RATIONALE-315: Patterns of Progression and Recurrence with Perioperative Tislelizumab in Resectable NSCLC

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CONCLUSIONS

- The addition of perioperative tislelizumab to neoadjuvant chemotherapy showed a lower incidence of disease progression precluding surgery, lower locoregional and distant recurrences rates regardless of disease stage, and a longer time to recurrence after surgery compared to placebo plus chemotherapy.
- Our findings further support perioperative tislelizumab plus chemotherapy as an effective treatment option for resectable stage II–IIIA NSCLC.

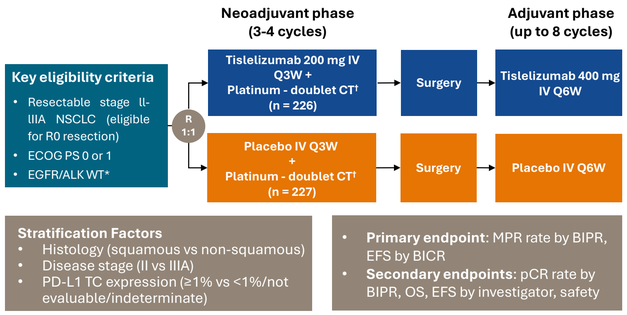
INTRODUCTION

- Perioperative immunotherapy has rapidly transformed the standard of care for resectable non-small cell lung cancer (NSCLC).[1]
- In the RATIONALE-315 trial, perioperative tislelizumab plus chemotherapy demonstrated statistically significant benefits for major pathological response (MPR), pathological complete response (pCR), event-free survival (EFS) and overall survival (OS) compared with placebo plus chemotherapy in patients with resectable NSCLC.[2-4]
- Currently, the differences in progression and recurrence between immunotherapy plus chemotherapy versus chemotherapy alone, as well as the recurrence patterns with perioperative immunotherapy are not well characterized.
- This post-hoc analysis explored the patterns of progression and recurrence in this patient population, and in the stage II and stage IIIA NSCLC subgroups.

METHODS

- The study design of RATIONALE-315 is shown in **Figure 1**.
- EFS event types were summarized in the randomized population; EFS was defined as the time from randomization to disease progression (either PD precluding surgery, or PD in the following visit after surgery was precluded for other reasons), postoperative recurrence, or death from any cause.
- Postoperative recurrence patterns were assessed by investigator among patients who underwent surgery and were classified as locoregional (L) or distant (D), with distant recurrence including concomitant locoregional and distant relapse.
- Time to (L/D) recurrence was defined as the time from randomization to postoperative (L/D) recurrence; patients with no (L/D) recurrence were censored at their EFS time.

Figure 1. RATIONALE-315 Study Design



*EGFR testing not required for squamous histology. †Squamous: cis/carbo + pac; nonsquamous: cis/carbo + pem.

Abbreviations: BICR, blinded independent central review; BIPR, blinded independent pathological review; carbo, carboplatin; cis, cisplatin; CT, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; IV, intravenous; MPR, major pathological response; NSCLC, non-small cell lung cancer; OS, overall survival; pac, paclitaxel; pCR, pathological complete response; PD-L1, programmed death-ligand 1; pem, pemetrexed; Q3W, every 3 weeks; Q6W, every 6 weeks; R0, pathological complete resection of the primary tumor; TC, tumor cell; WT, wild-type.

RESULTS

- A total of 453 patients were randomized to the tislelizumab (TIS; n=226) or placebo (PBO; n=227) arm.
- As of March 7, 2025 (median follow-up: 38.5 months [range, 0.1–57.0]), EFS events occurred in fewer patients in the TIS arm than in the PBO arm (31.9% vs 41.0%).
- Perioperative tislelizumab plus chemotherapy was associated with fewer proportions of patients having PD precluding surgery (3.1% vs 8.4%) and postoperative recurrence or death (26.5% vs 30.0%).
- Distribution of EFS event types in each arm is summarized in **Table 1**.

Table1. Summary of EFS Events

EFS event type*, n (%)	TIS arm (n=226)	PBO arm (n=227)
Total EFS events	72 (31.9)	93 (41.0)
PD precluding surgery	7 (3.1)	19 (8.4)
Stage II	1 (0.4)	8 (3.5)
Stage IIIA	6 (2.7)	11 (4.8)
Other reasons precluding surgery and had PD in the following visit	5 (2.2)	6 (2.6)
Postoperative recurrence or death	60 (26.5)	68 (30.0)

*EFS event types were assessed by investigator. **Abbreviations**: EFS, event-free survival; PD, progressive disease; PBO, placebo; TIS, tislelizumab.

Recurrence Patterns

- A total of 190 (84.1%) in TIS arm and 173 (76.2%) in PBO arm underwent surgery.
- Among patients who underwent surgery, postoperative recurrence was less frequent with TIS than PBO (26.3% vs 35.3%), with lower rates of both locoregional and distant recurrence; distant recurrence was the most common type (**Figure 2A**).
  - Locoregional recurrence: 9.5% (18/190) vs 15.0% (26/173); including lower pleural recurrence with TIS than PBO (**Figure 2B**).
  - Distant recurrence: 16.8% (32/190) vs 20.2% (35/173); including lower brain recurrence with TIS than PBO (**Figure 2C**).

Recurrence Patterns By Disease Stage

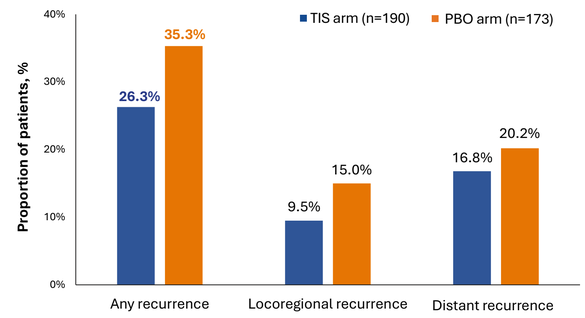
- In both stage II and stage IIIA NSCLC, distant recurrence is the predominant recurrence pattern post-surgery **(Figure 3)**.
- Consistently lower rates of locoregional and distant recurrence were observed in the TIS arm than in the PBO arm in both stage II and stage IIIA NSCLC (**Figure 3).**

Time To Recurrence

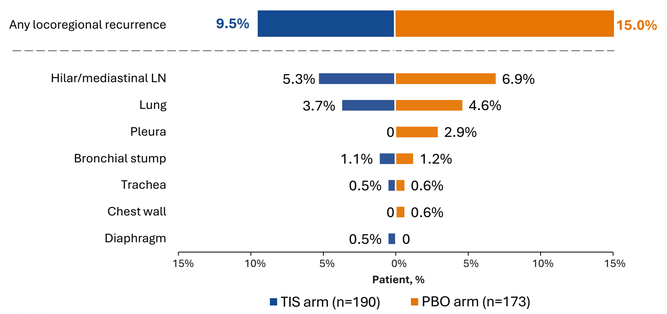
- Time to recurrence was prolonged in the TIS arm compared with the PBO arm (hazard ratio [HR], 0.61; 95% confidence interval [CI], 0.42–0.89) (**Figure 4A**):
  - Locoregional recurrence: HR, 0.52; 95% CI, 0.29–0.96 (**Figure 4B**).
  - Distant recurrence: HR, 0.68; 95% CI, 0.42–1.10 (**Figure 4C**).

Figure 2. Recurrence Patterns and Sites of Recurrence

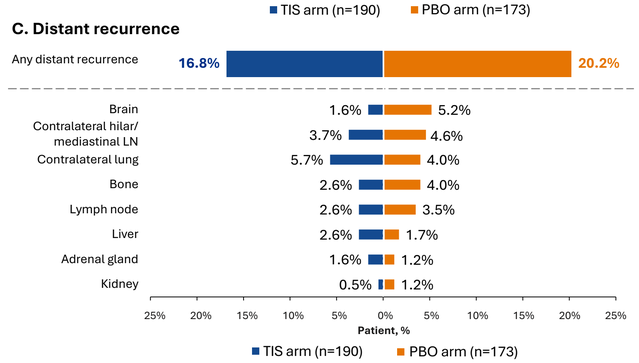
A. Recurrence patterns



B. Locoregional recurrence

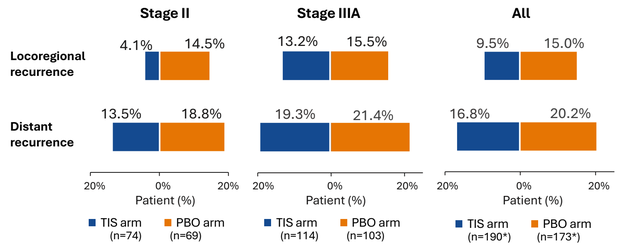


C. Distant recurrence



Abbreviations: LN, lymph node; PBO, placebo; TIS, tislelizumab.

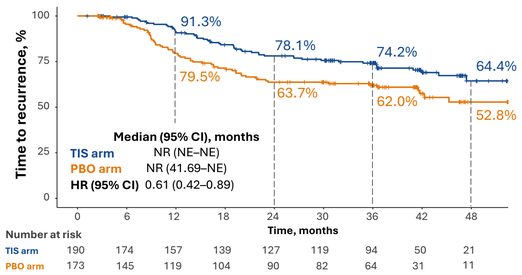
Figure 3. Recurrence Patterns by Disease Stage



*One patient with stage IB (one in TIS arm) and two patients with stage IIIB (one in each arm) were mistakenly enrolled.
Abbreviations: PBO, placebo; TIS, tislelizumab.

Figure 4. Time to Recurrence

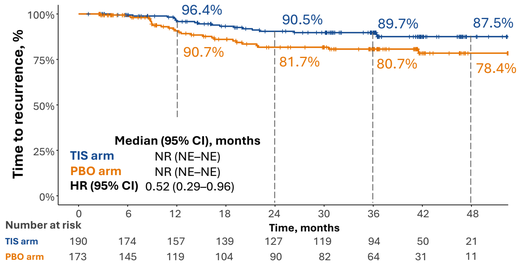
A. Any location



Number at risk

TIS arm	190	174	157	139	127	119	94	50	21
PBO arm	173	145	119	104	90	82	64	31	11

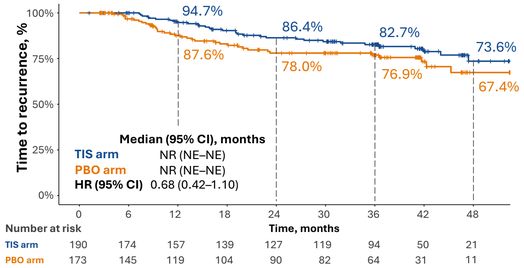
B. Locoregional recurrence



Number at risk

TIS arm	190	174	157	139	127	119	94	50	21
PBO arm	173	145	119	104	90	82	64	31	11

C. Distant recurrence



Number at risk

TIS arm	190	174	157	139	127	119	94	50	21
PBO arm	173	145	119	104	90	82	64	31	11

Abbreviations: CI, confidence interval; HR, hazard ratio; NE, not estimable; NR, not reached; PBO, placebo; TIS, tislelizumab.

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DISCLOSURES

The presenter has no conflict of interests to disclose.

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