

Onko-Sure[®] Proposed Mechanism of Action in Patients with Colorectal Cancer

Onko-Sure[®] is a simple, non-invasive, patent-pending and regulatory-approved in vitro diagnostic (IVD) blood test used both for monitoring colorectal cancer (CRC) during treatment and for post-treatment CRC recurrence. It is an ELISA-based assay that measures the accumulation of Fibrin/Fibrinogen Degradation Products (FDP) in the serum using a polyclonal antibody against the DR-70[®] blood biomarker.

For CRC, early identification of recurrence with prompt treatment can lead to a better survival rate and quality of life for the patients.¹ For the last 25 years, Carcinoembryonic Antigen (CEA) (sensitivity of 38-69%) and CA 19-9 (sensitivity of 23-65%) have been available blood biomarkers for colorectal cancer (CRC) treatment monitoring; however, similar to any other biomarker, they have their own limitations.¹ DR-70[®] (sensitivity of 54-87%) is the most recent biomarker cleared by the US FDA for the monitoring of colorectal cancer treatment and recurrence. It has been shown by two clinical studies performed in the UK and US in 2010 that combining CEA and DR-70[®] improves the test sensitivity to 50% higher than that of CEA alone.

Mechanism of Action of Onko-Sure[®]

The production of Fibrin and Fibrinogen Degradation Products (FDP) is restricted in healthy individuals by normal cells. However, cancer cells release proteolytic enzymes such as plasmin and thrombin as they grow and metastasize and they also redirect the coagulation cascade which leads to overproduction of FDP in the process of carcinogenesis.²⁻⁴

FDP level measurement is routinely performed for the detection of coagulopathies; however, the current assays for FDP measurement usually detect only one out of the many FDP components (D-dimer).⁵ There have been many publications studying the D-dimer level measurement in different malignancies including CRC⁶⁻⁹; however, it is not approved for detecting or monitoring malignancies.

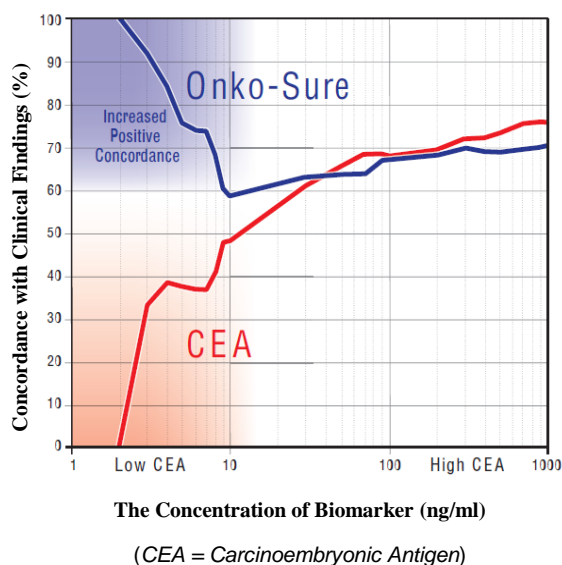
Onko-Sure[®] is the first blood test available for the monitoring of colorectal cancer treatment and recurrence based on FDP measurement. It is an ELISA-based test that uses DR-70[®] polyclonal antibody against the full array of FDP. Onko-Sure[®] detects all of the breakdown products of Fibrin and Fibrinogen, including a unique cancer-related breakdown product, Initial Plasmin Degradation Product (IPDP).¹⁰

Clinical data supports the medical utilization of Onko-Sure[®] for the monitoring of colorectal cancer. In these seven clinical studies, Onko-Sure[®] was used to measure DR-70 levels in about 6,000 patients and the results positively correlated with the progression of CRC.^{1,10-14} Furthermore, as reported by six other studies, the D-dimer level was also linked to CRC progression in about 500 patients.^{2,6-9}

Comparison of Onko-Sure[®] with CEA

CEA, an adhesion molecule, is firmly attached to cancer cells.¹⁵ Therefore, it is less abundant in blood and more difficult to be measured. However, DR-70 antigen is freely diffusible in blood and therefore easy to measure even in low concentrations in lower stages of the cancer. Approximately half of all CRC patients experience recurrence.¹⁶ Likewise, half of the CRC patients with recurrence, have low CEA values not detectable by CEA test.¹⁷⁻¹⁹ For this very reason, Onko-Sure[®] is advantageous over CEA in detecting lower levels of this biomarker leading to an early detection of recurrence.

Figure 1. Comparison of Onko-Sure[®] with CEA. Fifty percent or more CRC patients have low CEA values (<30). As demonstrated in the graph below, Onko-Sure[®] (blue line) showed increased positive concordance with clinical signs and symptoms, i.e., ability to monitor patients with low CEA (red line) values.



CEA has approximately a 20% chance of false positive in smokers²⁰ while Onko-Sure[®] measurements are not affected by smoking.

In general, a combination of several biomarkers provides more accurate information for CRC monitoring. Therefore, it is recommended that both CEA and Onko-Sure[®] are used in combination for the monitoring of post-surgery CRC recurrence²¹. More clinical studies are ongoing to verify the beneficial effect of CEA combination with Onko-Sure[®]. Furthermore, Onko-Sure[®] should be used in conjunction with other clinical modalities considered to be the standard of care for CRC disease progression monitoring.

Summary

Onko-Sure[®] is a simple, non-invasive, patent-pending blood test used both for monitoring colorectal cancer (CRC) during treatment and for post-treatment CRC recurrence. It is an ELISA-based assay that measures the accumulation of Fibrin/Fibrinogen Degradation Products (FDP) in the serum using a polyclonal antibody (DR-70) as a blood biomarker.

For the last 25 years, CEA has been the main routine biomarker for CRC monitoring. DR-70 is the most recent biomarker cleared by the US FDA for the monitoring of colorectal cancer treatment and recurrence. It is recommended to use these two tests in combination to increase the test sensitivity for the monitoring of CRC treatment and recurrence (supported by 2 clinical studies in 2011).

The information in this letter is intended for healthcare professionals practicing in the US. It is provided to you as a professional courtesy in response to your specific unsolicited request.

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