TPS8664 **Poster Session**

A randomized phase 3 study of ivonescimab plus chemotherapy versus pembrolizumab plus chemotherapy for the first-line treatment of metastatic non–small cell lung cancer: HARMONi-3.

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Background: The additionof antiangiogenic agents to standard first-line treatment with a programmed cell death protein 1 (PD-1) inhibitor and platinum doublet chemotherapy has shown efficacy in patients with metastatic non–small cell lung cancer (NSCLC). Ivonescimab is a novel tetravalent bispecific antibody that targets PD-1 and vascular endothelial growth factor. In a phase 2 trial, ivonescimab plus chemotherapy showed objective response rates (ORRs) of 71.4% and 54.2% and median progression-free survival (PFS) of 11.1 and 13.3 months in patients with metastatic squamous (SQ) and nonsquamous (NSQ) NSCLC, respectively (1). **Methods:** The multiregional, randomized, double-blind, phase 3 HARMONi-3 trial (NCT05899608) will compare the efficacy and tolerability of ivonescimab plus chemotherapy with pembrolizumab plus chemotherapy as first-line treatment in patients with metastatic SQ or NSQ NSCLC who have not previously received systemic treatment for metastatic disease and whose tumors have no known actionable mutations for which approved first-line therapies are available. Patients will be randomly assigned (1:1) to receive ivonescimab 20 mg/kg every 3 weeks (Q3W) or pembrolizumab 200 mg Q3W combined with chemotherapy (paclitaxel or nab-paclitaxel plus carboplatin for SQ or pemetrexed plus carboplatin for NSQ) for up to 4 cycles, followed by maintenance with ivonescimab or pembrolizumab alone for SQ or in combination with pemetrexed for NSQ for up to 24 months. Randomization will be done in blocks by histology (SQ and NSQ) and stratified by sex (female vs male), age ($<$65 vs $\geq$65 y), geographic region (East Asia vs rest of world), presence or absence of liver or brain metastases at baseline, previous PD-1 or programmed death ligand 1 (PD-L1) inhibitor treatment $>$6 months before the development of metastatic disease (yes vs no), and PD-L1 tumor proportion score ($\geq$1% or $<$1%). The dual primary end points are overall survival and PFS (assessed by investigators per RECIST v1.1). The secondary end points are ORR, disease control rate, duration of response, safety, pharmacokinetics, and immunogenicity. Patients are being recruited in Asia, Europe, and North America, with a target enrollment of 1080 patients (45-50% SQ and 50-55% NSQ). 1. Zhang L et al, ELCC 2024, FPN: 68P. Clinical trial information: NCT05899608. Research Sponsor: Summit Therapeutics, Inc.