Oncimmune

Frequently Asked Questions for Clinicians
For risk assessment of HCC in liver lesions

What is ***Early*CDT®—Liver**?

***Early*CDT—Liver** is a simple blood test to aid detection and confirmation of hepatocellular carcinoma ("HCC") in association with imaging in high-risk patients with liver lesions of all sizes.

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

- ***Early*CDT—Liver** is complementary to imaging for the diagnosis of HCC.
- The high specificity of the test makes it a clinically useful 'confirmation' test.
- It can detect HCC at all stages, with similar performance, for early– and late–stage disease.[1]
- ***Early*CDT—Liver** has high accuracy, similar to CT, MRI, and ultrasound (85% to 95% depending on risk).
- Both **Moderate** and **High Level** results are clinically actionable, for example by accelerating follow-up or clinical intervention.

How does ***Early*CDT—Liver** work?

Oncimmune's proprietary ***Early*CDT** cancer detection platform measures the presence in the blood of autoantibodies against specific tumor-associated antigens. These autoantibodies have the potential to signal the presence of cancer four years or more before diagnosis, and can be applied to a wide range of solid tumor types.[2,3] ***Early*CDT—Liver** measures a panel of seven autoantibodies, as well as alpha fetoprotein (AFP), to detect the presence of HCC.

Can you explain the possible test results?

***Early*CDT—Liver** test results are reported as **No Significant Level of Biomarkers Detected**, **Moderate Level** and **High Level**, depending on the level of biomarkers in the blood compared to appropriate cut-off values. The interpretation of these results is discussed below.

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

- The ***Early*CDT** cancer detection platform was exhaustively validated before launch with over 120,000 tests completed during development.
- The ***Early*CDT—Liver** test was developed and validated using samples from more than 1,500 patients with benign and malignant liver disease as well as healthy controls.

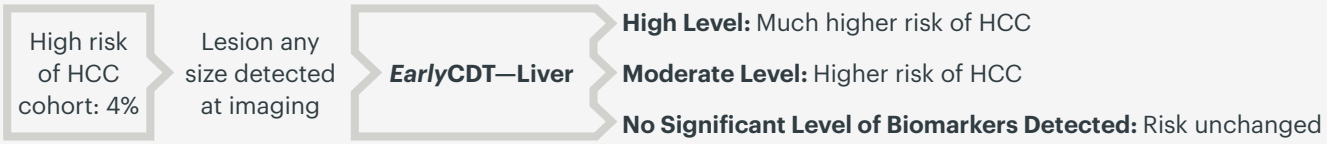
How does ***Early*CDT—Liver** performance complement imaging modalities used in diagnosis of HCC?

- Ultrasound scanning is the first–line screening test for patients at high risk of HCC according to AASLD, EASL and APASL guidelines.[4,5,6]
- Patients identified with a lesion by ultrasound are often followed up by contrast–enhanced CT or MRI to confirm the diagnosis of HCC. However, in a significant proportion of patients, the malignancy status of the patient's lesion cannot be determined from the results of the second imaging test.
- ***Early*CDT—Liver** also offers a complementary approach to contrast–enhanced CT or MRI in patients whose diagnosis of HCC can be neither confirmed nor ruled out using these imaging techniques.
- In addition, an ***Early*CDT—Liver High** result significantly enhances the chance of an ultrasound-identified liver nodule being malignant by three– to six–fold.
- As a simple blood test, ***Early*CDT—Liver** can be used as a rule-in test to give the clinician a high degree of certainty that a lesion is malignant.
- In patients with liver lesions less than 1cm, for which imaging modalities are less reliable, a **Moderate** or **High Level *Early*CDT—Liver** test result provides a higher level of certainty of cancer, which would indicate that accelerated follow-up is needed.
- If the ***Early*CDT—Liver** result is **No Significant Level of Biomarkers Detected**, then the patient's risk of malignancy does not change and they should be followed up according to your previously determined course of action.

How does a patient's estimated risk of liver cancer change following an ***Early*CDT—Liver** test?

***Early*CDT—Liver** positive test results signal a significantly increased risk of HCC. The test can be used in combination with all imaging modalities to add confirmatory value to imaging.

Figure 1. *Early*CDT—Liver test result.



The table below shows the risk after imaging, and the risk change with a positive test result based on the initial cohort risk of 4%[i] as seen in the USA.

			Positive Predictive Value (PPV)[iv] / Risk		
			When imaging is followed by ***Early*CDT—Liver**		
Imaging modality & combination[ii]	HCC prevalence of high-risk cohort[i]	Risk after positive imaging	High Level[iii]	High/Moderate combined[iii]	No Significant Level of Biomarkers Detected
Ultrasound only	4%	23%	80%	62%	No change from pre-test risk
Ultrasound + MRI	4%	81%	98%	96%	
Ultrasound + CT	4%	84%	99%	97%	
MRI only	4%	38%	89%	77%	
CT only	4%	43%	91%	81%	

(i) Initial cohort risk 4% taken from AASLD guidelines[1] (ii) Performance of MRI[1]: sensitivity 87%, specificity 94%; CT[1]: sensitivity 73%, specificity 96%; Ultrasound[3]: sensitivity 78%, specificity 89% (iii) Performance of ***Early*CDT—Liver**. High Level result: sensitivity 41%, specificity 97%; Moderate & High Level combined: sensitivity 54%, specificity 90% (Oncimmune data on file) (iv) PPV is the positive predictive value – the percentage chance of a positive being a "true cancer."

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

- A **High Level** test result is defined as one or more biomarkers in the ***Early*CDT—Liver** panel being above the high cut-off value.
- A **Moderate Level** test result is defined as one or more biomarkers in the ***Early*CDT—Liver** panel being above the low cut-off value, but all are below the high cut-off value.

A **High Level** or **Moderate Level** test result indicates that the patient's risk of having HCC is greater than that predicted pre-test for the lesion and other relevant HCC risk factors. This increased risk may warrant a recommendation for additional investigations. The recommendation should be consistent with the patient's history, overall risk profile, and guidelines.

If HCC is not found, consider continued additional testing in the future. Other age- and gender-specific screenings for other cancers (for example, breast and colon), such as those recommended by the American Cancer Society (*www.cancer.org*), should also be considered.*

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

- A **No Significant Level of Biomarkers Detected** test result is defined as all biomarkers in the ***Early*CDT—Liver** panel being below the low cut-off value.

This test result indicates a lower likelihood of HCC than a Moderate or High Level result; however, it does not rule out the possibility of the patient having HCC now or in the future. The patient's risk of having HCC is unchanged. Patients should continue to be treated in the normal course, as if there had been no ***Early*CDT—Liver** test performed.

You, their clinician, will determine continued monitoring and follow-up, consistent with the patient's history and overall risk profile.

How often do you recommend the patient have a repeat ***Early*CDT—Liver** test given a No Significant Level of Biomarkers Detected test result?

There is no recommended definitive repeat period, as the patient's ongoing risk will vary according to his or her risk factors.

Who should I test?

High–risk patients with a liver lesion of indeterminate malignancy after ultrasound (often a liver lesion <1cm), contrast–enhanced CT, or MRI scan. Patients should not be pregnant or have any personal history of any type of cancer (exception: basal cell carcinoma).

Why is ***Early*CDT—Liver** 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 liver cancer, not other types of cancer. Additionally the control population used to validate the test did not include any patients with a 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—Liver** result.

How is ***Early*CDT—Liver** different from other methods of liver cancer detection?

- ***Early*CDT—Liver** is a simple, affordable blood test with the goal of early cancer detection. Currently, most HCC cases are only detected once symptoms appear and usually in later stages of the disease.
- Measuring autoantibodies has the potential to detect liver cancer in its early stages of development, giving the patient more treatment options with subsequent improved prognosis.
- Some current methods of liver cancer detection, such as CT scanning, involve levels of radiation exposure.

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

***Early*CDT—Liver** is designed to indicate the presence of liver cancer cells in the body, i.e: liver cancer is present, not the likelihood of developing cancer in the future, which is what genetic predisposition testing is often looking for. Note: Currently there is no standardized genetic test for liver cancer.

Where can patients take the test?

In the US, you may request a kit for ***Early*CDT—Liver** using our website order form, by calling Oncimmune Client Services at **+1-888-583-9030**, or by emailing *clientservices@oncimmune.com*.

What is the sample provision process?

A blood or serum sample is all that is required. A simple finger stick sample collection is offered. Alternatively, one can complete a blood draw into a red-top serum tube or serum separator tube (SST). Return pre-paid packaging is supplied. Samples of both blood and serum are shipped at ambient temperature.

How are the test results reported?

Your patient's results are reported by fax only at present.

How long does it take to get results?

You should receive the results within 5–7 days from the time the sample is received at our laboratory in De Soto, Kansas.

Is ***Early*CDT—Liver** covered by Medicare, Medicaid and insurance plans in the US?

- It is required for ***Early*CDT—Liver** to be ordered only for patients being tested to assess the malignancy risk of indeterminate liver lesions identified by imaging.
- The cost of the test is low relative to many other tests, particularly as it is not a genetic test.
- Oncimmune works with all insurance carriers, including Medicare and Medicaid, and will file a claim with each patient's specific insurer.
- Oncimmune offers a Financial Assistance Plan to enable patients to be tested even if they are denied coverage by their plan provider.
- For further information contact Oncimmune Client Services at **+1 888 583 9030**, or by emailing *clientservices@oncimmune.com*.

Who is Oncimmune®?

- Oncimmune is a leader in the development, manufacture and commercialization of personalized 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 four 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.

Contact us

Within the US, please call **+1 888 583 9030**
or email *clientservices@oncimmune.com*

Outside the US, please call **+44 (0)115 823 1869**
or email *contact@oncimmune.co.uk*

References

1. Macdonald I, Welberry C, Murray A, et al. Development and validation of an ELISA test detecting a panel of autoantibodies in combination with AFP for early detection of hepatocellular carcinoma. Poster P-149 presented at: 12th International Liver Cancer Association Annual Conference, September 15th, 2018, London.
2. Jett J, Healey G, MacDonald I, et al. Determination of the detection lead time for autoantibody biomarkers in early stage lung cancer using the UKCTOCS cohort. *J Thorac Oncol*. 2017; 12(11, Suppl 2):S2170.
3. Zhong L, Coe SP, Stromberg AJ, et al. Profiling tumor-associated antibodies for early detection of non-small cell lung cancer. *J Thorac Oncol*. 2006; 1(6):513–519.
4. Heimbach JK, Kulik LM, Finn RS, et al. AASLD guidelines for the treatment of hepatocellular carcinoma. *Hepatology* 2018; 67(1):358–380.
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6. Omata M, Cheng A-L, Kokudo N, et al. Asia–Pacific clinical practice guidelines on the management of hepatocellular carcinoma: a 2017 update. *Hepatology International*. 2017;11(4):317–370.

* Follow up of patients always remains the sole responsibility of the treating clinician.