TPS8116 **Poster Session**

A randomized study of neoadjuvant REGN7075 + cemiplimab + chemotherapy (chemo) vs cemiplimab + chemo in patients (pts) with resectable non-small cell lung cancer (NSCLC).

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Background: Neoadjuvant chemo + anti–PD-1 checkpoint blockade, with/without adjuvant anti–PD-1, represents a new standard of care for pts with resectable NSCLC. However, most pts do not achieve major pathologic response (MPR) or pathologic complete response (pCR), and event-free survival (EFS) remains suboptimal; therefore, novel perioperative approaches are needed. REGN7075, a first-in-class costimulatory bispecific antibody, aims to bridge CD28+ T cells with EGFR-expressing tumor cells, facilitating T-cell activation through endogenous tumor antigens. Early efficacy and pharmacodynamic evidence suggest that REGN7075 can enhance immune responses and antitumor immunity even in "cold" tumors. In a first-in-human, open-label, Phase 1/2 study (NCT04626635), REGN7075 + cemiplimab (anti–PD-1) demonstrated clinical activity in PD-1–refractory, microsatellite stable colorectal cancer (Segal NH, et al. 2024). The addition of REGN7075 to cemiplimab + chemo may deepen antitumor responses in resectable NSCLC where EGFR is highly expressed, potentially representing a novel immunotherapy-based treatment (Tx) approach in this setting. In this perioperative platform study, multiple novel Tx approaches for resectable NSCLC will be evaluated in comparison to a control arm (cemiplimab + chemo). **Methods:** In this Phase 2, open-label, perioperative platform trial (NCT06465329), pts with resectable NSCLC will be randomized to an investigational arm (a novel antitumor agent + cemiplimab + chemo) or control arm (cemiplimab + chemo), stratified by tumor stage and PD-L1 expression. Here, we focus on the first investigational arm with REGN7075. The study will consist of neoadjuvant, surgical, and adjuvant periods. During the neoadjuvant period, pts assigned to the control arm will receive cemiplimab + chemo for up to 3 cycles before surgery. Pts in the investigational arm will receive REGN7075 with cemiplimab + chemo. Pts from both arms who proceed to surgery and undergo R0/R1 resection will then receive adjuvant cemiplimab. Eligibility criteria: histologically confirmed stage II–IIIB (N2) NSCLC considered resectable with curative intent (appropriate candidate for surgery), Tx naïve, no known *EGFR/ALK* alterations, ECOG PS ≤1. Primary endpoint: MPR. Secondary endpoints: safety, feasibility of surgery, pCR, and EFS. Pre-Tx and surgical tissue will be used for translational analysis and biomarker development. Up to 40 pts will be enrolled in each investigational arm, and the control arm will be open to enrollment throughout the study. A Bayesian statistical design will be used to evaluate the posterior probability of at least 15% improvement in MPR for investigational arms vs the control arm. This study is currently enrolling. Clinical trial information: NCT06465329. Research Sponsor: Regeneron Pharmaceuticals, Inc.