OUTCOMES FOLLOWING FIRST-LINE IMMUNOTHERAPY WITH OR WITHOUT CHEMOTHERAPY STRATIFIED BY KRAS MUTATIONAL STATUS – A REAL WORLD ANALYSIS IN PATIENTS WITH ADVANCED NSCLC

Charu Aggarwal, Halla Nimeiri, James Chen, Ker Huerga, Leora Horn, Nataliya Tuncu, Jyoti Patel. University of Pennsylvania, Philadelphia, PA, USA; Tempus, Chicago, IL, USA; Tempus and AstraZeneca, Chicago, IL, USA; AstraZeneca, Chicago, IL, USA; Northwestern University, Chicago, IL, USA; Robert H Lurie Comprehensive Cancer Center, Chicago, IL, USA

Background Recent meta-analysis from 12 registrational studies in patients with advanced non-small cell lung cancer (NSCLC) with KRAS mutations (mt), including G12C, evaluated efficacy outcomes of chemotherapy (CTx), immune checkpoint inhibitors (ICI), or ICI with CTx in the first line (1L) setting. Treatment with ICI + CTx provided superior efficacy, independent of KRAS and PD-L1 status and use of ICI + CTx was suggested as the preferred comparator arm in future 1L trials for patients with KRASmt. Herein, we report the largest, multimodal real world data (RWD) analysis for outcomes with 1L therapy in patients with advanced NSCLC stratified by KRASmt status.

Methods Deidentified multimodal RWD was accessed via the Tempus Lens database to retrospectively analyze 2,680 advanced 1L NSCLC patients. Patients were diagnosed between January 1, 2017 – December 31, 2021, had Tempus xT genomic sequencing and received CTx, ICI, or ICI + CTx. Patients were stratified by KRAS status: mutant (mt), G12C, or wildtype (wt). Median overall survival (mOS) was estimated using Kaplan-Meier methods. Subgroup analyses were performed using Cox model stratified by KRAS status, PD-L1 status [High (TPS > 50), Low (TPS ≥ 1-49), Negative (TPS < 1)] and pathogenic alterations in STK11, KEAP1 and TP53.

Results KRASmt were identified in 31.4% (840/2680), 11.3% (303/2680) were G12C. Proportion of patients with PD-L1 TPS ≥ 50% was highest in KRASmt and G12C groups compared to wt (30%, 31% vs 20% respectively). Demographics were balanced across all subgroups, except for a higher% of squamous histology (wt 25% vs 4% mt) and never-smokers (wt 14% vs. 5% mt). The prevalence of pathogenic variants between mt vs. wt groups were: STK11 (16% vs 10%), KEAP1 (9% vs 8%) and TP53 (48% vs 37%). OS results are shown in (table 1). In the mt subgroup, the greatest benefit was seen in PDL-1 High: mOS (months): High: 27.56, Low: 15.26, Negative: 14.1. Notably, the G12C + PDL-1 high group displayed the longest mOS (47.4). Patients with co-mutations had the worst outcome: KRASmt/STK11 (OS 11.53m) or KEAP1 (OS 11.33m) (table 2).

Conclusions Our analysis suggests that advanced NSCLC patients with KRASmt, including G12C with high PD-L1, had the best outcomes when treated with 1L ICI including ICI alone. Outcomes were significantly worse when STK11/KEAP1 co-mutations were present. This implies that patients with KRASmt NSCLC may represent a heterogeneous group requiring a tailored 1L trial design to account for variabilities in outcome.

REFERENCES