Title: A comparison of tislelizumab (TIS) plus chemotherapy (CT) vs programmed cell death protein-1 (PD-1) inhibitor monotherapy in first-line (1L) non-squamous (nsq) non-small cell lung cancer (nsclc) patients (pts) with programmed cell-death ligand 1 (PD-L1) ≥50%

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Background: PD-1/PD-L1 ± CT are approved 1L therapies for metastatic/locally advanced NSCLC. However, there are few studies comparing TIS + CT to PD-1 inhibitors alone in locally advanced/metastatic 1L nsq NSCLC with PD-L1 ≥50%. This exploratory analysis is the first to examine the risk-benefit of TIS + CT vs PD-1 inhibitor monotherapy (TIS and pembrolizumab [PEM] alone) in this pt population.

Methods: Locally advanced/metastatic 1L nsq NSCLC pts with PD-L1 ≥50% and no actionable mutations who received TIS + CT or TIS or PEM in the phase 3 RATIONALE-304 (NCT03663205) or AdvanTIG-302 (NCT04746924) trials, respectively, were compared. Average treatment effect on the treated (ATT) for overall survival (OS), progression-free survival (PFS) and overall response rate (ORR) was estimated using propensity score weighting (PSW) for all pts, smokers, nonsmokers and females. Unweighted safety was reported.

Results: As of April 26 2023 (RATIONALE-304) and May 30 2025 (AdvanTIG-302), 294 pts were included (n=74, RATIONALE-304; n=220, AdvanTIG-302 [52 TIS, 168 PEM]). In RATIONALE-304 and AdvanTIG-302, 58.1% and 88.1% of pts were ever smokers and 32.4% and 23.2% were female, respectively. The addition of CT to TIS suggested improved overall efficacy vs TIS or PEM alone (**Table**), with a trend for improved OS, PFS and ORR in smokers, nonsmokers and females. TIS + CT may also have improved efficacy over TIS or

PEM in pts with PD-L1 50-89%. For TIS + CT vs TIS or PEM alone, treatment-related treatment-emergent adverse events occurred in 100% and 79.5% of pts, and grade ≥3 immune-mediated adverse events in 10.8% and 11.9%, respectively.

Conclusion: In locally advanced/metastatic 1L nsq NSCLC pts with PD-L1 ≥50%, TIS + CT may have improved efficacy over TIS or PEM alone in females and pts with PD-L1 50-89%, regardless of smoking status.

Table (537/600 characters)

Endpoint	Unweighted	After PSW
OS		
HR (95% CI)	0.90 (0.61-1.35)	0.78 (0.50-1.21)
RMST difference (95% CI)*	0.74 (−2.75-4.23)	2.15 (−1.5-5.81)
Tau, months*	39.1	
PFS		
HR (95% CI)	0.83 (0.59-1.17)	0.73 (0.50-1.06)
ORR, % (95% CI)		
TIS + CT	70.3 (59.8-80.7)	70.3 (59.8-80.7)
TIS or PEM	56.4 (45.0-67.7)	50.8 (41.2-60.5)
Risk difference	13.9 (1.5-26.3)	19.4 (5.2-33.6)

*RMST provides an estimate of the average survival time up to a predefined ‘restriction time’ (denoted by Tau). RMST at time Tau means the mean survival time for those pts whose survival time ≤Tau.

CI confidence interval; HR, hazard ratio; RMST, restricted mean survival time.