Pathological response to neoadjuvant tislelizumab (TIS) plus platinum-doublet (PtDb) chemotherapy (CT) in resectable stage II-IIIa NSCLC patients (pts) in the phase 3 (Ph3) RATIONALE-315 trial

Authors: Federico Cappuzzo,[1*] Dongsheng Yue,[2] Wenxiang Wang,[3] Hongxu Liu,[4] Qixun Chen,[5] Chun Chen,[6] Jun Zhang,[7] Fan Bai,[8] Changli Wang[2]
*Presenting and corresponding author

Affiliations: [1]Istituto Nazionale Tumori IRCCS Regina Elena, Roma, Italy; [2]Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; [3]Hunan Cancer Hospital, Hunan, China; [4]Liaoning Cancer Hospital and Institute, Shenyang, China; [5]Zhejiang Cancer Hospital, Hangzhou, China; [6]Fujian Medical University Union Hospital, Fuzhou, China; [7]BeiGene USA, Inc., San Mateo, CA, USA; [8]BeiGene (Shanghai) Co., Ltd., Shanghai, China

ABSTRACT

Background: Neoadjuvant (NA) CT with anti-PD-(L)1 mAb has shown promising major pathological response (MPR) and pathological complete response (pCR] rates in pts with resectable NSCLC. The Ph3 RATIONALE-315 study (NCT04379635) investigated the efficacy and safety of NA TIS (anti-PD-1 mAb) or placebo (PBO) + CT, then adjuvant TIS or PBO, in pts with resectable stage II-IIIA NSCLC.

Material (Patients) and Methods: This study enrolled pts with treatment (tx)-naïve, resectable, confirmed squamous (sq) or non-sq (nsq) stage II-IIIA NSCLC who were eligible for PtDb CT, with no known *EGFR* mutation (nsq) or *ALK* gene translocation (sq & nsq). Pts were randomized (1:1) to 3-4 cycles of TIS 200 mg IV Q3W or PBO, + PtDb CT, followed by surgery + 8 cycles of adjuvant TIS 400 mg IV Q6W or PBO. Primary endpoints: MPR rate + EFS per RECIST v1.1 by blinded independent review committee (IRC). Key secondary endpoint: pCR rate.

Results: As of 20 Feb 2023 (median follow-up: 16.8 mo), 453 pts (TIS + CT, n=226; CT, n=227) were randomized (ITT population). Of 452 (99.8%; n=226 both arms) pts treated in the NA phase, 421 (92.9%) completed NA tx (TIS + CT, n=211 [93.4%]; CT, n=210 [92.5%]); 90 (19.9%) did not undergo surgery (TIS + CT, n=36 [15.9%]; CT, n=54 [23.8%]). Efficacy and safety data from the NA phase are summarized in the table; MPR and pCR rates were significantly improved with TIS + CT vs CT (P<0.0001). TIS + CT did not impact the feasibility of surgery.

Conclusions: TIS + CT showed clinically meaningful and statistically significant improvements in MPR and pCR rates vs PBO + CT as NA tx, and was manageable in pts with resectable stage II-IIIA NSCLC. These data support TIS + CT as a novel tx option for these pts.

Table.

	TIS + CT	CT
Efficacy	**ITT Analysis Set**	
	n=226	**n=227**
MPR, % (95% CI)[a]	56.2 (49.5-62.8)	15.0 (10.6-20.3)
Difference, % (95% CI); *P* value[b]	41.1 (33.2-49.1); *P*<0.0001	
OR (95% CI)	7.5 (4.8-11.8)	
pCR, % (95% CI)	40.7 (34.2-47.4)	5.7 (3.1-9.6)
Difference, % (95% CI); *P* value[b]	35.0 (27.9-42.1); *P*<0.0001	
OR (95% CI)	11.5 (6.2-21.5)	
Safety[c]	**Safety Analysis Set**	
TEAEs	**n=226**	**n=226**
	n (%)	
Pts with ≥1 TEAE	224 (99.1)	225 (99.6)
Grade ≥3	157 (69.5)	148 (65.5)
Serious	25 (11.1)	24 (10.6)

[a]Assessed by IRC

[b]1-sided

[c]Randomized pts who received ≥1 dose of any study drug; OR, odds ratio; TEAE, treatment-emergent adverse event.