A Follow-Up On Prospective Clinical Validation of the Envisia® Genomic Classifier

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RATIONALE

- The effectiveness of antifibrotics at delaying lung function decline in patients with IPF and progressive pulmonary fibrosis highlights the value of early and accurate diagnosis.
- Usual interstitial pneumonia (UIP) is a critical factor in determining diagnosis and prognosis of pulmonary fibrosis.
- UIP is often missed by high resolution CT scan (HRCT) alone.
- The Envisia Genomic Classifier (EGC) is a molecular test for UIP in transbronchial biopsies (TBBx) which was prospectively validated and showed utility in the multidisciplinary review and diagnosis of IPF patients.

OBJECTIVE OF THIS STUDY

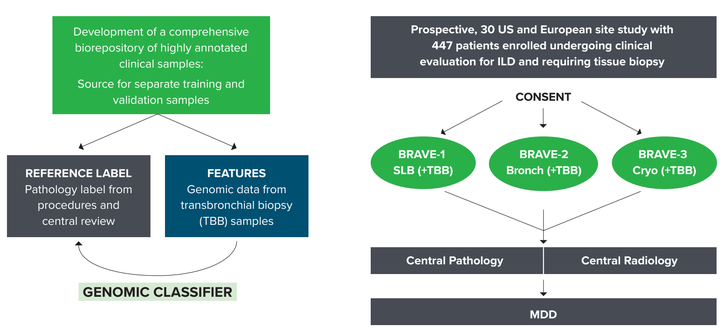
We conducted a prospective multi-center study in a second independent cohort of patients from the BRAVE study to further validate the Envisia Genomic Classifier performance.

METHODS

- Patients were allocated for this independent clinical validation from the BRAVE (Bronchial Sample Collection for a Novel Genomic Test) cohort.
- Histopathology diagnoses were used to derive UIP or non-UIP reference standard truth labels for each subject.
- Whole-transcriptome RNA-sequencing was performed on TBBx samples in the Veracyte CLIA certified reference laboratory.
- The test's previously validated and locked machine learning algorithm was used to classify each subject as UIP or non-UIP.
- After exclusions for non-diagnostic histopathology and process errors, 96 subjects remained for blinded testing against reference truth.

FIGURE 1.

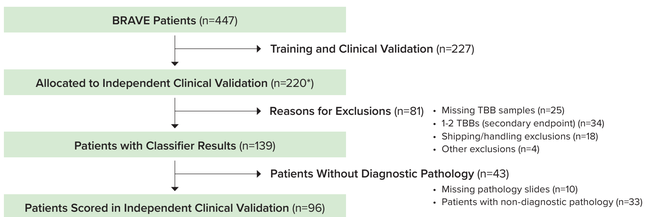
BRAVE: The Clinical Studies Supporting Algorithm Development Validation, and Clinical Utility of the Envisia Genomic Classifier



METHODS (CONT'D.)

FIGURE 2.

Derivation of Envisia Genomic Classifier Validation Cohort



* These 220 patients are independent of those used in the classifier development and the prior validation.

RESULTS

TABLE 1.

Clinical Demographics of the Envisia Genomic Classifier Validation Cohort

	Clinical Validation (N = 96)
Sex	
Women	41 (43%)
Men	55 (57%)
Age (years), mean (SD)	62.8 (12.1)
Smoker	
Yes	48 (50%)
No	48 (50%)
Study Site Type	
US academic	41 (43%)
US community	48 (50%)
European academic	7 (7%)
Biopsy Type	
Surgical	61 (64%)
TBBx	1 (1%)
Cryobiopsy	34 (35%)
UIP Frequency in Study	
By pathology	58 (60%)
By radiology	10/65 (15%)

SD, Standard Deviatio n; TBBx, transbronchial biopsy; UIP, Usual Interstitial Pneumonia

TABLE 2.

Clinical Validation Performance of the Envisia Genomic Classifier (n= 96)

		Reference Label	
		Non-UIP	UIP
Envisia Genomic Classifier	Non-UIP Call	35	23
	UIP Call	3	35
Sensitivity		60.3% [46.6 – 73.0]	
Specificity		92.1% [78.6 – 98.3]	
NPV		60.3% [46.6 – 73.0]	
PPV		92.1% [78.6 – 98.3]	
UIP Prevalence		60.4%	

UIP, Usual interstitial pneumonia; NPV, negative predictive value; PPV, positive predictive

RESULTS (CONT'D.)

FIGURE 3A.

Receiver Operating Characteristic (ROC) Curve for the Envisia Genomic Classifier Validation Cohort (n = 96)

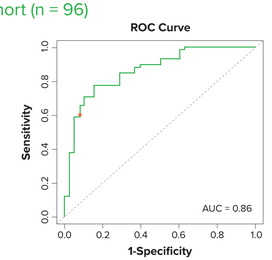
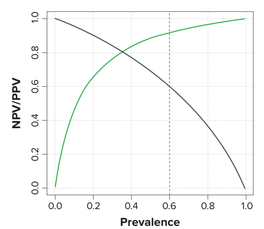


FIGURE 3B.

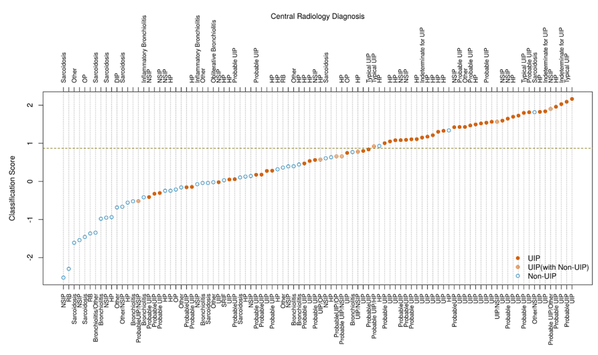
Prevalence Adjusted Positive and Negative Predictive Values for the Envisia Genomic Classifier



The positive (PPV) and negative (NPV) predictive values at the study UIP prevalence of 60% (dashed line).

FIGURE 4.

The Envisia Genomic Classifier Scores in the Validation Cohort



Scores above the boundary are molecular classifier UIP positive.

OP = organizing pneumonia
HP = hypersensitivity pneumonitis
RB = respiratory bronchiolitis
NSIP = non-specific interstitial pneumonia
DIP = desquamative interstitial pneumonia

CONCLUSIONS

- In this prospective multi-center independent clinical validation study, a molecular UIP pattern on TBBx from the Envisia Genomic Classifier shows high accuracy (PPV- 92%) for the detection of biopsy-proven UIP.
- These results suggest that recognition of a UIP pattern by the Envisia Genomic Classifier on TBBx specimens combined with HRCT and clinical factors in a multidisciplinary discussion may assist clinicians in making an ILD (especially IPF) diagnosis without the need for any additional biopsies (eg. SLB).

References

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Disclosures

1. Veracyte, Inc is the sponsor of this study. **2.** Dr Mary Beth Scholand is a clinical advisor for Boehringer-Ingelheim and Genentech: Speaker's bureau. **3.** Dr Ganesh Raghu is a consultant for Veracyte, Inc.