Neoadjuvant Tislelizumab or Placebo Plus 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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Objective: Adjuvant and neoadjuvant therapies have been proposed to improve the prognosis of patients (pts) with stage II/IIIA lung cancer. While programmed cell death protein-1/programmed death-ligand 1 (PD-1/PD-L1) inhibitors provide new treatment approaches for pts with advanced NSCLC, 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.

Methods: 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 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*) in combination with cisplatin/carboplatin + paclitaxel or pemetrexed on Day 1 of each 3-wk cycle for 3-4 cycles. 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 primary endpoints. Overall survival, objective response rate, disease-free survival, and pathological complete response rate are secondary efficacy endpoints. Safety/tolerability, assessed by monitoring incidence and severity of adverse events, and health-related quality-of-life measures will also be evaluated.