

Unveiling integrin beta-6: real-world data from the IB6 expression and clinical outcomes in non-small cell lung cancer study

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Conclusions

- This is the first real-world study to delineate the prevalence of IB6-high expression in mNSCLC within routine clinical practice
- IB6-high expression is common in mNSCLC in this diverse population in the US, particularly in nonsquamous histology, with an observed prevalence of 79.2% (95% CI, 71.0- 85.9)
- Demographics, clinical characteristics, and biopsy characteristics were generally consistent across IB6-high vs IB6-low subpopulations, except for histology
- No initial trends were observed between IB6 expression status and PD-L1 or ALK, but potential trends between IB6 expression status with KRAS and EGFR may merit future investigation
- This study begins to characterize IB6-high vs -low expressors using this novel IHC assay and associated cutoff in patients with mNSCLC to inform future developments of IB6-directed therapies

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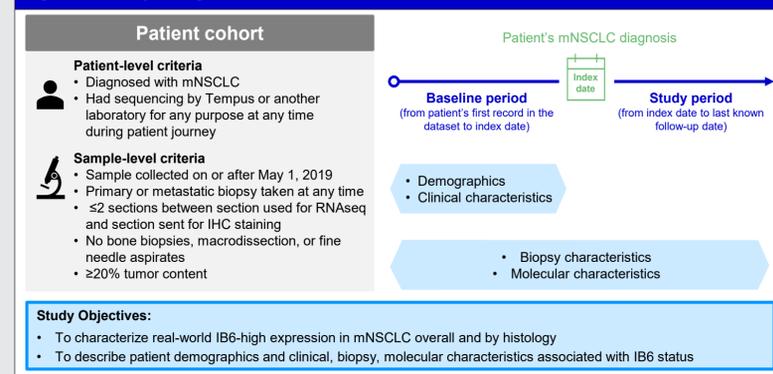
Background

- Integrin beta-6 (IB6), a member of the integrin superfamily of transmembrane adhesion proteins is overexpressed in several solid tumors, including non-small cell lung cancer (NSCLC)^{1,2}
- As IB6 is a novel potential target in oncology, several clinical trials of IB6-directed agents are ongoing³⁻⁸
 - Sigvotatug vedotin (SV), an investigational IB6-directed antibody-drug conjugate, has shown encouraging activity in a first-in-human phase 1 study and is the subject of two ongoing phase 3 NSCLC studies²⁻⁵
- Concurrent studies are also being conducted to characterize IB6 expression levels and patterns in patients with NSCLC⁹
 - Initial findings using commercially sourced non-squamous NSCLC samples estimated a high prevalence of patients (79%) with IB6-high status⁹
- Here, we present results of the retrospective real-world study, BEACON (IB6 Expression and Clinical Outcomes in NSCLC); we characterize IB6-high expression in real-world NSCLC tissue samples and describe characteristics associated with IB6 status

Methods

- This is a retrospective, observational study that used de-identified real-world clinical and molecular data from patients in the Tempus Database in the US
- Patients with metastatic NSCLC (mNSCLC) included in this study had to meet patient- and sample-level eligibility criteria (Figure 1)
- Patient demographics and clinical characteristics were obtained via electronic health record integration and clinical record abstraction
- These data were matched with tissue samples from primary or metastatic lesions collected on or after May 1, 2019, that subsequently underwent IB6 immunohistochemistry (IHC) and were manually scored by a pathologist to characterize IB6 at a central lab
 - IB6-high and IB6-low expression were defined as a percent positivity of tumor cells $\geq 50\%$ and $< 50\%$ positivity, respectively, of tumor cells at $\geq 2+$ intensity⁹
- Molecular characteristics were obtained from Tempus IHC if available or clinical notes (programmed death ligand 1 [PD-L1] status by IHC), DNA sequencing data (KRAS, ALK, and EGFR mutations), or RNA sequencing data (ALK mutations)
- Data cutoff was August 26, 2025, and data are presented descriptively for cohorts

Figure 1. Study design schematic



Results

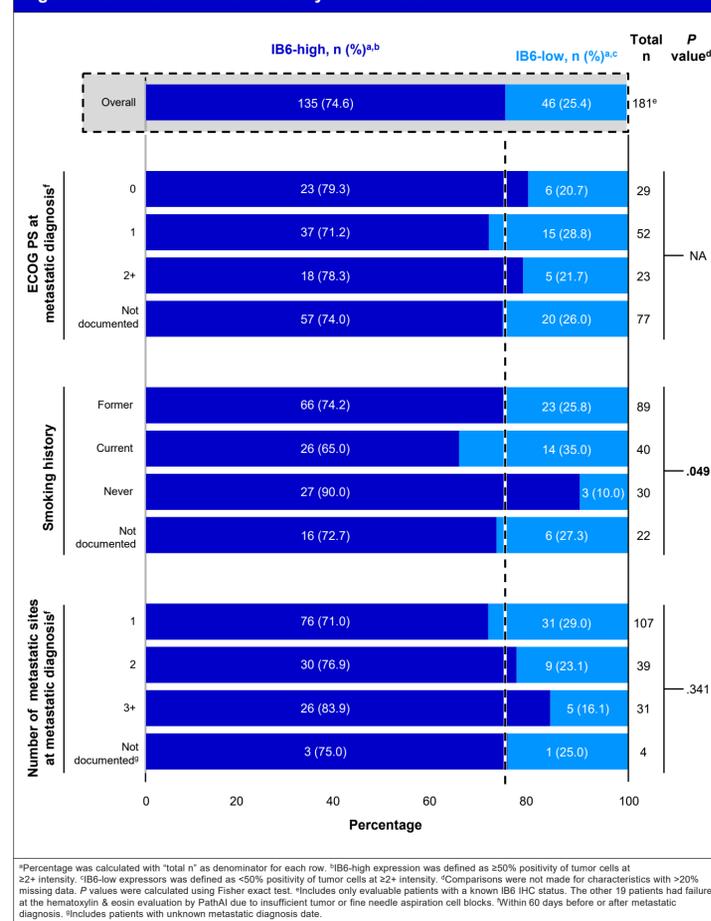
- After screening records for patients with NSCLC, 200 met eligibility criteria and were included in this study
- Overall, the median age was 67 years; 50.5% were male, 53.0% were White; and 70% had a nonsquamous cell carcinoma. Of the tissue samples, 34.0% were from primary tumors (Table 1)
- Demographic, clinical characteristics, and biopsy characteristics were generally consistent between the IB6-high vs IB6-low groups, except for histology (Figures 2-4)
- IB6-high expression was seen in 74.6% (95% CI, 67.6%-80.8%) of samples from the 181 patients with known IB6 IHC expression (Figure 4)
- IB6-high expression varied by histology, with IB6-high expression in 79.2% (95% CI, 71.0%- 85.9%) of nonsquamous samples and 59.4% (95% CI, 40.6-76.3) of squamous samples (Figure 4)
- PD-L1 expression was generally consistent across IB6-high and -low subgroups (Figure 5)
- Prevalence of KRAS G12C mutation and any EGFR mutation was slightly higher in the IB6-high vs the IB6-low subgroup
- Prevalence of ALK fusion was similar in the IB6-high and IB6-low subgroups

Table 1. Demographics, clinical, and biopsy characteristics of the overall population

	Overall (N=200)
Age at metastatic diagnosis	
Median (range), years	67.0 (37.0-85.0)
Sex, n (%)	
Male	101 (50.5)
Female	97 (48.5)
Not documented	2 (1.0)
Race, n (%)	
White	106 (53.0)
Black or African American	67 (33.5)
Asian	8 (4.0)
Other	16 (8.0)
Not documented	3 (1.5)
Ethnicity, n (%)	
Not Hispanic or Latino	184 (92.0)
Hispanic or Latino	13 (6.5)
Not documented	3 (1.5)
Institution type, n (%)	
Academic	190 (95.0)
Nonacademic	10 (5.0)
Primary tumor histology, n (%)^a	
Nonsquamous ^b	140 (70.0)
Squamous	33 (16.5)
Not otherwise specified	10 (5.0)
Unknown ^d	17 (8.5)
ECOG PS at metastatic diagnosis, n (%)^a	
0	35 (17.5)
1	59 (29.5)
2+	24 (12.0)
Not documented ^f	82 (41.0)
Smoking history, n (%)	
Former	97 (48.5)
Current	48 (24.0)
Never	31 (15.5)
Not documented	24 (12.0)
Number of metastatic sites at metastatic diagnosis, n (%)^a	
1	118 (59.0)
2	44 (22.0)
3+	34 (17.0)
Not documented	4 (2.0)
Biopsy type, n (%)	
Primary	68 (34.0)
Metastatic	132 (66.0)
Biopsy collection date	
Prior to metastatic diagnosis	31 (15.5)
On or after metastatic diagnosis	165 (82.5)
Not documented ^f	4 (2.0)

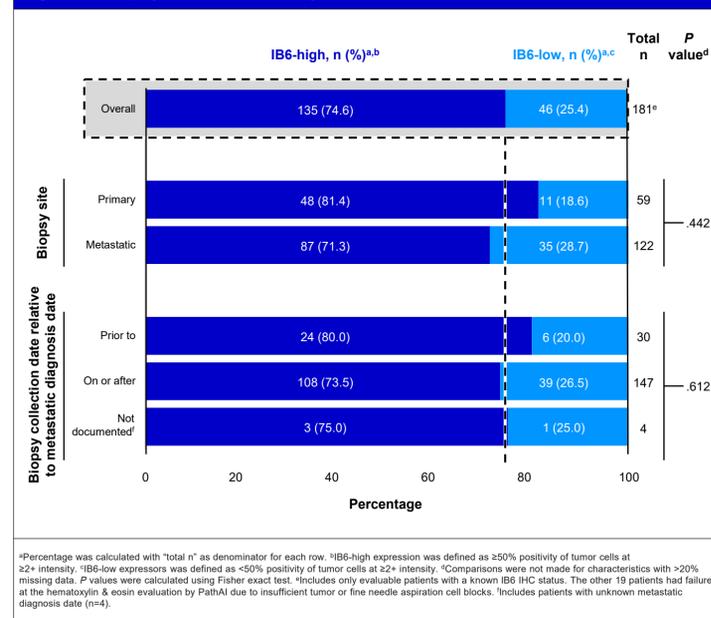
ECOG PS, Eastern Cooperative Oncology Group performance status. ^aIn this study, all patients with nonsquamous NSCLC had tumors classified as adenocarcinoma. ^bIncludes the following histologies: adenocarcinoma, non-small cell carcinoma, epithelioid hemangioendothelioma, carcinoma, no subtype, and bronchioalveolar carcinoma, mixed mucinous and nonmucinous. ^cIncludes patients with a primary tumor histology recorded > 30 days after metastatic diagnosis (n=13) and patients with unknown metastatic diagnosis date (n=4). ^dWithin 60 days before or after metastatic diagnosis. ^eIncludes patients with unknown metastatic diagnosis date (n=4).

Figure 2. Clinical characteristics by IB6 IHC status



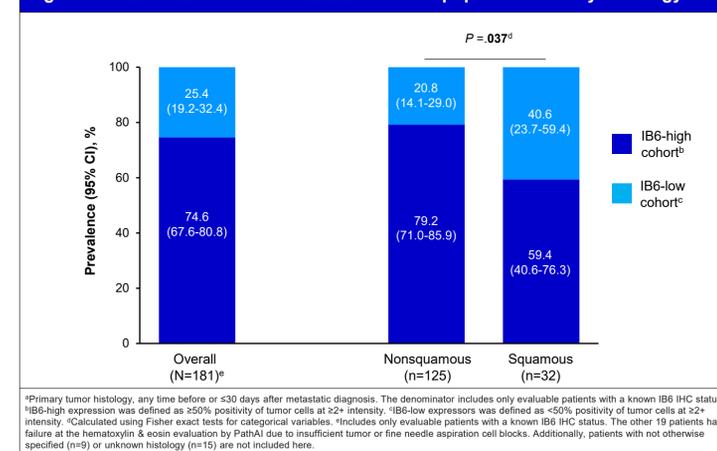
^aPercentage was calculated with "total n" as denominator for each row. ^bIB6-high expression was defined as $\geq 50\%$ positivity of tumor cells at $\geq 2+$ intensity. ^cIB6-low expressors was defined as $< 50\%$ positivity of tumor cells at $\geq 2+$ intensity. ^dComparisons were not made for characteristics with $> 20\%$ missing data. ^eP values were calculated using Fisher exact test. ^fIncludes only evaluable patients with a known IB6 IHC status. The other 19 patients had failure at the hematoxylin & eosin evaluation by PathAI due to insufficient tumor or fine needle aspiration cell blocks. ^gWithin 60 days before or after metastatic diagnosis. ^hIncludes patients with unknown metastatic diagnosis date.

Figure 3. Biopsy characteristics by IB6 IHC status



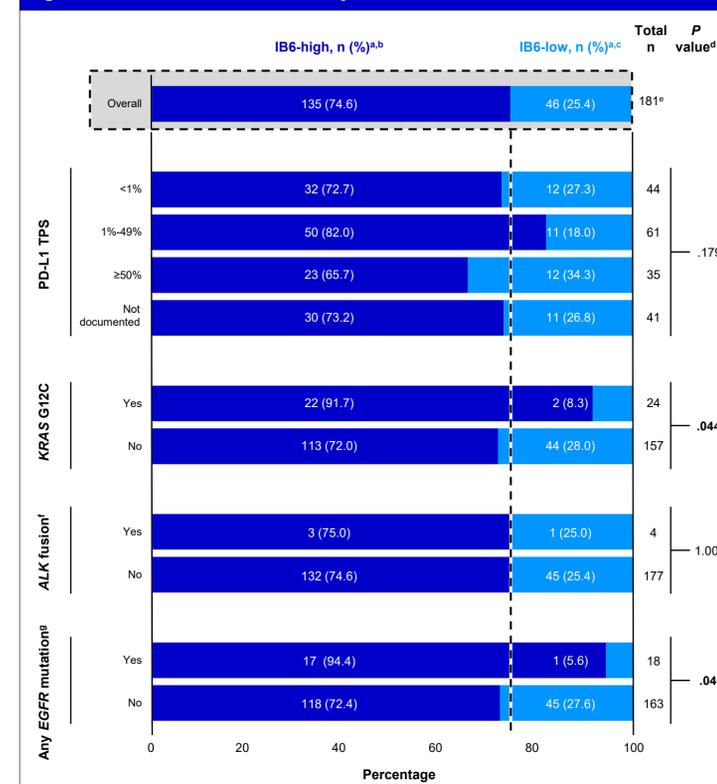
^aPercentage was calculated with "total n" as denominator for each row. ^bIB6-high expression was defined as $\geq 50\%$ positivity of tumor cells at $\geq 2+$ intensity. ^cIB6-low expressors was defined as $< 50\%$ positivity of tumor cells at $\geq 2+$ intensity. ^dComparisons were not made for characteristics with $> 20\%$ missing data. ^eP values were calculated using Fisher exact test. ^fIncludes only evaluable patients with a known IB6 IHC status. The other 19 patients had failure at the hematoxylin & eosin evaluation by PathAI due to insufficient tumor or fine needle aspiration cell blocks. ^gIncludes patients with unknown metastatic diagnosis date (n=4).

Figure 4. Prevalence of IB6 IHC status in overall population and by histology^a



^aPrimary tumor histology, any time before or ≤ 30 days after metastatic diagnosis. The denominator includes only evaluable patients with a known IB6 IHC status. ^bIB6-high expression was defined as $\geq 50\%$ positivity of tumor cells at $\geq 2+$ intensity. ^cIB6-low expressors was defined as $< 50\%$ positivity of tumor cells at $\geq 2+$ intensity. ^dCalculated using Fisher exact tests for categorical variables. ^eIncludes only evaluable patients with a known IB6 IHC status. The other 19 patients had failure at the hematoxylin & eosin evaluation by PathAI due to insufficient tumor or fine needle aspiration cell blocks. Additionally, patients with not otherwise specified (n=9) or unknown histology (n=15) are not included here.

Figure 5. Molecular characteristics by IB6 IHC status



PD-L1, programmed cell death ligand 1; TPS, tumor proportion score. ^aPercentage was calculated with "total n" as denominator for each row. ^bIB6-high expression was defined as $\geq 50\%$ positivity of tumor cells at $\geq 2+$ intensity. ^cIB6-low expressors was defined as $< 50\%$ positivity of tumor cells at $\geq 2+$ intensity. ^dComparisons were not made for characteristics with $> 20\%$ missing data. ^eP values were calculated using Fisher exact test. ^fIncludes only evaluable patients with a known IB6 IHC status. The other 19 patients had failure at the hematoxylin & eosin evaluation by PathAI due to insufficient tumor or fine needle aspiration cell blocks. ^gALK fusions were determined using DNA, a combination of DNA and RNA if DNA evidence was insufficient, or RNA only cells. ^hIncludes the following EGFR mutations: classic exon 19 deletion, L858R, exon 20 insertion, exon 19 in-frame deletion, exon 19 deletion-insertion, exon 19 in-frame insertion, exon 20 substitution, and exon 4 mutation.

Limitations

- This was a real-world retrospective dataset, which may be subject to unmeasured bias and not controlled for in the analyses
- Patient records were obtained from primarily two medical centers and may not be generalizable to the NSCLC population
- Tumor sample acquisition was heterogenous with respect to a NSCLC patient's journey and may not reflect natural changes to IB6 expression as the disease evolves