Tislelizumab (TIS) plus chemotherapy (CT) for first-line advanced or metastatic squamous non-small cell lung cancer (NSCLC): long-term overall survival (OS) subgroup analysis of RATIONALE-307

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Background: Long-term results of the open-label, randomised phase 3 RATIONALE-307 trial (NCT03594747) showed first-line TIS + CT maintained a clinically meaningful OS improvement vs placebo + CT and a tolerable safety profile, despite high in-study crossover for patients (pts) with locally advanced/metastatic squamous NSCLC. We report long-term OS outcomes among key subgroups in RATIONALE-307.

Methods: Adult pts with untreated, locally advanced (stage IIIB)/metastatic (stage IV) squamous NSCLC and an Eastern Cooperative Oncology Group performance status (ECOG PS) ≤1 were randomised (1:1:1) to receive TIS (200 mg intravenously once every 3 weeks) and carboplatin + paclitaxel (Arm A) or nab-paclitaxel (Arm B), or CT (paclitaxel + carboplatin) alone (Arm C). In-study crossover pts in Arm C could receive TIS upon disease progression. The primary endpoint was independent review committee-assessed progression-free survival. OS was a key secondary endpoint.

Results: 360 pts were randomised to Arm A (n=120), Arm B (n=119), and Arm C (n=121). The crossover rate was 58.7%. Minimum study follow-up was 46.5 months (data cutoff: Apr 28, 2023). OS outcomes generally favoured Arm A and B vs C in key subgroups. In Arm A vs C, a clinically meaningful improvement in OS was observed in pts aged <65 years (events/n=103/154; HR 0.68 [95% CI: 0.46, <1.00]), with an ECOG PS of 1 (events/n=127/178; HR 0.59 [95% CI: 0.41, 0.84]), and with stage IV disease (events/n=111/159; HR 0.64 [95% CI: 0.44, 0.93]). A clinically meaningful improvement in OS was observed in Arm B vs C in pts with an ECOG PS of 1 (events/n=136/186; HR 0.63 [95% CI: 0.45, 0.88]). OS HRs in Arm A vs C for pts with tumour PD-L1 expression <1% and ≥1% were 0.73 (95% CI: 0.45, 1.19; events/n=67/92) and 0.70 (95% CI: 0.47, 1.05; events/n=96/144), respectively, and 0.89 (95% CI: 0.56, 1.41; events/n=72/91) and 0.78 (95% CI: 0.53, 1.16; events/n=99/144) for Arm B vs C, respectively.

Conclusion: These long-term data demonstrate clinically meaningful improvements in OS with TIS + CT vs CT despite high in-study crossover across key subgroups of pts with locally advanced/metastatic squamous NSCLC.