

---

## **RATIONALE-307: Tislelizumab plus chemotherapy versus chemotherapy alone as first-line treatment for advanced squamous NSCLC in patients aged $\geq$ 65 years**

**Authors:** Jie Wang,<sup>1\*</sup>† Shun Lu,<sup>2</sup> Xinmin Yu,<sup>3</sup> Yanping Hu,<sup>4</sup> Yuping Sun,<sup>5</sup> Zhijie Wang,<sup>1</sup> Jun Zhao,<sup>6</sup> Yan Yu,<sup>7</sup> Chunhong Hu,<sup>8</sup> Kunyu Yang,<sup>9</sup> Guosheng Feng,<sup>10</sup> Kejing Ying,<sup>11</sup> Wu Zhuang,<sup>12</sup> Jianying Zhou,<sup>13</sup> Jingxun Wu,<sup>14</sup> Shiang Jiin Leaw,<sup>15</sup> Jing Zhang,<sup>15</sup> Xiao Lin,<sup>15</sup> Nong Yang<sup>16</sup>

\*Lead author

†Corresponding author

**Affiliations:** <sup>1</sup>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, China; <sup>2</sup>Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; <sup>3</sup>Zhejiang Cancer Hospital, Hangzhou, China; <sup>4</sup>Hubei Cancer Hospital, Wuhan, China; <sup>5</sup>Jinan Central Hospital, Shandong, China; <sup>6</sup>Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education, Beijing), Department of Thoracic Medical Oncology, Peking University Cancer Hospital & Institute, Beijing, China; <sup>7</sup>Harbin Medical University Cancer Hospital, Harbin, China; <sup>8</sup>The Second Hospital of Central South University, Changsha, China; <sup>9</sup>Union Hospital Tongji Medical College Huazhong University of Science and Technology, Hubei, China; <sup>10</sup>The People's Hospital of Guangxi Zhuang Autonomous Region, Nanning, China; <sup>11</sup>Sir Run Run Shaw Hospital, Zhejiang University, School of Medicine, Zhejiang, China; <sup>12</sup>Fujian Tumor Hospital, Fuzhou, China; <sup>13</sup>The First Affiliated Hospital, Zhejiang University, Zhejiang, China; <sup>14</sup>The First Affiliated Hospital of Xiamen University, Fujian, China; <sup>15</sup>BeiGene (Beijing) Co., Ltd., Beijing, China; <sup>16</sup>Department of Medical Oncology, Lung Cancer and Gastrointestinal Unit, Hunan Cancer Hospital/The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China.

### **Objective:**

Tislelizumab (TIS) is a humanized monoclonal antibody with high affinity and specificity for the programmed cell death protein-1. It has demonstrated antitumor activity in advanced lung cancers. We conducted a Phase 3, multicenter, randomized open-label study (NCT03594747) to assess the efficacy and safety of TIS plus chemotherapy in patients (pts) with advanced squamous NSCLC. TIS significantly improved progression-free survival (PFS) and reduced the risk of progression. We report sub-group results from pts aged  $\geq$  65 years.

### **Methods:**

Eligible pts (aged 18–75 years) enrolled in China were treatment-naïve for locally advanced or metastatic squamous NSCLC. Pts were stratified by disease stage (IIIB vs IV) and programmed death-ligand 1 (PD-L1) expression (< 1% vs 1–49% vs 50% tumor cells), and randomized 1:1:1 to Arm A: TIS 200 mg + paclitaxel (P) 175 mg/m<sup>2</sup> and carboplatin (C)

AUC-5 (every 3 weeks [Q3W] on Day 1); Arm B: TIS + *nab*-paclitaxel (*nab*-P) 100 mg/m<sup>2</sup> (Q3W on days 1, 8, and 15) + C (Q3W on Day 1); or Arm C: P + C (Q3W on Day 1). P, *nab*-P, and C were administered for 4–6 cycles. TIS was administered until loss of benefit, withdrawal, or start of a new therapy. In this sub-group analysis, pts aged ≥ 65 years were evaluated according to the primary endpoint (PFS) and key secondary endpoints (objective response rate [ORR] and safety).

**Results:**

Overall, 127 pts aged ≥ 65 years were randomized. Median age was 68.0 years and 120 pts (94.5%) were male. PFS and ORR were longer and higher, respectively, in Arms A and B, compared with Arm C (Table). Grade ≥ 3 treatment-related adverse events (TRAEs) occurred in 33 (84.6%), 44 (84.6%), and 28 (82.4%) pts aged ≥ 65 years in Arms A, B, and C, respectively, compared with 103 (85.8%), 99 (83.9%), and 94 (80.3%) pts of all ages. The most commonly reported TRAEs were anemia, decrease in neutrophil count, and alopecia.

**Conclusion:**

In this sub-group analysis, PFS and ORR were longer and higher, respectively, with TIS plus chemotherapy in pts aged ≥ 65 years with advanced squamous NSCLC. The safety profile of TIS in pts aged ≥ 65 years was similar to that in pts of all ages.

**Table:**

	<b>Arm A (N = 39)</b>	<b>Arm B (N = 52)</b>	<b>Arm C (N = 36)</b>
Median PFS, months (95% CI)	9.7 (5.59, NE)	9.7 (6.87, NE)	5.2 (4.14, NE)
HR (95% CI)	0.602 (0.309, 1.175)	0.564 (0.302, 1.052)	
ORR, % (95% CI)	69.2 (52.4, 83.0)	75.0 (61.1, 86.0)	50.0 (32.9, 67.1)