TPS8119 **Poster Session**

Neoadjuvant lazertinib with or without chemotherapy for patients with epidermal growth factor receptor (*EGFR*)-mutated resectable non-small cell lung cancer (NSCLC): NeoLazer trial.

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Background: While perioperative systemic treatment with checkpoint inhibitors plus chemotherapy has become a standard approach for resectable NSCLC, the benefit of systemic treatment in *EGFR*-mutated NSCLC remains unclear. In resectable *EGFR*-mutated NSCLC, adjuvant osimertinib has been shown to significantly improve disease-free survival and overall survival. However, neoadjuvant osimertinib alone has demonstrated limited efficacy, with a major pathologic response rate of less than 15% (NCT03433469). These data altogether highlight an unmet clinical need for optimizing perioperative systemic approach in resectable *EGFR*-mutated NSCLC. Lazertinib, a third-generation, central nervous system-penetrating EGFR tyrosine kinase inhibitor, has demonstrated superior efficacy compared to comparator EGFR tyrosine kinase inhibitor in treatment-naïve *EGFR*-mutated advanced NSCLC (NCT04248829). The NeoLazer trial (NCT06268210) is a phase II, randomized, controlled study designed to evaluate the efficacy and safety of neoadjuvant lazertinib with or without chemotherapy in patients with *EGFR*-mutated resectable NSCLC. **Methods:** Eligible patients must be ≥19 years of age, have an ECOG performance status of 0 or 1, non-squamous histology, stage IB–IIIB NSCLC based on the AJCC 8th edition, have confirmed sensitizing *EGFR* mutations (exon 19 deletion or L858R mutation), be deemed completely resectable by a multidisciplinary team, and demonstrate adequate organ and bone marrow function. The trial will enroll approximately 160 patients, who will be randomized 1:1 to receive either lazertinib (240 mg once daily) with chemotherapy (pemetrexed 500 mg/m^2 and carboplatin AUC5 every 3 weeks) or lazertinib alone (240 mg once daily) for three cycles before surgical resection. Randomization will be stratified by disease stage (IB–II vs. III) and *EGFR* mutation type (exon 19 deletion vs. L858R mutation). Following surgery, all patients will receive adjuvant lazertinib for three years. Neoadjuvant and adjuvant treatments will continue until unacceptable toxicity, disease progression or relapse, or patient withdrawal. The primary endpoint is major pathologic response, defined as ≤10% residual viable cancer cells in the surgical specimen. Secondary endpoints include safety based on CTCAE 5.0, type of surgical resection (segmentectomy vs. lobectomy), pathologic complete response, objective response rate based on RECIST 1.1, event-free survival, disease-free survival, and overall survival. In addition, the trial incorporates exploratory analyses, including whole-genome sequencing of tumor tissue and monitoring the dynamics of minimal residual disease through serial blood sampling. Clinical trial information: NCT06268210. Research Sponsor: None.