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

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Background

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

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 ECOG PS ≤1 and no known *EGFR* mutation (nsq) or *ALK* gene translocation (sq & nsq). Pts stratified by histology, disease stage, and PD-L1 expression (≥1% vs <1%) were randomized (1:1) to 3-4 cycles of TIS 200 mg IV Q3W or PBO, plus PtDb CT, followed by surgery + 8 cycles of adj TIS 400 mg IV Q6W or PBO. Primary endpoints: MPR rate after completion of NA tx + 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 to the intention-to-treat (ITT) population and had similar baseline characteristics. 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 & safety data from the NA phase are summarized in the table; MPR & 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. The safety profile of TIS + CT was consistent with known risks of each tx and was manageable in pts with resectable stage II-IIIA NSCLC, further supporting this tx combination for these pts.

Table. Efficacy and Safety Summary

	TIS + CT	**CT**
	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 Analysis Set[c]	
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.