*Early*CDT®–Lung

Test Name: *Early***CDT**®-**Lung**

Test Code: ECDTL09

CPT Code: 83520 x 7 units

Clinical Utility: *Early***CDT-Lung** is a blood test that aids in the risk assessment and early detection of lung cancer in high-risk patients and is complementary to annual CT screening[1-8].

- *Early***CDT-Lung** may encourage compliance for those who are eligible[9] and who have yet to commit to an annual CT screening program.
- *Early***CDT-Lung** may be used for at-risk patients who fall outside of the criteria for entry into a CT screening program.
- For patients with an indeterminate pulmonary nodule, *Early***CDT-Lung** can be used to further assess the risk of lung cancer being present[7].

The clinical sensitivity and specificity of *Early***CDT-Lung** is 41% and 93%[1,3], respectively, with specificity increasing to 98% for a High Level result[2]. The high specificity makes the test a rule in test where a Moderate or High Level result indicates that the patient is at increased risk of having lung cancer, while a Low Level result should not be used to rule out the presence of lung cancer.

This test is not recommended for patients with a history of cancer (exception: basal cell carcinoma).*

Background for Test Application: Cancer antigens are different to normal antigens so the body's immune system reacts to these antigens by producing autoantibodies. These autoantibodies, which can rise in the earliest stages of lung cancer and have been shown to be present in all types of lung cancer and at all stages, are produced in sufficient quantities to be measured in a patient's blood using a simple blood test, *Early***CDT-Lung**[1-5]. The *Early***CDT-Lung** test measures a panel of seven autoantibodies to detect the presence of lung cancer[1-3]. It is recommended that patients with elevated levels of autoantibodies be triaged for CT follow-up. This is not a genetic test for predisposition; a positive test may indicate the presence of the malignant disease.

Specimen Requirements:
- 0.5 mL serum is required.
- Blood should be collected, allowed to clot completely and centrifuged.
- Specimen can be shipped overnight at ambient temperature (U.S.) or frozen ice packs (outside U.S.).

Method: Enzyme-linked immunosorbent assay (ELISA) with 7 lung-cancer associated proteins as the bound antigen[3-7]. Relative autoantibody levels are compared to fixed cutoffs and reported accordingly[2]. The test was developed and its performance characteristics were determined by Oncimmune®. It has not been cleared by the FDA. Oncimmune is a high-complexity laboratory in compliance with all CLIA regulations.

Criteria for Lung Cancer Risk:
- ≥50 years old with ≥20 pack-years* smoking history
- 40-49 years old with ≥20 pack-years smoking history, plus at least 1 additional risk factor(s) (see below)
- Indeterminate pulmonary nodule(s)

Additional risk factors:
- Environmental exposures (e.g., radon, asbestos, radioactive substances)
- Emphysema or chronic obstructive pulmonary disease (COPD)
- Family history of lung cancer in a first degree relative

*Pack-years are calculated by multiplying the number of packs of cigarettes smoked per day by the number of years smoked.

References:
1. Jett JR, et al. Audit of the autoantibody test, *Early***CDT-Lung**, in 1600 patients: An evaluation of its performance in routine clinical practice. *Lung Cancer* 2014; 83:51-55.
2. Healey GF, et al. Signal stratification of autoantibody levels in serum samples and its application to the early detection of lung cancer. *J Thorac Dis* 2013; 5(5):618-625.
3. Chapman CJ, et al. *Early***CDT-Lung** test: improved clinical utility through additional autoantibody assays. *Tumor Biology* 2012; 33(5):1319-1326.
4. Lam S, et al. *Early***CDT-Lung**: an immuno-biomarker test as an aid to early detection of lung cancer. *Cancer Prev Res* 2011; 4(7):1126-1134.
5. Boyle P, et al. Clinical Validation of an Autoantibody test for lung cancer. *Ann Oncol* 2011; 22(2):383-389.
6. Murray A, et al. Technical validation of an autoantibody test for lung cancer. *Ann Oncol* 2010; 21(8):1687-1693.
7. Massion P, et al. Autoantibodies to a panel of lung cancer-associated antigens can provide significant discrimination between malignant and non-malignant lung nodules. *J Thoracic Oncology* 2013; 8(S2):S979.
8. Robertson JFR, et al. Tumour Markers. *U.S. Patent and Trademark Office* 2008; *7,402,403*.
9. US Preventive Services Task Force (USPSTF) Guidelines
* See *Early***CDT-Lung** FAQs

Understanding the *Early*CDT®-Lung Result

*Early*CDT®-Lung test results are reported as Low, Moderate or High Level depending on the number of autoantibodies in the blood compared to low and high cutoff values for each autoantibody. Answers to some frequently asked questions are given below. The patient should discuss the results with his/her physician for a clinical interpretation and recommendations for next steps.

What do I do if the result is Low Level?
A Low Level result suggests a lower likelihood of lung cancer than the Moderate Level or High Level results. However, it does not mean that the individual does not have lung cancer or could not develop lung cancer in the future. A physician may recommend that the patient continue a schedule of testing and examination based on the patient's personal history and/or clinical symptoms.

What do I do if the result is Moderate Level?
A Moderate Level result means that one or more autoantibodies were detected at an elevated level, which suggests that the likelihood of lung cancer is greater than predicted by the patient's gender, age, smoking history and other clinical factors. This result does not definitively mean that lung cancer is present. A physician may recommend additional testing, including a chest CT scan. If lung cancer is not found, a physician may recommend continued additional testing in the future. Other age- and gender-specific screenings for other cancers (for example, breast and colon), as recommended by the American Cancer Society (www.cancer.org), should also be considered.

What do I do if the result is High Level?
A High Level result means that one or more autoantibodies were detected at a very elevated level, which suggests that the likelihood of lung cancer is greater than predicted by the patient's gender, age, smoking history and other clinical factors. This result does not definitively mean that lung cancer is present. A physician may recommend additional testing, including a chest CT scan. If lung cancer is not found, a physician may recommend continued additional testing in the future. Other age- and gender-specific screenings for other cancers (for example, breast and colon), as recommended by the American Cancer Society (www.cancer.org), should also be considered.

What do these autoantibody levels have to do with lung cancer?
In all types of lung cancer, some individuals have been found to have elevated levels of one or more of these autoantibodies[a-b]. Autoantibodies have been shown to be present in the blood up to four years prior to a tumor becoming visible on a CT scan[c-f]. Early detection of lung cancer has been shown to increase the potential for an improved outcome[g].

References:
a) Chapman CJ, et al. *Early*CDT®-Lung test: improved clinical utility through additional autoantibody assays. *Tumor Biology* 2012; 33(5):1319-1326.
b) Lam S, et al. EarlyCDT-Lung: an immuno-biomarker test as an aid to early detection of lung cancer. *Cancer Prev Res* 2011; 4(7):1126-1134.
c) Chapman C, et al. The presence of autoantibodies to tumor-associated antigens can predate clinical diagnosis of small cell lung cancer. *Chest* 2010; 138:s775A.
d) Trivers GE, et al. Anti-p53 antibodies in sera from patients with chronic obstructive pulmonary disease can predate a diagnosis of cancer. *Clinical Cancer Res* 1996; 2:1767-1775.
e) Li Y, et al. p53 autoantibodies predict subsequent development of cancer. *Int J Cancer* 2005; 114:157-160.
f) Zhong L, et al. Profiling tumor-associated antibodies for early detection of non-small cell lung cancer. *JThor Oncol* 2006; 1:513-519.
g) The National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011; 365:395–409.

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