Frequently Asked Questions for Risk Assessment of Indeterminate Pulmonary Nodules

Clinical

*Early*CDT®–Lung

1. What is *Early*CDT®-Lung?

   *Early*CDT-Lung is a blood test that measures a panel of 7 autoantibodies for the early detection of lung cancer. The *Early*CDT® technology was invented at the University of Nottingham, UK, and Oncimmune® was subsequently established to further develop and market the clinical testing. It is not a genetic test, but rather provides information as to risk of a cancer being present.

2. What do my *Early*CDT-Lung results mean?

   For Intermediate risk nodules (10-65% risk), a High Level result shifts the nodule risk to Intervention risk level (>65%). A Moderate Level result will add more than 25% risk and shift some nodules from Intermediate risk to Intervention risk level.

3. What does a "No Significant Level of Autoantibodies Detected" result mean? Does it mean that the patient does not have lung cancer?

   This means all autoantibodies in the *Early*CDT-Lung panel are below the low cut-off value, and there is a lower likelihood of lung cancer than a Moderate or High Level result. The overall risk for lung cancer does not change. This is not a "rule-out" test and should not alter the treatment or follow-up that the physician would have followed in the absence of a test result.

4. Is there a correlation between nodule size and results?

   No, autoantibody production is not dependent on nodule size. The immune system responds aggressively when it encounters a tumor antigen, so it only takes a small amount of antigen to stimulate production of an abundance of autoantibodies. This is a key advantage of measuring autoantibodies for early cancer detection; autoantibodies may be elevated very early in the development of a cancer.

5. How does this work with PET?

   *Early*CDT-Lung is not intended to replace PET. The blood test is appropriate if there are no plans to utilize PET or if the PET scan is negative. A Moderate or High Level EarlyCDT-Lung result increases the risk of a nodule being malignant even after a positive PET scan. For example, there may be circumstances when it is deemed helpful if the PET result is inconclusive: a nodule with 20% risk increases to 60% with a positive PET, and with a High Level *Early*CDT-Lung result the risk increases further to 90%.

6. How many positives (Moderate or High Level results) can I expect?

   For intermediate risk nodules (10-65%), typically a Pulmonologist will see about 1 positive for every 7-10 tests ordered for nodule patients. The exact number of positives depends on the incidence of lung cancer in the overall population of nodules.

7. Examples of difficult clinical scenarios where *Early*CDT-Lung may help:

   - Patients with a nodule and chronic emphysema at higher biopsy risk.
   - Patients who refuse biopsy; to assist in identifying those at highest risk to help further inform the patient.

Technical

8. Does *Early*CDT-Lung detect all types of lung cancer at all stages?

   *Early*CDT-Lung detects all stages and types of lung cancer, including small cell and all sub-types of non-small cell. A key advantage of measuring autoantibodies is that they are can be detected at all stages of disease.

9. Which autoantibodies are measured by the test?

   The *Early*CDT-Lung panel includes: CAGE, GBU4-5, HuD, MAGE A4, NY-ESO-1, p53 and SOX-2.

10. Is there cross reactivity with other cancers among these autoantibodies? I recognize some of these biomarkers for other cancers. What are the chances that it's not lung cancer?

    The panel of autoantibodies was developed and validated for lung cancer; however, there is the potential for some of the autoantibodies to be elevated due to a different type of cancer. If a patient's result is Moderate or High Level and the patient has a pulmonary nodule, the risk of it being a lung cancer is much higher than the likelihood of the patient having another type of cancer. However, it is always good practice to ensure the patient is up-to-date on all other age- and gender-specific screenings for other cancers (for example, breast and colon), as recommended by the American Cancer Society (www.cancer.org).

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Technical (continued)

11. Why is *Early***CDT-Lung** not recommended for those with previous history of cancer, and why is basal cell carcinoma an exception?

    Test performance may vary for patients with a previous history of cancer or cancer treatment. The panel of autoantibodies measured has been optimized to detect lung cancer, not other types of cancer. And the control population used to validate the test did not include any patients with history of cancer. The exception to this recommendation is patients with history of basal cell carcinoma. A study was conducted, and the data suggested that basal cell carcinoma does not impact the *Early***CDT-Lung** result.

12. Is there mortality data for *Early***CDT-Lung**?

    The key to reducing mortality is early detection. *Early***CDT-Lung** has not been utilized in a clinical trial to show mortality benefit; however, the NLST trial demonstrated that annual screening of high-risk patients with low-dose CT resulted in a 20% reduction in mortality, which was attributable to early detection of the pulmonary nodule. Data have repeatedly demonstrated that *Early***CDT-Lung** can detect lung cancers early.

13. What is the specificity and positive predictive value (PPV) of *Early***CDT-Lung**?

    A High Level result has a specificity of 98% and PPV of more than 80%, where 4 out of 5 results are a true cancer. Considering both High and Moderate Level results, specificity is 93% and PPV is nearly 60%, where 3 out of 5 results are a true cancer.

14. What peer review publications support the test?

    Extensive data have been collected and published for *Early***CDT-Lung**, including more than 25 peer-reviewed publications and more than 50 peer-reviewed oral and poster presentations given at key conferences. Pierre Massion of Vanderbilt published a paper in *Journal of Thoracic Oncology* in 2017 showing the performance of EarlyCDT-Lung in patients with pulmonary nodules. A second key publication in *Journal of Cancer Therapy* in 2017 shows how *Early***CDT-Lung** enables risk re-classification of intermediate risk nodules to facilitate more appropriate intervention. A full list of key publications is available, and all are available at oncimmune.com/news-press/papers-publications/.

Ordering, Sample Collection & Transport

15. How do I order *Early***CDT-Lung**?

    *Early***CDT-Lung** is a simple blood test and is ordered as you would any blood work. The patient may be sent to the lab along with an *Early***CDT-Lung** kit/box. Results will be faxed directly to the physician, or other reporting options are available upon request, including online portal or File Transfer Protocol (FTP) interface; contact Oncimmune if interested in another reporting option.

16. How quickly will I get results?

    Typically results are reported out in 2-5 business days. High and Moderate Level results may take up to 4-7 days because of Oncimmune's policy to confirm all positive results.

Regulatory & Reimbursement

17. Is *Early***CDT-Lung** reimbursed?

    The test may be billed to Medicare, Medicaid and most Commercial Insurance. An ICD-10 for diagnosis of a pulmonary nodule can be used.

18. Is *Early***CDT-Lung** in guidelines?

    *Early***CDT-Lung** is not yet in guidelines however it provides a way to assess the risk of malignancy of a lung nodule, as recommended by ACCP guidelines. High and Moderate Level results add to the risk determined by risk calculators.

19. Is *Early***CDT-Lung** approved by the FDA?

    The test has been performed as a laboratory-developed test (LDT) in a CLIA-certified laboratory in De Soto, Kansas for over 8 years. FDA does not require approval of LDTs.

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