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Updated Efficacy and Safety of Taletrectinib in Chinese Patients With ROS1+ Non-Small Cell Lung Cancer: Phase 2 TRUST-I Study

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Background

- Taletrectinib is a next-generation, CNS-active, selective, oral ROS1 inhibitor with efficacy against the G2032R resistance mutation[1]
- Taletrectinib is currently approved in China and the United States for the treatment of adult patients with locally advanced or metastatic ROS1+ NSCLC[2,3]
- Taletrectinib demonstrated robust efficacy and favorable safety in patients with advanced or metastatic ROS1+ NSCLC from two Phase 2 studies: TRUST-I (NCT04395677) and TRUST-II (NCT04919811)[4–6]
- Here, we report updated efficacy data from the TRUST-I study, as well as safety 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; IQR, interquartile range; IRC, Independent Review Committee; mo, months; (m)RECIST v1.1, (modified) Response Evaluation Criteria in Solid Tumors version 1.1; NA, not available; 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; TRAE, treatment-related adverse event; TKI, tyrosine kinase inhibitor

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Methods

- The TRUST-I study design has been previously published[4]
- Efficacy is reported for patients with ROS1+ NSCLC who started treatment on taletrectinib 600 mg QD from TRUST-I with 11 months of additional follow-up[4]
- An integrated safety analysis is also reported for patients with ROS1+ NSCLC who received ≥1 dose(s) of taletrectinib 600 mg in Phase 1 or Phase 2 trials

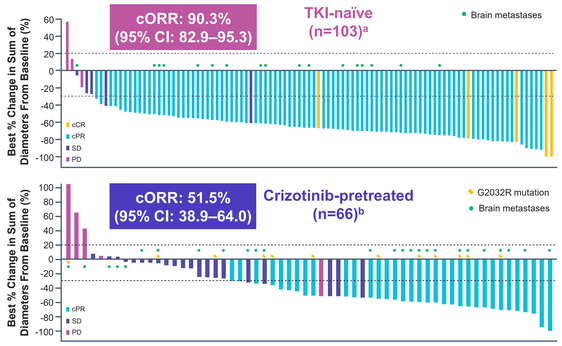
TRUST-I: Efficacy

Patient Demographics and Baseline Characteristics

Baseline Characteristics	TRUST-I		Integrated Safety Analysis (N=337)
	TKI-naïve (n=103)	Crizotinib-pretreated (n=67)	
Median age, years (range)	56 (26–78)	51 (31–77)	56 (26–83)
Female, n (%)	57 (55.3)	41 (61.2)	190 (56.4)
Stage IV disease, n (%)	94 (91.3)	65 (97.0)	318 (94.4)
ECOG PS 1, n (%)	83 (80.6)	48 (71.6)	228 (67.7)
Never smoker, n (%)	75 (72.8)	50 (74.6)	NA
Prior chemotherapy, n (%)	20 (19.4)	23 (34.3)	NA
Brain metastases,[a] n (%)	18 (17.5)	28 (41.8)	NA

[a]Assessed by IRC per mRECIST v1.1.

cORR by IRC According to RECIST v1.1

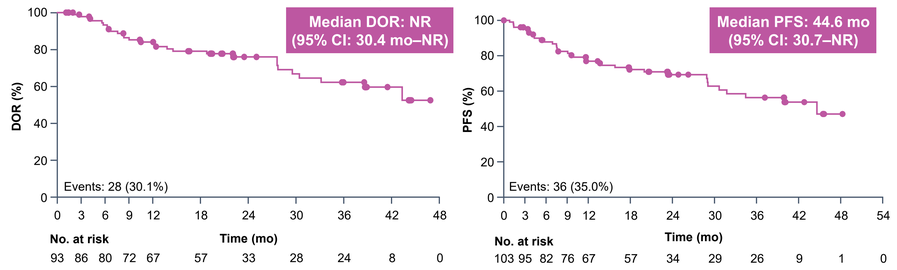


Data cutoff: October 28, 2024. [a]Two patients with confirmed BOR of NE are not shown in the figure. [b]One patient was excluded due to the presence of secondary cancer. One patient had a change of 136.5% which was cut at 100%. Six patients with confirmed BOR of NE are not shown in the figure.

Efficacy	TKI-naïve	Crizotinib-pretreated
cORR: G2032R mutations, % (95% CI)	–	(n=12) 66.7 (34.9–90.1)
cORR: Prior chemotherapy, % (95% CI)	(n=20) 85.0 (62.1–96.8)	(n=23) 43.5 (23.2–65.5)
IC efficacy[a]	**(n=8)**	**(n=16)**
IC-ORR, % (95% CI)	87.5 (47.4–99.7)	75.0 (47.6–92.7)

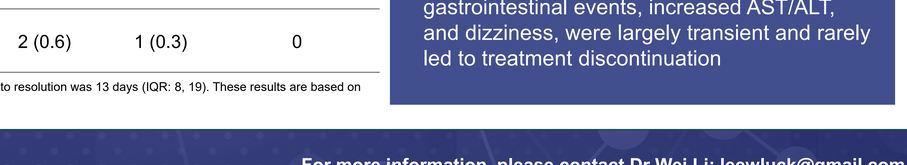
[a]Assesed by IRC per mRECIST v1.1 in patients with ≥1 measurable baseline brain metastasis.

DOR and PFS in TKI-naïve Patients (n=103)



Median follow-up: 40.9 mo (range, 22.0–50.1).

DOR and PFS in Crizotinib-pretreated Patients (n=66)



Median follow-up: 35.1 mo (range, 21.5–50.1).

- Median OS was NR for TKI-naïve patients and 25.6 mo for crizotinib-pretreated patients

Integrated Safety Analysis (N=337)

- The integrated safety analysis includes 337 patients with ROS1+ NSCLC from two Phase 2 trials (TRUST-I and TRUST-II) and a Phase 1 trial (J102)

Safety data from TRUST-I are available in the supplement, with no new safety signals identified with 11 months of additional follow-up

Overall Safety Summary (N=337)

Patients, n (%)	N=337
Any TEAEs	336 (99.7)
Any TRAEs	334 (99.1)
Serious TEAEs	103 (30.6)
Serious TRAEs	25 (7.4)
TEAEs leading to dose interruption	137 (40.7)
TRAEs leading to dose interruption	91 (27.0)
TEAEs leading to dose reduction	97 (28.8)
TRAEs leading to dose reduction	93 (27.6)
TEAEs leading to treatment discontinuation	22 (6.5)
TRAEs leading to treatment discontinuation	8 (2.4)

Data cutoff: June 7, 2024. Longer follow-up was not available at time of analysis after completion of the J102 trial.

TEAEs of Clinical Interest (N=337)

TEAE	Any Grade, n (%)	Median Time to Onset, Days (IQR)	Median Time to Resolution, Days (IQR)	Dose Interruption, n (%)	Dose Reduction, n (%)	Treatment Discontinuation, n (%)
Increased AST	256 (76.0)	16 (8, 43)[a]	50 (29, 148)[a]	23 (6.8)	17 (5.0)	1 (0.3)
Increased ALT				23 (6.8)	29 (8.6)	
Diarrhea	213 (63.2)	2 (1, 15)	1 (1, 3)	6 (1.8)	8 (2.4)	0
Nausea	159 (47.2)	2 (1, 13)	3 (1, 46)	5 (1.5)	4 (1.2)	0
Vomiting	146 (43.3)	3 (1, 35)	1 (1, 3)	10 (3.0)	5 (1.5)	0
Dizziness	71 (21.1)	34 (3, 199)	3 (1, 47)	2 (0.6)	1 (0.3)	0

[a]Median time to onset for Grade ≥3 increased AST/ALT was 43 days (IQR: 22, 86) and median time to resolution was 13 days (IQR: 8, 19). These results are based on laboratory data.

Conclusions

- In the TRUST-I study, taletrectinib continued to demonstrate meaningful efficacy in both TKI-naïve and crizotinib-pretreated patients with ROS1+ NSCLC
- High and durable response rates were observed, including high IC-ORR, efficacy against the G2032R resistance mutation, and encouraging PFS, regardless of line of therapy
- Taletrectinib demonstrated a favorable safety profile, with no new safety signals identified
- TEAEs of clinical interest, such as gastrointestinal events, increased AST/ALT, and dizziness, were largely transient and rarely led to treatment discontinuation

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TRUST-I: Baseline Characteristics

- Safety data reported here are for all patients from TRUST-I who received ≥1 dose(s) of taletrectinib

Baseline characteristics	Overall (N=173)
Median age, years (range)	55 (26–78)
Female, n (%)	100 (57.8)
Stage IV disease, n (%)	162 (93.6)
ECOG PS 1, n (%)	134 (77.5)
Never smoker, n (%)	128 (74.0)
Prior chemotherapy, n (%)	45 (26.0)
Brain metastases,[a] n (%)	46 (26.6)

[a]Assessed by IRC per mRECIST v1.1.
ECOG PS, Eastern Cooperative Oncology Group Performance Status; IRC, Independent Review Committee; mRECIST v1.1, modified Response Evaluation Criteria in Solid Tumors version 1.1.

TRUST-I Safety: TEAEs in ≥15% of Patients (N=173)[a]

Most frequent TEAEs (≥15% of patients), n (%)	Any Grade	Grade 1	Grade 2	Grade ≥3
Increased AST	131 (75.7)	90 (52.0)	26 (15.0)	15 (8.7)
Diarrhea	121 (69.9)	99 (57.2)	16 (9.2)	6 (3.5)
Increased ALT	117 (67.6)	80 (46.2)	27 (15.6)	10 (5.8)
Vomiting	94 (54.3)	76 (43.9)	16 (9.2)	2 (1.2)
Anemia	92 (53.2)	55 (31.8)	32 (18.5)	5 (2.9)
Nausea	74 (42.8)	64 (37.0)	8 (4.6)	2 (1.2)
Neutrophil count decreased	47 (27.2)	26 (15.0)	11 (6.4)	10 (5.8)
White blood cell count decreased	47 (27.2)	29 (16.8)	15 (8.7)	3 (1.7)
Blood bilirubin increased	46 (26.6)	35 (20.2)	8 (4.6)	3 (1.7)
Electrocardiogram QT prolonged	44 (25.4)	33 (19.1)	4 (2.3)	7 (4.0)
Dizziness	44 (25.4)	38 (22.0)	5 (2.9)	1 (0.6)
Blood creatinine increased	40 (23.1)	37 (21.4)	3 (1.7)	0
Weight increased	40 (23.1)	17 (9.8)	19 (11.0)	4 (2.3)
Proteinuria	40 (23.1)	35 (20.2)	5 (2.9)	0
Weight decreased	37 (21.4)	20 (11.6)	16 (9.2)	1 (0.6)
Hyperuricemia	36 (20.8)	34 (19.7)	2 (1.2)	0
Hypercholesterolemia	34 (19.7)	29 (16.8)	5 (2.9)	0
Decreased appetite	32 (18.5)	29 (16.8)	3 (1.7)	0
Bilirubin conjugated increased	30 (17.3)	22 (12.7)	5 (2.9)	3 (1.7)
Constipation	30 (17.3)	28 (16.2)	2 (1.2)	0
Hypertriglyceridemia	29 (16.8)	26 (15.0)	3 (1.7)	0
COVID-19	28 (16.2)	10 (5.8)	15 (8.7)	3 (1.7)
Urinary tract infection	28 (16.2)	20 (11.6)	8 (4.6)	0
Pyrexia	28 (16.2)	24 (13.9)	3 (1.7)	1 (0.6)
Rash	27 (15.6)	17 (9.8)	7 (4.0)	3 (1.7)
Blood creatine phosphokinase increased	26 (15.0)	20 (11.6)	6 (3.5)	0

Data cutoff: October 28, 2024.

[a]Safety is reported for all patients who received ≥1 dose(s) of taletrectinib.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; TEAE, treatment-emergent adverse event.