CT244

# Taletrectinib in TKI-Pretreated Patients With ROS1+ Non-Small Cell Lung Cancer: Updated Data From TRUST-I and TRUST-II

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## Background

- 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 or metastatic ROS1+ NSCLC[1–5]
- In the Phase 2 TRUST-I (NCT04395677) and TRUST-II (NCT04919811) studies, taletrectinib demonstrated robust efficacy, including IC activity and efficacy against G2032R mutations, with a manageable safety profile in TKI-naïve and TKI-pretreated patients with ROS1+ NSCLC[6–8]
- Here we report updated efficacy data in TKI-pretreated patients from TRUST-I and TRUST-II, and updated data from an integrated safety analysis

### Abbreviations

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BOR, best overall response; c, confirmed; CI, confidence interval; CNS, central nervous system; CR, complete response; 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; NE, not evaluable; NR, not reached; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; QD, once daily; ROS1, ROS proto-oncogene 1; SD, stable disease; TEAE, treatment-emergent adverse event; TKI, tyrosine kinase inhibitor; US, United States

### References

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## Methods

- The study designs of TRUST-I and TRUST-II have been previously reported[6]
- The efficacy populations reported here include TKI-pretreated patients from TRUST-I and TRUST-II with ≥1 measurable lesion at baseline per RECIST v1.1 by IRC who started treatment on taletrectinib 600 mg QD
- The safety population includes 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

## Efficacy in TKI-Pretreated Patients

### Demographics and Baseline Characteristics for TKI-Pretreated Patients[a]

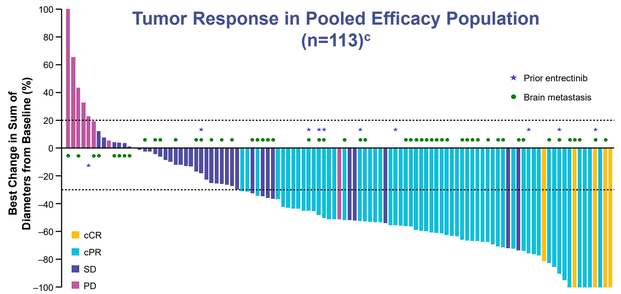
| Baseline Characteristics | TRUST-I (n=67) | TRUST-II (n=50) | Pooled Efficacy Population (N=113)[b] |
|---|---|---|---|
| **Median age, years (range)** | 51.0 (31–77) | 55.5 (27–79) | 53 (27–79) |
| **Female, n (%)** | 41 (61.2) | 27 (54.0) | 67 (59.3) |
| **Asian, n (%)** | 67 (100) | 23 (46.0) | 88 (77.9) |
| **Stage IV disease, n (%)** | 65 (97.0) | 49 (98.0) | 110 (97.3) |
| **ECOG PS 1, n (%)** | 48 (71.6) | 26 (52.0) | 73 (64.6) |
| **Never smoker, n (%)** | 50 (74.6) | 30 (60.0) | 78 (69.0) |
| **Prior chemotherapy, n (%)** | 23 (34.3) | 19 (38.0) | 42 (37.2) |
| **Brain metastases,[c] n (%)** | 28 (41.8) | 28 (56.0) | 55 (48.7) |
| **Prior crizotinib / entrectinib, n (%)** | 67 (100) / 0 | 40 (80.0) / 10 (20.0) | 103 (91.2) / 10 (8.8)[d] |

[a]Patients from TRUST-I and the registrational cohort 2 of TRUST-II who received one prior TKI. [b]Includes patients with ≥1 measurable baseline lesion per RECIST v1.1 by IRC. [c]Assessed by IRC per mRECIST v1.1. [d]Two patients were enrolled following crizotinib intolerance and 111 patients were enrolled following PD on a prior TKI.

### Tumor Response in TKI-Pretreated Patients

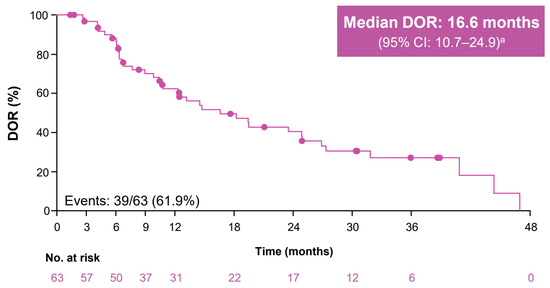
| Efficacy[a] | TRUST-I (n=66) | TRUST-II (n=47) | Pooled Efficacy Population (N=113) |
|---|---|---|---|
| **cORR, %** (95% CI) | **51.5** (38.9–64.0)[b] | **61.7** (46.4–75.5) | **55.8** (46.1–65.1) |
| Prior chemotherapy | (n=23) **43.5** (23.2–65.5) | (n=19) **78.9** (54.4–94.0) | (n=42) **59.5** (43.3–74.4) |

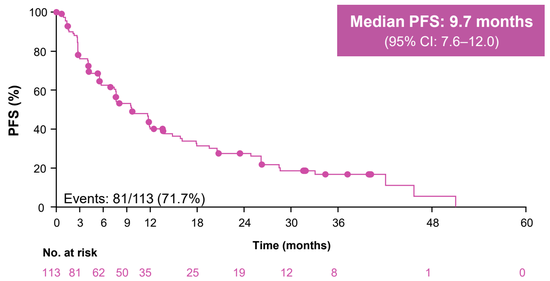
IC efficacy data are shown in the **Supplement**



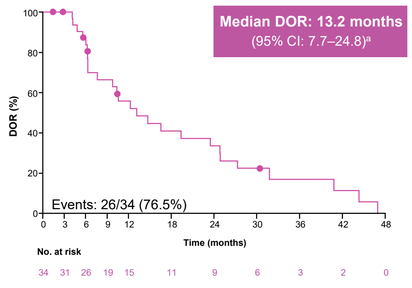

**Data cutoff: August 31, 2025.** [a]Assessed in patients with ≥1 measurable baseline lesion per RECIST v1.1 by IRC. [b]Responses were observed in 8/12 patients from TRUST-I with G2032R mutations (ORR 66.7% [95% CI: 34.9–90.1]). [c]One patient had a change of 136.5%, which is truncated at 100%. Six patients with cBOR of NE are not shown in the figure.

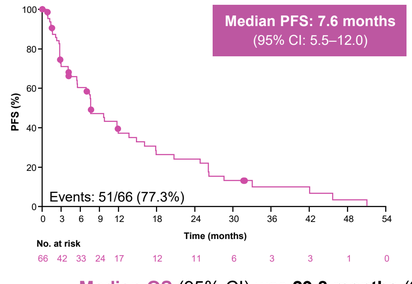
### Pooled (N=113) — Median follow-up: 35.8 months



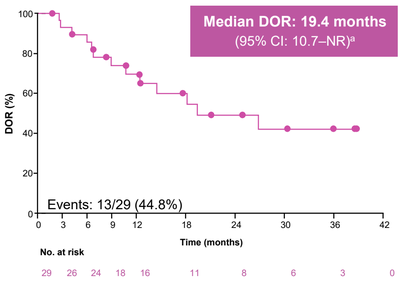



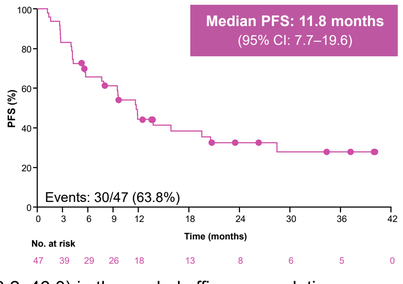

### TRUST-I (n=66) — Median follow-up: 45.2 months




### TRUST-II (n=47) — Median follow-up: 30.5 months




**Data cutoff: August 31, 2025.** [a]DOR reported only for patients with a CR or PR.

**Median OS** (95% CI) was **29.8 months** (23.2–46.0) in the pooled efficacy population, **25.6 months** (19.2–31.9) in TRUST-I, and **NR** (23.2–NR) in TRUST-II (**Supplement**)

## Integrated Safety Analysis (N=363)

- 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 (**Supplement**)
- With longer follow-up, no new safety signals were identified, and safety was consistent between the integrated safety population and TKI-pretreated patients (**Supplement**)
- The most common (any-grade) TEAEs were increased AST, increased ALT, diarrhea, nausea, and vomiting (**Supplement**)
- TEAEs led to dose interruptions in 42.7% of patients, dose reductions in 31.3%, and treatment discontinuations in 8.5%

## Conclusions

- With ~3 years of follow-up in the pooled analysis of TRUST-I and TRUST-II, taletrectinib maintained durable responses in TKI-pretreated patients with ROS1+ NSCLC
- With longer follow-up, taletrectinib demonstrated a manageable safety profile, with no new safety signals
- These data support taletrectinib as an effective and tolerable treatment option for patients with ROS1+ NSCLC after prior TKI therapy



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# IC Efficacy in TKI-Pretreated Patients

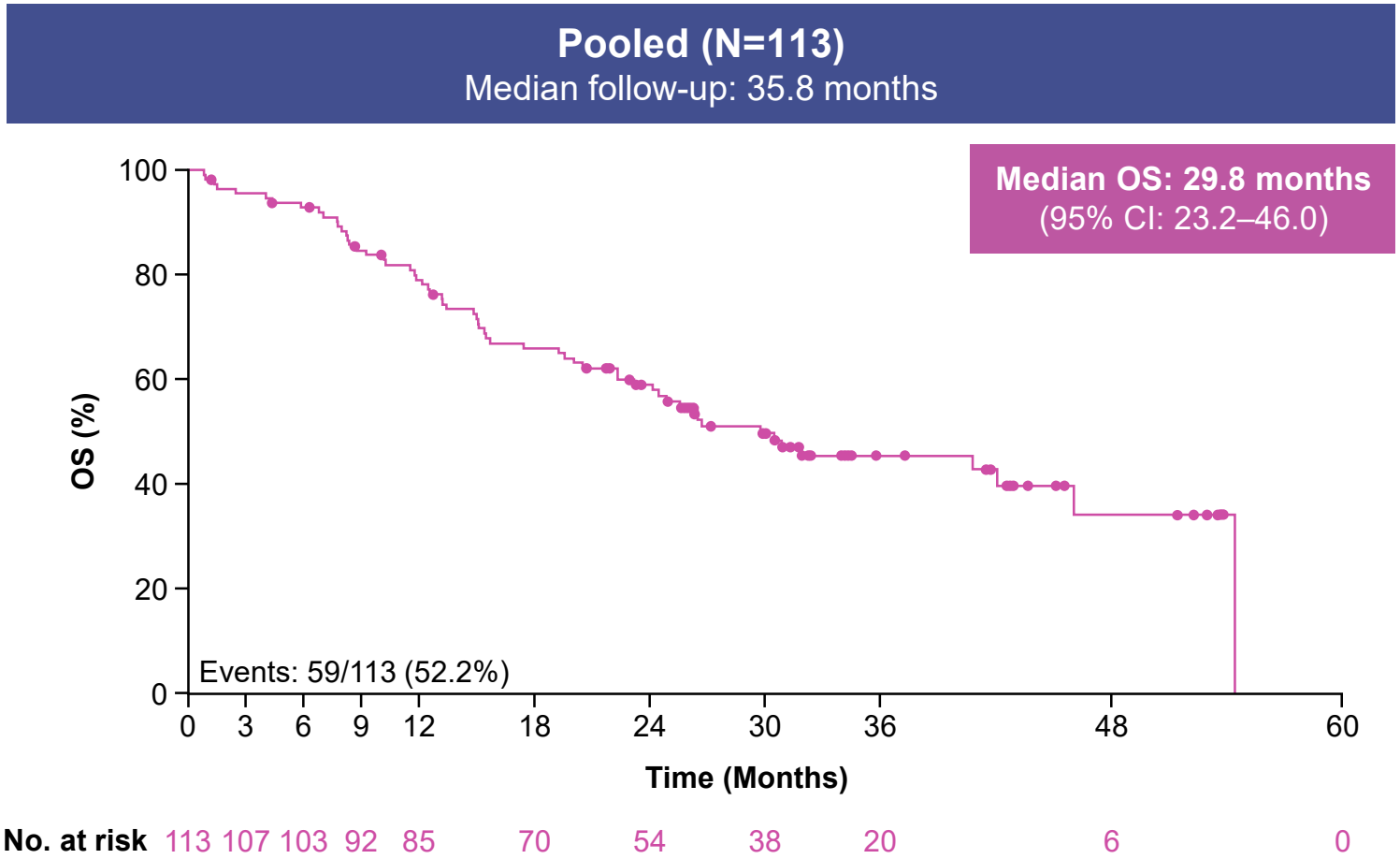
| IC Efficacy[a] | TRUST-I (n=16) | TRUST-II (n=16) | Pooled Efficacy Population (n=32) |
|---|---|---|---|
| **IC-cORR, %** (95% CI) | **75.0** (47.6–92.7) | **56.3** (29.9–80.3) | **65.6** (46.8–81.4) |

**Data cutoff: August 31, 2025.**

[a]Assessed by IRC per mRECIST v1.1 in patients with ≥1 measurable baseline brain metastasis. Among these, eight patients from TRUST-I and 12 from TRUST-II had been previously treated with IC radiotherapy.

c, confirmed; CI, confidence interval; IC, intracranial; IRC, independent review committee; mRECIST v1.1, modified Response Evaluation Criteria in Solid Tumors version 1.1; ORR, objective response rate; TKI, tyrosine kinase inhibitor.

# OS in TKI-Pretreated Patients From the Pooled Efficacy Analysis

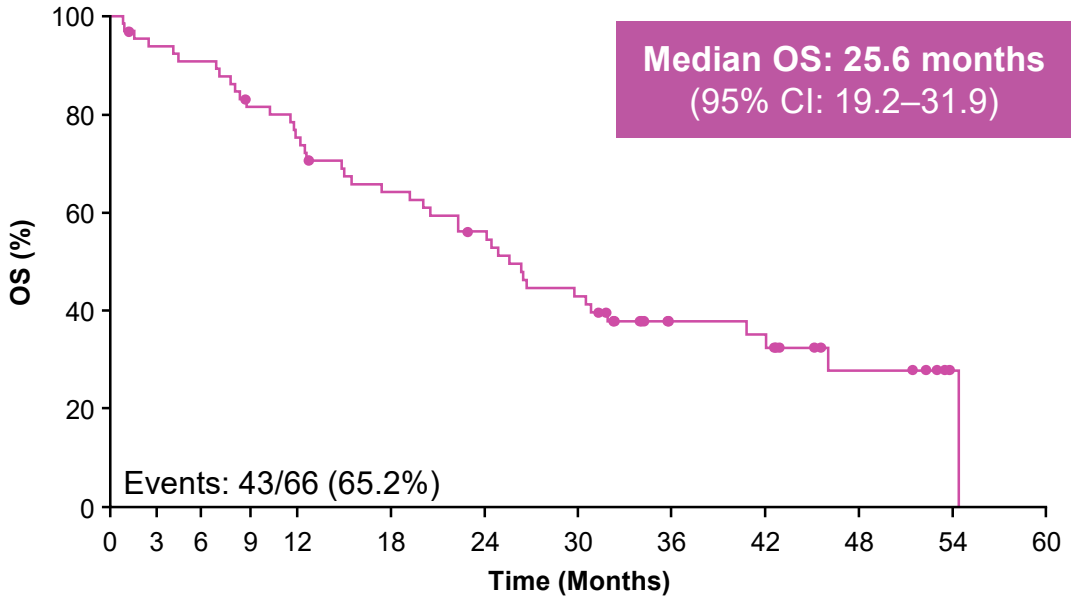



**Data cutoff: August 31, 2025.**

CI, confidence interval; OS, overall survival; TKI, tyrosine kinase inhibitor.

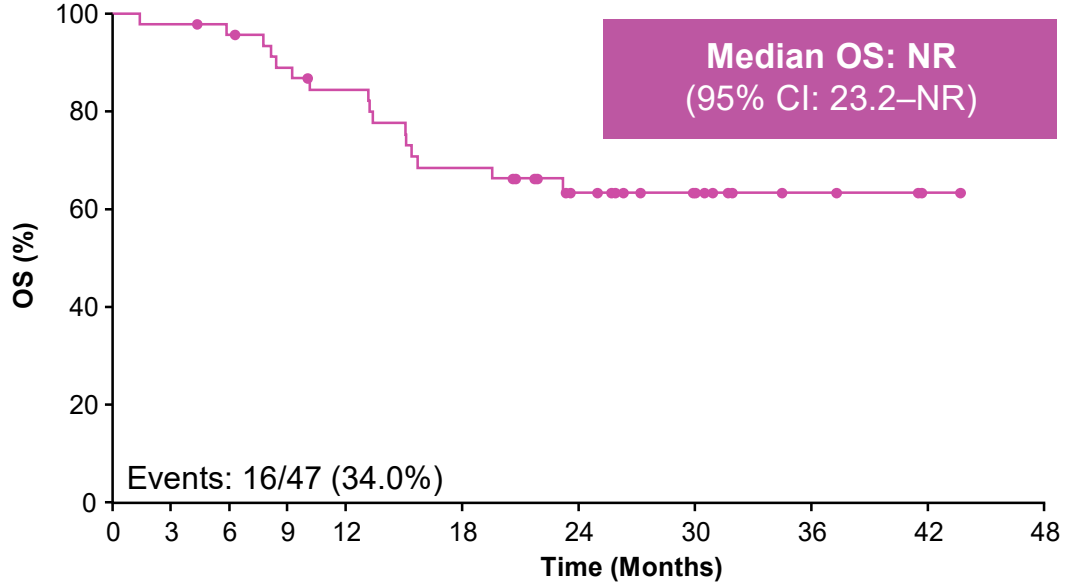
# OS in TKI-Pretreated Patients From TRUST-I and TRUST-II

## TRUST-I (n=66)
Median follow-up: 45.2 months




| No. at risk | 66 | 61 | 59 | 52 | 48 | 40 | 34 | 26 | 14 | 13 | 6 | 1 | 0 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

## TRUST-II (n=47)
Median follow-up: 30.5 months




| No. at risk | 47 | 46 | 44 | 40 | 37 | 30 | 20 | 12 | 6 | 1 |
|---|---|---|---|---|---|---|---|---|---|---|

**Data cutoff: August 31, 2025.**
CI, confidence interval; NR, not reached; OS, overall survival; TKI, tyrosine kinase inhibitor.

# Integrated Safety Population (N=363)[a]

| Baseline Characteristics | Integrated Safety Population (N=363) |
|---|---|
| **Median age, years (range)** | 56.0 (26–83) |
| **Female, n (%)** | 206 (56.7) |
| **Stage IV disease, n (%)** | 341 (93.9) |
| **ECOG PS 1, n (%)** | 244 (67.2) |

| Most Frequent TEAEs (≥20% of Patients), n (%) | Integrated Safety Population (N=363) | | TKI-Pretreated (n=182)[b] | |
|---|---|---|---|---|
| | Any Grade | Grade ≥3 | Any Grade | Grade ≥3 |
| **AST increased** | 261 (71.9) | 30 (8.3) | 120 (65.9) | 11 (6.0) |
| **ALT increased** | 248 (68.3) | 40 (11.0) | 116 (63.7) | 16 (8.8) |
| **Diarrhea** | 234 (64.5) | 9 (2.5) | 116 (63.7) | 3 (1.6) |
| **Nausea** | 174 (47.9) | 5 (1.4) | 91 (50.0) | 2 (1.1) |
| **Vomiting** | 164 (45.2) | 5 (1.4) | 83 (45.6) | 2 (1.1) |
| **Anemia** | 139 (38.3) | 15 (4.1) | 56 (30.8) | 7 (3.8) |
| **Dizziness** | 78 (21.5) | 1 (0.3) | 26 (14.3) | 0 |
| **Electrocardiogram QT prolonged** | 76 (20.9) | 13 (3.6) | 30 (16.5) | 5 (2.7) |
| **Constipation** | 74 (20.4) | 0 | 32 (17.6) | 0 |
| **Blood creatinine increased** | 73 (20.1) | 0 | 29 (15.9) | 0 |

**Data cutoff: August 31, 2025.**

[a]The integrated safety population includes TKI-naïve and TKI-pretreated patients with ROS1+ NSCLC who received ≥1 dose of taletrectinib 600 mg QD from Phase 2 trials (TRUST-I and TRUST-II) and a Phase 1 trial (J102). [b]Patients may have received ≥1 prior TKI.

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