Title: RATIONALE-315: post hoc analysis of event-free survival by surgically relevant subgroups treated with perioperative tislelizumab and neoadjuvant chemotherapy vs neoadjuvant chemotherapy

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Background:

RATIONALE-315 (NCT04379635) compared the efficacy and safety of perioperative tislelizumab (TIS) or placebo (PBO) + neoadjuvant chemotherapy (CT) in patients (pts) with resectable NSCLC. This post hoc analysis reports correlation of event-free survival (EFS) to key surgical outcomes.

Methods:

Pts with resectable stage II-IIIA NSCLC (N=453) were randomized 1:1 to 3-4 cycles of TIS 200 mg or PBO Q3W with neoadjuvant CT, followed by surgery and ≤8 cycles of adjuvant TIS 400 mg or PBO Q6W. Primary and key secondary endpoints were reported previously. Exploratory endpoints of surgical outcomes are presented here.

Results:

As of March 7, 2025, 190/226 pts in the TIS arm and 173/227 pts in the PBO arm underwent definitive surgery. EFS benefit with TIS vs PBO was observed in all surgically relevant subgroups (HR: 0.62; 95% CI: 0.44-0.88). Although R0 resection rates were similar between treatment arms, TIS showed greater EFS benefit vs PBO (HR: 0.62; 95% CI: 0.43-0.90). A similar trend was observed in R1/R2 pts (HR: 0.75; 95% CI: 0.19-3.05); however, data should be interpreted with caution due to small pt

numbers. Pts in the TIS arm who underwent open and minimally invasive surgery (n=179) achieved improved EFS benefit compared with those in PBO arm (n=157), regardless of disease stage and surgery type (**Table**).

In pts who underwent minimally invasive and open surgery, respectively, grade ≥3 treatment-emergent adverse events occurred in 77.2% and 78.8% of pts in the TIS arm and 71.3% and 81.7% in the PBO arm. In pts who underwent minimally invasive surgery in the TIS arm, grade ≥3 immune mediated adverse events were reported in 11.4% of all pts (13/114), 10.4% of pts in stage II (5/48), and 12.3% in stage IIIa (8/65).

Conclusions:

Perioperative TIS + neoadjuvant CT improved EFS in pts with resectable NSCLC across all surgically relevant subgroups regardless of disease stage or surgery type. These results further support TIS + CT as an efficacious and safe treatment option that may reduce the burden of invasive surgical intervention.

Table

	EFS rate, % (95% CI)					
	12 mo		**24 mo**		**48 mo**	
Approach to surgery, NSCLC stage	TIS	PBO	TIS	PBO	TIS	PBO
Minimally invasive						
Overall	89.7 (82.2-94.2)	79.0 (78.0-86.6)	81.0 (72.1-87.3)	63.8 (51.8-73.6)	74.3 (64.0-82.1)	55.4 (42.0-67.0)
Stage II	90.9 (82.8-99.8)	85.0 (73.7-98.0)	83.6 (73.1-95.5)	69.8 (55.8-87.4)	77.0 (64.6-91.8)	66.5 (52.1-84.8)
Stage IIIa	88.7 (77.8-94.5)	73.1 (56.7-84.1)	78.9 (66.5-87.2)	58.0 (41.3-71.4)	72.4 (58.6-82.3)	46.7 (29.0-62.6)
Open						
Overall	78.5 (65.9-86.9)	70.9 (57.8-80.6)	60.2 (46.7-71.2)	47.8 (34.9-59.6)	54.1 (40.4-66.0)	31.1 (17.3-45.8)
Stage II	85.7 (72.0-100)	80.0 (64.3-99.6)	76.2 (60.0-96.8)	55.0 (37.0-81.8)	71.4 (54.5-93.6)	NE (NE-NE)
Stage IIIa	74.1 (57.2-85.2)	66.4 (49.9-78.6)	50.3 (33.7-64.8)	44.3 (28.9-58.6)	NE (NE, NE)	28.7 (13.9-45.5)

NE, not evaluable.