**RATIONALE 307: A subgroup analysis of tislelizumab plus chemo vs chemo alone as 1L treatment for stage IIIB advanced sq NSCLC**

**Authors:** Prof Shun Lu[1]*, Prof Xinmin Yu[2], Prof Jie Wang[3], Dr Jun Zhao[4], Dr Yan Yu[5], Prof Chunhong Hu[6], Dr Guosheng Feng[7], Dr Kejing Ying[8], Dr Wu Zhuang[9], Dr Jianying Zhou[10], Dr Jingxun Wu[11], Dr Shiang Jiin Leaw[12], Dr Fan Bai[12], Dr Xiao Lin[12]

*Lead author

1. Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, 200030, China;
2. Zhejiang Cancer Hospital, Hangzhou, 310022, China;
3. State Key Laboratory of Molecular Oncology, Department of Medical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100730, China;
4. Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education, Beijing), Department of Thoracic Medical Oncology, Peking University Cancer Hospital & Institute, Beijing, 100142, China;
5. Harbin Medical University Cancer Hospital, Harbin, 150081, China;
6. The Second Hospital of Central South University, Changsha, 410011, China;
7. The People's Hospital of Guangxi Zhuang Autonomous Region, Nanning, 530021, China;
8. Sir Run RunShaw Hospital, Zhejiang University, School of Medicine, Zhejiang, 310009, China;
9. Fujian Tumor Hospital, Fuzhou, 350001, China;
10. The First Affiliated Hospital, Zhejiang University, Zhejiang, 310003, China;
11. The First Affiliated Hospital of Xiamen University, Fujian, 361003, China;
12. BeiGene (Beijing) Co., Ltd., Shanghai, 200040, China

## Introduction

Tislelizumab - a humanized, monoclonal antibody for programmed cell death protein 1 - has demonstrated significantly improved progression-free survival (PFS) and reduced risk of progression versus standard of care in advanced lung cancer (NCT03432598, NCT03594747). We conducted a Phase 3, multicenter, randomized, open-label study to assess the safety and efficacy of tislelizumab plus chemotherapy in patients with advanced squamous non-small cell lung cancer (NSCLC) (NCT03594747). Here, we report results from patients with stage IIIB disease.

## Methods

Adults in China with treatment-naïve histologically confirmed locally advanced or metastatic (stage IIIB or IV) squamous NSCLC not amenable to surgery or not suitable for chemoradiation were randomized 1:1:1 to Arm A: tislelizumab (200 mg) plus paclitaxel 175 mg/m$^2$ and carboplatin AUC 5 (every 3 weeks [Q3W] on day 1); Arm B: tislelizumab plus nab-paclitaxel 100 mg/m$^2$ (Q3W on days 1, 8 and 15) plus carboplatin (Q3W on day 1); or Arm C: paclitaxel plus carboplatin (Q3W on day 1). Paclitaxel, nab-paclitaxel and carboplatin were administered for 4–6 cycles. All treatments were administered intravenously. Stratification factors were disease stage (IIIB vs IV), and programmed death-ligand 1 expression (<1% vs 1–49% vs ≥50% tumor cells). Tislelizumab was administered until loss of benefit, withdrawal or start of new anticancer therapy. In this subgroup analysis, PFS, objective response rate (ORR) (assessed by independent review committee) and safety were evaluated in patients with stage IIIB disease.

## Results

Overall, 122/360 (33.9%) patients had stage IIIB NSCLC. Patients were randomized to Arm A (38 patients), B (40 patients) or C (44 patients). The median age was 61 years (range 34–74 years). At median follow-up time of 8.6 months across all arms, PFS was numerically longer, and ORR higher, respectively, with tislelizumab (Arms A and B) versus chemotherapy alone (Arm C) (**Table,** PFS: HR=0.402 [Arm A] vs 0.372 [Arm B]). The PFS benefit observed was consistent with the ITT population **(Table)**. TEAEs (≥1) and Grade ≥3 TEAEs were similar across all arms **(Table).** No new safety signals were observed. Laboratory abnormalities were the most commonly reported TEAEs across all arms.

## Conclusion

In this subgroup analysis, a clinically meaningful improvement in PFS and higher ORR was observed with tislelizumab plus chemotherapy versus standard of care in patients with stage IIIB advanced squamous NSCLC. The safety and efficacy profile of tislelizumab was consistent with the overall population.

## Table

| | Arm A (N = 38) | Arm B (N = 40) | Arm C (N = 44) |
|---|---|---|---|
| **Number of patients discontinued from the study** | 5 (13.2) | 5 (12.5) | 5 (11.4) |
| Primary reason for study discontinuation | | | |
| Death | 4 (10.5) | 3 (7.5) | 4 (9.1) |
| Voluntary withdrawal | 1 (2.6) | 2 (5.0) | 1 (2.3) |
| Number of patients remained on study | 33 (86.8) | 35 (87.5) | 39 (88.6) |

| **Efficacy*** | Arm A (N = 38) | Arm B (N = 40) | Arm C (N = 44) |
|---|---|---|---|
| **Median PFS in patients with stage IIIB disease, months** | 9.8 | 11.0 | 5.6 |
| 95% CI | 5.95, NE | 7.56, NE | 4.17, 7.43 |
| HR† (95% CI) | 0.402 (0.215, 0.750) | 0.372 (0.202, 0.686) | - |
| **ORR, n (%)** | 32 (84.2) | 33 (82.5) | 26 (59.1) |
| 95% CI | 68.7, 94.0 | 67.2, 92.7 | 43.2, 73.7 |

| | Arm A (N = 120) | Arm B (N = 119) | Arm C (N = 121) |
|---|---|---|---|
| **Median PFS in the ITT population, months** | 7.6 | 7.6 | 5.5 |
| 95% CI | 5.95, 9.79 | 5.75, 11.01 | 4.21, 5.65 |
| HR‡ (95% CI) | 0.524 (0.370, 0.742) | 0.478 (0.336, 0.679) | - |

| **Safety§, n (%)** | Arm A (N = 38) | Arm B (N = 40) | Arm C (N = 43) |
|---|---|---|---|
| **Patients with ≥1 TEAE** | 38 (100.0) | 39 (97.5) | 43 (100.0) |
| Related to any component of study treatment | 37 (97.4) | 39 (97.5) | 43 (100.0) |
| Related to tislelizumab | 34 (89.5) | 35 (87.5) | NA |
| Related to any component of chemotherapy | 37 (97.4) | 39 (97.5) | 43 (100.0) |
| **Grade ≥3 TEAEs** | 34 (89.5) | 35 (87.5) | 34 (79.1) |
| Related to any component of study treatment | 33 (86.8) | 34 (85.0) | 34 (79.1) |
| Related to tislelizumab | 14 (36.8) | 16 (40.0) | NA |
| Related to any component of chemotherapy | 33 (86.8) | 34 (85.0) | 34 (79.1) |
| Laboratory abnormalities | 25 (65.8) | 24 (60.0) | 18 (41.9) |
| **Serious TEAEs** | 12 (31.6) | 18 (45.0) | 7 (16.3) |
| Grade ≥3 | 11 (28.9) | 15 (37.5) | 4 (9.3) |
| Related to any component of study treatment | 8 (21.1) | 10 (25.0) | 6 (14.0) |
| Related to tislelizumab | 8 (21.1) | 7 (17.5) | NA |
| Related to any component of chemotherapy | 5 (13.2) | 7 (17.5) | 6 (14.0) |
| Laboratory abnormalities | 4 (10.5) | 2 (5.0) | 1 (2.3) |
| **TEAEs that led to permanent discontinuation of any component of study treatment** | 5 (13.2) | 12 (30.0) | 6 (14.0) |
| **TEAEs that led to death** | 0 (0.0) | 1 (2.5) | 1 (2.3) |

Data are reported for patients in the stage IIIB NSCLC subgroup unless otherwise indicated.

*Efficacy analysis set (includes all randomized patients); †Unstratified; ‡Stratified; §Safety analysis set (includes all randomized patients who received ≥1 dose of any component of study drug).

CI, confidence interval; HR, hazard ratio; ITT, intent-to treat; NA, not applicable; NE, not estimable; NSCLC, non-small cell lung cancer; ORR, objective response rate; PFS, progression-free survival; TEAE, treatment-emergent adverse event.