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

Authors: Jie Wang,[*1] Zhiyong Ma,[2] Dingzi Huang,[3] Yun Fan,[4] Xinmin Yu,[4] Sheng Hu,[5] Ziping Wang,[6] Zhihua Liu,[7] Devrim Cabuk,[8] Mahmut Gumus,[9] Yiyuan Ma,[10] Yan Wang,[10] Yan Ma,[10] Caicun Zhou[11]

Institutions:

[1]State Key Laboratory of Molecular Oncology, Department of Medical Oncology, National Cancer Centre/National Clinical Research Centre for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [2]The Affiliated Cancer Hospital of Zhengzhou University/Henan Cancer Hospital, Zhengzhou, China; [3]Department of Thoracic Medical Oncology, Lung Cancer Diagnosis and Treatment Centre, Key Laboratory of Cancer Prevention and Therapy, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Centre for Cancer, Tianjin, China; [4]Department of Thoracic Medical Oncology, Cancer Hospital of University of Chinese Academy of Sciences & Zhejiang Cancer Hospital, Hangzhou, China; [5]Hubei Cancer Hospital, Wuhan, China; [6]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/ Beijing), Department of Thoracic Medical Oncology, Peking University Cancer Hospital and Institute, Beijing, China; [7]Jiangxi Cancer Hospital, Nanchang, China; [8]Faculty of Medicine, Department of Medical Oncology, Kocaeli University, Kocaeli, Turkey; [9]Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey; [10]BeiGene (Beijing) Co., Ltd., Beijing, China; [11]Department of Medical Oncology, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, China.

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) population with a manageable safety profile. Given disease characteristics, standard of care treatment/prognosis differ between histologic types of NSCLC. Here we report the data on the sq population.

Methods

805 patients (pts) 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 IV or D 75 mg/m^2 IV every 3 weeks until disease progression, intolerable toxicity, or withdrawal. Histology (sq vs non-sq), was a stratification factor for randomization. Dual primary endpoints were OS in the ITT and PD-L1 ≥ 25% populations. The IA was conducted after ~426 deaths (76% of planned events). Efficacy and safety were assessed in 370 randomized pts with sq histology.

Results

Baseline characteristics of sq pts were balanced between treatment arms and similar to the ITT population. As of August 10, 2020, at median follow-up of 19.0 and 19.3 months (mo), respectively, median (95% CI) OS was longer with TIS (16.0 mo [13.8, 18.9]) vs D (11.3 mo [8.7, 12.7]) in the sq ITT population, and progression free survival (PFS), objective response rate (ORR) and duration of response (DoR) were also improved for TIS vs D (**Table**). 95.1% (TIS) and 99.1% (D) of pts had ≥ 1 treatment-emergent adverse event (TEAE) and 38.1% (TIS) and 79.5% (D) of pts had ≥ Grade 3 TEAEs. The most common TEAEs were anemia, cough and alanine amino transferase increased (TIS arm), and anemia, alopecia, and neutrophil count decreased (D arm).

Conclusions

TIS prolonged OS with a favorable safety profile in pts with advanced sq NSCLC who progressed after a Pt-containing regimen. The data are consistent with the overall ITT population.

Table

Efficacy[*]	**TIS (n=248)**		**D (n=122)**	
Median OS, mo (95% CI)	16.0 (13.80, 18.86)		11.3 (8.67, 12.68)	
OS HR (95% CI)[†]	0.58 (0.436, 0.761) P < 0.0001[‡§]			
Median PFS, mo (95% CI)	6.2 (4.21, 6.37)		2.3 (2.10, 3.38)	
PFS HR (95% CI)[†]	0.45 (0.343, 0.577) P < 0.0001[‡§]			
ORR, n (%)	57 (23.0)		5 (4.1)	
Median DoR, mo (95% CI)	16.7 (8.31, NE)		6.2 (2.10, 8.31)	
Safety[**]	**TIS (n=247)**		**D (n=117)**	
TEAEs ≥ 20% of patients in either arm, n (%)	**All grades**	**≥ Grade 3**	**All grades**	**≥ Grade 3**
Anemia	76 (30.8)	7 (2.8)	56 (47.9)	10 (8.5)
Decreased appetite	41 (16.6)	2 (0.8)	33 (28.2)	3 (2.6)
Asthenia	38 (15.4)	5 (2.0)	27 (23.1)	6 (5.1)
White blood cell count decreased	12 (4.9)	1 (0.4)	32 (27.4)	21 (17.9)
Leukopenia	9 (3.6)	1 (0.4)	31 (26.5)	19 (16.2)
Neutrophil count decreased	7 (2.8)	2 (0.8)	42 (35.9)	35 (29.9)
Alopecia	5 (2.0)	0 (0.0)	52 (44.4)	0 (0.0)
Neutropenia	2 (0.8)	0 (0.0)	37 (31.6)	34 (29.1)

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

CI; confidence interval; D, docetaxel; DoR, duration of response; HR, hazard ratio; mo, months; NE, not evaluable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; sq, squamous;

TEAE, treatment-emergent adverse event; TIS, tislelizumab

Data cut-off: August 10, 2020