Tislelizumab Versus Docetaxel as Second- or Third-Line Therapy in Previously Treated Patients With Advanced Non-Small Cell Lung Cancer (NSCLC): Asian and Non-Asian Subgroup Analysis of the RATIONALE-303 Study

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Conclusions

In the RATIONALE-303 study, tislelizumab improved OS and consistently demonstrated favorable efficacy benefits compared with docetaxel, including PFS, ORR, and DoR, in both Asian and non-Asian patients with previously treated advanced NSCLC.

In this final analysis of the Asian and non-Asian subgroups, tislelizumab treatment was generally well tolerated with a favorable safety profile compared with docetaxel, with fewer grade 3 or higher TEAEs in both subgroups.

Background

Anti-programmed cell death protein 1/death-ligand 1 (PD-[L]1) therapies have improved overall survival (OS) by 3-4 months vs docetaxel in patients with advanced NSCLC who progressed after prior platinum-based chemotherapy.[1-4]

Tislelizumab, a monoclonal antibody with high binding affinity to the PD-1 receptor, was specifically engineered to minimize Fcγ receptor binding on macrophages.[5,6]

In RATIONALE-303, tislelizumab significantly prolonged OS vs docetaxel in the intent-to-treat (ITT) population at the interim analysis (IA) (data cutoff: August 10, 2020),[7] leading to its approval in China for patients with advanced NSCLC whose disease progressed after chemotherapy.[8]

At the final analysis (FA) (data cutoff: July 15, 2021), tislelizumab continued to improve OS vs docetaxel in previously treated patients with advanced NSCLC.[9] Here, we report the FA of the Asian and non-Asian subgroups. (Clinicaltrials.gov: NCT03358875)

Methods

- Adult patients with histologically confirmed, locally advanced or metastatic squamous or nonsquamous NSCLC that progressed during or following treatment with at least one platinum-containing regimen (but no more than two prior lines of systemic chemotherapy) were randomized (2:1) to tislelizumab 200 mg intravenously (IV) or docetaxel 75 mg/m^2 IV every 3 weeks
- Co-primary endpoints were OS in the intent-to-treat (ITT) and PD-L1 tumor cell (TC) ≥25% populations. Secondary endpoints included investigator-assessed progression-free survival (PFS), objective response rate (ORR), duration of response (DoR), and safety

Results

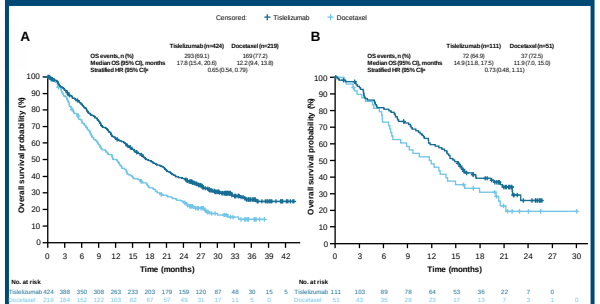
Patient Disposition and Baseline Characteristics

- Between November 2017 and April 2020, 643 Asian (641 from China) and 162 non-Asian patients were randomized
- At FA data cutoff, median study follow-up with tislelizumab vs docetaxel were 17.2 vs 10.7 months, respectively, in the Asian subgroup and 14.3 vs 10.4 months, respectively, in the non-Asian subgroup
- Sites in China initiated the study ~13.5 months earlier than sites outside of China
- Baseline characteristics were generally balanced between treatment arms in both subgroups

Efficacy Results

- An improved OS trend was observed with tislelizumab vs docetaxel in both the Asian (17.8 vs 12.2 months, respectively; stratified hazard ratio [HR] 0.65; 95% CI 0.54, 0.79) and non-Asian subgroups (14.9 vs 11.9 months, respectively; stratified HR 0.73; 95% CI 0.48, 1.11; **Figure 1**)
- Similarly, a longer median PFS was observed with tislelizumab vs docetaxel in both the Asian (HR 0.62; 95% CI 0.51, 0.75) and non-Asian (HR 0.67; 95% CI 0.45, 1.00) subgroups (**Figure 2**)
- Both subgroups demonstrated a favorable ORR and DoR with tislelizumab vs docetaxel (**Table 1**)

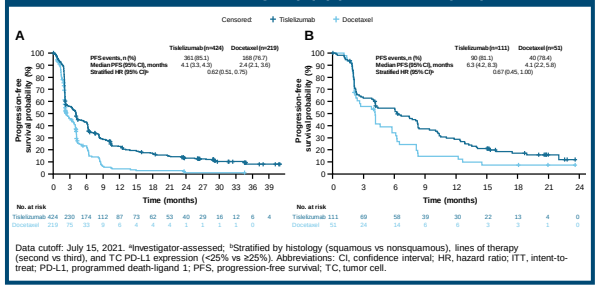
Figure 1. OS of Tislelizumab vs Docetaxel in the Asian Subgroup (A), and Non-Asian Subgroup (B) (ITT, Final Analysis)



Data cutoff: July 15, 2021. [a]Stratified by histology (squamous vs nonsquamous), lines of therapy (second vs third), and TC PD-L1 expression (<25% vs ≥25%). Abbreviations: CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; OS, overall survival; PD-L1, programmed death-ligand 1; TC, tumor cells.

- An ORR was achieved by 91 (21.5%) vs 13 (5.9%) and 30 (27.0%) vs six (11.8%) patients in the Asian and non-Asian subgroup, respectively

Figure 2. PFS[a] of Tislelizumab vs Docetaxel in the Asian Subgroup (A), and Non-Asian Subgroup (B) (ITT, Final Analysis)



Data cutoff: July 15, 2021. [a]Investigator-assessed; [b]Stratified by histology (squamous vs nonsquamous), lines of therapy (second vs third), and TC PD-L1 expression (<25% vs ≥25%). Abbreviations: CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; PD-L1, programmed death-ligand 1; PFS, progression-free survival; TC, tumor cell.

Table 1. Response Rate and Duration (ITT, Final Analysis)

	Asian Subgroup		Non-Asian Subgroup	
	Tislelizumab (n=424)	Docetaxel (n=219)	Tislelizumab (n=111)	Docetaxel (n=51)
ORR[a], n (%)	91 (21.5)	13 (5.9)	30 (27.0)	6 (11.8)
Median DoR[a], (95% CI), mo	13.8 (9.0, 21.8)	4.2 (2.1, 7.2)	10.3 (6.2, 19.9)	6.1 (2.1, 12.5)

Data cutoff: July 15, 2021. [a]Investigator assessed. ORR was assessed as the number of patients who had a best overall response of unconfirmed complete response or partial response. Abbreviations: CI, confidence interval; DoR, duration of response; HR, hazard ratio; ITT, intent-to-treat; mo, months; ORR, objective response rate.

Safety Results (Table 2)

- Fewer grade 3 or higher treatment-emergent adverse events (TEAEs) were reported in the tislelizumab arm than in the docetaxel arm for both Asian (41.1% vs 75.2%, respectively) and non-Asian (45.9% vs 72.9%, respectively) subgroups
- Serious TEAEs with tislelizumab vs docetaxel were experienced by 35.7% vs 31.4% of Asian patients and 29.7% vs 37.5% of non-Asian patients, respectively
- TEAEs leading to treatment discontinuation with tislelizumab vs docetaxel occurred in 10.6% vs 12.4% of Asian patients and 17.1% vs 16.7% of non-Asian patients

Table 2. TEAEs Occurring in ≥25% of Patients in the Tislelizumab or Docetaxel Arm[a] (Safety Population[b])

	Asian Subgroup				Non-Asian Subgroup			
	Tislelizumab (n=423)		Docetaxel (n=210)		Tislelizumab (n=111)		Docetaxel (n=48)	
n (%)	Any grade	≥grade 3	Any grade	≥grade 3	Any grade	≥grade 3	Any grade	≥grade 3
Anemia	135 (31.9)	17 (4.0)	99 (47.1)	15 (7.1)	21 (18.9)	1 (0.9)	16 (33.3)	3 (6.3)
Decreased appetite	72 (17.0)	5 (1.2)	47 (22.4)	2 (1.0)	16 (14.4)	0 (0)	15 (31.3)	1 (2.1)
Dyspnea	45 (10.6)	6 (1.4)	24 (11.4)	4 (1.9)	22 (19.8)	5 (4.5)	12 (25.0)	3 (6.3)
Nausea	42 (9.9)	0 (0)	31 (14.8)	1 (0.5)	19 (17.1)	0 (0)	12 (25.0)	0 (0)
WBC count decreased	20 (4.7)	1 (0.2)	72 (34.3)	46 (21.9)	0 (0)	0 (0)	2 (4.2)	1 (2.1)
Neutrophil count decreased	16 (3.8)	3 (0.7)	91 (43.3)	68 (32.4)	0 (0)	0 (0)	4 (8.3)	3 (6.3)
Leukopenia	15 (3.5)	1 (0.2)	62 (29.5)	36 (17.1)	2 (1.8)	0 (0)	11 (22.9)	5 (10.4)
Fatigue	12 (2.8)	0 (0)	12 (5.7)	6 (2.9)	24 (21.6)	3 (2.7)	13 (27.1)	2 (4.2)
Neutropenia	8 (1.9)	2 (0.5)	57 (27.1)	52 (24.8)	2 (1.8)	1 (0.9)	24 (50.0)	20 (41.7)
Alopecia	5 (1.2)	0 (0)	111 (52.9)	1 (0.5)	2 (1.8)	0 (0)	15 (31.3)	1 (2.1)

Data cutoff: July 15, 2021. Adverse event grades were evaluated based on NCI-CTCAE (version 4.03). [a]At any grade in either subgroup; [b]Safety population included all patients receiving any dose of study drug. Abbreviations: TEAE, treatment-emergent adverse event; WBC, white blood cell.

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