RATIONALE-315: Event-free survival (EFS) and overall survival (OS) of neoadjuvant tislelizumab (TIS) plus chemotherapy (CT) with adjuvant TIS in resectable non-small cell lung cancer (NSCLC)

Authors: Dongsheng Yue[1*]; Wenxiang Wang[2]; Hongxu Liu[3]; Qixun Chen[4]; Chun Chen[5]; Lunxu Liu[6]; Peng Zhang[7]; Guofang Zhao[8]; Fan Yang[9]; Guang Han[10]; Ying Cheng[11]; Bentong Yu[12]; Yue Yang[13]; Haiquan Chen[14]; Jie Jiang[15]; Bin Yao[16]; Shengfei Wang[17]; Ruihua Wang[17]; Wenjuan Zheng[16]; Changli Wang[1]
*Presenting author

Affiliations: [1]Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; [2]Hunan Cancer Hospital, Hunan, China; [3]Liaoning Cancer Hospital and Institute, Shenyang, China; [4]Zhejiang Cancer Hospital, Hangzhou, China; [5]Fujian Medical University Union Hospital, Fuzhou, China; [6]West China Hospital, Sichuan University, Chengdu, China; [7]Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, China; [8]Ningbo No.2 Hospital, Ningbo, China; [9]Peking University People's Hospital, Beijing, China; [10]Hubei Cancer Hospital, Wuhan, China; [11]Jilin Cancer Hospital, Changchun, China; [12]The First Affiliated Hospital of Nanchang University, Nanchang, China; [13]Beijing Cancer Hospital, Beijing, China; [14]Fudan University Shanghai Cancer Center, Shanghai, China; [15]The First Affiliated Hospital of Xiamen University, Xiamen, China; [16]BeiGene (Beijing) Co., Ltd, Beijing, China; [17]BeiGene (Shanghai) Co., Ltd, Shanghai, China

ABSTRACT

Background: The RATIONALE-315 study (NCT04379635) compared the efficacy and safety of neoadjuvant TIS (anti-PD-1) plus CT and adjuvant TIS vs placebo plus CT in patients with resectable NSCLC; here we report interim results for EFS and OS.

Methods: Patients with treatment-naïve resectable stage II–IIIA NSCLC eligible for platinum-doublet CT with no known EGFR mutations or ALK gene translocations were randomised (1:1) to either 3–4 cycles of neoadjuvant TIS 200 mg or placebo (IV Q3W) plus CT, then surgery and ≤8 cycles of adjuvant TIS 400 mg or placebo (IV Q6W). Dual primary endpoints were EFS by blinded independent central review and major pathological response by blinded independent pathology review. Secondary endpoints included pathological complete response, OS and safety.

Results: As of 21 Aug 2023 (median follow-up: 22.0 mo), 453 patients were randomized (TIS, n=226; placebo, n=227). Of these, 452 received neoadjuvant treatment (n=226 both arms [99.8%]), 421 (92.9%) completed neoadjuvant treatment (TIS, n=211 [93.4%]; placebo, n=210 [92.5%]), 363 (80.1%) had surgery (TIS, n=190 [84.1%]; placebo, n=173 [76.2%]), 315 (69.5%) received adjuvant treatment (TIS, n=168 [74.3%]; placebo, n=147 [64.8%]) and 207 (45.7%) completed adjuvant treatment (TIS, n=106 [46.9%]; placebo, n=101 [44.5%]). Median EFS or OS were not reached for either arm; however, a statistically significant difference in EFS (HR [95% CI], 0.56 [0.40–0.79]; 1-sided P=.0003) and an OS benefit trend (HR [95% CI], 0.62 [0.39–0.98]; 1-sided P=.0193) were observed favouring TIS. In the safety population (n=226 both arms), 224 (99.1%) patients on TIS vs 225 (99.6%) on placebo experienced ≥1 treatment-related adverse event (TRAE); 163 (72.1%) vs 150 (66.4%) experienced Grade ≥3 TRAEs and 35 (15.5%) vs 18 (8.0%) experienced serious TRAEs, respectively.

Conclusions: Neoadjuvant TIS plus CT with adjuvant TIS demonstrated a clinically meaningful and statistically significant benefit for EFS and an OS benefit trend vs placebo plus CT. Regimen safety was manageable and consistent with known treatment risks. These data support this combination as a new standard of care for patients with resectable NSCLC.