TPS8648 **Poster Session**

SOHO-02: Phase III trial of BAY 2927088 in patients with locally advanced or metastatic NSCLC with *HER2*-activating mutations.

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Background: Approximately 2-4% of non-small cell lung cancer (NSCLC) harbor activating human epidermal growth factor receptor 2 (*HER2*) mutations. This represents a major area of unmet medical need as no first-line HER2-targeted therapies are currently approved for patients with locally advanced or metastatic NSCLC with *HER2*-activating mutations. BAY 2927088 is an oral, reversible tyrosine kinase inhibitor that potently targets HER2 and mutant epidermal growth factor receptor. Preliminary evidence from the Phase I/II SOHO-01 trial has demonstrated anti-tumor activity and a manageable safety profile in previously treated patients with NSCLC with *HER2*-activating mutations (PL04.03 presented at IASLC 2024 World Conference on Lung Cancer). Here we introduce the SOHO-02 trial evaluating the efficacy and safety of BAY 2927088 as first-line therapy in patients with locally advanced or metastatic NSCLC with *HER2*-activating mutations. **Methods:** SOHO-02 is an ongoing Phase III, open-label, randomized, multicenter trial of BAY 2927088 in patients with locally advanced or metastatic NSCLC with *HER2*-activating mutations (NCT06452277). Eligibility criteria include patients aged ≥18 years with: documented histologically or cytologically confirmed, locally advanced or metastatic non-squamous NSCLC; documented activating mutation in the tyrosine kinase domain of HER2; measurable disease per RECIST v1.1; no previous systemic therapy for locally advanced or metastatic disease; and eligibility to receive treatment with the selected platinum-based doublet-chemotherapy and pembrolizumab. Overall, 278 eligible patients will be randomized to BAY 2927088 p.o. 20 mg twice daily or standard of care (SoC; pembrolizumab in combination with cisplatin/pemetrexed or carboplatin/pemetrexed) in 21-day cycles. The primary endpoint is BAY 2927088 efficacy vs. SoC on progression-free survival per RECIST v1.1 as assessed by blinded independent central review (BICR). Key secondary endpoints include BAY 2927088 efficacy vs. SoC on overall survival, overall response rate, disease control rate, and duration of response per RECIST v1.1 by BICR, and BAY 2927088 safety and tolerability vs. SoC. Impact of BAY 2927088 on patient health-related quality of life and symptom severity will be evaluated using EORTC QLQ-C30 and NSCLC-SAQ. Enrollment is ongoing. Clinical trial information: NCT06452277. Research Sponsor: Bayer AG.