HOST IMMUNE PROFILING IN FIRST-LINE IMMUNOTHERAPY TREATED ADVANCED STAGE NON-SMALL CELL LUNG CANCER: RESULTS FROM THE INSIGHT REGISTRY STUDY

Background Immune checkpoint inhibitor therapies (ICI) have revolutionized the treatment of advanced stage non-small cell lung cancer (NSCLC) yielding 5 year-survival in ~30% for ICI treated patients and PD-L1 expression (≥50%) with median survival of 26.3 months (m).1 New treatment biomarkers have the potential to improve these results. Here we report the updated interim analysis results from the INSIGHT study, evaluating the extensively validated blood-based proteomic test, the Host Immune Classifier (HIC).2

Methods INSIGHT (NCT03289780) is a prospectively designed multicenter observational clinical study, having enrolled over 4,500 patients with NSCLC, across all stages and histologies. Pre-treatment blood samples were evaluated with the HIC test, which classifies patients as either HIC-Hot (HIC-H) or HIC-Cold (HIC-C). An interim analysis of exploratory endpoints was performed once patients had at least 12 months of follow up in the first 3,035 patients enrolled.

Results In the analysis population, 564 advanced stage (Stages IIIb & IV) patients were treated with a 1st line ICI containing regimen (ICI monotherapy [ICI-m] n=204 and ICI+Platinum based Chemotherapy [ICI+PC] n=360). Real-world median Overall Survival (mOS) for the ICI-m and ICI+PC cohorts was 12.9m and 13.0m, respectively. mOS for the ICI-m cohort stratified by the HIC test was 17.5m (HIC-H) vs. 5.6m (HIC-C), Hazard Ratio (HR): 0.49 (CI 0.23-0.76), p-value = 0.001. Similarly, stratification of the ICI+PC cohort indicated that patients classified as HIC-H had a mOS of 17.1m vs. 8.2m in HIC-C (HR 0.49 (CI 0.34-0.71), p-value=0.0001. Evaluation of the ICI-m treated patients with PD-L1 expression ≥50% demonstrated a similar survival stratification, 16.4m vs 5.3m (HR 0.49 [0.32-0.76], p-value=0.001, Figure 1A) for HIC-H and HIC-C, respectively. However, in the ICI+PC PD-L1 high cohort, OS did not significantly differ between patients classified as HIC-H and HIC-C (Not Reached vs. 14.3, HR 0.49 [0.23-1.03], p value=0.06). Furthermore, the HIC test classifications were independent of PD-L1 expression (p-value=0.196) and remained an independent predictor of OS in ICI-treated patients, when covariates such as PS and PD-L1 expression were adjusted for in a multivariate analysis (HR 0.54 [0.45-0.64], p-value=0.0001).

Conclusions HIC-C patients with PD-L1 expression ≥50% treated with ICI+PC had better survival than those treated with ICI-m (mOS 14.3m vs 5.3m) suggesting that a blood-based HIC test provides clinically meaningful information that may aid in selecting 1st line immunotherapy containing regimens. Additionally, in the real-world setting mOS of patients treated with ICI-m was reduced as compared to survival reported in registrational clinical trials (i.e. 26.3m). 1

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Trial Registration Clinicaltrial.gov: NCT03289780

REFERENCES

Ethics Approval INSIGHT (NCT03289780) is an ongoing registry study involving over 30 academic and community oncology practices across the United States of America. The study has been reviewed and approved by an accredited central IRB (Advava; formerly Quorum), as well as multiple institutional review boards and conducted in accordance with the International Conference on Harmonization guidelines for Good Clinical Practice and the Declaration of Helsinki. All patients have provided written informed consent for participation.

Abstract 580 Figure 1 Overall survival stratification of patients with PD-L1 ≥50% expression treated with either ICI-m (A) or ICI+PC (B). In patients treated with ICI-m, mOS differed significantly between HIC-H and HIC-C, HR 0.49 (CI 0.32-0.76), p-value = 0.001. Conversely, in patients with PD-L1 ≥50% expression treated with ICI+PC, overall survival did not significantly differ between HIC-H and HIC-C, HR 0.49 (0.23-1.0), P-value = 0.06.