TPS8113 **Poster Session**

Comparing impact of treatment before or after surgery in patients with stage II-IIIb resectable non-small cell lung cancer (NSCLC; Alliance A082304-SWOG S2402).

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Background: There are currently three approved approaches for patients with resectable NSCLC including neoadjuvant chemoimmunotherapy, adjuvant chemoimmunotherapy and perioperative treatment with neoadjuvant chemoimmunotherapy followed by adjuvant immunotherapy. All regimens were approved after showing event-free survival (EFS) or disease-free survival (DFS) benefit with the addition of immunotherapy to chemotherapy compared to chemotherapy alone. Each approach has its benefits and risks. Starting immunotherapy prior to surgery may improve treatment compliance and efficacy of immunotherapy. Nevertheless, neoadjuvant chemoimmunotherapy may result in missing an opportunity for curative surgery and increase the complexity of tumor resection. PROSPECT-LUNG (NCT06632327) is a randomized study evaluating whether starting chemoimmunotherapy before or after surgery leads to better outcomes. **Methods:** This is a randomized phase 3 trial in which patients will be randomized 1:1 to surgery followed by chemoimmunotherapy (adjuvant arm) or neoadjuvant chemoimmunotherapy followed by surgery and adjuvant therapy (perioperative arm). Patients with histologic or cytologic confirmation of surgically resectable stage IIA-IIIB NSCLC (per AJCC 9th edition) or stage IIA to IIIB per AJCC 8th edition up to single ipsilateral mediastinal station (N2a), ECOG PS $\leq$ 2 (or Karnofsky $\geq$ 60%), no prior treatment for NSCLC and no previous malignancy within 3 years are eligible. The dual primary endpoints are real-world event free survival (rwEFS) defined as date from randomization to date of the first of the following events: failure to undergo resection for any reason, progression prior to surgery that precludes resection, recurrence or progression at any time after surgery or death from any cause, and overall survival (OS) defined as time from randomization to death from any cause. The target accrual is 1,100 patients assuming one-sided type I error of 0.03 for OS endpoint and 0.02 for rwEFS endpoint. This sample size will enable the detection of a 3-year rwEFS improvement from 55% in the adjuvant therapy arm to 64% in the perioperative arm with an 84% power. This sample size would detect an HR of 0.73 (improvement in median OS from 8.1 to 11 years in favor of the perioperative arm, 5-year OS from 65% in the adjuvant arm to 73% in the perioperative arm, assuming exponential survival) with 83.6% power. The study has a pragmatic design with minimal data collection, reporting of adverse events that lead to discontinuation of therapy, hospitalization or death only. It allows providers to choose therapy per standard of care (FDA approved or on NCCN), includes patients with ECOG performance status 2, permits use of local laboratory testing and imaging studies and determination of recurrence/progression will be done by local treating physicians with no use of RECIST. Clinical trial information: NCT06632327. Research Sponsor: National Cancer Institute; U10CA180821.