Tislelizumab Versus Docetaxel in Patients With Previously Treated Advanced Squamous Non-Small Cell Lung Cancer: Sub-Analysis From Phase 3 RATIONALE-303 Randomized Clinical Study

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Abstract:

Objectives: At a predefined interim analysis (IA), RATIONALE-303 (NCT03358875) demonstrated improved overall survival (OS) for tislelizumab versus docetaxel in the intent-to-treat (ITT) population with a manageable safety profile. Given disease characteristics, standard of care treatment/prognosis differ between histologic types of non-small cell lung cancer (NSCLC). Here we report the data on the squamous population.

Methods: Eight hundred five patients with histologically confirmed, advanced NSCLC with progressive disease during or after ≥1 platinum-containing chemotherapy regimen were randomized (2:1) to tislelizumab 200 mg IV or docetaxel 75 mg/m^2 IV every 3 weeks until disease progression, intolerable toxicity, or withdrawal. Histology (squamous vs nonsquamous) was a stratification factor for randomization. Dual primary endpoints were OS in the ITT and PD-L1 ≥25% populations. The IA was conducted after ~426 deaths (76% of planned events). Efficacy and safety were assessed in 370 randomized patients with squamous histology.

Results: Baseline characteristics of squamous patients were balanced between treatment arms and similar to the ITT population. As of August 10, 2020, at median follow-up of 19.0 and 19.3 months, respectively, median (95% CI) OS was longer with tislelizumab (16.0 months [13.8, 18.9]) versus docetaxel (11.3 months [8.7, 12.7]) in the squamous ITT population, and progression-free survival, objective response rate, and duration of response were also improved for tislelizumab versus docetaxel (**Table**). Among tislelizumab and docetaxel patients, 95.1% and 99.1% had ≥1 treatment-emergent adverse event (TEAE), respectively, and 38.1% (tislelizumab) and 79.5% (docetaxel) of patients

had ≥ grade 3 TEAEs. The most common TEAEs were anemia, cough, and increased alanine amino transferase (tislelizumab arm), and anemia, alopecia, and decreased neutrophil count (docetaxel arm).

Conclusions: Tislelizumab prolonged OS with a favorable safety profile in patients with advanced squamous NSCLC who progressed after a platinum-containing regimen. The data are consistent with the overall ITT population.

Table

Efficacy[a]	**Tislelizumab (n=248)**		**Docetaxel (n=122)**	
Median OS, months (95% CI)	16.0 (13.80, 18.86)		11.3 (8.67, 12.68)	
OS HR (95% CI)[b]	0.58 (0.436, 0.761) *P*<0.0001[c,d]			
Median PFS, months (95% CI)	6.2 (4.21, 6.37)		2.3 (2.10, 3.38)	
PFS HR (95% CI)[b]	0.45 (0.343, 0.577) *P*<0.0001[c,d]			
ORR, n (%)	57 (23.0)		5 (4.1)	
Median DoR, months (95% CI)	16.7 (8.31, NE)		6.2 (2.10, 8.31)	
Safety[e]	**Tislelizumab (n=247)**		**Docetaxel (n=117)**	
TEAEs ≥20% of patients in either arm, n (%)	**All grades**	**≥ Grade 3**	**All grades**	**≥ Grade 3**
Anemia	76 (30.8)	7 (2.8)	56 (47.9)	10 (8.5)
Decreased appetite	41 (16.6)	2 (0.8)	33 (28.2)	3 (2.6)
Asthenia	38 (15.4)	5 (2.0)	27 (23.1)	6 (5.1)
White blood cell count decreased	12 (4.9)	1 (0.4)	32 (27.4)	21 (17.9)
Leukopenia	9 (3.6)	1 (0.4)	31 (26.5)	19 (16.2)
Neutrophil count decreased	7 (2.8)	2 (0.8)	42 (35.9)	35 (29.9)
Alopecia	5 (2.0)	0 (0.0)	52 (44.4)	0 (0.0)
Neutropenia	2 (0.8)	0 (0.0)	37 (31.6)	34 (29.1)

[a]Efficacy analysis set: squamous patients; [b]Stratified; [c]One-sided stratified log-rank test; [d]Descriptive *P*-value; [e]Safety analysis set: squamous patients.
CI, confidence interval; DoR, duration of response; HR, hazard ratio; NE, not evaluable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; TEAE, treatment-emergent adverse event.
Data cut-off: August 10, 2020.