Subgroup Analysis of Japanese Patients in the Phase II Study of Taletrectinib in Patients with ROS1+ NSCLC: The Global TRUST-II Study

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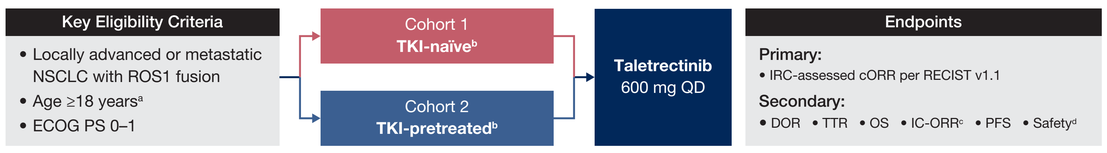
Background & Methods

- Taletrectinib is an oral, CNS-active, selective next-generation ROS1 inhibitor that is approved for use in Japan, China, and USA.
- TRUST-II is a global, multicenter, single-arm pivotal phase 2 study of taletrectinib once-daily in ROS1+ tumors composed of several cohorts (cohort 1-5) (NCT04919811).
- This analysis was conducted based on a further 5 months of follow-up data since our publication was published (cutoff: October 2024)[1]. Median follow-up was 20.5 months (range: 8.3–34.5) for TKI-naïve cohort and 20.4 months (range: 8.6–34.5) for TKI-pretreated cohort.
- Among the 105 patients enrolled globally in the registrational cohorts (cohort 1 and 2), 25 (24%) were Japanese, providing a sufficient dataset to explore potential ethnic differences in efficacy and safety compared with the overall population. Here, we report updated efficacy (cohort 1 and 2) and safety (cohort 1-5) for Japanese patients in TRUST-II.

Study Design



[a]Or ≥20 years, as required by local regulations. [b]Registrational cohorts are shown. [c]Assessed by IRC per mRECIST v1.1. [d]Safety population includes all patients who received ≥1 dose of taletrectinib 600 mg.

Results

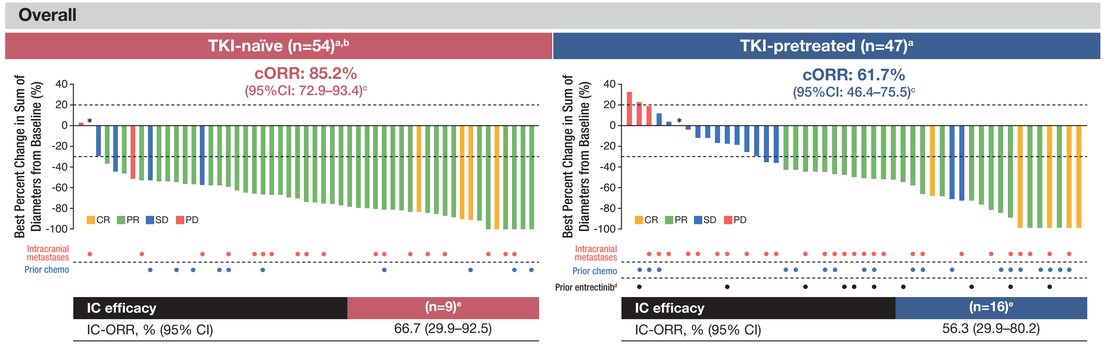
Baseline Characteristics

Baseline Characteristics	Overall[1]			Japanese patients		
	TKI-naïve[a] (n=55)	TKI-pretreated[b] (n=50)	Safety Population[c] (N=171)	TKI-naïve[a] (n=14)	TKI-pretreated[b] (n=11)	Safety Population[c] (N=38)
Median age, years (range)	57.0 (27-83)	55.5 (27-79)	57.0 (27-83)	58.5 (27-73)	45.0 (27-77)	53.5 (27-83)
Female, n (%)	31 (56.4)	27 (54.0)	96 (56.1)	7 (50.0)	6 (54.5)	21 (55.3)
Never smoker, n (%)	28 (50.9)	30 (60.0)	95 (55.6)	6 (42.9)	5 (45.5)	17 (44.7)
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)	6 (42.9) / 8 (57.1)	6 (54.5) / 5 (45.5)	19 (50.0) / 19 (50.0)
Stage IV disease, n (%)	49 (89.1)	49 (98.0)	162 (94.7)	13 (92.9)	11 (100.0)	37 (97.4)
Prior chemotherapy, n (%)	11 (20.0)	19 (38.0)	67 (39.2)	1 (7.1)	3 (27.3)	15 (39.5)
Intracranial metastases at baseline, n (%)	19 (34.5)	28 (56.0)	78 (45.6)	6 (42.9)	7 (63.6)	20 (52.6)
Prior crizotinib / entrectinib, n (%)	-	40 (80.0) / 10 (20.0)	86 (50.3) / 29 (17.0)	-	8 (72.7) / 3 (27.3)	18 (47.4) / 12 (31.6)

Data cutoff: October 28, 2024.
[a]Registrational cohort are shown (Cohort 1). [b]Registrational cohort are shown (Cohort 2). [c]Safety population includes all patients who received ≥1 dose of taletrectinib 600 mg (all cohorts in TRUST-II).

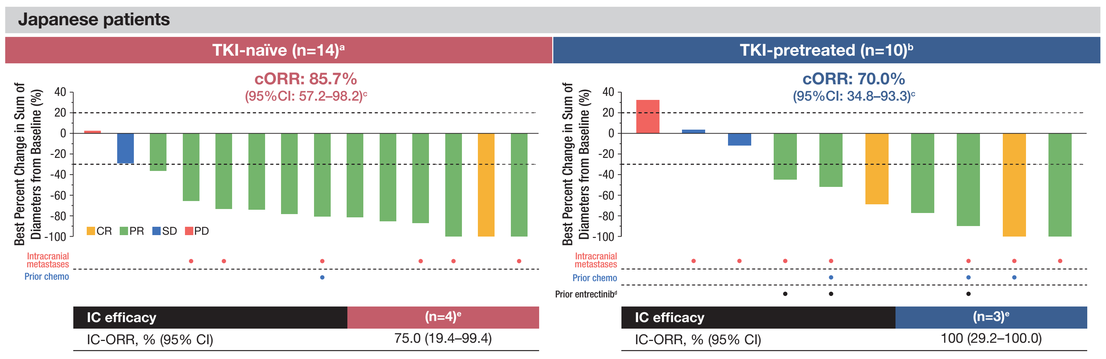
Efficacy: cORR/IC-ORR

Overall



[a]Response evaluable population (REP) includes patients with ≥1 measurable lesion at baseline who received ≥1 dose of taletrectinib. [b]One patient with best overall response (BOR) of NE is not shown in the waterfall plot. [c]Clopper-Pearson method was used to calculate CI. [d]All other patients received prior crizotinib. [e]Patients with ≥1 measurable intracranial metastases at baseline. *One patient with cBOR of SD had a best percent change of 0%.

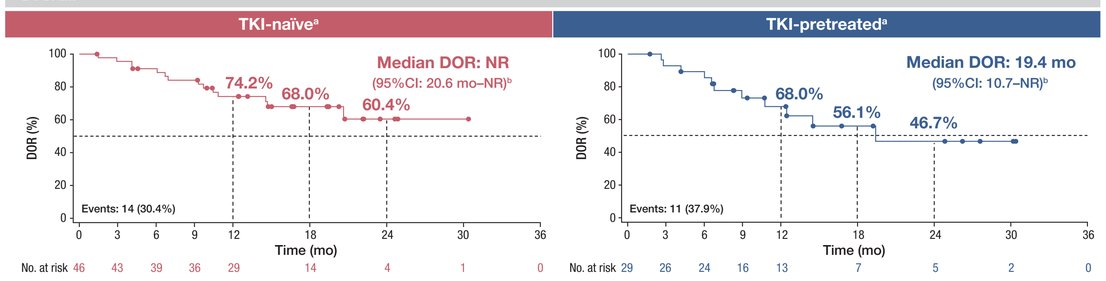
Japanese patients



[a]14 enrolled in Cohort 1 and 14 participants were efficacy evaluable by IRC; 14 participants were evaluable by investigator.
[b]11 enrolled in Cohort 2 and 10 participants were efficacy evaluable by IRC with 1 participant excluded due to not having a measurable lesion at baseline per IRC; 11 participants were evaluable by investigator. [c]Clopper-Pearson method was used to calculate CI. [d]All other patients received prior crizotinib. [e]IC-ORR is based on the IAP population, which is a subset of REP and includes all participants who have at least 1 measurable intracranial metastases at baseline per mRECIST v1.1 by IRC.

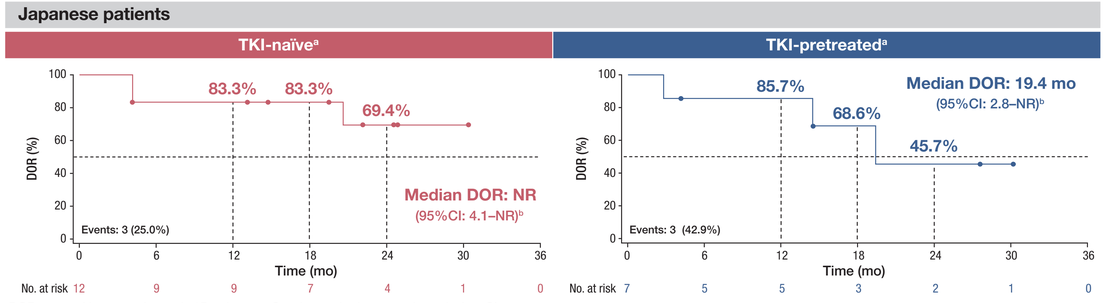
Efficacy: DOR

Overall



[a]DOR reported in responders only. [b]Brookmeyer-Crowley method was used to calculate CI.

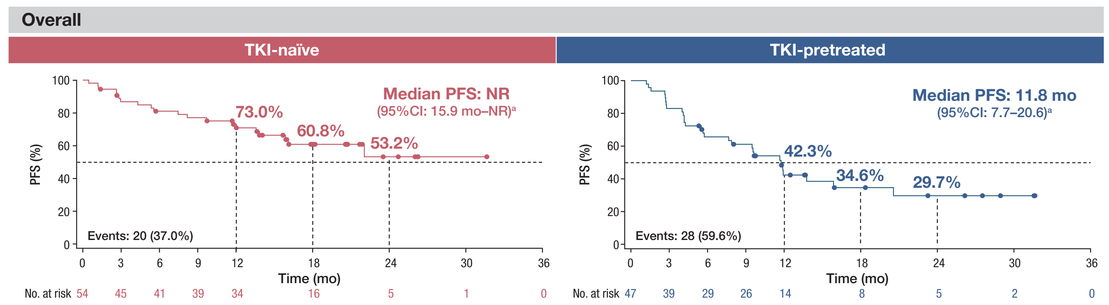
Japanese patients



[a]DOR reported in responders only. [b]Brookmeyer-Crowley method was used to calculate CI.

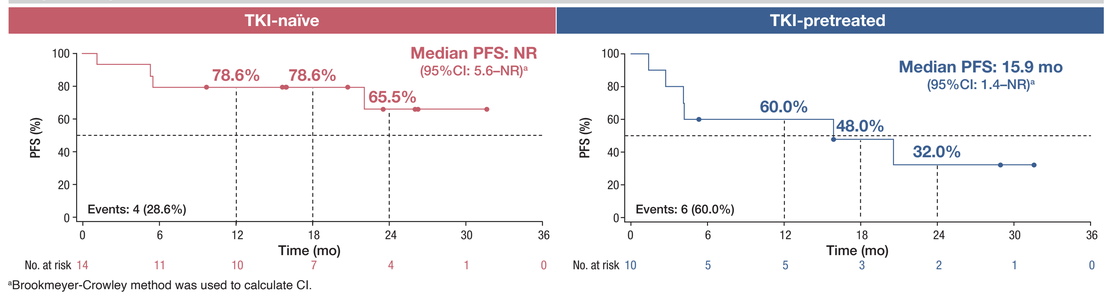
Efficacy: PFS

Overall



[a]Brookmeyer-Crowley method was used to calculate CI.

Japanese patients



[a]Brookmeyer-Crowley method was used to calculate CI.

Safety: TEAEs in ≥15% of Overall patients

(Overall, N=171; Japanese patients, N=38)

Patients, n (%)	Overall		Japanese patients	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any TEAEs	**169 (98.8)**	**90 (52.6)**	**38 (100.0)**	**16 (42.1)**
Most frequent TEAEs (≥15% of Overall patients)				
Increased ALT	115 (67.3)	26 (15.2)	27 (71.1)	7 (18.4)
Increased AST	112 (65.5)	12 (7.0)	27 (71.1)	1 (2.6)
Diarrhea	99 (57.9)	1 (0.6)	26 (68.4)	0
Nausea	89 (52.0)	3 (1.8)	21 (55.3)	0
Vomiting	59 (34.5)	2 (1.2)	12 (31.6)	0
Constipation	41 (24.0)	0	13 (34.2)	0
Anemia	34 (19.9)	7 (4.1)	6 (15.8)	0
Increased blood CPK	34 (19.9)	6 (3.5)	5 (13.2)	2 (5.3)
Dysgeusia	33 (19.3)	0	12 (31.6)	0
Dizziness	30 (17.5)	0	4 (10.5)	0
Electrocardiogram QT prolonged	28 (16.4)	6 (3.5)	9 (23.7)	2 (5.3)
Decreased appetite	26 (15.2)	1 (0.6)	6 (15.8)	0

Summary

- There were 14 efficacy-evaluable patients in TKI-naïve cohort, with cORR of 85.7%, IC-ORR of 75.0%, and median DOR not reached.
- In 10 TKI-pretreated patients (7 crizotinib, 3 entrectinib), cORR was 70.0%, IC-ORR was 100%, and median DOR was 19.4 months.
- Median PFS was not reached in TKI-naïve and 15.9 months in TKI-pretreated.
- Most common TEAEs were increased ALT (71.1%), AST (71.1%), and diarrhea (68.4%). Higher tendency for increased ALT and AST in Japanese patients were observed, mostly Grade 1 or 2.
- Regarding neurologic TEAEs, dysgeusia was 31.6%, dizziness was 10.5%, mostly Grade 1 or 2.
- Only 1 patient (2.6%) discontinued due to TEAEs.

Conclusions

- Taletrectinib continues to show high and durable overall responses, robust intracranial activity, in Japanese ROS1+ NSCLC both in TKI-naïve and -pretreated in the TRUST-II study.
- The safety profile, including low neurologic adverse events, was consistent with entire cohort, supporting its efficacy and tolerability in this population.

Abbreviations

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BOR, best overall response; CI, confidence interval; CNS, central nervous system; cORR, confirmed objective response rate; CPK, creatine phosphokinase; CR, complete response; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IAP, intracranial analysis population; IC-ORR, intracranial objective response rate; IRC, independent review committee; mo, months; (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; REP, response evaluable population; ROS1, c-ros oncogene 1; ROS1+, ROS1-positive; SD, stable disease; TEAE , treatment-emergent adverse event; TKI, tyrosine kinase inhibitor; TTR, time to response

References

1. Liu G, et al. J Thorac Oncol. 2025;20:S56 (suppl 1).

Acknowledgments

- We would like to thank all patients who participated in this study, the study investigators, and their staff.
- This study was sponsored by Nuvation Bio Inc.
- Medical writing support was provided by Flaminia Fenoaltea, MSc, of Ashfield MedComms, an Inizio company, and was funded by Nuvation Bio Inc. and Nippon Kayaku Co. Ltd.

Disclosures

The presenting author, Takashi Seto, declares the following potential conflicts of interest:
Invited speaker: Amgen, AnHeart Therapeutics, AstraZeneca, Bristol-Myers Squibb, Chugai Pharmaceutical, Eli Lilly Japan, MSD, Novartis Pharma, Ono Pharmaceutical, Pfizer Japan and Takeda Pharmaceutical; Writing engagement: Eli Lilly Japan and Novartis Pharma; Full or part-time employment: Precision Medicine Asia; Member of board of directors: West Japan Oncology Group.