An Audit of the Clinical Performance of EarlyCDT®-Lung

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PURPOSE

EarlyCDT®-Lung, a clinical blood test that detects autoantibodies to lung cancer associated antigens, has shown high specificity in case-control validation studies[1] and currently serves as an aid to early detection. We investigated the performance of this test in routine use by auditing clinical outcomes of the initial series of patients tested by EarlyCDT-Lung who also signed HIPAA authorization permitting disclosure of their health information to Oncimmune®.

METHODS

1613 patients in the U.S. at high risk for lung cancer (mean 5-year risk = 3.08%, as calculated using the Spitz model[2]) were included. The EarlyCDT-Lung panel was modified in November 2010 from 6 antigen (Ag) to 7Ag to improve specificity of the test[1]; this report includes data on both the 6Ag (n=752) and 7Ag (n=861) panels. Tests were ordered by 810 physicians in 48 states. Information as to whether a patient was diagnosed with cancer was requested at specific intervals based upon the EarlyCDT-Lung result:

- Positives: Physicians were contacted immediately and contact maintained to determine what course of action was being taken; follow-up was then structured around the physician-described follow-up plan. Follow-up was requested for all patients at 6 months following EarlyCDT-Lung.
- Negatives: Follow-up was requested at 6 months for all negatives. Subsequent follow-up was requested annually thereafter.

Six month follow-up for the positives/negatives was 100%/97% for the 6Ag panel and 98%/91% for the 7Ag panel. This report will focus on the 6 month results.

Pathology reports, when available, were reviewed for diagnostic classification. Staging was assessed on histology where surgery was performed, otherwise on imaging. A lung cancer was classified as early-stage if it was a Stage I or II NSCLC or limited disease SCLC. The clinical/pathological diagnosis was compared to the EarlyCDT-Lung result, and the performance of EarlyCDT-Lung was evaluated.

RESULTS

Clinical Performance (Table 1). Sixty-one patients (3.8%) were identified with lung cancer within 6 months after EarlyCDT-Lung; 25 of whom tested positive by EarlyCDT-Lung giving a sensitivity of 41%: sensitivity for the 6Ag (46%) and the 7Ag panels (37%) were not statistically different (p=0.5). The positive predictive value (PPV) for the 6Ag panel was 8.6% (1 in 11.6) and 16% (1 in 6.4) for the 7Ag panel. For patients testing negative on the 7Ag panel, 22/764 (2.9%) were found to have a lung cancer (i.e., 1 in 34.7). Thus for the current 7Ag panel, a positive result represents a 5.4-fold increase in risk of lung cancer.

Table 1. Clinical performance of the 6Ag and 7Ag panels calculated from the clinical audit dataset.

	Specificity (%)[a]	Sensitivity (%)[b]	PPV
6Ag panel	599/726 (83%)	12/26 (46%)	1 in 11.6 (8.6%)
7Ag panel	742/812 (91%)	13/35 (37%)	1 in 6.4 (16%)

[a]The 7Ag panel shows a highly statistically significant improvement in specificity of EarlyCDT-Lung ($p<0.0001$).
[b]The sensitivities of the 6Ag and 7Ag panels were not statistically different ($p=0.5$).

Detection of all types of lung cancer. Of the 61 lung cancer cases diagnosed in this cohort, 49 (80%) were non-small cell lung cancer (NSCLC), 4 (6.6%) were small cell lung cancer (SCLC), 1 was mixed NSCLC-SCLC and type was unknown for 7 cases (Table 2).

Table 2. Breakdown of cancer type/sub-type for the 61 lung cancer cases.

Lung Cancer Type/Sub-type	Number
Adenocarcinoma	30 (49.2%)
Squamous	14 (22.9%)
Small Cell Lung Cancer (SCLC)	4 (6.6%)
Mixed SCLC+NSCLC	1 (1.6%)
NSCLC, Unknown Sub-type*	5 (8.2%)
Unknown Type	7 (11.5%)

* 4 clinical diagnosis with no tissue diagnosis; 1 tissue diagnosis of NSCLC not otherwise specified.

Detection of all stages of lung cancer. Of the 49 NSCLCs, 28 were early-stage (I or II), 17 were late-stage (III or IV) and 4 were stage unknown. Importantly, 56% (9/16) of NSCLCs detected by EarlyCDT-Lung (where stage was known) were early-stage. Stage was unknown for an additional 2 NSCLCs detected by EarlyCDT-Lung.

CONCLUSIONS

- The performance of EarlyCDT-Lung in this clinical audit mirrors that of the extensive case-control validation studies previously reported, showing significant improvements in specificity of the 7Ag panel while maintaining sensitivity.
- A positive test for EarlyCDT-Lung carries a 5.4-fold increase in risk of lung cancer in this population.
- The high specificity of EarlyCDT-Lung with its high PPV confirmed in this audit makes it a potentially complementary tool to CT for lung cancer detection.

COMMENT

- These figures take no account of occult lung cancers, which may present over the next few years as cancers have been shown to stimulate a cancer antigen-specific autoimmune response up to 5 years before detection by current imaging methods.[3] Any “yet to present” cancers will likely increase sensitivity and specificity for this cohort.

REFERENCES

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