Tislelizumab (TIS) versus docetaxel (D) in patients with previously treated advanced non-squamous (non-sq) non-small-cell lung cancer (NSCLC): subanalysis from the RATIONALE-303 Phase 3 randomized clinical study

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Abstract:

Background

At a predefined interim analysis (IA), RATIONALE-303 (NCT03358875) demonstrated improved overall survival (OS) for TIS vs D in the intent-to-treat (ITT), with a manageable safety profile. Disease characteristics, standard of care and treatment/prognosis differ between histologic types of NSCLC. Here, we report on the non-sq population.

Methods

805 patients with histologically confirmed, advanced NSCLC with progressive disease during or after ≥ 1 platinum (Pt)-containing chemotherapy regimen were randomized (2:1) to TIS 200 mg or D 75 mg/m^2 every 3 weeks until disease progression, intolerable toxicity, or withdrawal. Histology (sq vs non-sq) 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 non-sq histology.

Results

Baseline characteristics of non-sq 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 (mo), respectively, median (95% CI) OS was longer with TIS (18.6 mo [15.41, 23.16]) vs D (13.8 mo [9.43, 17.94]) in the non-sq ITT population, and objective response

rate (ORR) and duration of response (DoR) were also improved for TIS vs D (**Table**). 95.5% (TIS) and 97.9% (D) of patients had ≥ 1 treatment-emergent adverse event (TEAE) and 39.0% (TIS) and 70.9% (D) of patients had ≥ Grade 3 TEAEs. The most common TEAEs were anemia, aspartate aminotransferase increased and alanine aminotransferase increased (TIS arm), and alopecia, anemia and neutrophil count decreased (D arm).

Conclusions

TIS prolonged OS, consistent with the overall ITT population, with a favorable safety profile in patients with advanced non-sq NSCLC who progressed after a Pt-containing regimen.

Table

Efficacy[*]	**TIS (n=287)**		**D (n=148)**	
Median OS, mo (95% CI)	18.6 (15.41, 23.16)		13.8 (9.43, 17.94)	
OS HR (95% CI)[†]	0.71 (0.538, 0.929) P=0.0064[‡,§]			
Median PFS, mo (95% CI)	2.5 (2.14, 4.01)		3.6 (2.17, 4.14)	
PFS HR (95% CI)[†]	0.84 (0.660, 1.062) P=0.0686[‡,§]			
ORR, n (%)	60 (20.9)		14 (9.5)	
Median DoR, mo (95% CI)	11.7 (6.80, 14.65)		6.2 (2.10, 7.16)	
Safety[**]	**TIS (n=287)**		**D (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)

[*]Efficacy analysis set - non-sq patients; [†]Stratified; [‡]One-sided stratified log-rank test; [§]Descriptive P-value; [**]Safety analysis set - non-squamous patients

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI; confidence interval; DoR, duration of response; HR, hazard ratio; mo, months; NE, not evaluable; ORR, objective response rate; PFS, progression-free survival; TEAE, treatment-emergent adverse event

Data cut-off: August 10, 2020