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

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Disclosures for Dr. Zhou

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Background

- Anti-PD-(L)1 therapies have improved 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 ITT population at the 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 FA (data cutoff: July 15, 2021), tislelizumab continued to improve OS vs docetaxel in previously treated patients with advanced NSCLC[9]
- The final analysis of the Asian and non-Asian subgroups report is presented here (Clinicaltrials.gov: NCT03358875)

IA, interim analysis; ITT, intent to treat; NSCLC, non-small cell lung cancer; OS, overall survival; PD-(L)1, protein death-(ligand) 1.

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Methods

- Adult patients with histologically confirmed, locally advanced or metastatic squamous or non-squamous NSCLC that progressed during or following treatment with at least one platinum-containing regimen (but no more than two prior lines of systemic chemotherapy)
- Treatment: tislelizumab 200 mg IV or docetaxel 75 mg/m^2 IV every 3 weeks (2:1 randomization)
- Co-primary endpoints were OS in the ITT and PD-L1 TC ≥ 25% populations
- Secondary endpoints included investigator-assessed PFS, ORR, DoR, and safety

Duration of response, DoR; ITT, intent to treat; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; TC, tumor cell.

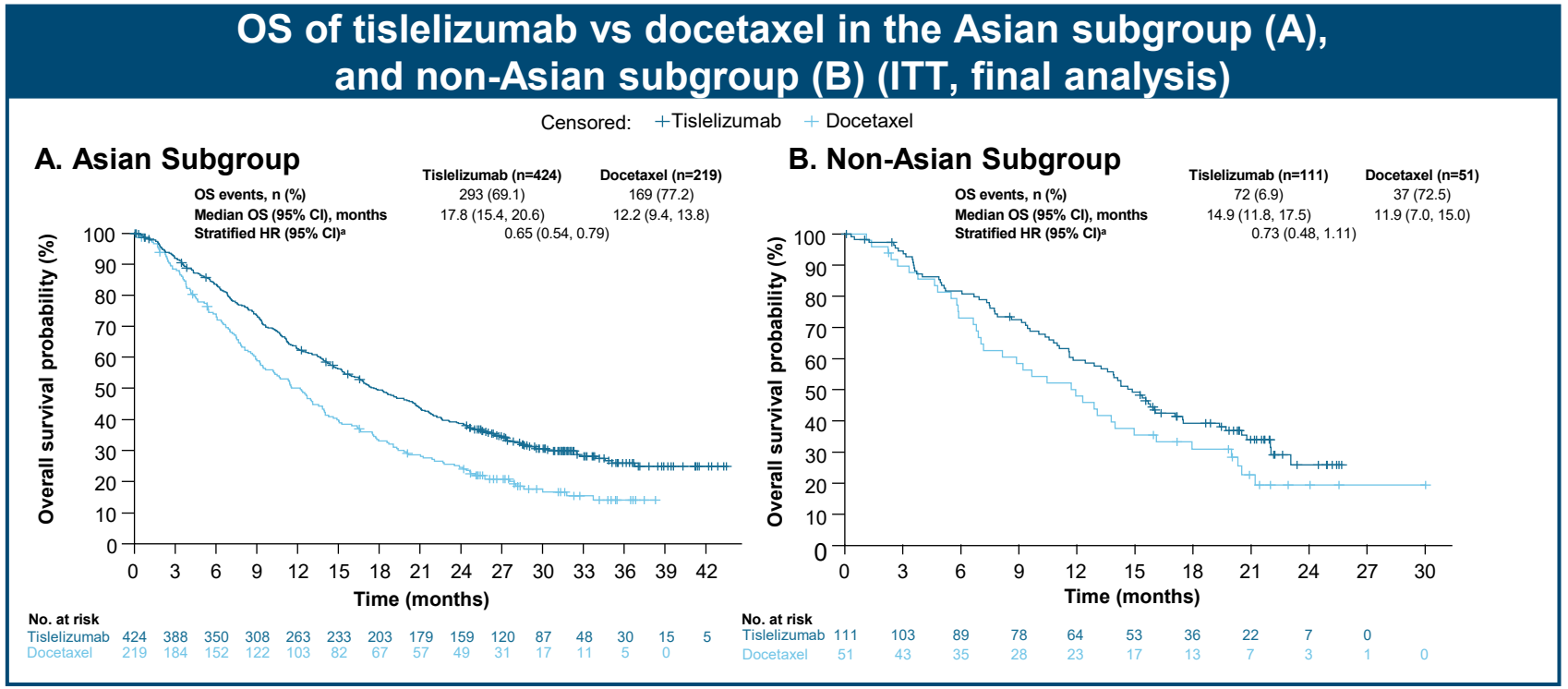
Patient Disposition & Baseline Characteristics

- 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

FA, final analysis.

An Improved OS Trend was Observed with Tislelizumab vs Docetaxel

- Asian subgroup: 17.8 vs 12.2 months; stratified HR, 0.65 (95% CI, 0.54, 0.79)
- Non-Asian subgroup: 14.9 vs 11.9 months; stratified HR, 0.73 (95% CI, 0.48, 1.11)

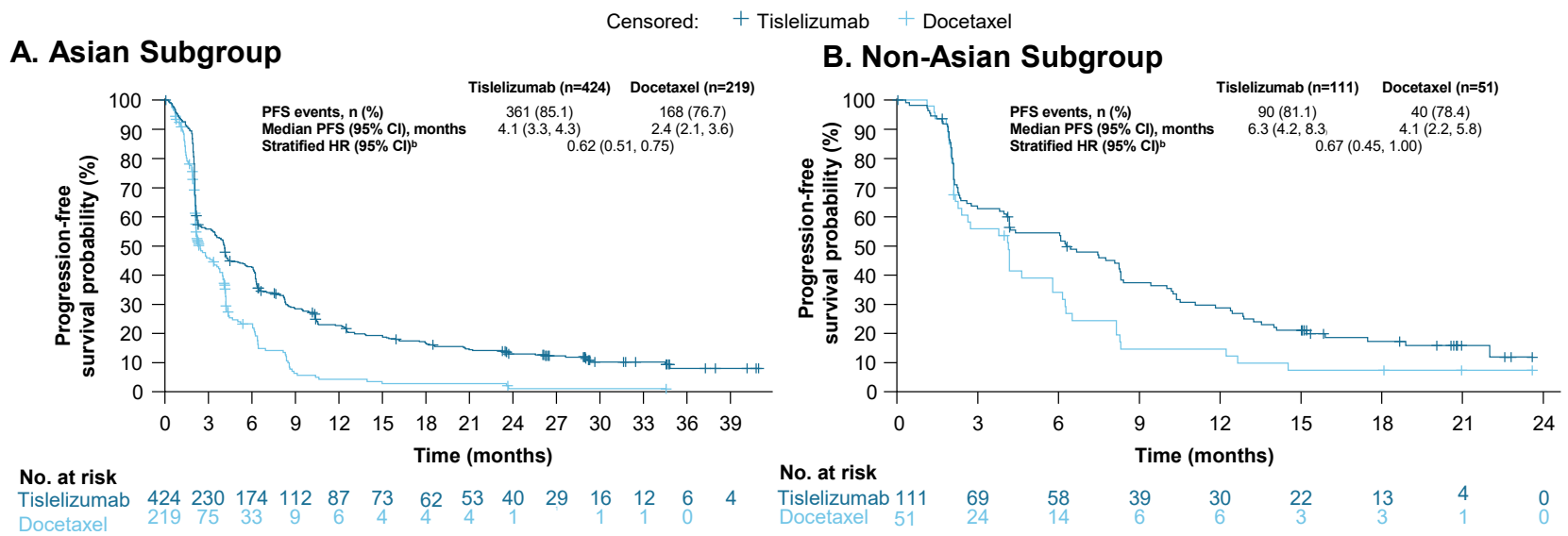


Data cutoff: July 15, 2021. [a]Stratified by histology (squamous vs nonsquamous), lines of therapy (second vs third), and TC PD-L1 expression (<25% vs ≥25%).
CI, confidence interval; HR, hazard ratio CI, confidence interval; HR, hazard ratio; ; ITT, intent-to-treat; OS, overall survival; PD-L1, programmed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

A Longer Median PFS was Observed with Tislelizumab vs Docetaxel

- Asian subgroup: 4.1 vs 2.4 months; stratified HR, 0.62 (95% CI, 0.51, 0.75)
- Non-Asian subgroup: 6.3 vs 4.1 months; stratified HR, 0.67 (95% CI, 0.45, 1.00)

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 non-squamous), lines of therapy (second vs third), and TC PD-L1 expression (<25% vs ≥25%).
CI, confidence interval; ITT, intent-to-treat; PD-L1, programmed death-ligand 1; HR, hazard ratio; PFS, progression free survival; TC, tumor cell.

Both Subgroups Demonstrated a Favorable ORR and DoR with Tislelizumab vs Docetaxel

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)

- An ORR was achieved by 91 (21.5%) vs 13 (5.9%) patients and 30 (27.0%) vs 6 (11.8%) patients in the Asian and non-Asian subgroups for tislelizumab vs docetaxel, respectively

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.
CI, confidence interval; DoR, duration of response; HR, hazard ratio; ITT, intent-to-treat; mo, months; ORR, objective response rate.

Fewer Grade ≥ 3 TEAEs were Reported with Tislelizumab vs Docetaxel

- Grade ≥ 3 TEAEs with tislelizumab vs docetaxel
  - Asian subgroup: 41.1% vs 75.2%
  - Non-Asian subgroup: 45.9% vs 72.9%
- Serious TEAEs with tislelizumab vs docetaxel
  - Asian subgroup: 35.7% vs 31.4%
  - Non-Asian subgroup: 29.7% vs 37.5%
- TEAEs leading to treatment discontinuation with tislelizumab vs docetaxel
  - Asian subgroup: 10.6% vs 12.4%
  - Non-Asian subgroup: 17.1% vs 16.7%

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.
TEAEs, treatment emergent adverse events; WBC, white blood cell.

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

DoR, duration of response; NSCLC, non small cell lung cancer; ORR, overall response rate; OS, overall survival; PFS, progression free survival; TEAEs, treatment emergent adverse events.

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