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

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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. Disease characteristics, standard of care, and treatment/prognosis differ between histologic types of non-small cell lung cancer (NSCLC). Here, we report on the nonsquamous 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 or docetaxel 75 mg/m^2 every 3 weeks until disease progression, intolerable toxicity, or withdrawal. Histology (squamous vs nonsquamous) was a randomization stratification factor. Dual primary endpoints were OS in the ITT and PD-L1 ≥25% populations. A prespecified IA was conducted after ~426 deaths (76% of planned events). Efficacy and safety were assessed in 435 randomized patients with nonsquamous histology

Results: Baseline characteristics of nonsquamous patients were balanced between treatment arms and similar to the ITT population. As of August 10, 2020, at median follow-up of 20 and 17 months, respectively, median (95% CI) OS was longer with tislelizumab (18.6 months [15.41, 23.16]) versus docetaxel (13.8 months [9.43, 17.94]) in the nonsquamous ITT population, and objective response rate and duration of response were also improved for tislelizumab versus docetaxel (**Table**). In tislelizumab and docetaxel patients, 95.5% and 97.9% had ≥1 treatment-emergent adverse event (TEAE), respectively, and 39.0% (tislelizumab) and 70.9% (docetaxel) of patients had ≥ grade 3 TEAEs. The most common TEAEs were anemia, increased aspartate aminotransferase, and increased alanine aminotransferase (tislelizumab arm), and alopecia, anemia, and decreased neutrophil count (docetaxel arm).

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

Table

Efficacy[a]	**Tislelizumab (n=287)**		**Docetaxel (n=148)**	
Median OS, months (95% CI)	18.6 (15.41, 23.16)		13.8 (9.43, 17.94)	
OS HR (95% CI)[b]	0.71 (0.538, 0.929) *P*=0.0064[c,d]			
Median PFS, months (95% CI)	2.5 (2.14, 4.01)		3.6 (2.17, 4.14)	
PFS HR (95% CI)[b]	0.84 (0.660, 1.062) *P*=0.0686[c,d]			
ORR, n (%)	60 (20.9)		14 (9.5)	
Median DoR, months (95% CI)	11.7 (6.80, 14.65)		6.2 (2.10, 7.16)	
Safety[e]	**Tislelizumab (n=287)**		**Docetaxel (n=141)**	
TEAEs ≥15% of patients in either arm, n (%)	**All grades**	**≥ Grade 3**	**All grades**	**≥ Grade 3**
Anemia	76 (26.5)	11 (3.8)	56 (39.7)	6 (4.3)
AST increased	64 (22.3)	5 (1.7)	18 (12.8)	0 (0.0)
ALT increased	63 (22.0)	4 (1.4)	24 (17.0)	0 (0.0)
Cough	59 (20.6)	4 (1.4)	25 (17.7)	0 (0.0)
Weight decreased	44 (15.3)	2 (0.7)	13 (9.2)	0 (0.0)
Decreased appetite	41 (14.3)	3 (1.0)	26 (18.4)	0 (0.0)
Hypoalbuminemia	37 (12.9)	0 (0.0)	23 (16.3)	0 (0.0)
Nausea	37 (12.9)	0 (0.0)	22 (15.6)	0 (0.0)
Constipation	31 (10.8)	0 (0.0)	22 (15.6)	0 (0.0)
Asthenia	29 (10.1)	1 (0.3)	29 (20.6)	8 (5.7)
Neutrophil count decreased	8 (2.8)	1 (0.3)	53 (37.6)	36 (25.5)
White blood cell count decreased	8 (2.8)	0 (0.0)	42 (29.8)	26 (18.4)
Neutropenia	7 (2.4)	3 (1.0)	44 (31.2)	38 (27.0)
Leukopenia	6 (2.1)	0 (0.0)	38 (27.0)	22 (15.6)
Alopecia	0 (0.0)	0 (0.0)	70 (49.6)	2 (1.4)

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