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Comparable Efficacy and Safety of Taletrectinib for Advanced *ROS1*+ Non-small Cell Lung Cancer Across Pivotal Studies and Between Races and World Regions

Maurice Pérol,[1] Wei Li,[2] Nathan A. Pennell,[3] Geoffrey Liu,[4] Filippo De Braud,[5] Misako Nagasaka,[6] Enriqueta Felip,[7] Anwen Xiong,[2] Yongchang Zhang,[8] Huijie Fan,[9] Xicheng Wang,[10] Feiwu Ran,[11] Xianyu Zhang,[11] Wenfeng Chen,[11] Wei Wang,[11] Lyudmila Bazhenova,[12] Caicun Zhou[2,13]

[1]Department of Medical Oncology, Léon Bérard Cancer Center, Lyon, France; [2]Department of Medical Oncology, Shanghai Pulmonary Hospital and Thoracic Cancer Institute, Tongji University School of Medicine, Shanghai, China; [3]Cleveland Clinic Taussig Cancer Institute, Cleveland, OH, USA; [4]Princess Margaret Cancer Centre, Temerty School of Medicine, University of Toronto, Toronto, Canada; [5]University of Milan, Milan, Italy; [6]University of California Irvine School of Medicine and Chao Family Comprehensive Cancer Center, Orange, CA, USA; [7]Vall d'Hebron University Hospital, Barcelona, Spain; [8]Hunan Cancer Hospital, The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China; [9]The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; [10]The First Affiliated Hospital/School of Clinical Medicine Guangdong Pharmaceutical University, Guangzhou, China; [11]Nuvation Bio, New York, NY, USA; [12]University of California San Diego Moores Cancer Center, San Diego, CA, USA [13]Department of Medical Oncology, East Hospital, Tongji University School of Medicine, Shanghai, China

Supplementary Materials

Background & Methods

- Taletrectinib is an oral, potent, CNS-active, selective, next-generation ROS1 TKI that was evaluated in 2 pivotal *ROS1*+ NSCLC phase 2 trials: the global TRUST-II (NCT04919811) and regional TRUST-I (NCT04395677) studies
- The study designs of TRUST-II[1] and TRUST-I[2] have been previously published
- Here, we compare the efficacy and safety of taletrectinib within and between the pivotal global TRUST-II and regional TRUST-I studies through predefined subgroup analyses

Conclusions

- Taletrectinib demonstrated similar efficacy and safety across the TRUST-II and TRUST-I trials and across subgroups including race, geographic region, and prior chemotherapy status
- TEAEs of special interest, including GI events, occurred early and decreased over time
- Efficacy was unaffected by dose reduction across the two cohorts

Abbreviations

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; CNS, central nervous system; cORR, confirmed objective response rate; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; GI, gastrointestinal; IRC, independent review committee; m, median; mRECIST, modified Response Evaluation Criteria in Solid Tumors; NR, not reached; NSCLC, non-small cell lung cancer; PFS, progression-free survival; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; REP, response evaluable population; ROS1, c-ros oncogene 1; *ROS1*+, *ROS1*-positive; RR, relative risk; TEAE, treatment-emergent adverse event; TKI, tyrosine kinase inhibitor.

References

1. Pérol M, et al. *J Clin Oncol*. 2025;epub April 3, 2025.
2. Li W, et al. *J Clin Oncol*. 2024;42:2660-2670.

Acknowledgments

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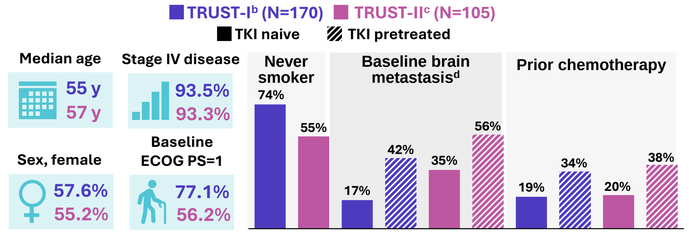
Results

Demographics and Baseline Characteristics[a]



Data cutoff: October 28, 2024

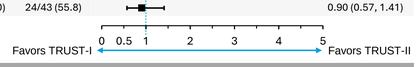
[a]In patients treated with taletrectinib 600 mg QD. [b]TRUST-I was conducted in China. [c]The TRUST-II population included only TKI-naive and TKI-pretreated patients, 47% of whom were geographically Western (North America or Europe) and 53% were Asian (Japan: 24%; Korea: 16%; China: 13%). [d]By IRC per mRECIST v1.1.

TRUST-II and TRUST-I: Efficacy

- Efficacy was assessed in the REP which included patients with ≥1 measurable baseline lesion per RECIST v1.1 who initiated taletrectinib treatment at 600 mg QD across TKI-naive (n=157) and TKI-pretreated (n=113) cohorts in TRUST-II and TRUST-I

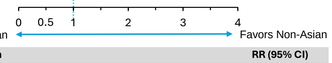
TRUST-II and TRUST-I: Comparable Efficacy Across Studies[a]

Endpoint	TRUST-II	TRUST-I	RR (95% CI)
cORR			
TKI naive	46/54 (85.2)	93/103 (90.3)	0.94 (0.83, 1.07)
With prior chemotherapy	9/10 (90.0)	17/20 (85.0)	1.06 (0.80, 1.40)
Without prior chemotherapy	37/44 (84.1)	76/83 (91.6)	0.92 (0.80, 1.06)
TKI pretreated	29/47 (61.7)	34/66 (51.5)	1.20 (0.87, 1.66)
With prior chemotherapy	15/19 (78.9)	10/23 (43.5)	1.82 (1.08, 3.06)
Without prior chemotherapy	14/28 (50.0)	24/43 (55.8)	0.90 (0.57, 1.41)



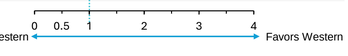
TRUST-II and TRUST-I: Comparable Efficacy Across Race and Region[a]

	Endpoint	Non-Asian	Asian	RR (95% CI)
Race	**cORR**			
	TKI naive	16/19 (84.2)	123/138 (89.1)	0.94 (0.77, 1.16)
	With prior chemotherapy	6/6 (100)	20/24 (83.3)	1.20 (1.00, 1.44)
	Without prior chemotherapy	10/13 (76.9)	103/114 (90.4)	0.85 (0.63, 1.15)
	TKI pretreated	16/25 (64.0)	47/88 (53.4)	1.20 (0.84, 1.71)
	With prior chemotherapy	8/10 (80.0)	17/32 (53.1)	1.51 (0.96, 2.36)
	Without prior chemotherapy	8/15 (53.3)	30/56 (53.6)	1.00 (0.58, 1.70)



	Endpoint	Western	Non-Western	RR (95% CI)
Region	**cORR**			
	TKI naive	17/21 (81.0)	122/136 (89.7)	0.90 (0.73, 1.12)
	With prior chemotherapy	6/6 (100)	20/24 (83.3)	1.20 (1.00, 1.44)
	Without prior chemotherapy	11/15 (73.3)	102/112 (91.1)	0.81 (0.59, 1.10)
	TKI pretreated	17/26 (65.4)	46/87 (52.9)	1.24 (0.88, 1.74)
	With prior chemotherapy	8/10 (80.0)	17/32 (53.1)	1.51 (0.96, 2.36)
	Without prior chemotherapy	9/16 (56.3)	29/55 (52.7)	1.07 (0.65, 1.76)

[a]An RR of 1 indicates there is no difference between groups.



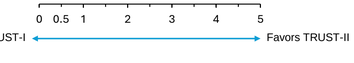
- Comparable efficacy was observed across race and region within TRUST-II (**Supplement**)

TRUST-II and TRUST-I: Safety

TRUST-II and TRUST-I: Comparable Safety Across Studies[a,b]

- Safety was assessed in all patients who received ≥1 dose of taletrectinib in TRUST-II (n=171)[1] and TRUST-I (n=173)[2]

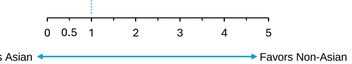
Endpoint	TRUST-II	TRUST-I	RR (95% CI)
Grade ≥3 TEAE	90/171 (52.6)	94/173 (54.3)	0.97 (0.80, 1.18)
Grade ≥3 ALT/AST elevation	31/171 (18.1)	35/173 (20.2)	0.90 (0.58, 1.38)
Grade ≥3 GI disorders	7/171 (4.1)	10/173 (5.8)	0.71 (0.28, 1.82)



[a]An RR of 1 indicates there is no difference between groups.
[b]The TRUST-II population included patients across cohorts 1 to 5 treated with taletrectinib 600 mg QD.[1]

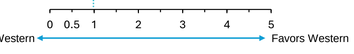
TRUST-II[a] and TRUST-I: Comparable Safety Across Race and Region[a]

	Endpoint	Non-Asian	Asian	RR (95% CI)
Race	**Grade ≥3 TEAE**	50/91 (54.9)	134/253 (53.0)	1.04 (0.83, 1.29)
	Grade ≥3 ALT/AST elevation	19/91 (20.9)	47/253 (18.6)	1.12 (0.70, 1.81)
	Grade ≥3 GI disorders	5/91 (5.5)	12/253 (4.7)	1.16 (0.42, 3.20)



[a]An RR of 1 indicates there is no difference between groups.

	Endpoint	Western	Non-Western	RR (95% CI)
Region	**Grade ≥3 TEAE**	54/97 (55.7)	130/247 (52.6)	1.06 (0.85, 1.31)
	Grade ≥3 ALT/AST elevation	20/97 (20.6)	46/247 (18.6)	1.11 (0.69, 1.77)
	Grade ≥3 GI disorders	5/97 (5.2)	12/247 (4.9)	1.06 (0.38, 2.93)



[a]An RR of 1 indicates there is no difference between groups.

TRUST-II and TRUST-I: TEAEs of Special Interest

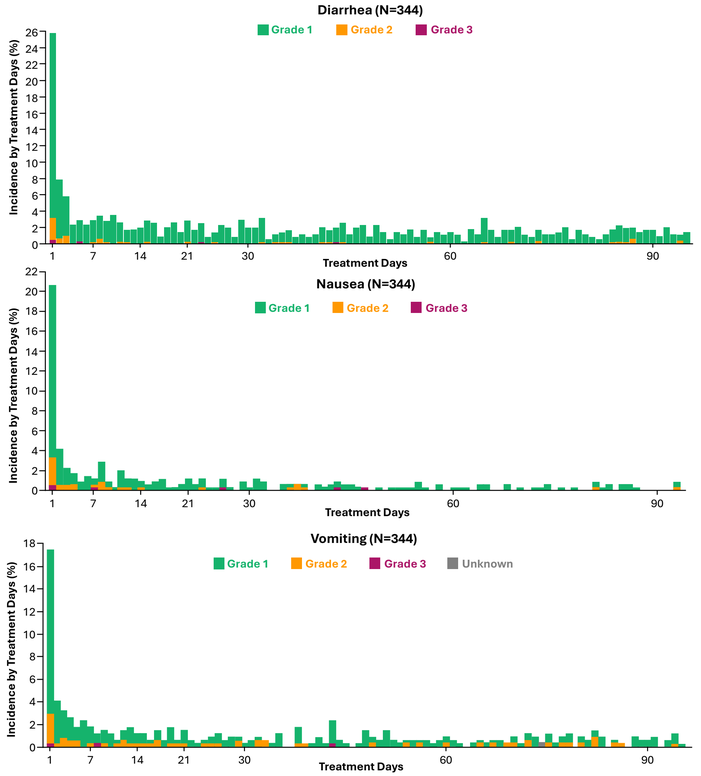
- Due to comparable overall safety across TRUST-II and TRUST-I, a detailed safety characterization of TEAEs of special interest was conducted in a combined population from both studies (Table below and **Supplement**)

TRUST-II[a] and TRUST-I: GI Events Across Studies

GI Events	TRUST-II (n=171) All grades, n (%)	TRUST-II (n=171) Grades ≥3, n (%)	TRUST-I (n=173) All grades, n (%)	TRUST-I (n=173) Grades ≥3, n (%)
Diarrhea	99 (57.9)	1 (0.6)	121 (69.9)	6 (3.5)
Vomiting	59 (34.5)	2 (1.2)	94 (54.3)	2 (1.2)
Nausea	89 (52.0)	3 (1.8)	74 (42.8)	2 (1.2)

[a]The TRUST-II population included patients across cohorts 1 to 5 treated with taletrectinib 600 mg QD.[1]

Most GI Events Occurred Early in Treatment and Decreased Over Time



Dose Reduction[a] Does Not Compromise Efficacy

- DOR and PFS across the efficacy population were comparable regardless of dose reduction status (**Supplement**)

	TKI-naive (n=157)		TKI-pretreated (n=113)	
	With Dose Reduction	Without Dose Reduction	With Dose Reduction	Without Dose Reduction
Median follow-up time, months	23.9	27.1	22.1	27.3
N	46	111	28	85
cORR,% (95 CI%)	95.7 (85.2, 99.5)	85.6 (77.6, 91.5)	71.4 (51.3, 86.8)	50.6 (39.5, 61.6)
DCR, % (95% CI)	97.8 (88.5, 99.9)	93.7 (87.4, 97.4)	92.9 (76.5, 99.1)	85.9 (76.6, 92.5)
Median DOR, months [95% CI] (Range)	38.6 [14.7, NR] (1.1–46.9)	NR	12.5 [8.9, NR] (4.1–31.8)	16.6 [10.4, 27.3] (1.4–38.7)

[a]Following grade ≥3 increased ALT/AST, patients in TRUST-I could resume taletrectinib at their original dose or a reduced dose while patients in TRUST-II were required to resume taletrectinib at a reduced dose