.1

Secondary:
- DOR
- TTR
- OS
- IC-ORR[d]
- PFS
- Safety[e]

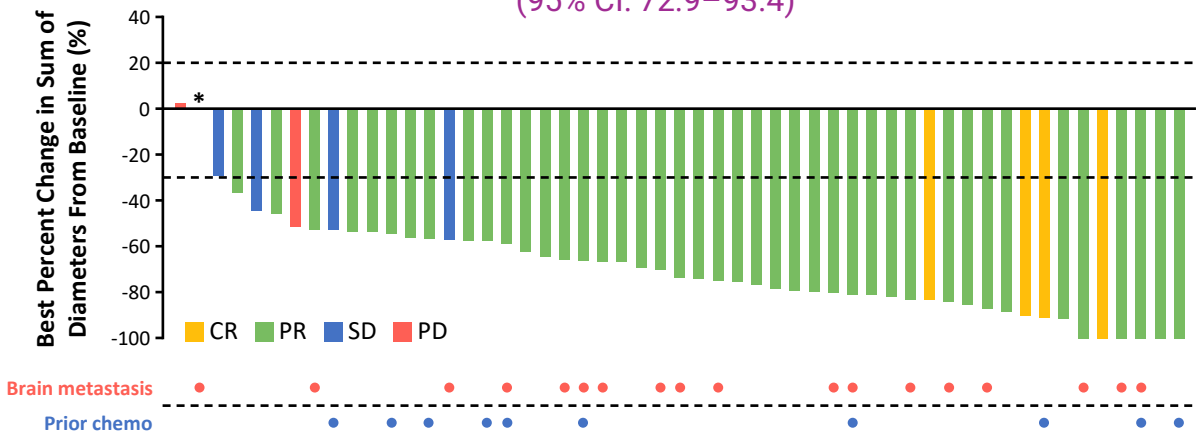
Baseline Characteristics	TKI-naïve (n=55)[c]	TKI-pretreated (n=50)[c]	Safety Population (N=171)[e]
Median age, years (range)	57.0 (27–83)	55.5 (27–79)	57.0 (27–83)
Female, n (%)	31 (56.4)	27 (54.0)	96 (56.1)
Never smoker, n (%)	28 (50.9)	30 (60.0)	95 (55.6)
Region: Asia / non-Asia, n (%)	34 (61.8) / 21 (38.2)	22 (44.0) / 28 (56.0)	74 (43.3) / 97 (56.7)
ECOG PS: 0 / 1, n (%)	22 (40.0) / 33 (60.0)	24 (48.0) / 26 (52.0)	70 (40.9) / 101 (59.1)
Stage IV disease, n (%)	49 (89.1)	49 (98.0)	162 (94.7)
Prior chemotherapy, n (%)	11 (20.0)	19 (38.0)	67 (39.2)
Brain metastases at baseline,[d] n (%)	19 (34.5)	28 (56.0)	78 (45.6)
Prior crizotinib / entrectinib, n (%)	-	40 (80.0) / 10 (20.0)	86 (50.3) / 29 (17.0)

Data cutoff: October 28, 2024. c, confirmed; DOR, duration of response; 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; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; QD, once daily; TKI, tyrosine kinase inhibitor; TTR, time to response.
[a]NCT04919811. [b]Or ≥20 years, as required by local regulations. [c]Registrational cohorts are shown. [d]Assessed by IRC per mRECIST v1.1. [e]Safety population includes all patients who received ≥1 dose of taletrectinib 600 mg.

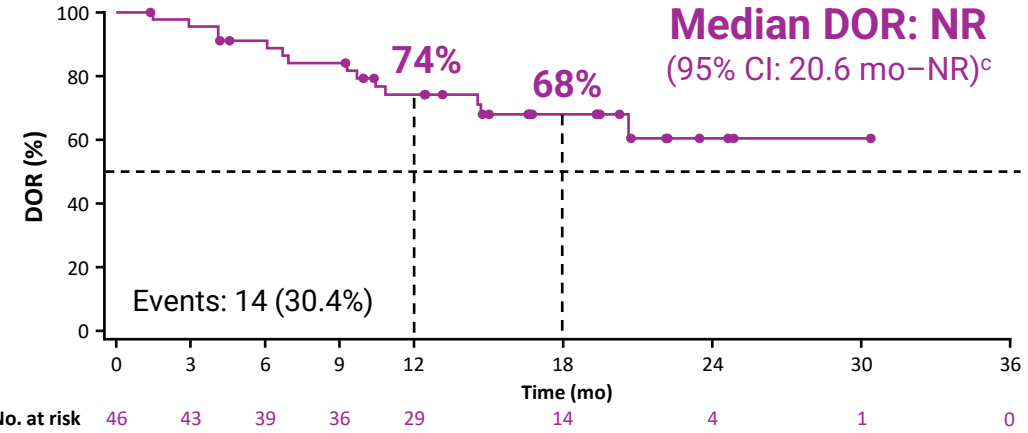
Taletrectinib: Efficacy Outcomes in TKI-naïve ROS1+ NSCLC

TKI-naïve (n=54)[a,b]
Median follow-up: 20.5 mo (range: 8.3–34.5)

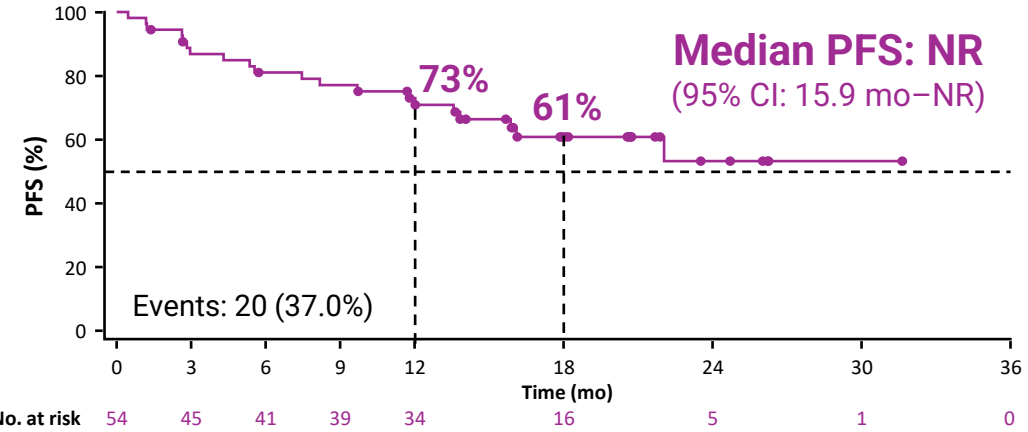
cORR: 85.2%
(95% CI: 72.9–93.4)



Median DOR: NR
(95% CI: 20.6 mo–NR)[c]



Median PFS: NR
(95% CI: 15.9 mo–NR)



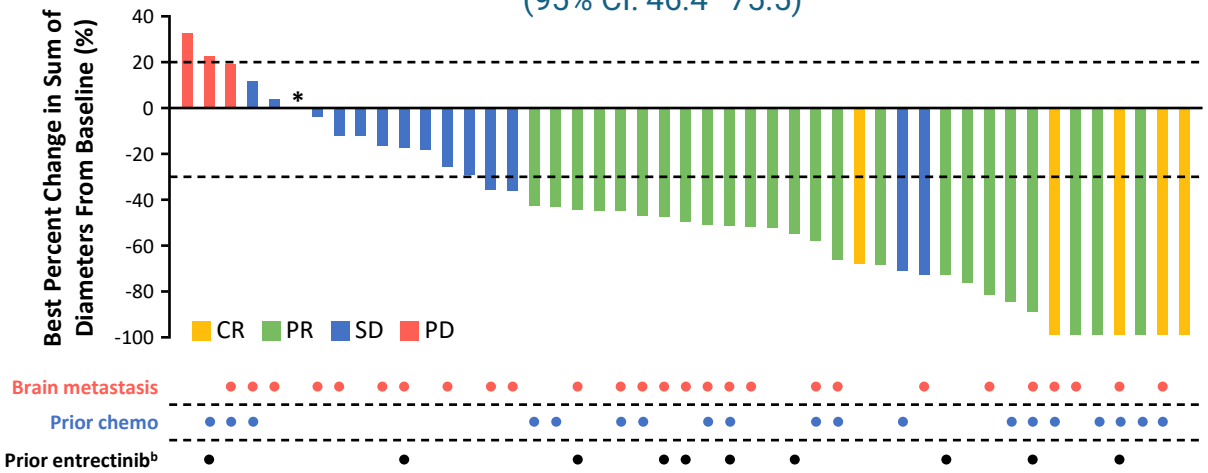
Efficacy	TKI-naïve (n=54)
cORR: prior chemo, yes / no, n/N (%)	9/10 (90.0) / 37/44 (84.1)
Median TTR,[c] mo (95% CI)	1.4 (1.3–1.4)
IC efficacy	**(n=9)[d]**
IC-ORR, % (95% CI)	66.7 (29.9–92.5)

Data cutoff: October 28, 2024. BOR, best overall response; CI, confidence interval; CR, complete response; mo, months; NE, not evaluable; NR, not reached; PD, progressive disease; PR, partial response; SD, stable disease.
[a]Response evaluable population includes patients with ≥1 measurable lesion at baseline who received ≥1 dose of taletrectinib. [b]One patient with cBOR of NE is not shown in the waterfall plot. [c]TTR and DOR reported in responders only.
[d]Patients with ≥1 measurable brain metastasis at baseline. *One patient with cBOR of SD had a best percent change of 0%.

Taletrectinib: Efficacy Outcomes in TKI-pretreated ROS1+ NSCLC

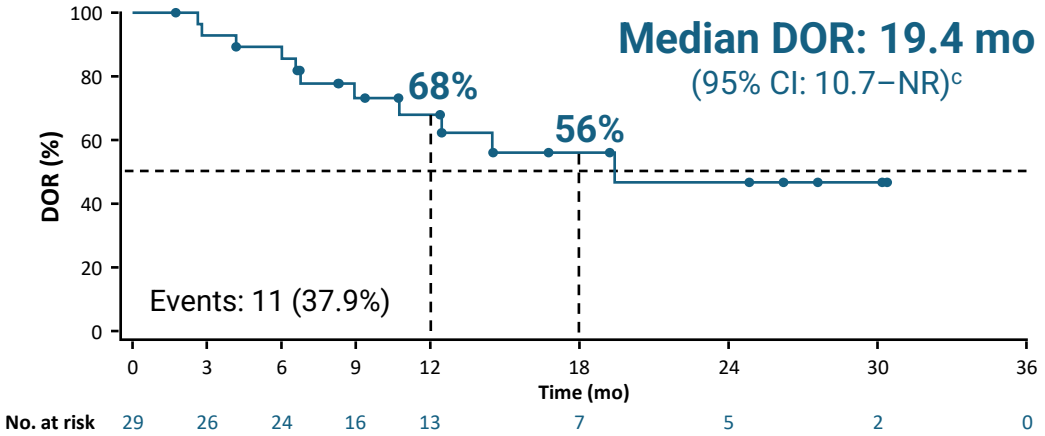
TKI-pretreated (n=47)[a]
Median follow-up: 20.4 mo (range: 8.6–34.5)

cORR: 61.7%
(95% CI: 46.4–75.5)

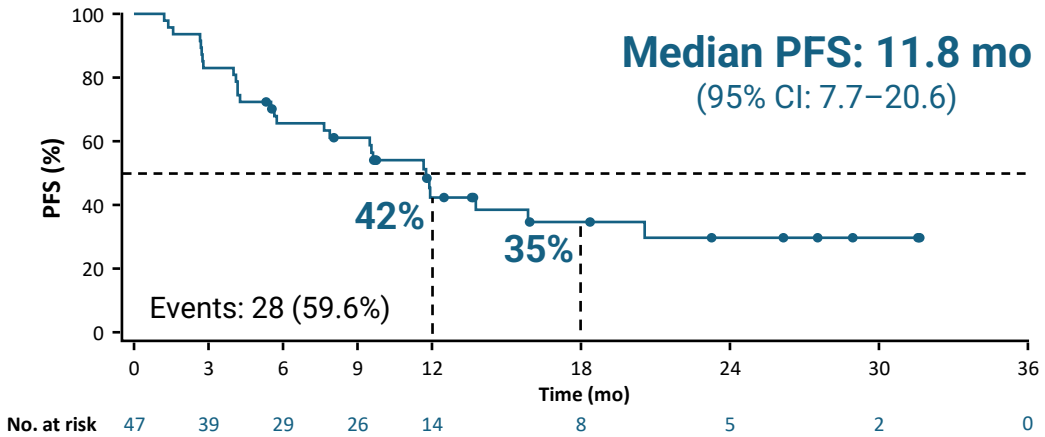


Efficacy	TKI-pretreated (n=47)
cORR: prior chemo, yes / no, n/N (%)	15/19 (78.9) / 14/28 (50.0)
Median TTR,[c] mo (95% CI)	1.4 (1.4–1.6)
IC efficacy	**(n=16)[d]**
IC-ORR, % (95% CI)	56.3 (29.9–80.3)

Median DOR: 19.4 mo
(95% CI: 10.7–NR)[c]



Median PFS: 11.8 mo
(95% CI: 7.7–20.6)



Data cutoff: October 28, 2024. [a]Response evaluable population includes patients with ≥1 measurable lesion at baseline who received ≥1 dose of taletrectinib. [b]All other patients received prior crizotinib. [c]TTR and DOR reported in responders only. [d]Patients with ≥1 measurable brain metastasis at baseline. *One patient with cBOR of SD had a best percent change of 0%.

Taletrectinib Safety: TEAEs in ≥15% of Patients (N=171)[a]

Patients, n (%)	Any grade	Grade ≥3
Any TEAEs	**169 (98.8)**	**90 (52.6)**
Most frequent TEAEs (≥15% of patients)		
Increased ALT	115 (67.3)	26 (15.2)
Increased AST	112 (65.5)	12 (7.0)
Diarrhea	99 (57.9)	1 (0.6)
Nausea	89 (52.0)	3 (1.8)
Vomiting	59 (34.5)	2 (1.2)
Constipation	41 (24.0)	0
Anemia	34 (19.9)	7 (4.1)
Increased blood CPK	34 (19.9)	6 (3.5)
Dysgeusia	33 (19.3)	0
Dizziness	30 (17.5)	0
Electrocardiogram QT prolonged	28 (16.4)	6 (3.5)
Decreased appetite	26 (15.2)	1 (0.6)

- With 5 months of additional follow-up,[1] no new safety signals were identified
- Rates of neurologic TEAEs were low and limited to Grade 1 or 2
  - **Dysgeusia:** 15.2% Grade 1; 4.1% Grade 2
  - **Dizziness:** 15.2% Grade 1; 2.3% Grade 2
- **2.3%** of patients discontinued treatment due to treatment-related AEs
  - No patients in TRUST-II discontinued treatment due to increased ALT or AST

Data cutoff: October 28, 2024. AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; TEAE, treatment-emergent adverse event.
[a]Safety population includes all patients who received ≥1 dose of taletrectinib 600 mg. Median exposure to taletrectinib was 9.7 mo (range: 0.2–31.8).
1. Liu G, et al. *J Thorac Oncol.* 2024;19:S72–S73.

Conclusions

- In the global **TRUST-II study**, taletrectinib demonstrated **high overall and IC response rates** in both TKI-naïve and TKI-pretreated patients with advanced ROS1+ NSCLC
- With 5 months of additional follow-up,[1] **responses remained durable with encouraging PFS;** OS remained immature
- Taletrectinib demonstrated a **favorable safety profile**, with low rates of neurologic AEs and treatment discontinuations
- Post-FDA approval,[2] these results further support taletrectinib as an effective treatment option for patients with advanced ROS1+ NSCLC, regardless of prior TKI exposure

Other presentations on taletrectinib at WCLC 2025

Tuesday 9 September 10:00 AM – 11:30 AM (Poster Session)

TRUST-I study update (P3.12.69), TRUST-III trial in progress (P3.18.62), Clinical pharmacologic characteristics (P3.12.12)

1. Liu G, et al. *J Thorac Oncol.* 2024;19:S72–S73. 2. IBTROZI™ (taletrectinib). Prescribing Information. Nuvation Bio Inc.; 2025.

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