Neoadjuvant Tislelizumab or Placebo + Platinum-Based Chemotherapy Followed by Adjuvant Tislelizumab or Placebo in Patients With Resectable Non-Small Cell Lung Cancer (NSCLC): A Phase 3 Trial in Progress

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Background: Adjuvant and neoadjuvant therapies have been proposed to improve the prognosis of patients (pts) with stage II/IIIA lung cancer but have provided only modest survival benefits. When added to chemotherapy, PD-(L)1 inhibitors have resulted in enhanced antitumor activity versus chemotherapy alone, but their ability to limit relapse in pts who have undergone surgical resection has not yet been fully elucidated. Tislelizumab, a monoclonal antibody with high affinity and specificity for PD-1, was engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis. Tislelizumab, as a single agent and in combination with chemotherapy, has demonstrated a manageable tolerability profile and efficacy in pts with advanced NSCLC.

Trial design: This phase 3, randomized, double-blind study (NCT04379635) compares the efficacy of neoadjuvant tislelizumab or placebo + platinum-based doublet chemotherapy followed by adjuvant tislelizumab or placebo. Adult pts (n≈380) with histologically confirmed, squamous (sq) or nonsquamous (nsq) stage II/IIIA resectable NSCLC are eligible; key exclusion criteria include prior systemic anticancer treatment for lung cancer or known *EGFR* mutations or *ALK* rearrangements. In the neoadjuvant phase, pts will be randomized 1:1 to receive tislelizumab (*Arm A*) or placebo (*Arm B*) plus cisplatin/carboplatin + paclitaxel or pemetrexed on Day 1 of each 3-wk cycle for 3-4 cycles. Patients will be stratified by histology (sq vs nsq), disease stage (II vs IIIA), and PD-L1 expression (≥1% vs <1%). After surgery, adjuvant therapy (tislelizumab [*A*]; placebo [*B*]) will be administered on Day 1 of each 6-wk cycle for up to eight cycles. Major pathological response rate (proportion of pts with ≤10% residual viable tumors) and event-free survival per RECIST v1.1 are dual primary endpoints. Secondary endpoints include overall survival, objective response rate, disease-free survival, pathological complete response rate, safety/tolerability (assessed by monitoring incidence and severity of adverse events), and health-related quality-of-life measures.