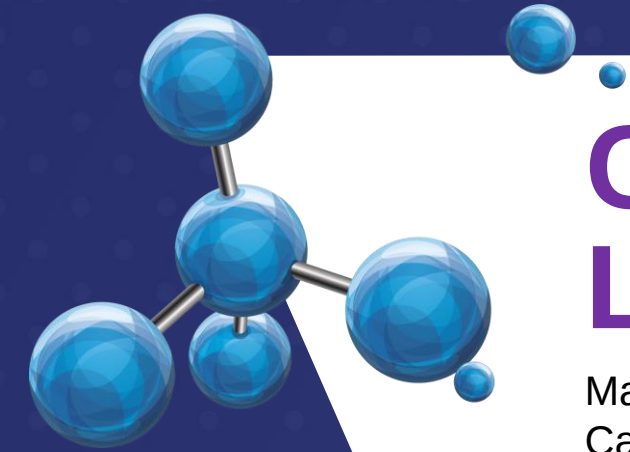




Comparable Efficacy and Safety of Taletrectinib for Advanced *ROS1*+ Non-small Cell Lung Cancer Across Pivotal Studies and Between Races and World Regions

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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-II¹ and TRUST-I² 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

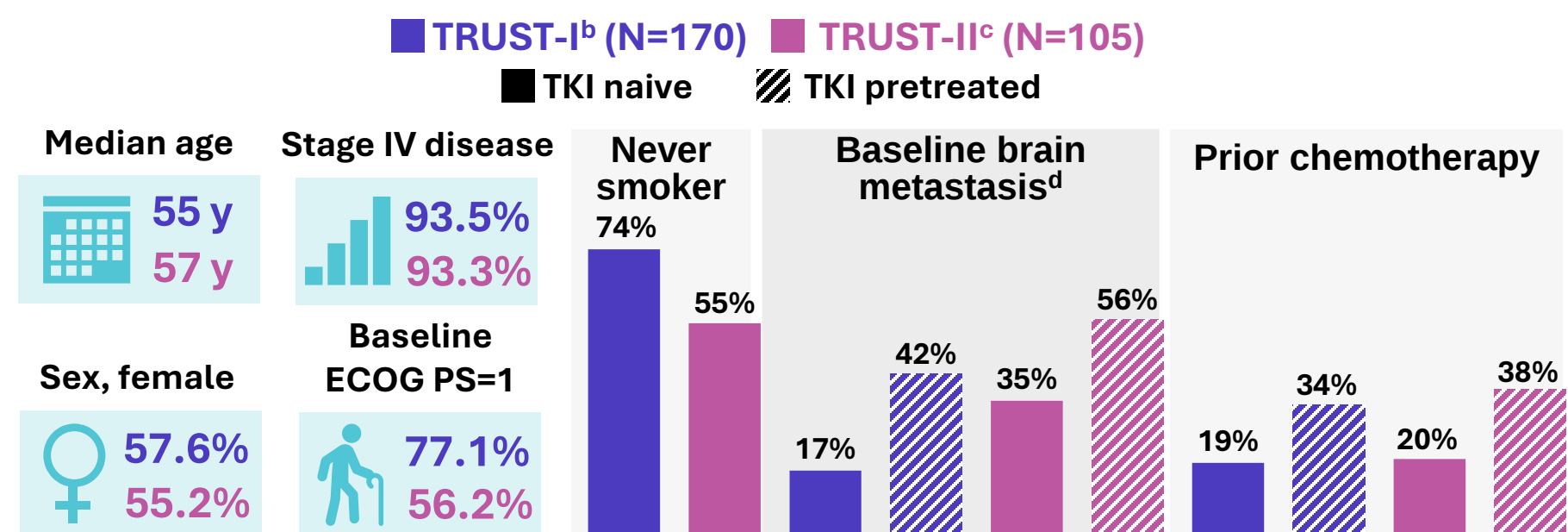
- Pérol M, et al. *J Clin Oncol*. 2025; epub April 3, 2025.
- Li W, et al. *J Clin Oncol*. 2024;42:2660-2670.

Acknowledgments

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Results

Demographics and Baseline Characteristics^a



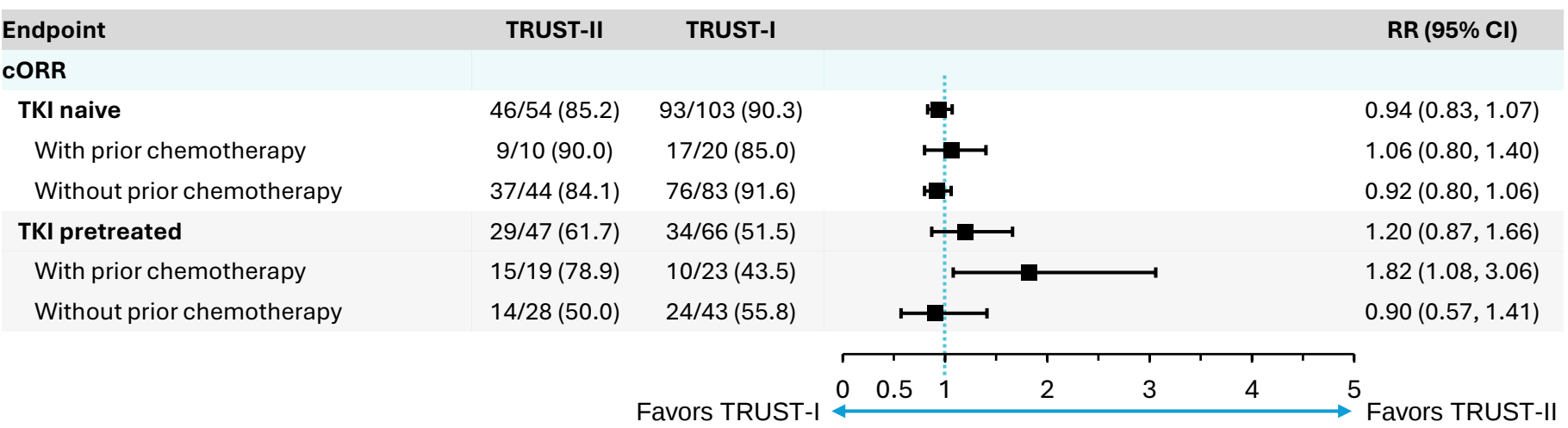
Data cutoff: October 28, 2024

^aIn patients treated with taletrectinib 600 mg QD. ^bTRUST-I was conducted in China. ^cThe TRUST-II population included only TKI-naïve and TKI-pretreated patients, 47% of whom were geographically Western (North America or Europe) and 53% were Asian (Japan: 24%; Korea: 16%; China: 13%). ^dBy IRC per mRECIST v1.1.

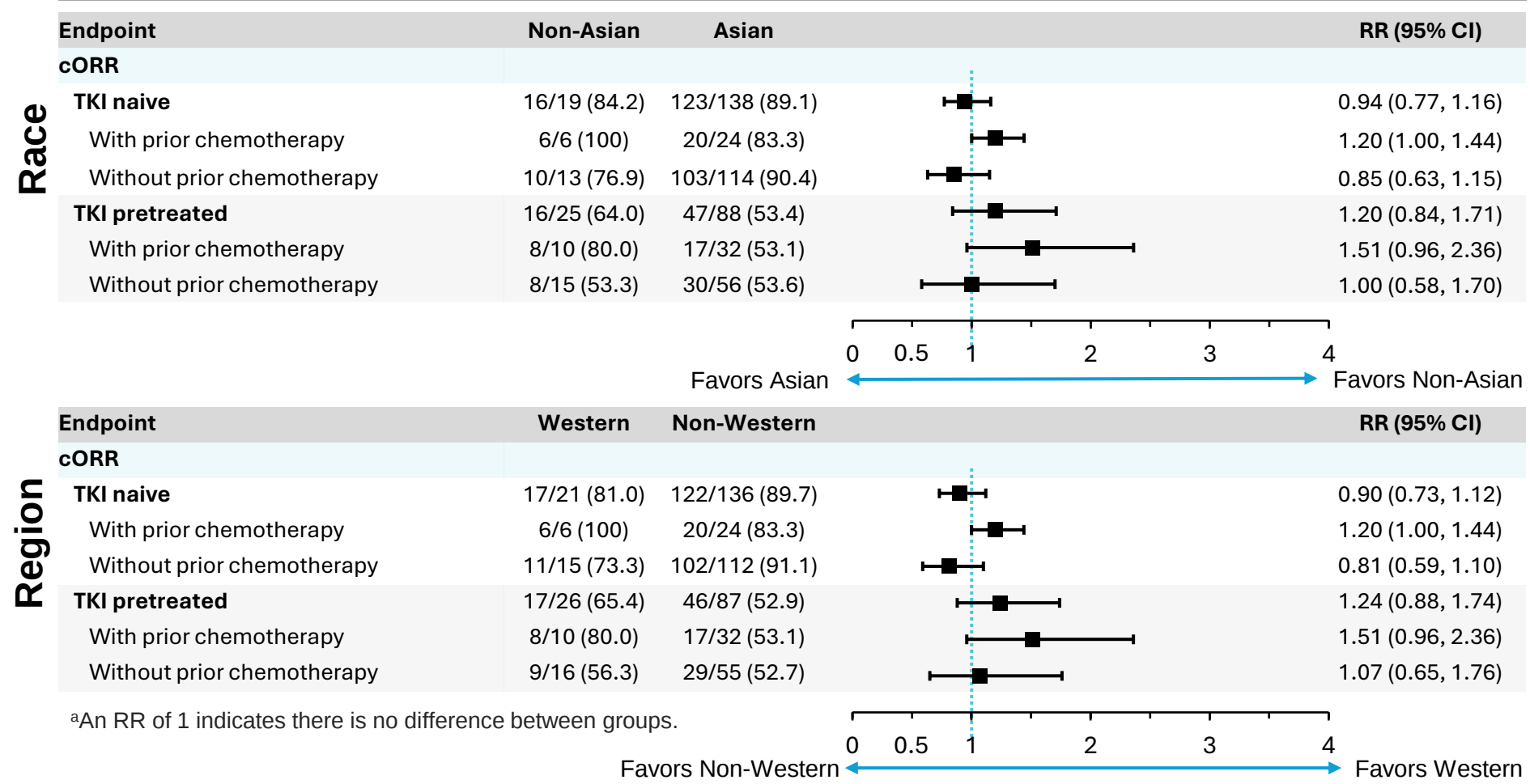
TRUST-II and TRUST-I: Efficacy

- 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-naïve (n=157) and TKI-pretreated (n=113) cohorts in TRUST-II and TRUST-I

TRUST-II and TRUST-I: Comparable Efficacy Across Studies^a



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



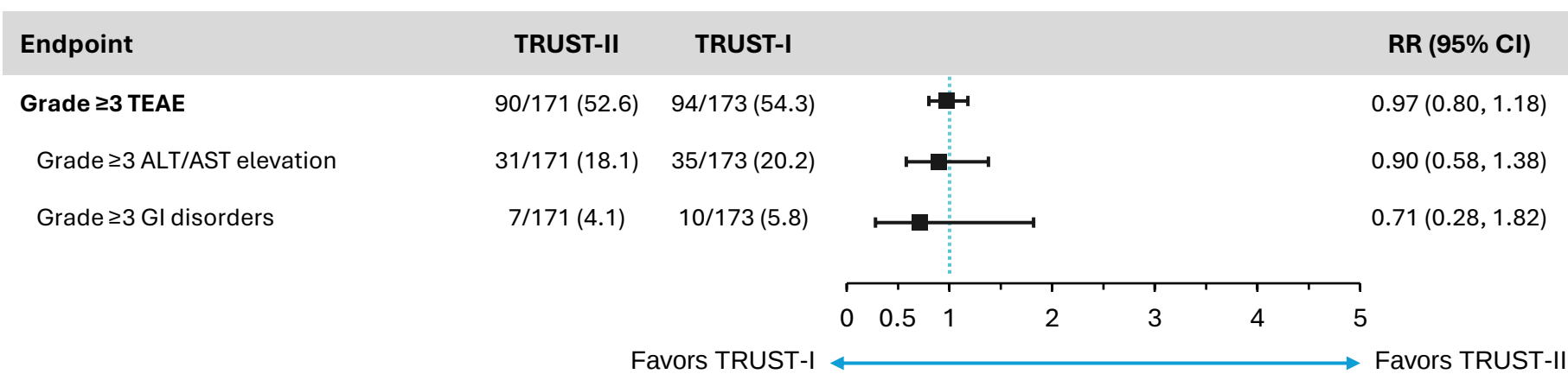
^aAn RR of 1 indicates there is no difference between groups.

- 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}

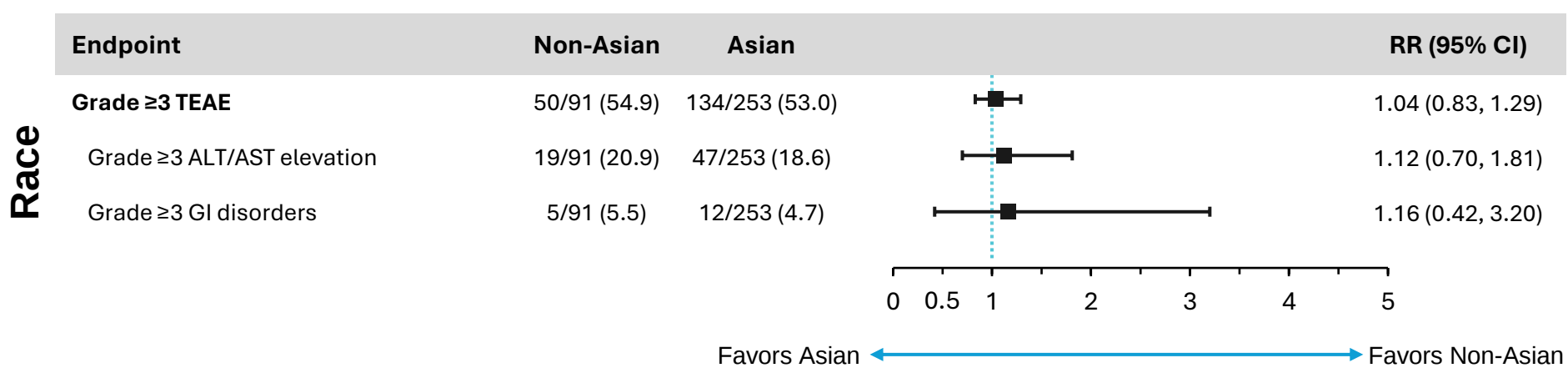
- Safety was assessed in all patients who received ≥ 1 dose of taletrectinib in TRUST-II (n=171)¹ and TRUST-I (n=173)²



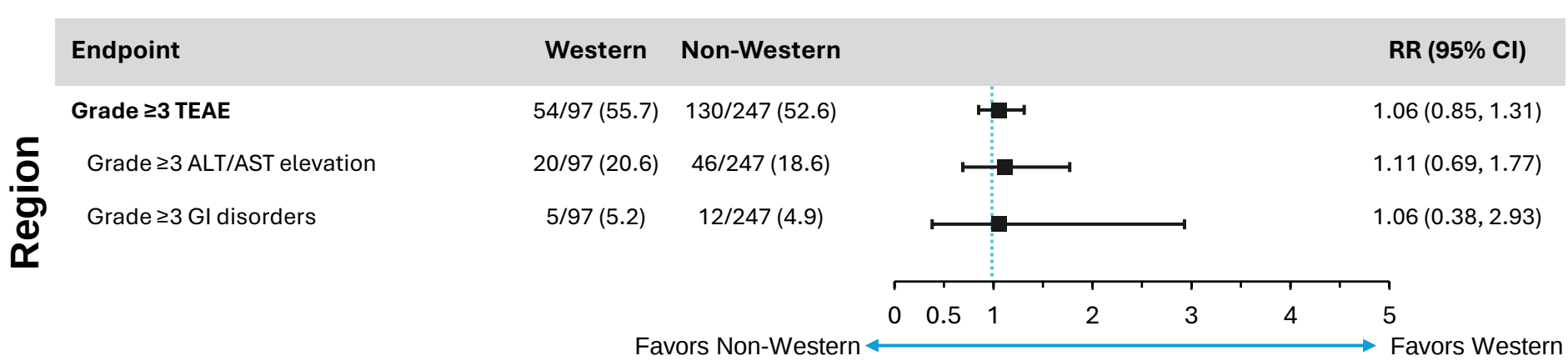
^aAn RR of 1 indicates there is no difference between groups.

^bThe 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



^aAn RR of 1 indicates there is no difference between groups.



^aAn RR of 1 indicates there is no difference between groups.

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

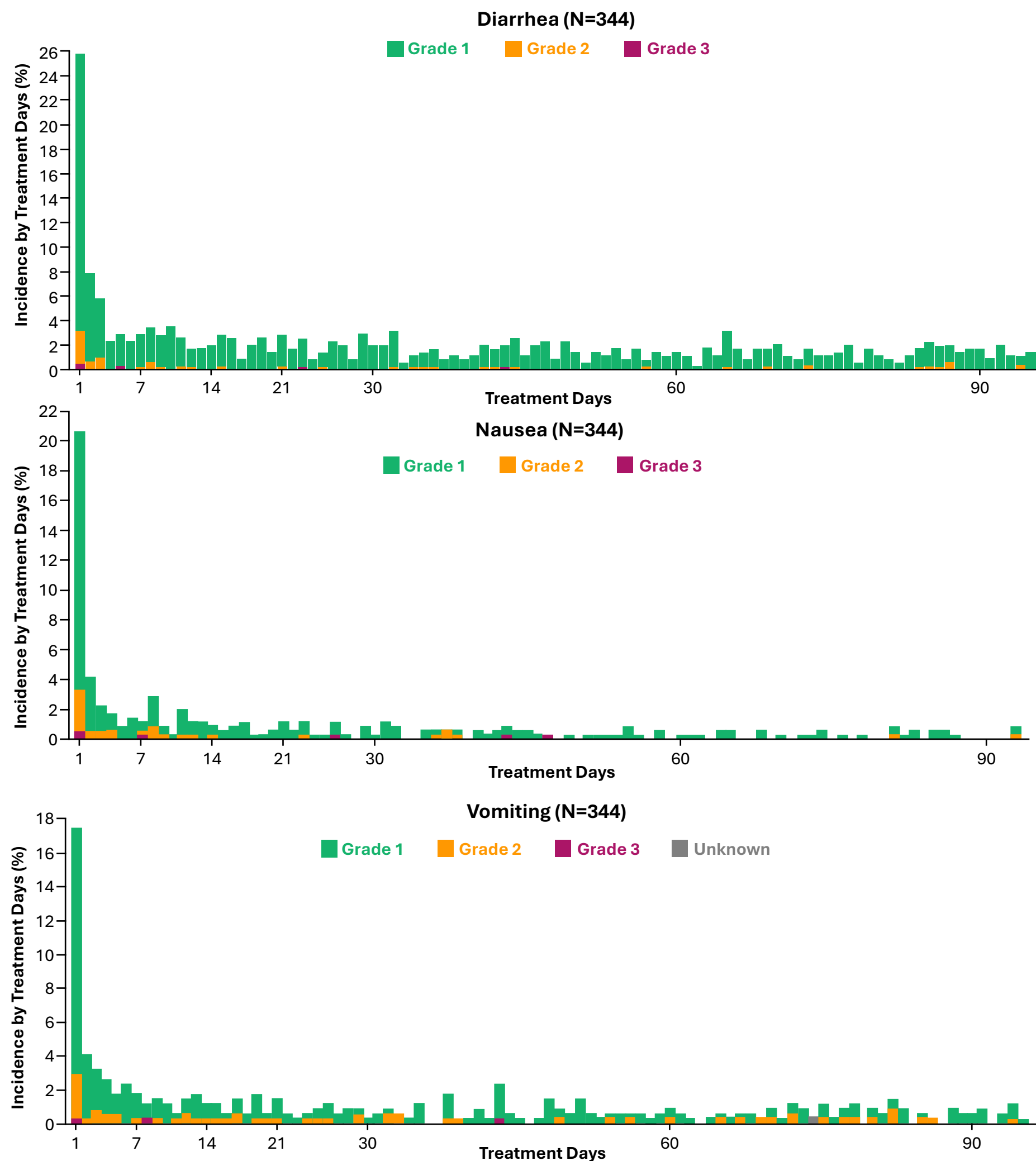
- Due to comparable overall safety across TRUST-II and TRUST-I, a detailed safety characterization of TEAEs of special interest was conducted in a combined population from both studies (Table below and Supplement)

TRUST-II^a and TRUST-I: GI Events Across Studies

GI Events	TRUST-II (n=171)		TRUST-I (n=173)	
	All grades, n (%)	Grades ≥ 3 , n (%)	All grades, n (%)	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)

^aThe 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

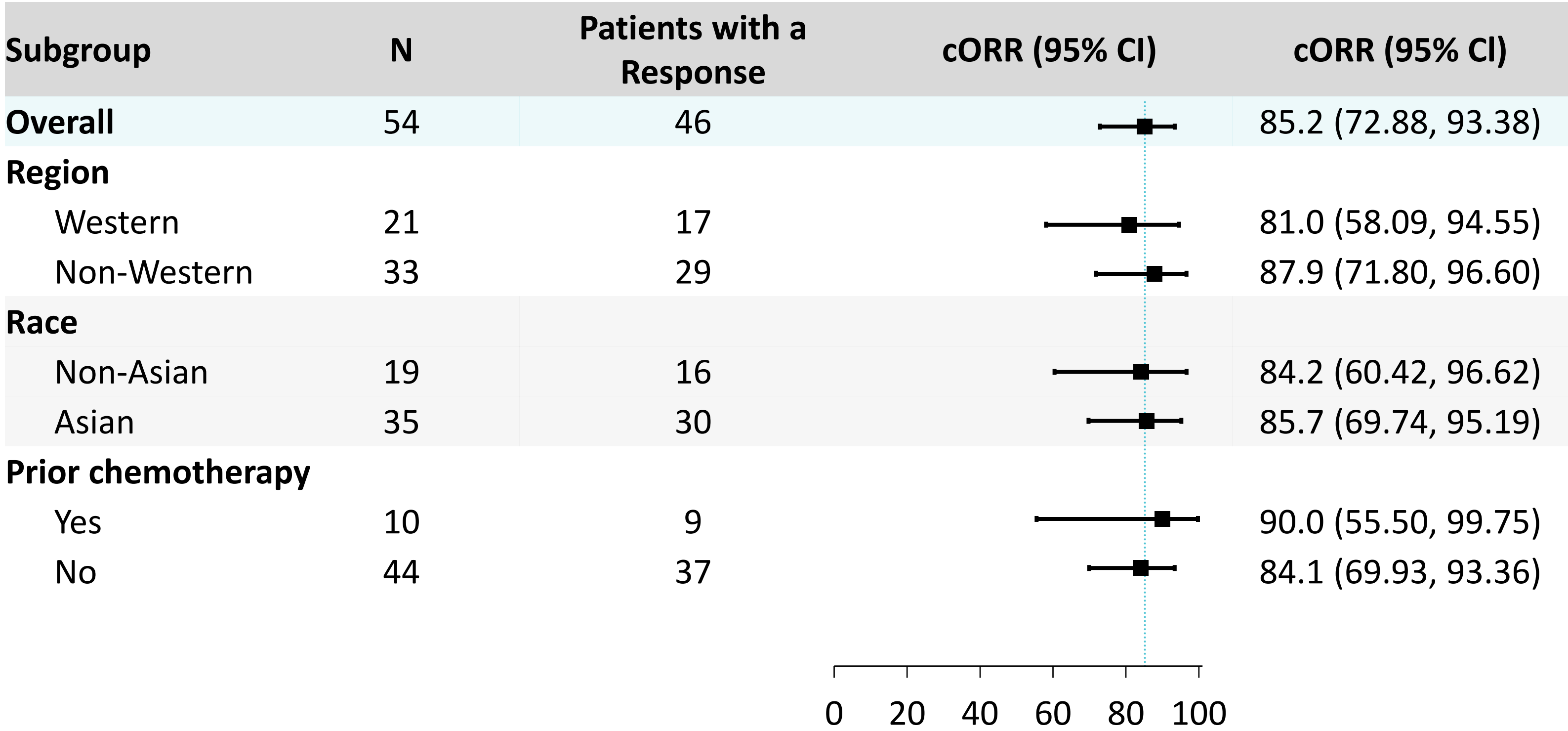
- DOR and PFS across the efficacy population were comparable regardless of dose reduction status (Supplement)

	TKI-naïve (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)

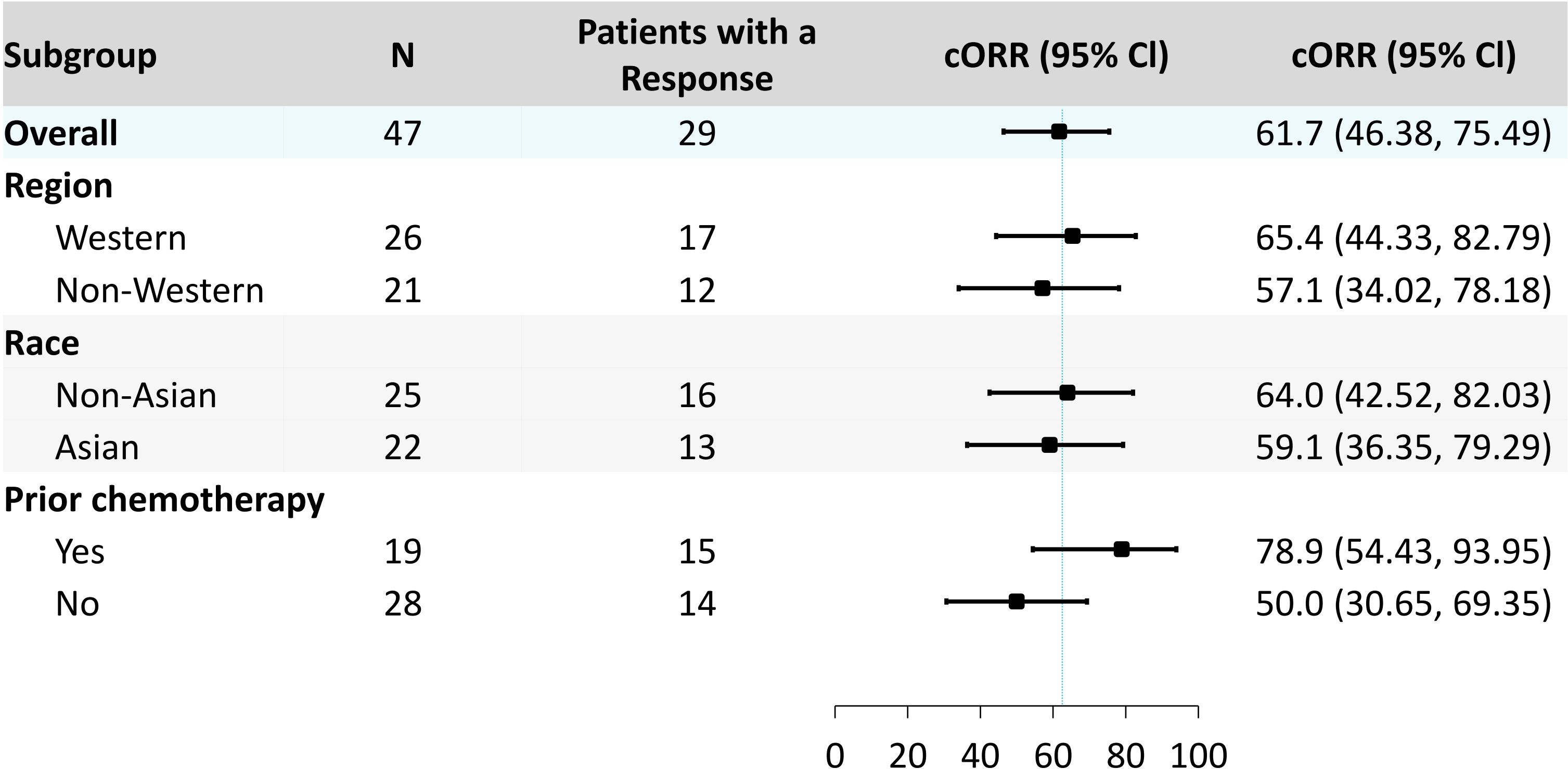
^aFollowing grade ≥ 3 increased ALT/AST, patients in TRUST-I could resume taletrectinib at their original dose or a reduced dose while patients in TRUST-II were required to resume taletrectinib at a reduced dose

TRUST-II: Comparable Efficacy Across Race, Region, and Prior Chemotherapy in Patients with Advanced *ROS1*+ NSCLC Treated with Taletrectinib 600 mg QD

TKI Naive

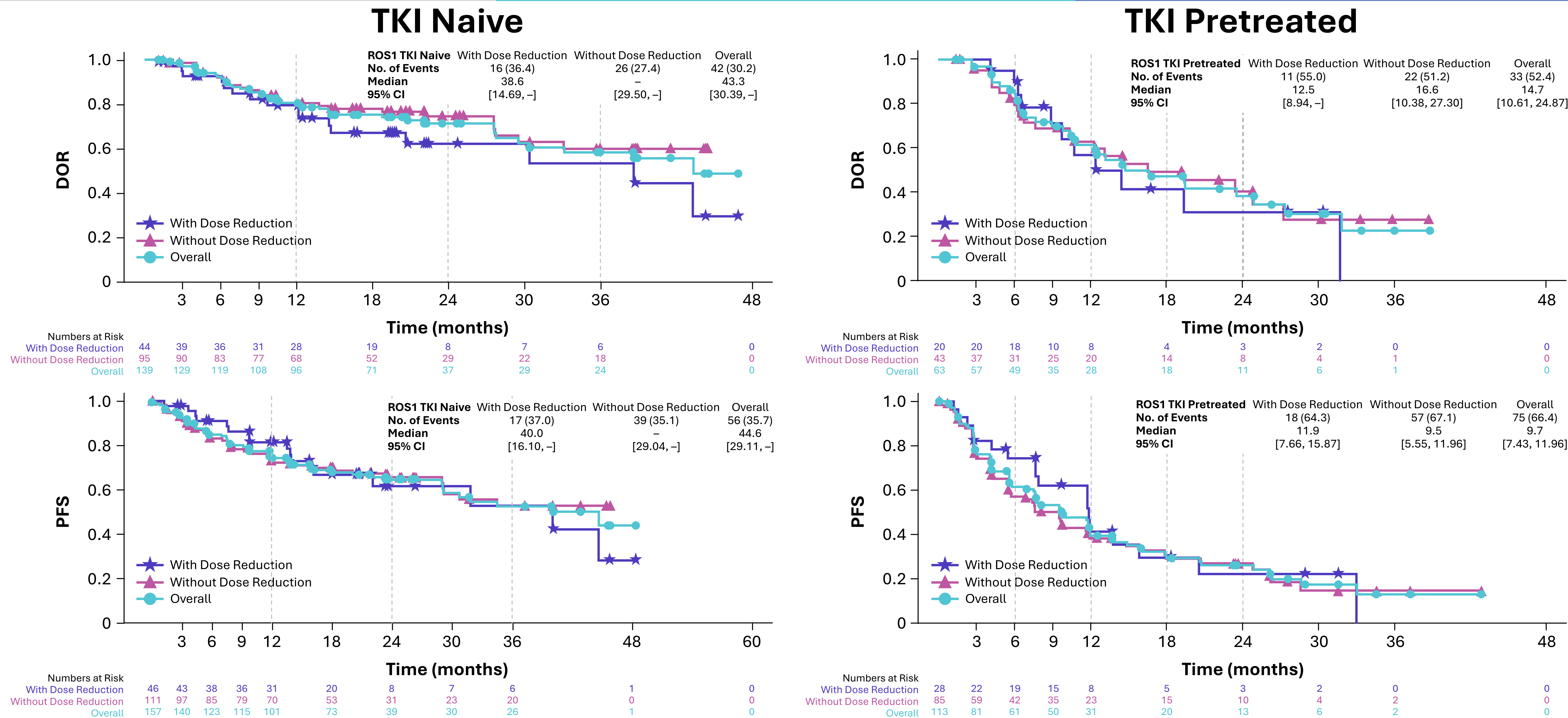


TKI Pretreated



Data cutoff: October 28, 2024.
Dashed vertical line represents the overall cORR for TKI-naive patients.
CI, confidence interval; cORR, confirmed objective response rate; NSCLC, non-small cell lung cancer; QD, once daily; TKI, tyrosine kinase inhibitor.

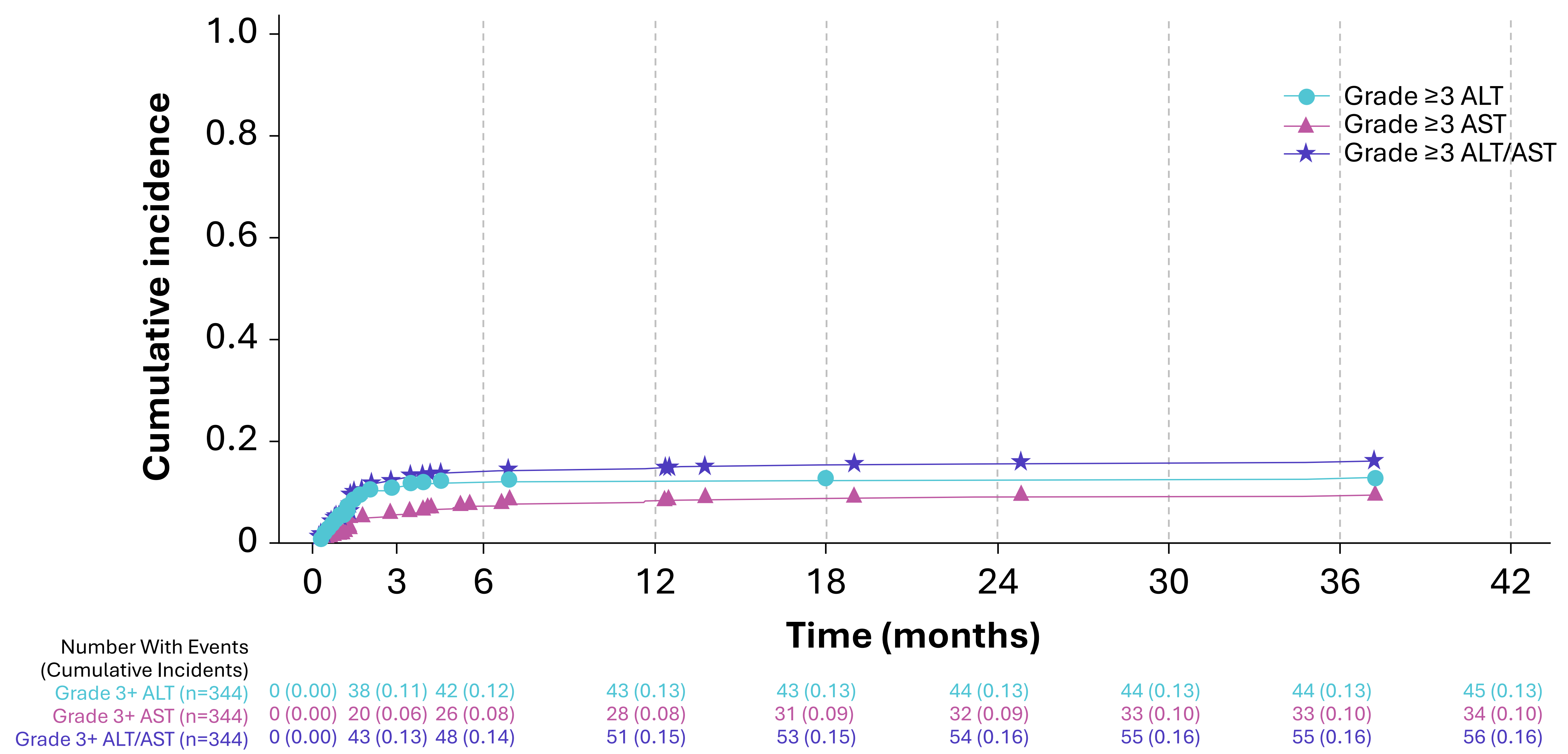
TRUST-II and TRUST-I^a: DOR and PFS Across the Efficacy Population Were Similar Regardless of Dose Reduction Status



Data cutoff: October 28, 2024.

^aEfficacy was assessed in the REP which included patients with advanced *ROS1*+ NSCLC 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. DOR, duration of response; NSCLC, non-small cell lung cancer; PFS, progression-free survival; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; TKI, tyrosine kinase inhibitor; REP, response evaluable population; *ROS1*, c-ros oncogene 1; *ROS1*+, *ROS1*-positive; TKI, tyrosine kinase inhibitor.

TRUST-II and TRUST-I: Most Grade ≥ 3 ALT/AST Increase Occurred Early and Were Not Cumulative^{a,b}



Data cutoff: October 28, 2024.

^aCumulative incidence was calculated as the cumulative number of patients with first onset grade ≥ 3 ALT/AST evaluation events during treatment period divided by the total number of patients who had at least 1 ALT/AST laboratory assessment. ^bSafety was assessed in all patients who received ≥ 1 dose of taletrectinib in TRUST-II (n=171) and TRUST-I (n=173). ALT, alanine aminotransferase; AST, aspartate aminotransferase.