Neoadjuvant Tislelizumab (TIS) Plus Chemotherapy (CT) with Adjuvant TIS vs. Neoadjuvant Placebo (PBO) Plus CT with Adjuvant PBO in Resectable Non-Small Cell Lung Cancer (NSCLC): Patient-Reported Outcomes (PRO) in the RATIONALE-315 Trial

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Background: In the pivotal phase 3 RATIONALE-315 trial (NCT04379635) of patients with resectable stage II to IIIA NSCLC, perioperative TIS plus (+) neoadjuvant platinum-based CT led to a significant improvement in event-free survival [HR=0.56, p=0.0003] compared to placebo + neoadjuvant platinum-based CT. Here, we report results for PRO instruments from RATIONALE-315.

Methods: PROs were secondary endpoints assessed using the EORTC QLQ-C30 and QLQ-LC13 instruments. Key PRO endpoints included QLQ-C30 GHS/QoL, physical function, as well as QLQ-LC13 symptoms of dyspnea, cough, and chest pain. A mixed model for repeated measures was performed at Cycle 1 (baseline), Cycle 3 of neoadjuvant phase, the Cycles 3 and 7 of adjuvant phase. Time to deterioration (TTD) was examined using Kaplan-Meier method. All HRQoL analysis were performed on the intent-to-treat analysis set.

Results: A total of 453 pts were randomized (1:1) to receive neoadjuvant TIS (n=226) or PBO (n=227). By Cycle 7, no meaningful differences in least-squares (LS) mean change from baseline between arms were observed for GHS/QoL, physical functioning, and fatigue, or chest pain and dyspnea (**Table**); however, the TIS + CT arm experienced a meaningful improvement in LS mean for coughing (-4.37 [95% CI: -9.46 to 0.21]). TTD analysis showed that pts in the TIS + CT arm were at lower risk of worsening for chest pain (HR 0.59 [95% CI: 0.38-0.91]); risk of worsening was similar between the arms in all other PRO endpoints.

Conclusions: Pts in the TIS + chemo arm experienced better HRQoL outcomes than those in the PBO + CT arm in this population of patients with resectable NSCLC, with improvements in coughing and lower risk of chest pain

Table

HRQoL endpoint	Least Squares Mean (95% CI)			
	Cycle 3: adjuvant phase		Cycle 7: adjuvant phase	
	TIS	PBO	TIS	PBO
QLQ-C30				
GHS/QoL	-1.14 (-3.79, 1.52)	-1.97 (-4.77, 0.83)	1.09 (-1.34, 3.53)	1.90 (-0.66, 4.46)
Physical functioning	-3.57 (-5.10, -2.05)	-3.61 (-5.22, -2.01)	-2.60 (-4.20, 1.00)	-2.23 (-3.92, -0.54)
Fatigue	2.52 (0.23, 4.81)	2.97 (0.57, 5.37)	2.54 (0.09, 4.99	2.87 (0.30, 5.45)
QLQ-LC13				
Coughing	-4.58 (-7.75, -1.42)	-5.63 (-8.97, -2.29)	-12.15 (-15.60, -8.71)	-7.52 (-11.16, -3.89)
Chest pain	0.43 (-2.42, 3.28)	5.42 (2.39, 8.44)	0.36 (-2.34, 3.05)	1.89 (-0.96, 4.75)
Dyspnea	4.62 (2.57, 6.67)	6.57 (4.41, 8.74)	3.18 (0.82, 5.55)	4.56 (2.07, 7.06)