RATIONALE-307: Tislelizumab plus chemotherapy versus chemotherapy alone as first-line treatment for advanced squamous NSCLC in patients aged ≥ 65.

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Background:

Tislelizumab is a humanized, monoclonal antibody with high affinity and specificity for the programmed cell death protein 1 (PD-1). It has demonstrated antitumor activity in advanced lung cancers. We conducted a Phase 3, multicenter, randomized open-label study (NCT03594747) to assess the safety and efficacy of tislelizumab plus chemotherapy in patients (pts) with advanced squamous NSCLC. As previously reported, tislelizumab (TIS) significantly improved progression free survival (PFS) and reduced the risk of progression. Here, we report results from a sub-group of pts aged ≥ 65 years.

Methods:

Eligible pts (aged 18-75 years) enrolled in China were treatment-naive for locally advanced or metastatic squamous NSCLC. Pts were stratified by disease stage (IIIB vs IV), and programmed death-ligand 1 (PD-L1) expression (< 1% vs

1-49% vs 50% tumor cells), and randomized 1:1:1 to Arm A: TIS 200 mg + paclitaxel (P) 175 mg/m^2 and carboplatin (C) area under the plasma concentration 5 (every 3 weeks [Q3W] on day 1); Arm B: TIS + *nab*-paclitaxel (*nab*-P) 100 mg/m^2 (Q3W on days 1, 8 and 15) + C (Q3W on Day 1); or Arm C: P + C (Q3W on day 1). P, *nab*-P and C were administered for 4 to 6 cycles. TIS was administered until loss of benefit, withdrawal of consent or start of a new anticancer therapy. In this sub-group analysis, pts aged ≥ 65 years were evaluated according to the primary endpoint (PFS) and key secondary endpoints (objective response rate and safety).

Results:

Overall, 127 pts aged ≥ 65 years were randomized to receive treatment. Median age of pts aged ≥ 65 was 68.0 years and 120 pts (94.5%) were male. In total, 18 (46.2%), 20 (38.5%), and 34 (94.4%) pts in Arms A, B and C, respectively, had discontinued treatment. In Arm C 22/34 pts had completed chemotherapy. The primary and secondary endpoints, PFS and ORR, were longer and higher, respectively, in Arms A and B, compared with Arm C (**Table**). Grade ≥ 3 treatment related adverse events (TRAEs) occurred in 33 (84.6%), 44 (84.6%) and 28 (82.4%) pts aged ≥ 65 years in Arms A, B and C, respectively, compared with 103 (85.8%), 99 (83.9%) and 94 (80.3%) pts aged ≥ 18 years enrolled in the study. The most commonly reported TRAEs in pts aged ≥ 65 years were anemia, decrease in neutrophil count, and alopecia.

Conclusions:

In this sub-group analysis, PFS and ORR were longer and higher, respectively, with TIS in pts aged ≥ 65 years with advanced squamous NSCLC. The safety profile of TIS in pts aged ≥ 65 years was similar to the safety profile for all aged pts aged ≥ 18 years.

Table

	Arm A (N = 39)	**Arm B (N = 52)**	**Arm C (N = 36)**
Median PFS, months (95% CI)	9.7 (5.59, NE)	9.7 (6.87, NE)	5.2 (4.14, NE)
HR (95% CI)	0.602 (0.309, 1.175)	0.564 (0.302, 1.052)	
ORR, % (95% CI)	69.2 (52.4, 83.0)	75.0 (61.1, 86.0)	50.0 (32.9, 67.1)

CI, confidence interval; HR, hazard ratio; NE, not estimable; ORR, objective response rate; PFS, progression free surviva