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

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Objectives: In RATIONALE-303 (NCT03358875), tislelizumab significantly improved overall survival (OS) versus docetaxel in the intent-to-treat population (ITT) at the interim analysis (IA). Tislelizumab was later approved in China for advanced or metastatic non-small cell lung cancer (NSCLC) after progression on prior platinum-based chemotherapy. At the final analysis (FA), the co-primary endpoint of OS in the programmed death-ligand 1 (PD-L1, VENTANA SP263 assay) tumor cell ≥25% population was met, and tislelizumab continued to improve OS compared with docetaxel in the ITT. Here we report FA results from the Asian versus non-Asian subgroups.

Methods: A total of 805 patients with histologically confirmed locally advanced or metastatic NSCLC that progressed during or following treatment with ≥1 platinum-based regimen were randomized 2:1 to receive tislelizumab 200 mg or docetaxel 75 mg/m^2 intravenously once every 3 weeks until disease progression, intolerable toxicity, or withdrawal of consent. Dual primary endpoints were OS in the ITT and PD-L1 ≥25% populations. Secondary endpoints included investigator-assessed progression-free survival (PFS), objective response rate (ORR), duration of response (DoR), and safety. A prespecified IA was conducted in ITT after ≈426 deaths (76% of planned events).

Results: In total, 643 Asian and 162 non-Asian patients were randomized. Baseline characteristics were balanced between treatment arms in both subgroups. Both subgroups demonstrated favorable OS, PFS, DoR, and ORR with tislelizumab versus docetaxel (**Table**). Treatment-emergent adverse events (TEAEs) of ≥ grade 3 with tislelizumab

versus docetaxel were experienced by 41.1% versus 75.2% of Asian patients and 45.9% versus 72.9% of non-Asian patients, respectively. Serious TEAEs with tislelizumab versus docetaxel were experienced by 35.7% versus 31.4% of Asian patients and 29.7% versus 37.5% of non-Asian patients, respectively.

Conclusions: In both Asian and non-Asian patients, tislelizumab demonstrated favorable efficacy benefits compared with docetaxel and was generally well tolerated.

Table

	Asian		**Non-Asian**	
ITT analysis set	**Tislelizumab (n=424)**	**Docetaxel (n=219)**	**Tislelizumab (n=111)**	**Docetaxel (n=51)**
Median study follow-up, months	17.2	10.7	14.3	10.4
Deaths, n (%)	293 (69.1)	169 (77.2)	72 (64.9)	37 (72.5)
mOS, months	17.8	12.2	14.9	11.9
HR[a] (95% CI)	0.65 (0.54, 0.79); *P* < 0.0001		0.73 (0.48, 1.11); *P*=0.0674	
mPFS, months	4.1	2.4	6.3	4.1
HR[a] (95% CI)	0.62 (0.51, 0.75); *P* < 0.0001		0.67 (0.45, 1.00); *P*=0.0241	
ORR, %	21.5	5.9	27.0	11.8
Odds ratio (95% CI)	4.41 (2.41, 8.07); *P* < 0.0001		2.84 (1.12, 7.20); *P*=0.0226	
mDoR, months	13.8	4.2	10.3	6.1

P values are descriptive. [a]Stratified by histology, lines of therapy, and PD-L1 expression.
CI, confidence interval; HR, hazard ratio; m, median.