Perioperative tislelizumab for resectable non-small cell lung cancer: final analysis of RATIONALE-315

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ABSTRACT

Introduction: Interim analyses (IAs) from RATIONALE-315 demonstrated that perioperative tislelizumab plus neoadjuvant chemotherapy had clinically meaningful and statistically significant improvement in major pathological response (MPR), event-free survival (EFS), and pathological complete response (pCR), with a manageable safety/tolerability profile, compared with neoadjuvant chemotherapy in patients with resectable non-small cell lung cancer (NSCLC). We report results of the prespecified EFS/OS final analysis (FA).

Methods: Adults with untreated, resectable, stage II-IIIA NSCLC were randomised 1:1 to neoadjuvant tislelizumab 200 mg or placebo every 3 weeks plus platinum-based doublet chemotherapy for 3-4 cycles, followed by surgery and adjuvant tislelizumab 400 mg or placebo every 6 weeks for ≤8 cycles. As MPR, EFS, and pCR were statistically significant at IAs, only OS was statistically tested at FA.

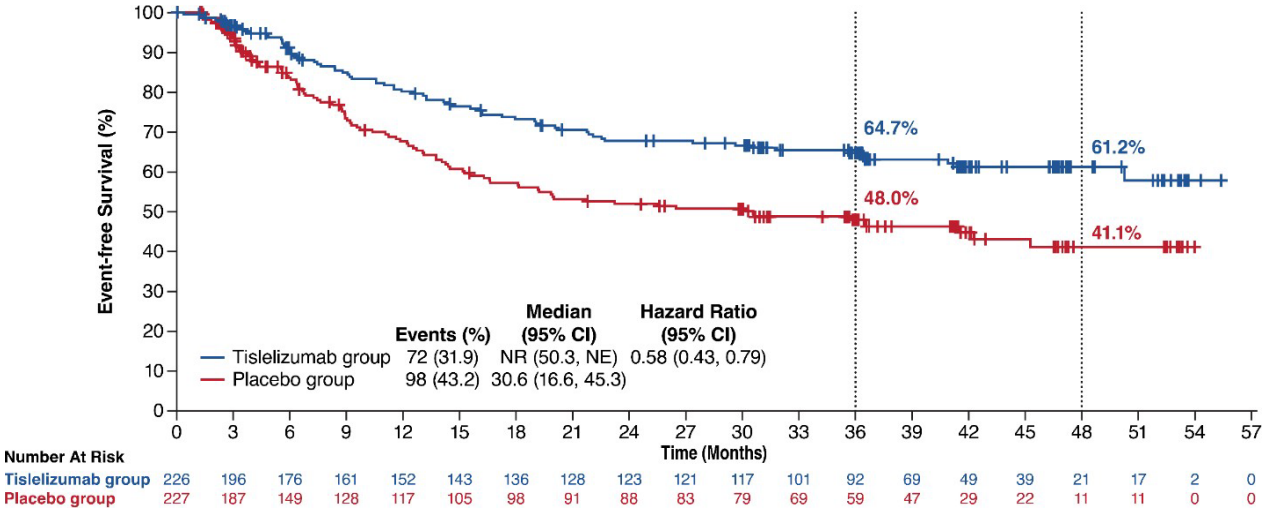
Results: Overall, 453 patients were randomised (tislelizumab, n=226; placebo, n=227). Over 90% of patients completed neoadjuvant treatment (tislelizumab, n=211; placebo, n=210), 363 (80.1%) had surgery (tislelizumab, n=190; placebo, n=173), and 224 (49.4%) completed adjuvant treatment (tislelizumab, n=115; placebo, n=109).

With a median study follow-up of 38.5 months (data cutoff: Mar 7, 2025), a statistically significant and clinically meaningful OS benefit was observed in the tislelizumab arm vs placebo arm (HR=0.65 [95% CI: 0.45, 0.93]; one-sided *P*=.0093). The significant EFS benefit reported with tislelizumab over placebo in the IAs was sustained (**Figure 1**; HR=0.58 [95% CI: 0.43, 0.79]), and improvement in EFS was consistent whether assessed by independent review committee (IRC) or the investigator. EFS_{IRC} and OS benefits observed with tislelizumab were also observed across major subgroups, regardless of PD-L1 expression, disease stage, and histology type. Disease-free survival, assessed by IRC, was also improved with tislelizumab vs placebo in patients with complete resection.

With the longer follow-up, safety/tolerability profiles were consistent with IAs, and no new or worsening signals emerged. Rates of grade ≥3 and serious TRAEs were 73.0% vs 67.3% and 15.5% vs 8.8% in the tislelizumab and placebo arms, respectively. The most frequently reported TRAEs of any grade were neutropenia (tislelizumab, 78.8%; placebo, 78.3%) and leukopenia (tislelizumab, 63.3%; placebo, 67.3%); these were also the most common grade ≥3 TRAEs in both arms (neutropenia: tislelizumab, 61.5%; placebo, 59.3%; leukopenia: tislelizumab, 16.8%; placebo, 14.2%).

Conclusions: Neoadjuvant tislelizumab plus chemotherapy and adjuvant tislelizumab demonstrated statistically significant, clinically meaningful OS benefit and sustained significant EFS improvement compared with neoadjuvant chemotherapy in patients with resectable NSCLC, potentially offering a new treatment paradigm that is generally well tolerated and safe for this population.

Figure 1. Event-Free Survival Assessed by Independent Review Committee



CI, confidence interval; NE, not estimable; NR, not reached.