Real-World Performance of Blood-Based Proteomic Profiling in Immunotherapy Treatment in Advanced Stage NSCLC

Patricia Rich (Thompson), MD[1], Joanna Roder, PhD[2], John Dubay, MD, PhD[3], David Oubre, MD[4], Emily Pauli, PharmD[5], James Orsini, MD[6], Edgardo Santos, MD[7], Morton Coleman, MD[8], Waseemullah Khan, MD[9], Wallace Akerley, MD[10], Robert Siegel, MD[11], Linda Traylor, PhD[12], Paul Walker, MD[13]

1. Cancer Treatment Centers of America, Newnan, GA, 2. Biodesix Inc., Steamboat Springs, CO, 3. Lewis & Faye Manderson Cancer Center , Tuscaloosa, AL, 4. Pontchartrain Cancer Center, Covington, LA, 5. Clearview Cancer, Institute, Huntsville, AL, 6. Essex Oncology, Belleville, NJ, 7. Lynn Clinical Research Institute, Boca Raton, FL 8. Clinical Research Alliance, Lake Success, NY, 9. Cancer Care of North Florida, Lake City, FL 10. Huntsman Cancer Center, Salt Lake City, UT, 11. Bon Secours St. Francis Cancer Center, Greenville, SC 12. Biodesix, Boulder, CO 13. Leo W. Jenkins Cancer Center, ECU, Greenville, NC

INSIGHT Study Overview

- INSIGHT is an ongoing registry study (NCT03289780) including 33 US sites.
- All enrolled patients receive blood-based proteomic testing and are assigned a result of VeriStrat Poor (VSP) or VeriStrat Good (VSG) prior to therapy initiation.
- Patient characteristics, therapeutic decisions, staging, disease monitoring metrics and available biomarker data have been collected.
- Patient follow-up occurs for up to 18 months.
- First patient first visit for study initiation was May 16, 2016
- Last patient first visit for the first 1000 patient cohort was October 31, 2017
- Database lock was November 15, 2018

Statistical Methods

A pre-specified interim analysis was performed on the first 1000 patients enrolled in the study with at least 1 year follow up. Overall survival (OS) in months (mo) is summarized as median and 95% confidence interval (CI) and as Kaplan-Meier plots and compared between proteomic-defined subgroups or between therapies by log-rank p values and Cox Proportional hazard ratios and p values. Data from the frontline patient subgroup (N = 419) and the 2nd and higher lines (N = 297) are presented here.

Figure 1. Patient population summary

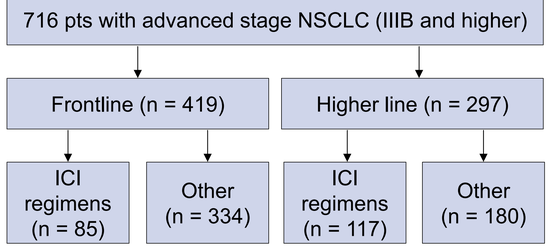


Table 1. PD-L1 Expression by VeriStrat in Frontline Subgroup

PD-L1 Expression, n (%) Frontline Subgroup	VeriStrat Good	VeriStrat Poor	P Value
≤1%	67 (23.0)	17 (13.3)	0.119
>1% and <50%	24 (8.3)	13 (10.2)	
≥50%	42 (14.4)	23 (18.0)	
NA	158 (54.3)	75 (58.6)	

Table 2. Multivariate Analysis of OS for subjects in frontline receiving an immunotherapy-containing regimen, including VS and therapy type

Covariate		Hazard Ratio (95% CI)	CPH p-value
VeriStrat (vs VSP)	VSG	0.27 (0.13-0.55)	<0.001
Therapy (vs Monotherapy)	With chemotherapy	0.32 (0.13-0.81)	0.015
Therapy (vs Monotherapy)	With other	1.67 (0.48-5.78)	0.422
Gender (vs Male)	Female	1.50 (0.76-2.95)	0.241
Disease Stage (vs IV)	IIIB	1.78 (0.58-5.39)	0.312
Smoking Status (vs Ever)	Never	2.83 (0.43-18.66)	0.281
ECOG PS (vs 0)	1	0.84 (0.37-1.89)	0.665
ECOG PS (vs 0)	2+	1.46 (0.62-3.43)	0.392
Histology (vs Non-Squamous)	Squamous Cell	0.40 (0.11-1.44)	0.159
Histology (vs Non-Squamous)	Undetermined	0.63 (0.26-1.52)	0.298
Age (vs ≥ 65)	< 65	0.74 (0.37-1.47)	0.388
PD-L1 Status (vs<50%)	≥ 50%	0.50 (0.18-1.37)	0.177
PD-L1 Status (vs<50%)	NA	1.13 (0.41-3.11)	0.813

RESULTS

Table 3. Patient demographics by line of therapy

Advanced Stage NSCLC (IIIB and IV)	Frontline	Second and Higher Lines
	N = 419	N = 297
Age		
Mean (SD)	67.4 (10.7)	65.6 (10.7)
Median (Range)	67 (35-95)	66 (27-95)
VeriStrat Classification, n (%)		
Good	291 (69.5)	223 (75.1)
Poor	128 (30.6)	74 (24.9)
Gender, n (%)		
Female	200 (47.7)	153 (51.5)
Male	219 (52.3)	144 (48.5)
Line of Therapy, n (%)		
2nd	NA	133 (44.8)
3rd	NA	98 (33.0)
4th	NA	39 (13.1)
5th	NA	27 (9.1)
Disease Stage at Study Entry, n (%)		
IIIB	52 (12.4)	31 (10.4)
IV	367 (87.6)	266 (89.6)
Histology, n (%)		
Adenocarcinoma	256 (61.1)	160 (53.9)
Bronchioalveolar	1 (0.2)	NA
Carcinoma NOS	12 (2.9)	1 (0.3)
Large Cell	4 (1.0)	3 (1.0)
Neoplasm	5 (1.2)	4 (1.4)
NSCLC	55 (13.1)	51 (17.2)
Squamous	86 (20.5)	78 (26.3)
Smoking Status, n (%)		
Current Smoker	149 (35.6)	70 (23.6)
Ex Smoker	225 (53.7)	192 (64.7)
Never Smoker	45 (10.7)	35 (11.8)
ECOG PS at Study Entry, n (%)		
0	101 (24.1)	77 (25.9)
1	201 (48.0)	146 (49.2)
2	93 (22.2)	61 (20.5)
3	21 (5.0)	12 (4.0)
4	3 (0.7)	1 (0.3)
KRAS Mutation Status, n (%)		
Mutated	52 (12.4)	22 (7.4)
Wild-Type	316 (75.4)	219 (73.7)
NA	51 (12.2)	56 (18.9)
PD-L1 Expression, n (%)		
≤1%	84 (20.1)	39 (13.1)
>1% and <50%	37 (8.8)	11 (3.7)
≥50%	65 (15.5)	24 (8.1)
NA	233 (55.6)	223 (75.1)
Treatment Regimen, n (%)		
Carboplatin-based chemotherapy	222 (53.0)	50 (16.8)
Cisplatin-based chemotherapy	14 (3.3)	2 (0.7)
Immunotherapy combination	39 (9.3)	4 (1.4)
Immunotherapy (monotherapy)	46 (11.0)	113 (38.1)
None/Hospice/BSC/Observation	34 (8.1)	44 (14.8)
Non-platinum-based chemotherapy	11 (2.6)	32 (10.8)
Radiation	22 (5.3)	10 (3.4)
Surgery	1 (0.2)	0 (0.0)
TKI	17 (4.1)	35 (11.8)
Other	13 (3.1)	7 (2.4)

Table 4. Summary statistics for front-line therapy and second line+

Therapy	N	mOS	N: VSG/VSP	mOS: VSG	mOS: VSP	HR	CPH p
Frontline Therapies	**419**	**10.5 (8.9-13.0)**	**291/128**				
All Immunotherapy (ICI)	85	14.8 (7.8-und)	54/31	Not reached (14.8-und)	4.1 (2.0-7.8)	0.33 (0.18-0.61)	<0.001
ICI Monotherapy	46	9.3 (4.1-und)	28/18	14.8 (8.0-und)	3.3 (1.4-7.8)	0.45 (0.21-0.96)	0.039
ICI + Chemotherapy (CT)	33	Not reached (12.4-und)	23/10	Not Reached (15.4-und)	5.9 (1.9-und)	0.23 (0.07-0.74)	0.014
All Platinum-based CT	237	12.2 (9.5-15.6)	172/65	14.3 (10.9-und)	7.9 (5.0-12.2)	0.63 (0.43-0.92)	0.016
Carboplatin-based Therapy	222	12.2 (9.5-15.8)	160/62	14.3 (10.6-und)	8.5 (5.0-12.2)	0.65 (0.44-0.96)	0.031
Carboplatin + Paclitaxel	119	14.0 (10.2-16.4)	81/38	14.8 (10.5-und)	10.5 (5.2-16.4)	0.73 (0.43-1.22)	0.230
Carboplatin + Pemetrexed	92	12.7 (8.7-und)	76/16	17.6 (9.2-und)	5.0 (3.3-und)	0.50 (0.25-0.98)	0.044
Platinum-based CT + Bevacizumab	46	8.8 (6.3-10.6)	40/6	8.8 (6.3-13.1)	7.3 (2.0-und)	1.05 (0.37-3.00)	0.929
No Active Therapy	55	3.6 (2.1-6.9)	35/20	4.8 (2.4-11.6)	2.1 (0.6-4.9)	0.51 (0.26-1.01)	0.052
Higher Line Therapies	**297**	**11.5 (9.7-14.6)**	**223/74**				
ICI Monotherapy (2nd Line+)	113	10.7 (9.1-14.9)	80/33	14.9 (10.4-und)	6.0 (2.5-9.1)	0.32 (0.19-0.55)	<0.001
ICI Monotherapy (3rd Line+)	59	Not reached (9.7-undefined)	49/10	Not reached (10.7-undefined)	6.0 (1.3-und)	0.25 (0.10-0.65)	0.005
All CT (2nd line+)	84	12.4 (8.8-15.5)	59/25	15.6 (12.0-19.4)	5.2 (3.1-8.2)	0.26 (0.14-0.46)	<0.001
Non-platinum CT (2nd line+)	32	14.9 (10.1-und)	24/8	15.5 (12.0-und)	9.7 (2.9-12.9)	0.32 (0.12-0.85)	0.022

Figure 2. Kaplan-Meier plot of OS by treatment regimen (ICI vs. chemotherapy) without VeriStrat stratification for advanced stage patients: **2A)** frontline platinum-containing regimens vs immunotherapy-containing regimens **2B)** second or higher line chemotherapy vs immunotherapy **2C)** second or higher line non-platinum chemotherapy vs immunotherapy.

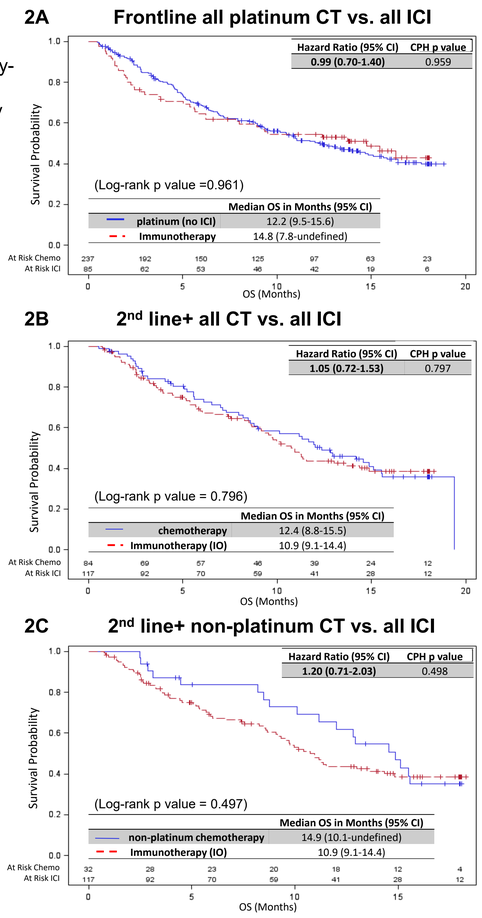
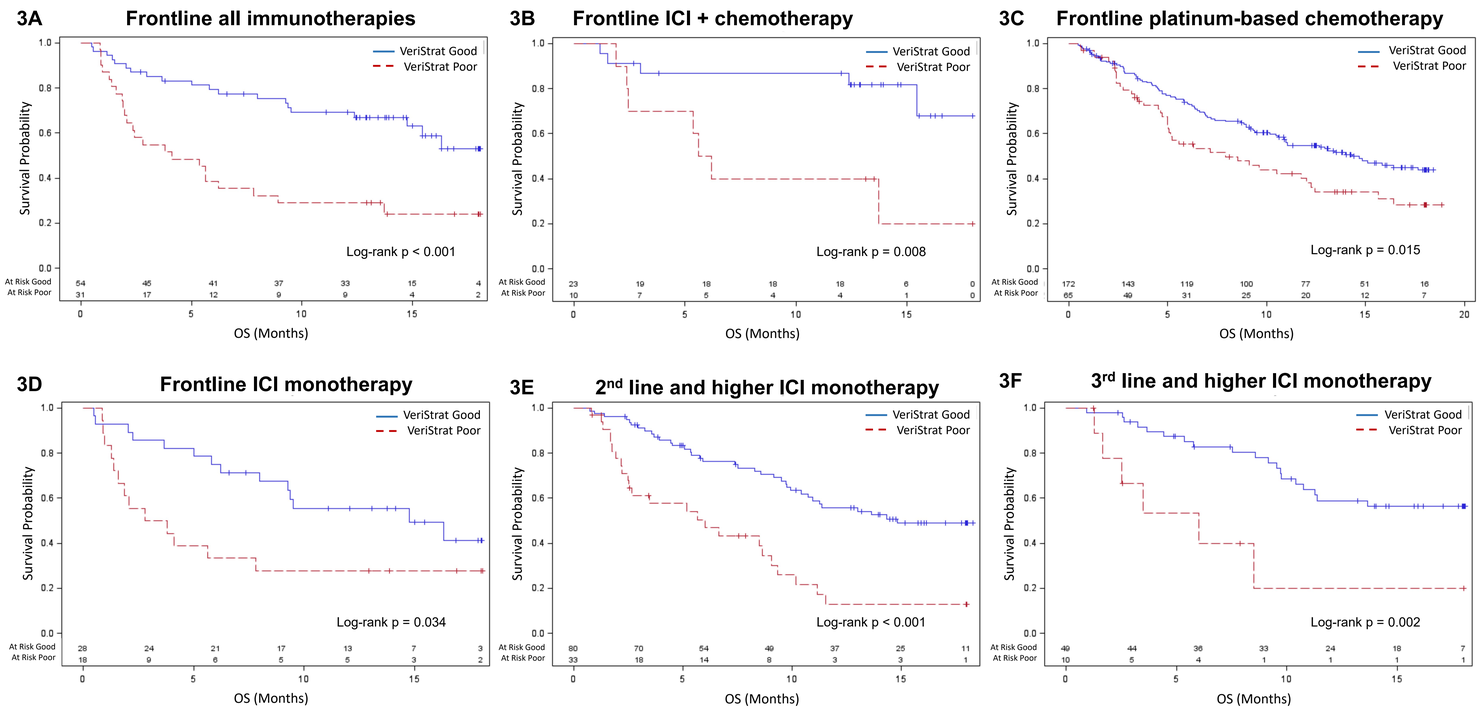


Figure 3. Kaplan-Meier plot of OS by VeriStrat classification for advanced stage NSCLC patients receiving: **3A)** frontline immunotherapy (all) using ICI monotherapy or ICI combination therapies; **3B)** frontline immunotherapy combinations with chemotherapy; **3C)** frontline platinum-based chemotherapy (all); **3D)** frontline ICI monotherapy; **3E)** second-line+ ICI monotherapy; **3F)** third-line+ ICI monotherapy.

VeriStrat classification was not significantly associated with PD-L1 status (p=0.119, Table 1) and was predictive of outcomes for ICI treatment when adjusted for PD-L1 (p<0.001, Table 2).



CONCLUSION

The INSIGHT study is an ongoing observational study evaluating the real world use of VeriStrat blood-based proteomic testing in the treatment of lung cancer patients. Based on the current interim analysis results, the VeriStrat test is predictive of overall survival in immunotherapy treated patients at all lines of therapy in advanced stage NSCLC, even when adjusted for PD-L1 status in a multi-variate analysis, suggesting that the test may provide clinically meaningful information for immunotherapy treatment.

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