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 (NCT04919811): Phase 2 Trial of Taletrectinib in ROS1+ NSCLC[a]

Key Eligibility Criteria

Inclusion Criteria:

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

Cohort 1: ROS1 TKI naive
Taletrectinib 600 mg QD

Cohort 2: 1 Prior ROS1 TKI
Taletrectinib 600 mg QD

Endpoints

Primary:

- IRC-assessed cORR per RECIST v1.1

Secondary:

- DOR
- BOR
- TTR
- Safety[c]
- IC-ORR
- DCR
- PFS

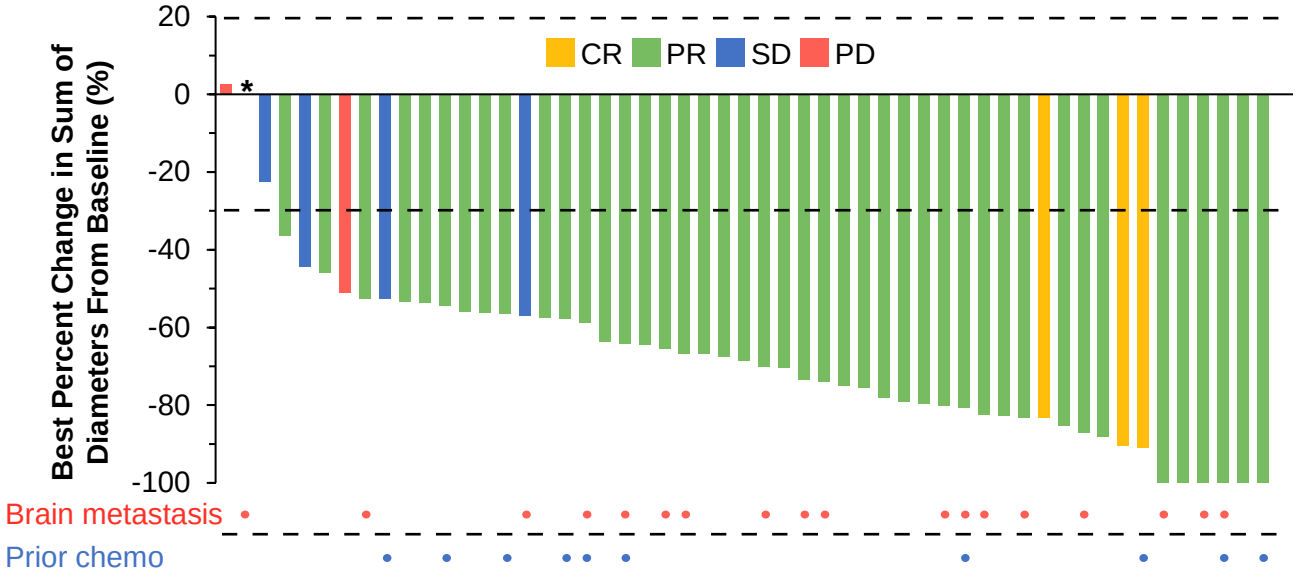
Category	TKI Naive (n=55)[a]	TKI Pretreated (n=50)[a]	Overall (N=159)[c]
Median age, years (range)	57.0 (27–82)	55.0 (27–79)	57.0 (27–83)
Female, n (%)	31 (56.4)	27 (54.0)	89 (56.0)
Never smoker, n (%)	28 (50.9)	30 (60.0)	90 (56.6)
Region, Asia/Non-Asia, n (%)	34 (61.8)/21 (38.2)	22 (44.0)/28 (56.0)	74 (46.5)/85 (53.5)
ECOG PS 0/1, n (%)	22 (40.0)/33 (60.0)	24 (48.0)/26 (52.0)	66 (41.5)/93 (58.5)
Stage IV disease, n (%)	49 (89.1)	49 (98.0)	151 (95.0)
Prior anticancer chemotherapy, n (%)	11 (20.0)	19 (38.0)	64 (40.3)
Brain metastasis, n (%)	19 (34.5)	28 (56.0)	72 (45.3)
Prior crizotinib/entrectinib, n (%)	–	40 (80.0)/10 (20.0)	82 (51.6)/27 (17.0)

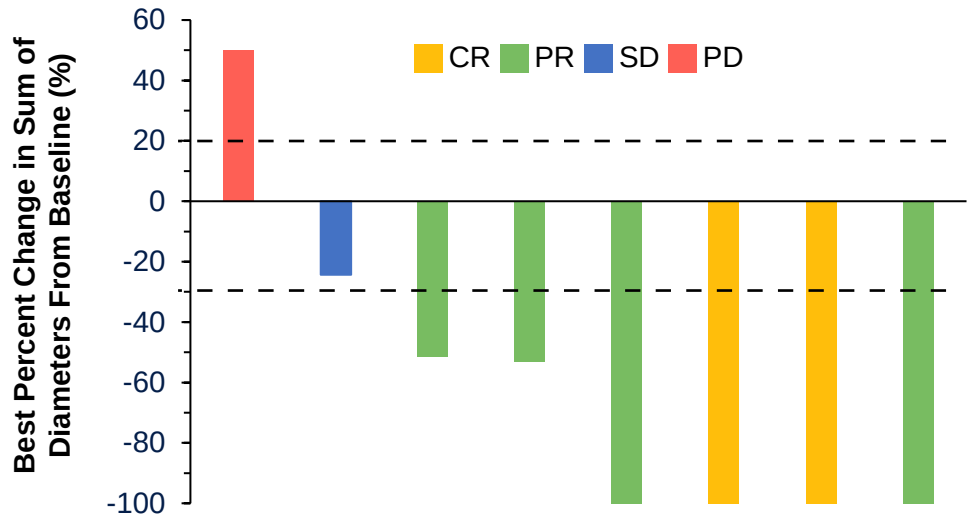
Data cutoff: June 7, 2024. [a]Registrational cohorts are shown. [b]Or ≥20 years, as required by local regulations. [c]Safety population includes all patients who received ≥1 dose of taletrectinib 600 mg. BOR, best overall response; cORR, confirmed objective response rate; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IC, intracranial; IRC, independent review committee; NSCLC, non–small cell lung cancer; PFS, progression-free survival; QD, every day; RECIST, Response Evaluation Criteria in Solid Tumors; TKI, tyrosine kinase inhibitor; TTR, time to response.

Taletrectinib Responses in TKI-Naive ROS1+ NSCLC[a,b]

	TKI Naive (n=54)
cORR, % (95% CI)	85.2 (72.88, 93.38)
Asia ORR (n=33)	87.9 (71.80, 96.60)
Non-Asia ORR (n=21)	81.0 (58.09, 94.55)

Measurable baseline brain metastases	TKI Naive (n=9)
IC-ORR, % (95% CI)	66.7 (29.93, 92.51)
CR, n (%)	2 (22.2)
PR, n (%)	4 (44.4)





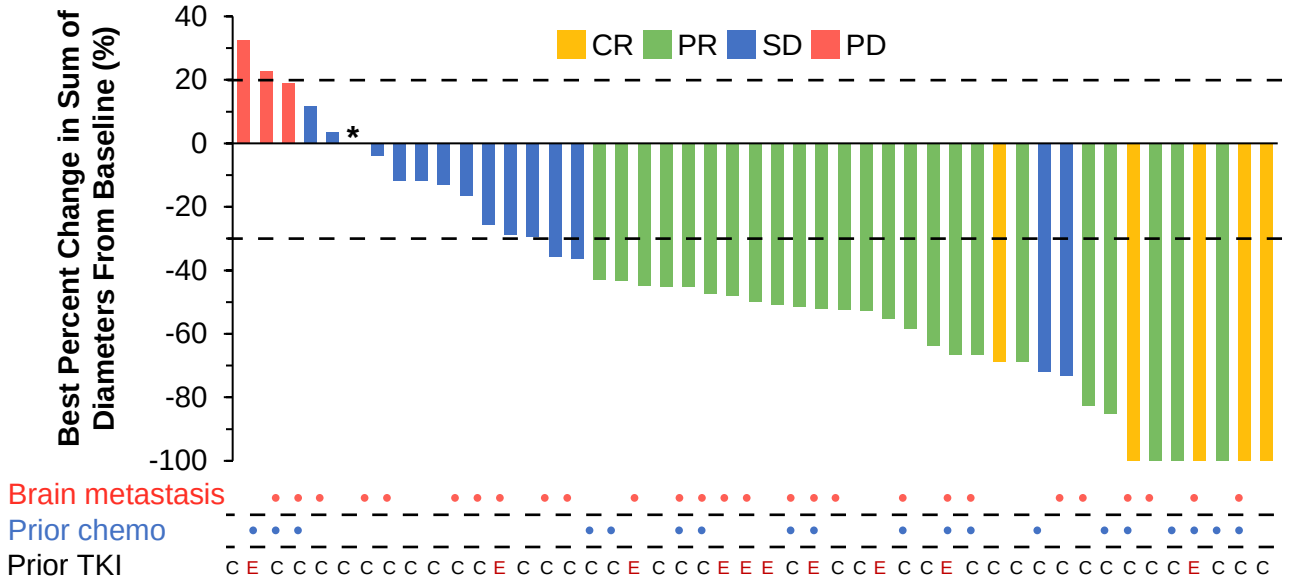
Median follow-up: 15.8 mo (range: 3.6–29.8)

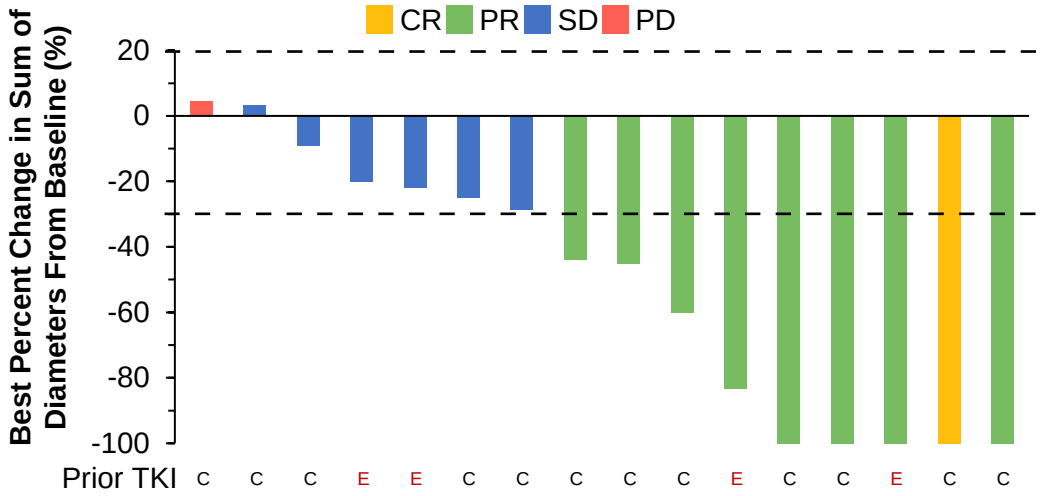
Data cutoff: June 7, 2024. [a]Response evaluable population (patients with ≥1 measurable lesion at baseline who received ≥1 dose of taletrectinib). [b]Patients with confirmed BOR as not evaluable are not displayed in the waterfall plots. *One patient had a best percent change of 0%. BOR, best overall response; CI, confidence interval; cORR, confirmed objective response rate; CR, complete response; IC, intracranial; DOR, duration of response; NR, not reached; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; TKI, tyrosine kinase inhibitor.

Taletrectinib Responses in TKI-Pretreated ROS1+ NSCLC[a,b]

	TKI Pretreated (n=47)
cORR, % (95% CI)	61.7 (46.38, 75.49)
Asia ORR (n=21)	57.1 (34.02, 78.18)
Non-Asia ORR (n=26)	65.4 (44.33, 82.79)

Measurable baseline brain metastases	TKI Pretreated (n=16)
IC-ORR, % (95% CI)	56.3 (29.88, 80.25)
CR, n (%)	1 (6.3)
PR, n (%)	8 (50.0)





Median follow-up: 15.7 mo (range: 3.9–29.8)

Data cutoff: June 7, 2024. [a]Response evaluable population (patients with ≥1 measurable lesion at baseline who received ≥1 dose of taletrectinib). [b]Patients with confirmed BOR as not evaluable are not displayed in the waterfall plots. *One patient had a best percent change of 0%. C, crizotinib; CI, confidence interval; cORR, confirmed objective response rate; CR, complete response; E, entrectinib; IC, intracranial; DOR, duration of response; NR, not reached; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; TKI, tyrosine kinase inhibitor.

Taletrectinib Safety: TEAEs in ≥15% of Patients (N=159)

	Any grade, n (%)	Grade ≥3, n (%)
Increased ALT	108 (67.9)	24 (15.1)
Increased AST	107 (67.3)	11 (6.9)
Diarrhea	90 (56.6)	1 (0.6)
Nausea	82 (51.6)	3 (1.9)
Vomiting	53 (33.3)	2 (1.3)
Constipation	40 (25.2)	0 (0)
Anemia	32 (20.1)	7 (4.4)
Dysgeusia	31 (19.5)	0 (0)
Increased blood CPK	29 (18.2)	6 (3.8)
Dizziness	27 (17.0)	0 (0)
Prolonged QT	24 (15.1)	5 (3.1)

- Median exposure of taletrectinib was 8.4 months (range: 0.1–28.9)
- 37.1% of patients had a TEAE leading to a dose reduction
  - The most common events leading to dose reduction were elevated liver enzymes (16.4%)
- 7.5% of patients had a TEAE leading to treatment discontinuation; 1.3% were treatment-related
- Rates of neurologic TEAEs were low (dysgeusia: 19.5%; dizziness: 17.0%); none were grade ≥3
- No treatment-related AE led to death

Data cutoff: June 7, 2024. AE, adverse event; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatinine phosphokinase; TEAE, treatment-emergent adverse event.

Conclusions

- With full enrollment of patients in geographically diverse regions, taletrectinib continues to demonstrate meaningful efficacy in both TKI-naive and TKI-pretreated patients with ROS1+ NSCLC
  - Robust overall and intracranial responses were observed
  - Comparable efficacy between patients in Asia vs non-Asia
  - At the time of analysis, DOR and PFS were immature for both cohorts
- Taletrectinib demonstrated a favorable safety profile
  - Treatment discontinuations due to TEAEs were low
  - The rate of neurologic TEAEs was low and most were grade 1–2
  - No treatment-related death
- The efficacy and safety of taletrectinib in the global TRUST-II trial remains highly consistent with findings from the regional TRUST-I trial

DOR, duration of response; IC, intracranial; NSCLC, non–small cell lung cancer; PFS, progression-free survival; TKI, tyrosine kinase inhibitor; TEAE, treatment-emergent adverse event.

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