TPS8115 **Poster Session**

KEYMAKER-U01E: A phase 2 umbrella study with rolling arms of investigational agents with or without chemotherapy plus pembrolizumab for resectable stage II–IIIB (N2) non–small-cell lung cancer (NSCLC).

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Background: Neoadjuvantpembrolizumab (pembro) + chemotherapy (CT) followed by adjuvant pembro significantly improved event-free survival (EFS), pathological complete response (pCR), major pathological response, and overall survival (OS) in early-stage NSCLC. Despite the expanding number of therapeutic options for early-stage NSCLC, there remains an unmet need to improve outcomes. Sacituzumab tirumotecan (sac-TMT/MK-2870/SKB264) is an antibody-drug conjugate composed of an anti-trophoblast cell surface antigen 2 antibody, a hydrolytically cleavable linker, and a belotecan-derivative topoisomerase I inhibitor payload (average drug-to-antibody ratio, 7.4). Sac-TMT monotherapy demonstrated encouraging antitumor activity in a phase 1/2 study in heavily pretreated, advanced NSCLC. The phase 2 KEYMAKER-U01E study (NCT06788912) is evaluating the addition of multiple investigational agents ± CT to pembro followed by surgery and adjuvant pembro in resectable stage II–IIIB (N2) NSCLC; the treatment arm presented here includes sac-TMT + pembro. **Methods:** This open-label, adaptive design study is enrolling participants (pts) aged ≥18 years with previously untreated, pathologically confirmed, resectable stage II, IIIA, or IIIB (N2) NSCLC (AJCC v8) with no *EGFR* mutations, and measurable disease per RECIST v1.1. Pts must be able to undergo surgery, have ECOG PS 0 or 1, and provide a tumor sample for biomarker analysis. Approximately 60 pts will be randomized 1:1 to Arm 1 or 2. In Arm 1 (reference arm), pts will receive neoadjuvant therapy of 4 cycles of pembro 200 mg intravenously (IV) + CT IV Q3W (cisplatin 75 mg/m^2 or carboplatin area under the curve 5 or 6 mg/mL/min on day 1 with gemcitabine 1000 mg/m^2 on days 1 and 8 for squamous histology, with pemetrexed 500 mg/m^2 on day 1 for nonsquamous, or with paclitaxel 175 or 200 mg/m^2 on day 1 for any histology). Pts in Arm 2 will receive 4 cycles of pembro 200 mg IV Q3W + 6 cycles of sac-TMT 4 mg/kg IV Q2W (treatment arm). Following surgery, all pts will receive up to 13 cycles of adjuvant pembro 200 mg IV Q3W. Additional agents may be included when available. Randomization will be stratified by histology (squamous vs nonsquamous) and tumor stage (II vs III). Dual primary endpoints are pCR (ypT0/ypN0) and percentage of residual viable tumor, assessed by blinded independent pathology review. Secondary endpoints are EFS and distant metastasis-free survival per investigator review, OS, objective response rate during neoadjuvant therapy, and safety. Postoperative tumor imaging occurs ≤4 weeks before the start of adjuvant therapy, with pts followed per study protocol until disease recurrence, development of new primary NSCLC, pregnancy, death, pt withdrawal, or end of study. AEs will be graded per NCI CTCAE v5.0. Enrollment is scheduled to begin in March 2025 at 34 sites globally. Clinical trial information: NCT06788912. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.