RATIONALE-307: Safety analysis of patients (pts) receiving tislelizumab (TIS) plus chemotherapy (chemo) vs chemo alone in advanced squamous (sq) NSCLC

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Background:

Primary results from the Phase 3 RATIONALE-307 study (NCT03594747) showed significantly prolonged PFS, higher ORR, and a tolerable safety profile for TIS + chemo as first-line treatment for sq NSCLC. We report results from a *post-hoc* safety analysis of TIS + chemo vs chemo alone.

Methods:

Eligible pts (18–75 years) with treatment-naïve locally advanced or metastatic sq NSCLC were randomized 1:1:1 to Arm A: TIS 200 mg + paclitaxel (P) 175 mg/m^2 and carboplatin (C) AUC 5 (every 3 weeks [Q3W], day [D] 1); Arm B: TIS + *nab*-paclitaxel 100 mg/m^2 (Q3W, D 1, 8, and 15) + C (Q3W, D 1); or Arm C: P + C (Q3W, D 1). Chemo was administered for 4–6 cycles, after which, pts in Arms A and B continued TIS alone, and pts in Arm C were permitted to crossover to receive TIS alone upon disease progression. The safety analysis set (SAS) included all randomized

patients who received at least 1 dose of study treatment. The differences between incidence rates of treatment-emergent adverse events (TEAEs) were compared between pts treated with TIS plus chemo vs chemo alone for the first 4–6 cycles of treatment when chemo was administered in combination with TIS (Arms A and B) or alone (Arm C). All statistical analysis results were *post-hoc* exploratory and P-values are descriptive.

Results:

In total, 355 pts were included in the SAS (Arm A: 120; Arm B: 118; Arm C: 117). There were no notable differences in safety results for pts receiving TIS + chemo vs chemo alone (**Table**). P-values between Arms A vs C, and Arms B vs C were > 0.01. Confidence intervals (CIs) of the differences between Arms A vs C and Arms B vs C all included 0, except between Arms B vs C for TEAEs leading to discontinuation. There was a numerical difference between Arms B vs C for TEAEs leading to discontinuation during the chemo co-administrated period, but this was not clinically meaningful.

Conclusion:

TIS + chemo had a tolerable safety profile. TIS did not add toxicity or impact treatment when added to chemo.

Table:

	TIS + chemo		**Chemo**
	Arm A (n=120)	**Arm B (n=118)**	**Arm C (n=117)**
All TEAEs, n (%)	120 (100.0)	117 (99.2)	117 (100.0)
Rate diff (95% CI)	NA*	–0.8 (–4.7, 2.4)	-
Grade ≥ 3 TEAEs, n (%)	105 (87.5)	100 (84.7)	98 (83.8)
Rate diff (95% CI)	3.7 (–5.3, 13.0)	1.0 (–8.5, 10.5)	-
Serious TEAEs, n (%)	37 (30.8)	37 (31.4)	29 (24.8)
Rate diff (95% CI)	6.0 (–5.4, 17.4)	6.6 (–5.0, 18.0)	-
TEAEs leading to any drug discontinuation, n (%)	12 (10.0)	31 (26.3)	18 (15.4)
Rate diff (95% CI)	–5.4 (–14.2, 3.2)	10.9 (0.5, 21.3)	-
TEAEs leading to death, n (%)	3 (2.5)	4 (3.4)	5 (4.3)
Rate diff (95% CI)	–1.8 (–7.5, 3.4)	–0.9 (–6.7, 4.7)	-

*NA due to 100% TEAE incidence rate in both comparison arms
diff, difference; NA, not available