Abstract 1117

Immunotherapy alone or with chemotherapy in advanced NSCLC? Utility of clinical factors and blood-based host immune profiling.

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Introduction

Immune checkpoint inhibitors (ICI) have revolutionized cancer care with greater overall survival (OS) in patients with advanced stage non-small cell lung cancer (aNSCLC). However, even for patients with good ECOG performance status (PS) 0-1 and high PD-L1 expression, the overall response rate to single-agent ICI in the treatment naïve population is only 45%. Combination treatments might increase efficacy but add toxicity and higher cost. Better predictors of response to treatment are needed to guide treatment decisions. A prospectively designed, observational study assessed the ability of clinical factors and a clinically validated, blood-based, host immune classifier (HIC) to predict ICI therapy outcomes.

Methods

Over 3,500 NSCLC patients at any stage and line of therapy across 33 US sites have been enrolled in the prospective observational study (NCT03289780) that assesses subject sera by the proteomic HIC test (HIC-Hot or HIC-Cold) prior to treatment initiation. An interim analysis was performed after 12-18 months follow-up with the first 2,000 enrolled subjects. The correlation of various factors, including PD-L1 expression, age, histology, PS, smoking history, gender and the HIC result, with OS of subjects receiving ICI alone (ICI, n=86) or in combination with platinum-doublet chemotherapy (ICI+PD, n=98) was assessed.

Results

In a real-world clinical setting, OS of subjects with newly diagnosed aNSCLC did not differ significantly between ICI and ICI+PD (median OS (mOS): 9.4 vs. 12.5 months, hazard ratio 0.80 [95% confidence interval: 0.54-1.19], P-value=0.28). Survival analysis for subjects receiving ICI indicated that HIC-Hot, better PS and younger age, but not high PD-L1 expression (either 50% or 90% cutoff) were significantly associated with longer OS according to univariate analyses (see table). When adjusted for covariates in a multi-variate analysis, HIC and age remained significant predictors of OS (p=0.0006 and p=0.005), while PS did not (p=0.40). For patients receiving ICI+PD, only high PD-L1 expression was significantly associated with increased OS. While HIC individually trended towards significance, its inclusion in a multi-variate analysis of gender, smoking history (ever vs. never) and PD-L1 expression (<50% vs. ≥50%) did not improve the fit, indicating that HIC is not independently associated with OS in subjects receiving ICI+PD (p=0.27).

Association of selected clinical factors and HIC individually with OS of patients receiving ICI or ICI+PD.

Treatment Type	Univariates	mOS	Hazard Ratio (95% confidence interval)	P-value
ICI	**HIC-Cold (N=30) vs. HIC-Hot (N=56)**	2.2 months vs. 16.3 months	2.61 (1.49-4.56)	0.0008
ICI	**PS 2+ (N=24) vs. PS 0-1 (N=62)**	4.2 months vs. 16.3 months	2.10 (1.19-3.73)	0.011
ICI	**Age >65 years (N=48) vs. Age <65 years (N=38)**	6.7 months vs. not reached	1.80 (1.01-3.20)	0.046

ICI	**PD-L1 <50% (N=12) vs. PD-L1 ≥50% (N=74)**	10.1 months vs. 9.3 months	1.32 (0.64-2.72)	Not significant (0.45)
ICI	**PD-L1 <90% (N=57) vs. PD-L1 ≥90% (N=29)**	8.0 months vs. 9.4 months	1.43 (0.77-2.65)	Not significant (0.25)
ICI+PD	**PD-L1 <50% (N=59) vs. PD-L1 ≥50% (N=39)**	8.5 months vs. not reached	2.02 (1.08-3.77)	0.028
ICI+PD	**HIC-Cold (N=33) vs. HIC-Hot (N=65)**	7.0 months vs. 17.3 months	1.76 (0.99-3.11)	Not significant (0.053)
ICI+PD	**PS 2+ (N=17) vs. PS 0-1 (N=81)**	8.5 months vs. 16.0 months	1.42 (0.74-2.85)	Not significant (0.33)

Conclusion

The HIC test provides clinically meaningful information in addition to currently utilized clinical factors to potentially help guide immunotherapy treatment decisions for patients with newly diagnosed aNSCLC. HIC stratified survival for patients receiving ICI but not ICI+PD, suggesting that patients classified HIC-Cold may benefit from addition of chemotherapy to ICI.

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