The Impact of Blood-Based Host Immune Profiling to Identify Aggressive Early-Stage NSCLC

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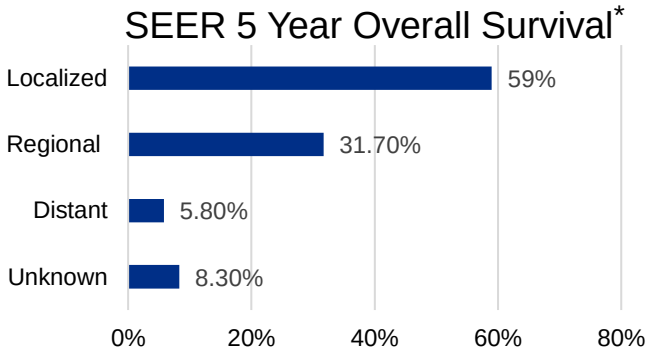
DISCLOSURES

I do not have any relevant financial relationships to disclose.

Introduction & Background

Early-Stage NSCLC:

- Early detection of non-small cell lung cancer (NSCLC) provides the greatest opportunity for a cure.
- However, even when NSCLC is identified early, 30-60% of patients diagnosed with stage I-IIIA disease will experience local and/or distant recurrences, respectively.
- More precise tools are needed to refine lung cancer staging and identify patients that have a more aggressive disease who may benefit from additional treatment or enhanced disease surveillance following curative intent.



INSIGHT observational trial (NCT03289780):

- Currently >3900 subjects enrolled across 35 sites in the US (goal N=5000)
- NSCLC of all stages, all histologies, all lines of therapies, all ECOG PS eligible; up to 3-year follow-up
- **Host Immune Classifier:**
  - Clinically validated, blood-based proteomic classifier that utilizes mass spectrometry and machine learning algorithm to designate labels: HIC-Hot or HIC-Cold
  - HIC-Cold: chronic inflammatory disease state associated with poor prognosis

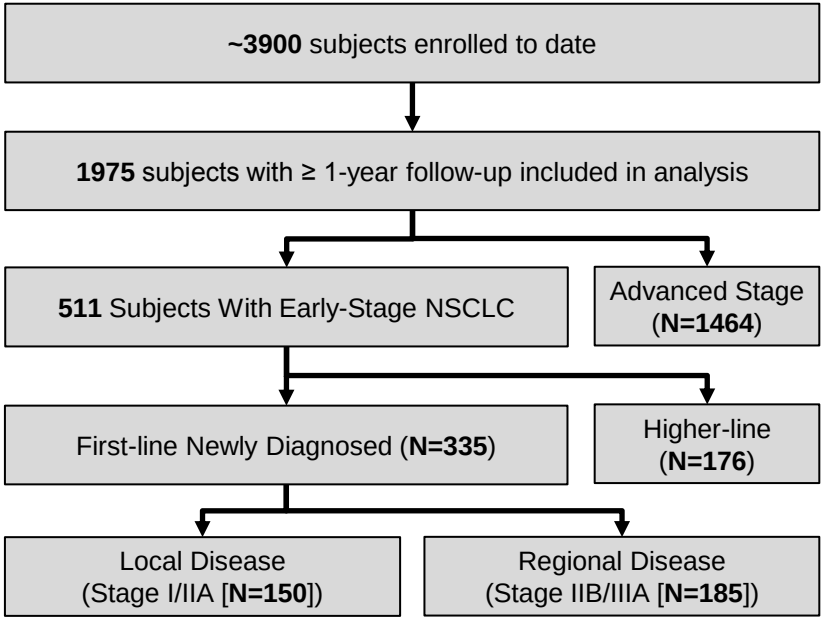
Reference: *https://seer.cancer.gov/statfacts/html/lungb.html

Methods

Statistical Methods:

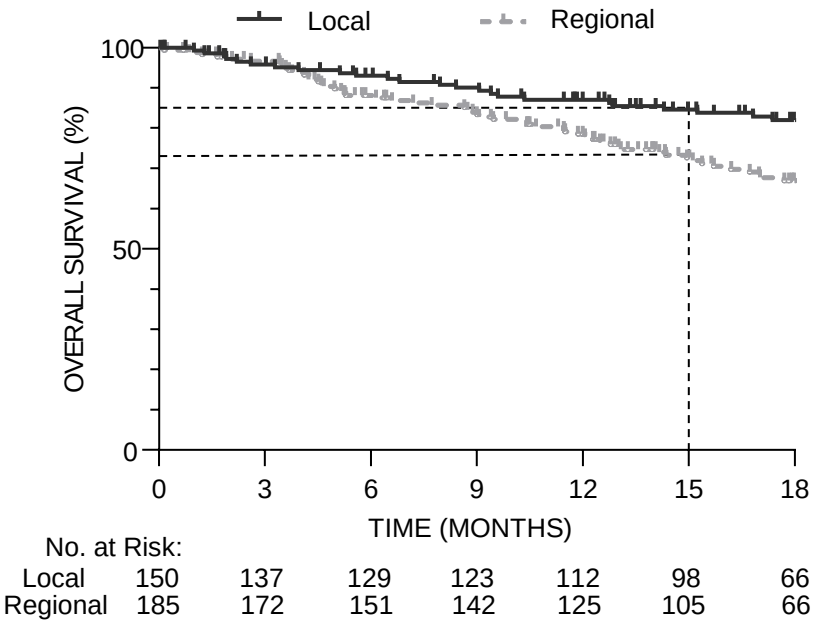
- A study interim analysis of secondary and exploratory endpoints was performed after 12-18 months (mo) follow-up with the first 2,000 enrolled patients
- We report the overall survival (OS) and disease-free survival (DFS) of HIC-defined subgroups comprising patients with stage I through stage IIIA
  - Defined by the AJCC seventh edition staging system
  - Patients treated according to standard of care practice
- Overall survival (OS) summarized as percent 12 mo and 15 mo landmark survival, 95% confidence interval (CI) and as Kaplan-Meier plots
- OS compared between HIC-defined subgroups by Cox Proportional hazard ratios and P values

Subject Population Summary



Overall Survival of Early-Stage NSCLC Patients Enrolled in the INSIGHT Study

Landmark Overall Survival

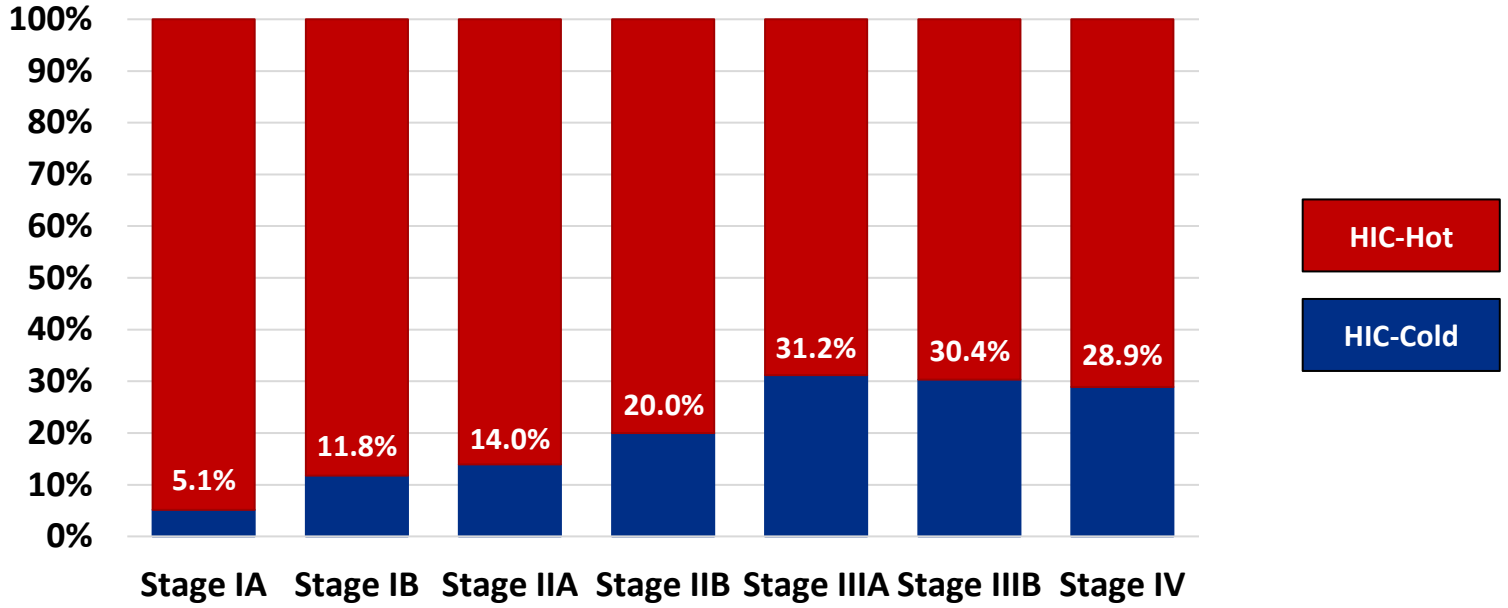


Sub-Group	N	12 Month OS Rate (95% CI)	15 Month OS Rate (95% CI)
Local (Stage I/IIA)	150	87% (80-92)	85% (78-90)
Regional (Stage IIB- IIIA)	185	79% (72-84)	73% (65-79)

Study Subject Population Summary

	Local (N=150)	Regional (N=185)
Age		P value 0.251
Mean Years (SD)	68.9 (9.01)	67.7 (9.79)
Median Years (Range)	69.8 (31.5-90.2)	68.9 (29.3-88.2)
Gender, % (N)		P value 0.189
Female	53.3% (N=80)	45.9% (N=85)
Male	46.7% (N=70)	54.1% (N=100)
Disease Stage, % (N)		
Stage IA	45.3% (N=68)	--
Stage IB	30.0% (N=45)	--
Stage IIA	24.7% (N=37)	--
Stage IIB	--	23.8% (N=44)
Stage IIIA	--	76.2% (N=141)
Histology, % (N)		P value <0.001
Adenocarcinoma	68.0% (N=102)	43.8% (N=81)
Squamous	27.3% (N=41)	43.8% (N=81)
NSCLC Other	4.7% (N=7)	12.4% (N=23)
Smoking Status, % (N)		P value 0.089
Currently Smokers	3.3% (N=50)	41.1% (N=76)
Former-Smokers	54.7% (N=82)	53.0% (N=98)
Never smokers	12.0% (N=18)	5.9% (N=11)

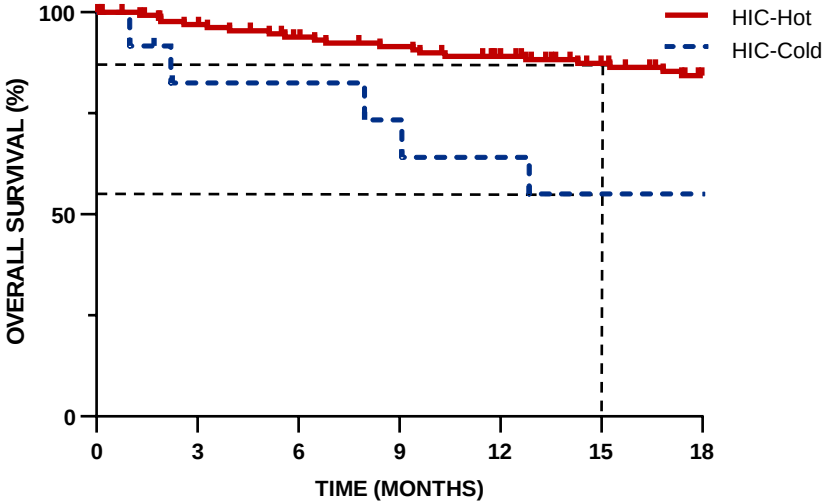
Incidence of HIC-Cold Classification Across NSCLC Stages



Increasing Proportion of HIC-Cold classification with more advanced disease stages

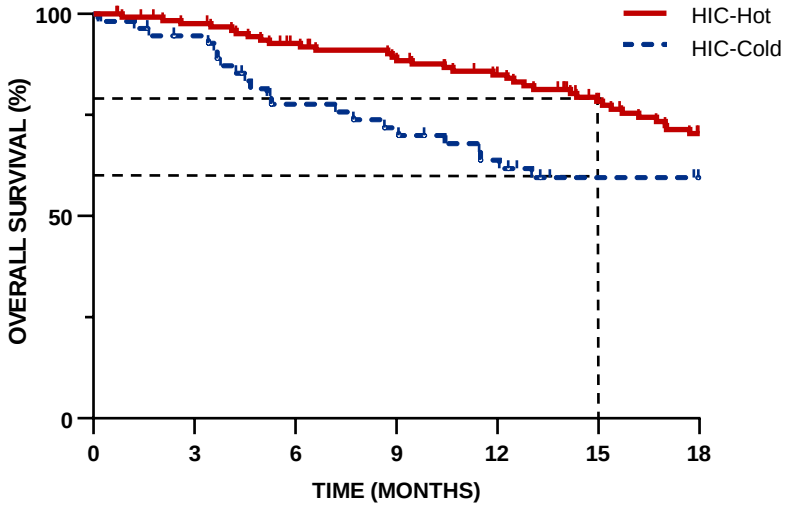
Impact of HIC-Cold Classification On Patient Overall Survival

Local (Stage I/IIA)



	12 Month OS Rate (95% CI)	15 Month OS Rate (95% CI)
HIC-Hot = 138	89% (82-93)	87% (80-92)
HIC-Cold = 12	64% (30-85)	55% (23-78)
Hazard Ratio (95% CI) HIC-Cold vs. Hot	**3.68** (1.38-9.87)	P value **0.010**

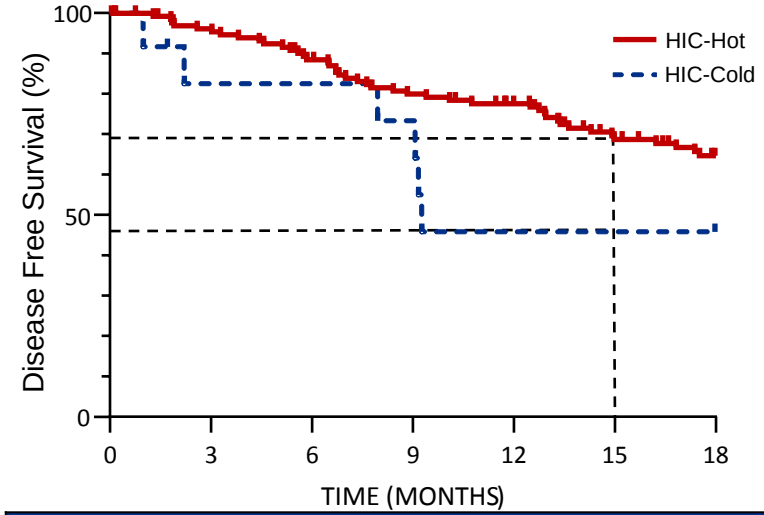
Regional (Stage IIB/IIIA)



	12 Month OS Rate (95% CI)	15 Month OS Rate (95% CI)
HIC-Hot = 128	85% (77-90)	79% (70-85)
HIC-Cold = 57	64% (49-75)	60% (45-72)
Hazard Ratio (95% CI) HIC-Cold vs. Hot	**1.77** (1.02-3.06)	P value **0.041**

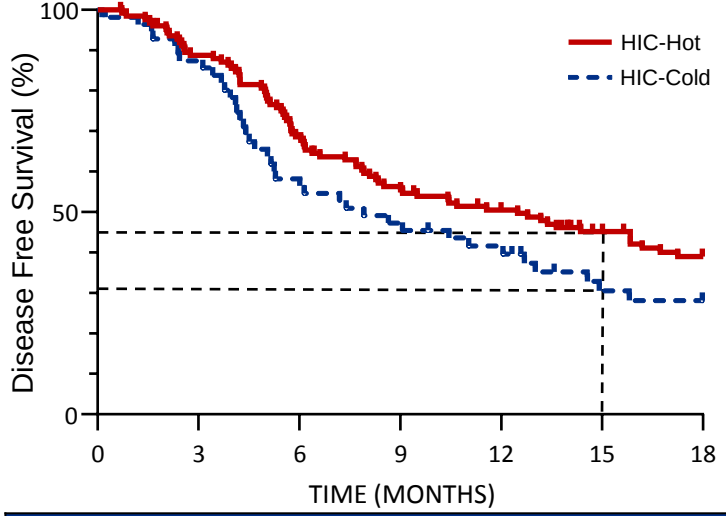
Impact of HIC-Cold Classification On Patient Disease Free Survival

Local (Stage I/IIA)



	12 Month DFS Rate (95% CI)	15 Month DFS Rate (95% CI)
HIC-Hot = 138	78% (70-84)	69% (60-76)
HIC-Cold = 12	46% (17-71)	46% (17-71)
Hazard Ratio (95% CI) HIC-Cold vs. Hot	1.94 (0.83-4.57)	P value 0.128

Regional (Stage IIB/IIIA)



	12 Month OS Rate (95% CI)	15 Month OS Rate (95% CI)
HIC-Hot = 128	51% (41-59)	45% (36-54)
HIC-Cold = 57	42% (28-54)	31% (19-44)
Hazard Ratio (95% CI) HIC-Cold vs. Hot	1.39 (0.94-2.06)	P value 0.101

Multivariate Analysis For Overall Survival

Covariate		Hazard Ratio (95% CI)	CPH p-value
HIC Classification (vs Hot)	**HIC-Cold**	**1.89 (1.15-3.12)**	**0.012**
Treatment Regimen (vs platinum-based chemotherapy)	**Surgery**	0.54 (0.18-1.64)	0.276
	Other	1.23 (0.71-2.12)	0.454
Gender (vs Female)	**Male**	1.04 (0.65-1.65)	0.878
ECOG PS (vs 0)	**1**	1.05 (0.57-1.91)	0.886
	2+	1.93 (1.02-3.68)	0.045
Histology (vs Other)	**Squamous**	1.29 (0.81-2.04)	0.287
Age (vs ≥ 65)	**< 65**	1.07 (0.66-1.75)	0.789
Stage (vs Local)	**Regional**	1.36 (0.76-2.43)	0.300

Summary & Conclusions

1. Blood-based immune profiling with the HIC test identifies an aggressive disease state (HIC-Cold) associated with a chronic inflammation.
2. The HIC-Cold disease state can be identified across all NSCLC stages. The proportion of HIC-Cold classifications increased with disease stage
3. HIC-Cold Classification is associated with significantly reduced OS in both local (I/IIA) and regional disease (IIB/IIIA) patients.
4. HIC Test classification was found to be associated with OS, independent of other covariates.

The use of blood-based immune profiling may identify early-stage lung cancer patients with aggressive disease that could potentially benefit from enhanced disease surveillance or additional treatment.