TPS2700 **Poster Session**

A phase 2 basket trial of tarlatamab in patients with advanced DLL3-expressing tumors: University of California Lung Cancer Consortium UCCC-01/UCLA L-10.

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Background: Delta-like ligand 3 (DLL3) is an inhibitory Notch ligand that is aberrantly expressed on the surface of tumor cells, in particular on those with neuroendocrine differentiation. Tarlatamab is a bispecific T cell engager that binds to DLL3 and CD3 to promote T cell killing of DLL3-expressing cells. Prior studies of tarlatamab have demonstrated encouraging antitumor activity and manageable toxicity in patients with small cell lung cancer (SCLC; DeLLphi-301) and neuroendocrine prostate cancer (NEPC; DeLLpro-300). Meanwhile, DLL3 has been reported to be highly expressed in multiple tumor types, including in many neuroendocrine neoplasms (NENs) other than SCLC and NEPC. The role of anti-DLL3 therapies in these cancers has not been established. **Methods:** This is a phase 2, multicenter, open-label, basket study designed to evaluate the efficacy of tarlatamab in patients with DLL3-expressing cancers. Key inclusion criteria include presence of advanced stage disease with progression following ≥1 prior line of therapy and positive tumor DLL3 expression by immunohistochemistry (Ventana SP347 assay). Patients with de novo SCLC or NEPC are excluded, but all other tumor types and NENs are eligible, including large cell neuroendocrine carcinoma and SCLC transformed from previously treated NSCLC. Tarlatamab will be administered at an initial step-up dose (1 mg on D1 and 10 mg on D8 and D15 of cycle 1) followed by 10 mg every 2 weeks. Treatment will continue until unacceptable toxicity, progressive disease, or withdrawal of consent. The study will follow a Simon's two-stage design: in Stage 1, 10 patients with tumor DLL3 expression ≥25% will be enrolled, and the study will be stopped if ≤1 patient achieves an objective response; otherwise, an additional 19 patients with tumor DLL3 expression ≥1% will be enrolled for Stage 2. The primary endpoint is the objective response rate. Secondary endpoints include safety, progression free survival, duration of response, and overall survival. Exploratory studies will evaluate correlation of antitumor activity with tissue and blood-based biomarkers, such as DLL3 expression on tumor and liquid biopsies. This study is currently enrolling patients through the University of California Lung Cancer Consortium (UCLCC). Clinical trial information: NCT06788938. Research Sponsor: None.