A BLOOD-BASED AUTOANTIBODY TEST TO HELP IDENTIFY LIKELY MALIGNANT INDETERMINATE PULMONARY NODULES: AN OPPORTUNITY FOR EARLY DIAGNOSIS OF LUNG CANCER

Trevor Pitcher[1], Laura J Peek[1], Rachel Hartfield[1], Robbie Lunt[1], Steven C Springmeyer[1] and James R Jett[1,2]

[1]Biodesix, Inc. Boulder, CO, [2]National Jewish, Denver, CO

Introduction

- Current guideline-recommended cancer risk prediction for indeterminate pulmonary nodules (IPN) is imprecise, leading to overtreatment of benign nodules and delayed diagnosis of malignancies [1]. Clinical follow-up is less clear for moderate risk nodules (pCa 5-65%), which comprise 75% of IPNs.
- A blood test (the Nodify CDT® test [CDT]) evaluates the levels of autoantibodies (AAbs) against a panel of 7 lung cancer associated proteins to identify "likely malignant" IPNs may expedite diagnosis.
- This retrospective analysis of the PANOPTIC clinical trial (NCT01752114) further reports on the AAbs profiles in patients with incidentally discovered IPNs.

Methods

The Nodify CDT Test Overview:

- CDT measures blood levels of a panel of 7 AAbs to tumor associated antigens that have been shown to be elevated for all types of lung cancer from the earliest stage of the disease [2].
- The AAbs measured in the test panel target the following tumor antigens: p53, NY-ESO-1, CAGE, GBU4-5, SOX2, HuD and MAGE A4.
- Samples were classified as positive if the concentration of at least one autoantibody was above predefined cutoffs (i.e. HL or ML) [2,3]:
  - High Level (HL)
  - Moderate Level (ML)
  - No Significant Level of AAbs Detected (NSLAD)

Clinical Sample Set:

- Samples from the PANOPTIC study meeting the following criteria were evaluated by the CDT test (N=263). Testing criteria were defined as:
  - Lung nodule diameter 8-30 mm
  - ≥40 years of age
  - No previous history of cancer

Results

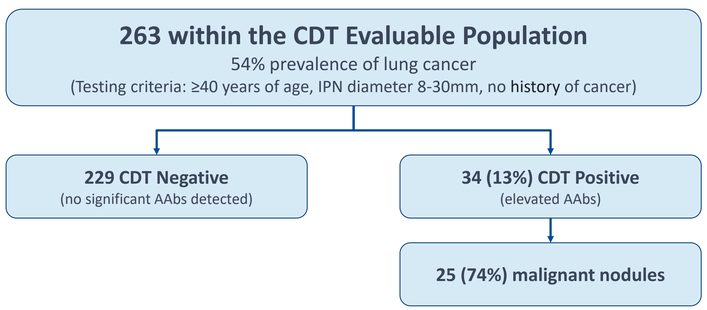

Figure 1: Sample Flow Diagram. In the overall PANOPTIC patient cohort (N=317), 263 patient samples met the clinical use criteria. In this population, there was a cancer prevalence of 54%. Analysis with CDT identified 34 patients with elevated levels of tumor associated autoantibodies, with 25 (74%) diagnosed with a malignancy within the 2-year follow-up of the study.

Results Continued

Table 1: Patient Clinical Characteristics

Characteristic	All Patients	Benign	Cancer	CDT Positive Patients	*P*-value
No. Patients	263	121	142	34	
Age (Years)	65.89 ± 9.76	65.12 ± 10.66	66.55 ± 8.91	66.67 ± 9.53	0.5315
Sex					0.6832
Female	128 (49%)	72 (51%)	56 (46%)	15 (44%)	
Male	135 (51%)	70 (49%)	65 (54%)	19 (56%)	
Smoking History					0.0021
Current/Former	219 (83%)	91 (75%)	128 (90%)	31 (91%)	
Never Smoker	44 (17%)	30 (25%)	14 (10%)	3 (9%)	
Lung Nodule					
CT Nodule Diameter (mm)	17.1 ± 6.2	14.9 ± 5.8	19.1 ± 5.8	19.3 ± 6.3	<0.0001
Nodule Location					0.0004
Mid/Lower Lung	108 (41%)	64 (53%)	44 (31%)	12 (35%)	
Upper Lung	155 (59%)	57 (47%)	98 (69%)	22 (65%)	
Spiculation					0.0002
Not Spiculated	157 (60%)	88 (73%)	69 (49%)	24 (71%)	
Spiculated	106 (40%)	33 (27%)	73 (51%)	10 (29%)	

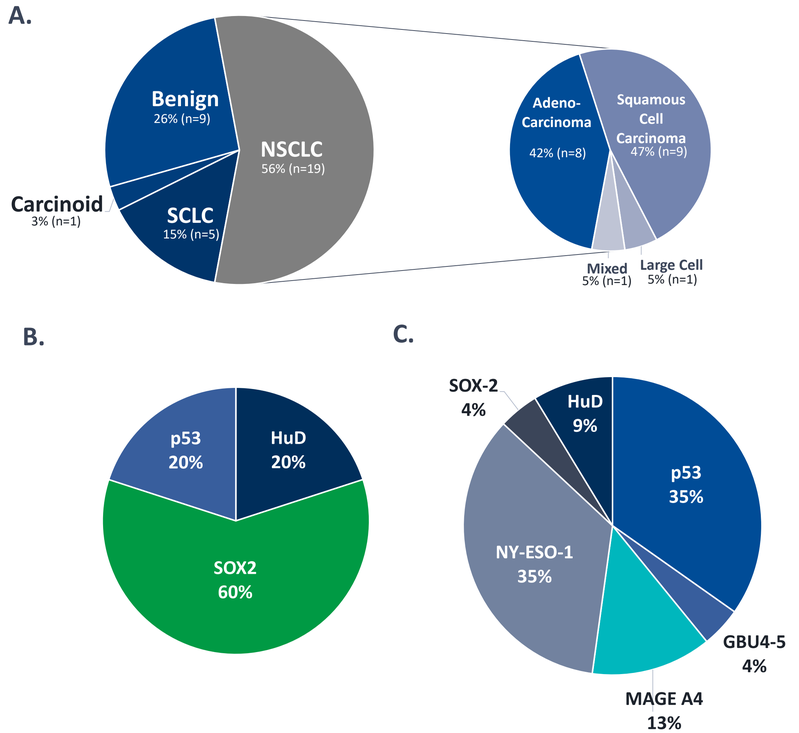

Figure 2: CDT Autoantibody Positivity:
(A) Diagnoses of patients identified as CDT positive (n=34), autoantibody profiles in patients diagnosed with (B) small cell lung cancer (SCLC; n=5) and (C) non-small cell lung cancer (NSCLC; n=19), respectively.

Results Continued

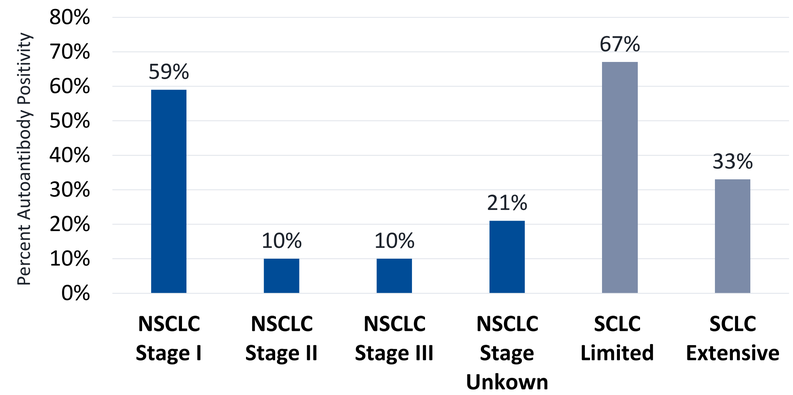

Figure 3: CDT Autoantibody Positivity by Lung Cancer Stage:
CDT was able to identify NSCLC across stages: I-III NSCLC, with stage I the most prevalent (58%, 11/19), stage II (10%, 2/19), stage III (10% 2/19) and (21%, 4/19) with staging unknown. Due to PANOPTIC inclusion/exclusion criteria, no stage IV patients were enrolled in this study. Among SCLC diagnoses, limited (67% 3/5) and extensive (33% 2/5) stage disease were both detected by CDT.

Table 2: Individual Autoantibody Performance

Tumor Associated Autoantibody	Specificity
p53	**96%** (95% CI 91-99%)
NY-ESO-1	**99%** (95% CI 95-100%)
MAGE A4	**100%** (95% CI 97-100%)
GBU4-5	**98%** (95% CI 94-100%)
CAGE	ND*
HuD	**98%** (95% CI 93-99%)
SOX-2	**99%** (95% CI 95-100%)
Total Ab Panel	**93%** (95% CI 86-97%)

*ND: Not Detected

Conclusions & Clinical Implications

Conclusions: A majority of the malignant IPNs with a CDT positive result were diagnosed with Stage I NSCLC or Limited Stage SCLC, indicating that the AAbs in the test are elevated early in lung cancer disease progression. This elevated AAb profile is apparent across cancer type and histology.

Clinical Implications: Implementing blood-based testing in nodule patient evaluation may improve early diagnosis of lung cancer by identifying likely malignant nodules at an early stage when they would be otherwise considered indeterminate and may be subject to a diagnostic odyssey.

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Trevor.Pitcher@biodesix.com