RATIONALE-303: post-hoc analysis of tislelizumab monotherapy in previously treated non-small cell lung cancer with metastases

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ABSTRACT

Introduction: The global, open-label, randomised, multicentre phase 3 RATIONALE-303 trial (NCT03358875) demonstrated superior overall survival (OS) with tislelizumab (anti-programmed cell death protein-1 antibody) vs docetaxel in patients with locally advanced or metastatic (squamous or non-squamous) non-small cell lung cancer (NSCLC) who progressed after platinum-based chemotherapy. Results are reported on subgroup analyses of patients with metastases, including liver metastases, who historically have poor prognosis.

Methods: Eligible patients aged ≥18 years were randomised (2:1) to receive intravenous tislelizumab 200 mg or docetaxel 75 mg/m^2 once every 3 weeks. Efficacy (OS and investigator-assessed progression-free survival [PFS_{INV}] and objective response rate [ORR_{INV}]) and safety outcomes were analysed based on the number of metastatic sites (locally advanced [ie, no metastatic sites], one or two metastatic sites, or three or more metastatic sites) and presence or absence of liver metastases at baseline.

Results: Among the 805 randomised patients (tislelizumab, n=535; docetaxel, n=270), 106 (13.2%) had liver metastases at baseline (tislelizumab, n=73; docetaxel, n=33). As of January 18, 2024 (median study follow-up: 16.6 months for tislelizumab and 10.7 months for docetaxel), sustained OS, PFS_{INV}, and ORR benefit was observed among tislelizumab- vs docetaxel-treated patients, regardless of the number of metastatic sites at baseline (Table 1). OS, PFS_{INV}, and ORR benefit among patients treated with tislelizumab vs docetaxel was maintained in those with and without liver metastases at baseline (Table 2). Safety outcomes were consistent with the known safety profile of tislelizumab, with tislelizumab demonstrating a more favourable safety profile compared with docetaxel across all subgroups (Tables 1 and 2).

Conclusion: This post-hoc analysis of RATIONALE-303 demonstrated a clinically meaningful OS, PFS_{INV}, and ORR_{INV} benefit with tislelizumab vs docetaxel in pretreated patients with locally advanced or metastatic squamous or non-squamous NSCLC, regardless of the number of metastatic sites, including liver metastases.

Table 1. Efficacy and Safety Outcomes by Number of Metastatic Sites at Baseline in the RATIONALE-303 Trial

	Locally Advanced (No Metastatic Sites)		One or Two Metastatic Sites		Three or More Metastatic Sites	
Efficacy Outcomes	**Tislelizumab (n=84)**	**Docetaxel (n=33)**	**Tislelizumab (n=328)**	**Docetaxel (n=172)**	**Tislelizumab (n=123)**	**Docetaxel (n=65)**
Median OS (95% CI), months	24.5 (20.7, 29.5)	14.9 (12.6, 19.3)	17.5 (15.8, 20.0)	12.7 (9.7, 15.2)	11.2 (7.6, 12.9)	7.8 (5.8, 10.5)
Unstratified HR (95% CI)	0.52 (0.33, 0.83)		0.71 (0.57, 0.87)		0.68 (0.49, 0.94)	
Median PFS_{INV} (95% CI), months	8.3 (5.5, 13.1)	3.7 (2.1, 6.9)	4.2 (3.6, 6.2)	2.6 (2.1, 4.0)	2.3 (2.1, 4.0)	2.2 (1.9, 4.0)
Unstratified HR (95% CI)	0.58 (0.35, 0.96)		0.62 (0.50, 0.76)		0.65 (0.46, 0.92)	
ORR_{INV}, n (%) [95% CI]	26 (31.0) [21.3, 42.0]	4 (12.1) [3.4, 28.2]	73 (22.3) [17.9, 27.2]	15 (8.7) [5.0, 14.0]	22 (17.9) [11.6, 25.8]	2 (3.1) [0.37, 10.7]
Safety Outcomes	**Tislelizumab (n=84)**	**Docetaxel (n=33)**	**Tislelizumab (n=327)**	**Docetaxel (n=165)**	**Tislelizumab (n=123)**	**Docetaxel (n=60)**
Patients with ≥1 TEAE, n (%)	83 (98.8)	33 (100.0)	316 (96.6)	163 (98.8)	119 (96.7)	58 (96.7)
Patients with ≥1 TRAE, n (%)	71 (84.5)	32 (97.0)	248 (75.8)	156 (94.5)	85 (69.1)	54 (90.0)
Serious TEAEs, n (%)	21 (25.0)	12 (36.4)	119 (36.4)	48 (29.1)	52 (42.3)	24 (40.0)
TEAEs leading to death, n (%)	1 (1.2)	2 (6.1)	22 (6.7)	5 (3.0)	12 (9.8)	5 (8.3)
TEAEs leading to treatment discontinuation, n (%)	9 (10.7)	8 (24.2)	41 (12.5)	17 (10.3)	17 (13.8)	9 (15.0)

Data cutoff: January 18, 2024.

Abbreviations: CI, confidence interval; HR, hazard ratio; ORR_{INV}, investigator-assessed objective response rate; OS, overall survival; PFS_{INV}, investigator-assessed progression-free survival; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Table 2. Efficacy and Safety Outcomes in Patients With or Without Liver Metastases at Baseline in the RATIONALE-303 Trial

	With Liver Metastases		Without Liver Metastases	
Efficacy Outcomes	**Tislelizumab (n=73)**	**Docetaxel (n=33)**	**Tislelizumab (n=462)**	**Docetaxel (n=237)**
Median OS (95% CI), months	13.4 (7.9, 17.3)	6.8 (4.1, 7.8)	17.6 (15.8, 20.4)	12.9 (11.3, 14.0)
Unstratified HR (95% CI)	0.48 (0.30, 0.78)		0.69 (0.58, 0.82)	
Median PFS_{INV} (95% CI), months	2.1 (2.0, 4.0)	2.0 (1.8, 4.0)	4.3 (4.1, 6.2)	2.9 (2.3, 4.0)
Unstratified HR (95% CI)	0.53 (0.33, 0.85)		0.62 (0.52, 0.74)	
ORR_{INV}, n (%) [95% CI]	11 (15.1) [7.8, 25.4]	2 (6.1) [0.7, 20.2]	110 (23.8) [20.0, 28.0]	19 (8.0) [4.9, 12.2]
Safety Outcomes	**Tislelizumab (n=72)**	**Docetaxel (n=29)**	**Tislelizumab (n=462)**	**Docetaxel (n=229)**
Patients with ≥1 TEAE, n (%)	69 (95.8)	28 (96.6)	449 (97.2)	226 (98.7)
Patients with ≥1 TRAE, n (%)	53 (73.6)	26 (89.7)	351 (76.0)	216 (94.3)
Serious TEAEs, n (%)	30 (41.7)	11 (37.9)	162 (35.1)	73 (31.9)
TEAEs leading to death, n (%)	6 (8.3)	2 (6.9)	29 (6.3)	10 (4.4)
TEAEs leading to treatment discontinuation, n (%)	10 (13.9)	3 (10.3)	57 (12.3)	31 (13.5)

Data cutoff: January 18, 2024.

Abbreviations: CI, confidence interval; HR, hazard ratio; ORR_{INV}, investigator-assessed objective response rate; OS, overall survival; PFS_{INV}, investigator-assessed progression-free survival; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.