Oncimmune

Frequently Asked Questions for Clinicians

For screening of lung cancer in high-risk patients

What is ***Early*CDT®—Lung**?

***Early*CDT—Lung** is a **simple**, **affordable blood test** for the early detection of lung cancer. It has two uses:

1. to aid in the risk assessment and early detection of lung cancer in high-risk patients where CT screening is not available, outside the US;
2. to assess indeterminate pulmonary nodules (IPNs) for the risk of malignancy.

These FAQs relate to use (1). They are intended for reading by clinicians who practice outside the US and in countries where annual CT screening in accordance with US guidelines is not available.

What are the key benefits of ***Early*CDT—Lung**?

***Early*CDT—Lung** can detect autoantibodies to lung cancer four years or more before clinical diagnosis via standard care pathways.[1,2] This benefit may translate into improved patient outcomes and a better chance of improving survival.

How does it work?

***Early*CDT—Lung** measures blood levels of a panel of seven autoantibodies* to tumour-associated antigens that are linked to lung cancer. These seven autoantibodies have been shown to be elevated for all types of lung cancer, and from the earliest stage of the disease.[3,4]

Autoantibody levels can be measured easily and accurately, thanks to the signal magnification created by the body's immune response to cancer. The test runs on a simple enzyme-linked immunosorbent assay (ELISA) platform.

* The seven autoantibodies are CAGE, HuD, NY-ESO-1, SOX-2, GBU4-5, MAGE A4, and p53.

How accurate is ***Early*CDT—Lung** and what are the performance statistics?

***Early*CDT—Lung** is a rule-in test for lung cancer, validated with high specificity to complement other technologies such as CT scanning. Table 1 shows that ***Early*CDT—Lung** performs favourably when compared with other established cancer detection tests.

Table 1. Performance of ***Early*CDT—Lung** compared to other established cancer detection tests.[5]

	Accuracy	Performance (PPV)[a]
***Early*CDT—Lung** (High)[b]	**97%**	**1 in 5**
***Early*CDT—Lung** (Moderate & High)[b]	**92%**	**1 in 10**
CT Screening (Annual)[c]	73%	1 in 25
Mammography[d]	92%	1 in 26
Cologuard®[e]	84%	1 in 27

Assumed cancer rates[f]: ***Early*CDT—Lung** & CT Screening = 1.2%, Mammography = 0.8%, Cologuard® = 0.6%

● True Positive = cancer ● False Positive = no cancer

Are the performance claims for the ***Early*CDT—Lung** test supported?

The ***Early*CDT—Lung** test has been extensively studied, with data reported in more than 25 peer-reviewed clinical publications and more than 60 peer-reviewed oral and poster presentations at key conferences.

The test has been clinically validated in seven independent cohorts and more than 120,000 patient samples, generating 12 million data points.

The test has also been independently audited since commercial launch in clinical practice on a large sample set of 1,600 patients and the results have been published.[6] The results have consistently demonstrated that the test performs as expected.

What is the NHS (or ECLS) study?

The National Health Service (NHS) Scotland is conducting the world's largest randomised, controlled clinical trial for the early detection of lung cancer using biomarkers. The trial, known as ECLS, is using ***Early*CDT—Lung** to select patients for x-ray and CT surveillance in order to determine if the test generates a diagnostic stage shift compared to normal UK clinical practice, which is to wait until symptoms present.

Interim findings from 12,210 high-risk patients show that the performance of ***Early*CDT—Lung** is as expected. Most importantly, the study is demonstrating a significant diagnostic stage shift: 75% of all lung cancers found (n=16) have been at stage I or II; in normal practice 80% of lung cancers are diagnosed at stage III or IV, a 55% stage shift.[7]

How does ***Early*CDT—Lung** performance compare to annual CT screening?

***Early*CDT—Lung** offers a complementary approach to annual CT screening. As a simple blood test, ***Early*CDT—Lung** can be used when an individual is at increased risk but does not meet the high-risk criteria for annual CT screening, and only 26.7% of lung cancers fall into these critieria.[8] It can also be used when individuals are unwilling or unable to undergo lifelong annual CT screening.

Alternatively, ***Early*CDT—Lung** can be used as a rule-in test to qualify patients for annual CT screening, as is being investigated by the NHS in Scotland. This strategy, using lower risk thresholds for inclusion, is demonstrating a diagnostic stage shift compared to normal UK clinical practice.

In any case, a **Moderate** or **High Level *Early*CDT—Lung** result can be followed by suitable CT scans to confirm the presence of lung cancer earlier, with the patient and clinicians better aware of the risk of lung cancer developing.

How does a patient's estimated 1-year risk of having lung cancer change following an ***Early*CDT—Lung** test?

The following table illustrates the example of a 65-year-old male with a 45 pack-year smoking history:

Table 2. The effect of ***Early*CDT—Lung** test results on the 1-year risk of having lung cancer

Test Result	1-Year Risk	Increase in 1-Year Risk
No Significant Level of Autoantibodies Detected	1.2%	Unchanged at 1.2%
Moderate Level	3.5%	3 ×
High Level	19.3%	16 ×

A personalised report reflecting the estimated risk of your specific patient, as calculated based upon age, gender, smoking history and their ***Early*CDT—Lung** test result, is available online at: *http://oncimmune.com/smoking-calculator*

What if the patient's test result is High Level or Moderate Level?

A **High Level** or **Moderate Level** test result indicates that the patient's risk of having lung cancer is greater than that predicted by their gender, age, smoking history and other risk factors.

This increased risk may warrant a recommendation for additional testing, which may include CT imaging. The recommendation will be consistent with the patient's history and overall risk profile, which could include prior radiological findings.

What if further testing does not detect lung cancer?

If lung cancer is not found, you may recommend continued additional testing in the future. You should also consider other age- and gender-specific screenings for other cancers (for example, breast and colon), such as those recommended by the World Health Organisation (WHO, *http://www.who.int/cancer/prevention/diagnosis-screening/en/*).

What if the patient's test result is No Significant Level of Autoantibodies Detected?

A **No Significant Level of Autoantibodies Detected** test result is defined as all autoantibodies in the ***Early*CDT—Lung** panel being below the low cut-off value. This would indicate a lower likelihood of having lung cancer than a **Moderate** or **High Level** result; however, this would not rule out lung cancer now or in the future because in order to be eligible for the test your patient was already at an elevated risk of lung cancer, as predicted by age, gender, smoking history and other risk factors. The patient's risk has not changed. You, the patient's clinician, will determine continued monitoring and follow-up, consistent with the patient's history and overall risk profile.

For a patient receiving a No Significant Level of Autoantibodies Detected test result, how often do you recommend a repeat ***Early*CDT—Lung** test?

There is no recommended definitive repeat period, as you will have to take into account your patient's ongoing risk. The general advice for repeat testing is between one and two years, to test for new lung cancers that may have developed since the previous test was undertaken.

Who should I test?

You should test high-risk patients – those who are at risk of lung cancer due to a combination of age, gender, smoking history and other risk factors such as environmental exposures (radon, dust, asbestos, radioactive substances), those with a history of emphysema/COPD, or first-degree relative family history.

Patients should not have any personal history of any type of cancer (exception: basal cell carcinoma). ***Early*CDT—Lung** is not recommended for use in patients younger than 40 years of age.

A full list of lung cancer risk factors is available at:
http://oncimmune.com/risk-factors

Why is ***Early*CDT—Lung** not recommended for those with a 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 optimised to detect lung cancer, not other types of cancer, and the control population used to validate the test did not include any patients with a history of cancer. The exception to this recommendation is for patients with a history of basal cell carcinoma (BCC). Data suggest that BCC does not impact the ***Early*CDT—Lung** result.

How is ***Early*CDT—Lung** different from other methods of lung cancer detection?

***Early*CDT—Lung** is a simple, affordable blood test measuring blood levels of a panel of autoantibodies to tumour-associated antigens that are linked to lung cancer. Autoantibodies benefit from signal magnification created by

the body's immune response to cancer, so this approach has the potential to detect lung cancer in its early stages of development, giving the patient more treatment options with subsequent improved prognosis. The ***Early*CDT—Lung** test parameters have been set to be complementary to other lung cancer detection techniques, such as low dose CT scanning.

Is ***Early*CDT—Lung** different from genetic testing? How?

***Early*CDT—Lung** is designed to indicate the presence of lung cancer cells in the body (i.e., lung cancer is present). Genetic propensity testing, by contrast, is conducted to assess the likelihood of developing cancer in the future.
Note: Currently, there is no standardised genetic test for lung cancer.

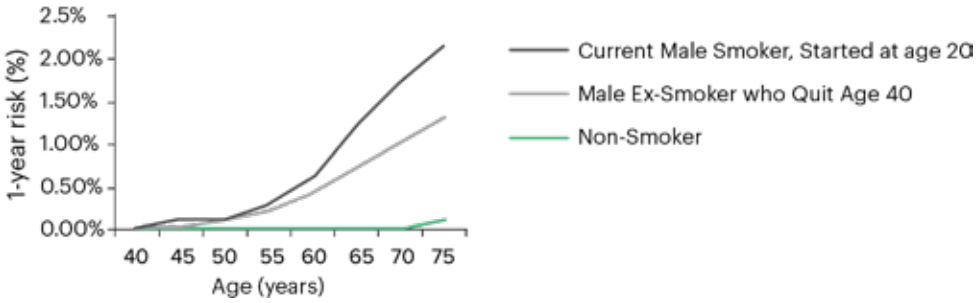
What is a pack-year?

A pack-year is a measurement to quantify the amount a person has smoked over a long period of time, calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked. For example, one pack-year is equal to smoking 20 cigarettes (one pack) per day for one year.

How does smoking cessation affect risk?

As the following graph illustrates, stopping smoking reduces lung cancer risk; however, it is important to note that early cessation is key to reducing risk, as the effects of smoking accrue over time. The graph compares the one-year risk of developing lung cancer in a current smoker, an ex-smoker who quit at the age of 40, and a non-smoker.[9] The graph assumes that at age 40, both the current smoker and the ex-smoker had a 20-pack year smoking history, and that the current smoker continues to smoke at the same level.

Graph 1. Comparison of 1-year risk on male current, ex-smoker and non-smoker



Where can patients take the test?

Current distributors and test providers are listed on the website: *http://oncimmune.com/distributors/*

What is the sample provision process?

Blood should be drawn into a serum separator tube and sent at ambient temperature to your test provider, who will then separate the serum and analyse the sample. In some territories, a simple finger stick sample collection is offered. Contact the test provider for full sample collection and sending instructions.

How are the test results reported?

You can obtain your results directly from the test provider, and you should then discuss them with your patient. The test provider does not send results to the patient.

How long does it take to get results?

Timeframes may vary depending on test provider, but the test provider should report the results to you 5–7 days from the time the sample is received at the laboratory.

How much does ***Early*CDT—Lung** cost and is it covered by medical insurance?

The cost of the ***Early*CDT—Lung** test is low relative to many other tests, particularly as it is not a genetic test. Patients with private insurance need to confirm coverage with their insurance provider. For information on the self-pay price for the test, please contact your local test provider.

Who is Oncimmune?

Oncimmune is a leader in the development, manufacture and commercialisation of personalised immunodiagnostics for the screening, detection and care of cancer. Changing how clinicians, researchers and patients view, diagnose and treat cancer, our technology detects evidence of the body's natural response to cancer, enabling detection 4 years or more before standard clinical diagnosis. Our tests facilitate clinical decision-making and are complementary to diagnostic technologies, making them valuable additions to established and new care pathways. We partner with leading developers and distributors to make our technology available globally. Oncimmune was founded in 2002 and launched its platform technology in 2009, followed by its first commercial tests, ***Early*CDT—Lung** and ***Early*CDT—Liver**. Oncimmune is headquartered in Nottingham, UK with a CLIA lab in Kansas, US and offices in London, UK and Shanghai, China.

For additional information please call +44 (0)115 823 1869 or email: *contact@oncimmune.co.uk*

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