TPS8114 **Poster Session**

GEMINI-NSCLC study: Integrated longitudinal multi-omic biomarker profiling study of non-small cell lung cancer (NSCLC) patients.

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Background: Lung cancer is the global leading cause of cancer deaths. Despite treatment advances, NSCLC outcomes remain poor. The molecular landscape of NSCLC has identified various subtypes allowing targeted therapies, but some tumors lack a biomarker-directed therapy. Identifying improved surrogates of immunotherapy (IO) response is key to stopping ineffective treatments and empowering patients to switch therapies more rapidly. Combining next-generation sequencing (NGS) and circulating tumor DNA (ctDNA) technologies with high-resolution multi-omic data may revolutionize NSCLC management by enabling non-invasive monitoring, personalized treatment strategies, and the development of next-generation therapies to improve patient outcomes. **Methods:** The Gemini-NSCLC study is a multicenter, real-world observational study profiling patients with NSCLC undergoing IO standard-of-care (SOC) therapy. Cohort 1 (C1) includes patients with early-stage disease treated with curative intent therapies. Cohort 2 (C2) includes patients with late-stage disease receiving first-line IO, excluding those with targetable genomic drivers. Patients will have blood and tissue collected at study entry and longitudinally. They will undergo testing with DNA and RNA sequencing and novel assays, including baseline spatial transcriptomic profiling, serial tumor-informed ctDNA profiling, and scRNA sequencing with T-Cell receptor seq of peripheral immune cells. All patients will be assessed with cohort-relevant real-world endpoints, allowing correlation with longitudinal multi-omic data for biomarker discovery. Information from novel multi-omic assays will be descriptive and hypothesis-generating. For C1, the primary endpoint is real-world disease-free survival (rwDFS). Secondary endpoints include pathologic complete response (pCR) rate and real-world overall survival (rwOS) stratified by ctDNA status. Molecular endpoints include sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of minimal residual disease (MRD) assay vs. conventional imaging. Patients are followed until recurrence or five years post-therapy. Patients in whom disease recurs may roll over to C2 for continued data collection. For C2, the primary endpoint is rwOS, with rwPFS as a secondary endpoint. Molecular endpoints include ctDNA dynamics with IO and correlation with rwOS. Exploratory endpoints include evolving genomic variants as resistance mechanisms. As of 01/2025, the study is enrolling and active at 49 of 60 planned sites, with accruals of 48/500 in C1, 20/700 in C2. Clinical trial information: NCT05236114. Research Sponsor: Tempus, AI, Inc.; AstraZeneca.