RATIONALE 304: Tislelizumab (TIS) plus chemotherapy (chemo) vs chemo alone as first-line (1L) treatment for non-squamous (non-sq) non-small cell lung cancer (NSCLC) in patients (pts) who are smokers vs non-smokers

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Background

Primary results from the Phase 3 RATIONALE-304 study (NCT03663205) showed efficacy and a manageable safety/tolerability profile for TIS, an anti-programmed cell death protein 1 monoclonal antibody, plus chemo, as 1L treatment for advanced or metastatic non-sq NSCLC. Here, we report results based on smoking status.

Methods

Eligible pts (aged 18–75 years) who were treatment-naïve for locally advanced or metastatic non-sq NSCLC were stratified by disease stage and programmed death-ligand 1 expression, and randomized 2:1 to receive TIS (200 mg intravenously [IV]) plus platinum (carboplatin AUC 5 or cisplatin 75 mg/m^2 IV) + pemetrexed 500 mg/m^2 (PP) every three weeks followed by maintenance TIS + pemetrexed (Arm A), or PP followed by maintenance pemetrexed (Arm B). Chemo was administered for 4–6 cycles. Progression free survival (PFS) by independent review committee (IRC), objective response rate (ORR) by IRC, and safety were assessed in pts who were smokers (former/current) and non-smokers.

Results

213 pts who were smokers with a median age of 61 years and 121 pts who were non-smokers with a median age of 59 years were randomized. PFS was longer with TIS plus chemo vs chemo alone for pts who were smokers (**Table**). ORR was higher with TIS plus chemo vs chemo alone for both smokers and non-smokers. Treatment emergent adverse events (TEAEs) occurring in smokers and non-smokers are summarized in the **Table**.

Conclusions

Clinically meaningful improvements in PFS were observed with TIS plus chemo in pts with advanced non-sq NSCLC who were smokers. The safety and efficacy profile of TIS was consistent with the overall population of this Phase 3 study.

Table

	Smokers		Non-smokers	
	Arm A (n=147)	**Arm B (n=66)**	**Arm A (n=76)**	**Arm B (n=45)**
n, (95% CI)				
Median PFS, months	9.7 (7.72, 11.53)	4.6 (4.11, 7.62)	8.5 (5.75, 11.86)	7.7 (5.82, 11.73)
Hazard ratio*	0.466 (0.311, 0.697)	-	1.075 (0.596, 1.940)	-
ORR, %	61.2 (52.8, 69.1)	31.8 (20.9, 44.4)	50.0 (38.3, 61.7)	44.4 (29.6, 60.0)
	n=146	**n=66**	**n=76**	**n=44**
n (%)				
Grade ≥ 3 TEAEs	99 (67.8)	36 (54.5)	51 (67.1)	23 (52.3)
Serious TEAEs	52 (35.6)	15 (22.7)	22 (28.9)	8 (18.2)
Immune-related TEAEs	38 (26.0)	NA	19 (25.0)	NA

*Unstratified