Surgical outcomes from RATIONALE-315: Randomized, double-blind, phase 3 study of periopeoative tislelizumab with neoadjuvant chemotherapy in resectable NSCLC

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ABSTRACT

Background: RATIONALE-315 (NCT04379635) investigated the efficacy and safety of perioperative tislelizumab (TIS) or placebo (PBO) with neoadjuvant chemotherapy (CT) in patients (pts) with resectable NSCLC. Here, we report key surgery outcomes from the study.

Methods: Pts in China with treatment-naïve resectable stage II-IIIA NSCLC, with ECOG PS ≤1 and no known *EGFR* mutations or *ALK* gene translocations were enrolled. Pts were randomized (1:1) to 3-4 cycles of TIS 200 mg or PBO, IV Q3W, plus CT, followed by surgery and up to 8 cycles of adjuvant TIS 400 mg or PBO, IV Q6W. Primary endpoints were major pathological response (MPR, reported previously) and event-free survival. Key secondary endpoint was pathological complete response (pCR) rate. Surgery outcomes were exploratory endpoints.

Results: 453 pts were enrolled and baseline characteristics were similar between arms. 190/226 pts (84.1%) in the TIS arm and 173/227 pts (76.2%) in the PBO arm underwent definitive surgery (Table). Main reasons for surgery cancellation were pt withdrawal (20 vs 28 pts), progressive disease (6 vs 17 pts) and adverse events (AEs) (6 vs 2 pts), respectively. Surgery delays occurred in 31 (16.3%) vs 22 (12.7%) pts, mainly due to AEs in 12 (6.3%) vs 6 (3.5%) pts in TIS vs PBO arms, mostly within two weeks. R0 resection was achieved in 95.3% pts in TIS vs 93.1% in PBO arm. Median duration of surgery (2.7 vs 2.8 hours) and length of hospitalization (7 vs 7 days) were similar between arms. In the TIS vs PBO arms, any-grade AEs and grade ≥3 post-operative complication rates were 63.7% vs 61.3%, and 11.1% vs 15.6%, and 90-day post-surgery mortality was 3 pts (1.3%) vs 4 pts (1.8%), respectively.

Conclusion: Perioperative TIS plus neoadjuvant CT did not impact the feasibility and completeness of surgery, and was accompanied by statistically significant improvement in MPR and pCR, and manageable safety, indicating TIS is a perioperative treatment option for pts with resectable NSCLC.

Table. Types and Approaches of Surgery in the RATIONALE-315 Study		
	TIS Arm (n=190)	**PBO Arm (n=173)**
Type of surgery, n (%)		
Lobectomy	135 (71.1)	106 (61.3)
Pneumonectomy	16 (8.4)	21 (12.1)
Sleeve lobectomy	20 (10.5)	16 (9.2)
Bilobectomy	18 (9.5)	29 (16.8)
Segmentectomy	1 (0.5)	1 (0.6)
Approach of surgery, n (%)		
Open	65 (34.2)	70 (40.5)
Minimally invasive	114 (60.0)	87 (50.3)
Minimally invasive to thoracotomy	11 (5.8)	16 (9.2)
Data cutoff: August 21, 2023. **Abbreviations:** PBO, placebo; TIS, tislelizumab.		