Tislelizumab (TIS) treatment beyond progression in advanced sq-NSCLC after 1l chemoimmunotherapy: Results from randomized, phase III RATIONALE-307 study

Zhijie Wang[1], Xinmin Yu[2], Jun Zhao[3], Yan Yu[4], Jingxun Wu[5], Rui Ma[6], Zhiyong Ma[7], Jiuwei Cui[8], Na Zhao[9], Ding Wang[10], Jie Wang[1]

[1]Department of Medical Oncology, Cancer Hospital Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
[2]Department of Medical Oncology, Zhejiang Cancer Hospital, Institute of Basic Medicine and Cancer (IBMC), Chinese Academy of Sciences, Hangzhou, China
[3]Department of Medical Oncology, Beijing Cancer Hospital, Beijing, China
[4]Department of Medical Oncology, Harbin Medical University Cancer Hospital, Harbin, China
[5]Department of Medical Oncology, The First Affiliated Hospital of Xiamen University, Xiamen, China
[6]Department of Chest Internal Medicine, Liaoning Cancer Hospital & Institute, Shenyang, China
[7]Department of Medical Oncology, The Affiliated Cancer Hospital of Zhengzhou University/Henan Cancer Hospital, Zhengzhou, China
[8]Cancer Center Department, The First Hospital of Jilin University, Changchun, China
[9]BeiGene (Shanghai) Co., Ltd., Shanghai, China
[10]BeiGene (Beijing) Co., Ltd., Beijing, China

Background: ICI transformed the treatment of NSCLC; however, subsequent treatment options after PD remain limited. Continued ICI treatment beyond progression (TBP) is allowed in patients (pts) who may benefit from immunotherapy in numerous phase III clinical trials, yet TBP benefits after 1L ICI + chemo in NSCLC remain unclear. Here we evaluated the efficacy and safety of TIS TBP in RATIONALE-307, a phase III study of TIS plus chemo vs chemo in 1L sq-NSCLC, and further explored the potential beneficial population.

Methods: Pts with PD from TIS + chemo arms were divided into 3 groups based on subsequent treatments: TBP group (continuing TIS monotherapy), OT group (switching to other anti-cancer treatment) and NT group (receiving no treatment). Post-PD OS (data cut-off: Apr 28, 2023) was evaluated in 3 groups. In TBP group, we further assessed treatment exposure and safety of TIS TBP; post-PD OS in pts with varying PD patterns (low risk: PD of existing lesions; intermediate risk: new lesions; high risk: both) was also analyzed to explore the potential beneficial population.

Results: Among 162 pts with PD, 67 (41.3%) continued TIS monotherapy, 55 (34.0%) switched to other treatments, and 40 (24.7%) received no further treatment. Characteristics at baseline and at PD, 1L efficacy, and 1L PD patterns were shown in Table. The mOS from PD was 18.4 mo for TBP group, 7.9 mo for OT, and 7.2 mo for NT. In TBP group, median TIS cycles from PD was 4 (range 1-53). No new safety signals were observed with TIS TBP. The mOS from PD for low, intermediate and high-risk pts were 22.8, 16.1 and 8.3 mo, respectively.

Conclusions: Within the limitations of retrospective analysis, TIS TBP might bring survival benefits for sq-NSCLC pts after disease progression on 1L chemoimmunotherapy, without increasing safety risks. Pts with low or intermediate risk tended to have longer OS, representing a potentially beneficial population that may offer insights for clinical decision-making in TBP.

Table

	TBP (n=67)	OT (n=55)	NT (n=40)
Baseline Characteristics*			
Age<65 yrs	39 (58.2)	41 (74.5)	24 (60.0)
ECOG PS=1	48 (71.6)	46 (83.6)	31 (77.5)
PD-L1 <1%	30 (44.8)	20 (36.4)	19 (47.5)
1L efficacy			

ORR*	52 (77.6)	43 (78.2)	29 (72.5)
mPFS (95% CI), mo	9.7 (7.7-11.8)	7.6 (6.7-9.7)	7.6 (5.7-9.7)
Characteristics change at PD*			
Without worsening of ECOG PS	64 (95.5)	50 (90.9)	34 (85.0)
Weight drop ≥10%	2 (3.0)	0	1 (2.5)
1L PD patterns			
Progressive lesions, mean (range)	1.67 (1–5)	1.85 (1–7)	1.95 (1–7)
Specific PD patterns*			
Only existing lesions	38 (56.7)	36 (65.5)	22 (55)
Only new lesions	21 (31.3)	8 (14.5)	10 (25)
Both	8 (11.9)	11(20)	8 (20)
Post-PD OS			
Median (95% CI), mo	18.4 (5.5-22.8)	7.9 (7.4-13.7)	7.2 (4.7-10.5)

* n (%)