

Onko-Sure[®] Clinical FAQs*

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ONKO-SURE[®] INTRODUCTION

General Background

1. Onko-Sure[®] is a simple, non-invasive 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 assay that measures the accumulation of Fibrin/Fibrinogen Degradation Products (FDP) in the serum using a polyclonal antibody against the DR-70) tumor marker.
2. For CRC, early identification of recurrence with proper treatment can lead to a better survival rate and quality of life for the patients.¹ For the last 25 years, Carcino-Embryogenic Antigen (CEA) has been the only available tumor marker for colorectal cancer (CRC) monitoring; however, similar to any other tumor marker, it has its own limitations.¹ DR-70 is the only other available tumor marker cleared by the US FDA for the monitoring of colorectal cancer treatment and recurrence.

Mechanism of Action of Onko-Sure[®]

1. 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
2. Onko-Sure[®] is the first blood test available for the monitoring of colorectal cancer 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
3. Clinical data supports the medical utilization of Onko-Sure[®] for the monitoring of colorectal cancer treatment and recurrence. In these clinical studies, Onko-Sure[®] was used to measure DR-70[®] levels in 226 patients and the results positively correlated with the progression of CRC.^{1,10-12} Furthermore, as reported by four other studies, the D-dimer level was also linked to CRC progression in 298 patients.⁶⁻⁹

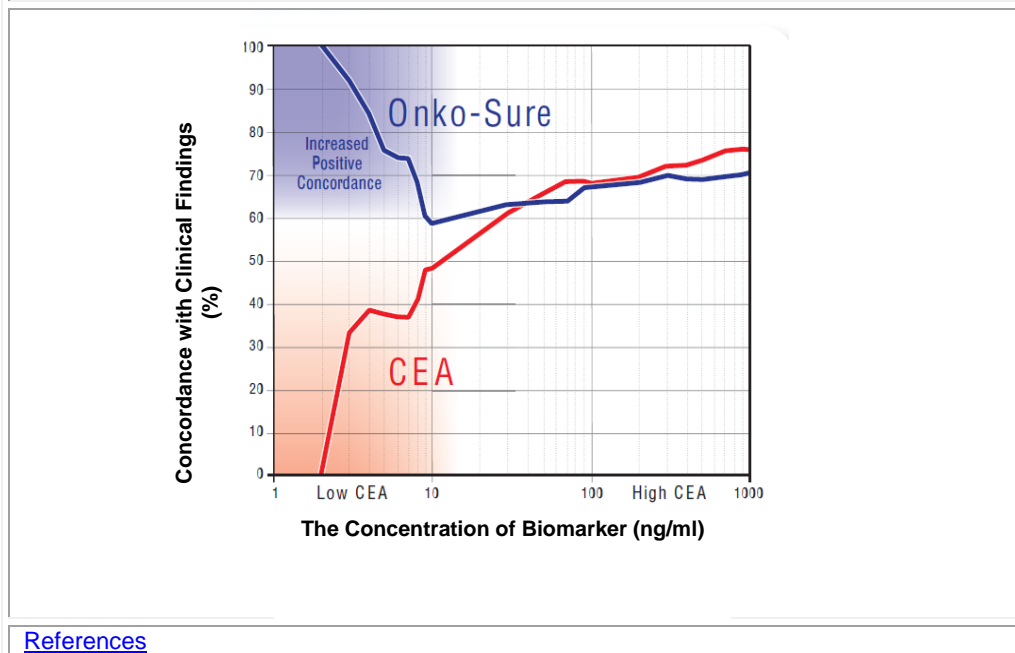
ONKO-SURE[®] INTRODUCTION (CONT.)

Comparison of Onko-Sure[®] with CEA

1. 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.
2. CEA has approximately a 20% chance of false positive in smokers²⁰ while Onko-Sure[®] measurements are not affected by smoking.
3. 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.

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, i.e., ability to monitor patients with low CEA (red line) values.



Summary

1. 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.
2. 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)

ONKO-SURE[®] INTRODUCTION (CONT.)

References

1. Anthony T. Colorectal cancer follow-up in 2005. *Surg Oncol Clin N Am.* 2006;15:175-193.
2. Okholm M, Iversen, LH, Thorlacius-Ussing O, Ejleron E, Boesby S. Fibrin and fibrinogen degradation products in plasma of patients with colorectal adenocarcinoma. *Dis Colon Rectum.* 1996;39:1102-1106.
3. Hatton MW. Fibrinogen catabolism within the procoagulant VX-2 tumor of rabbit lung in vivo: Effluxing fibrin(ogen) fragments contain antiangiogenic activity. *J Lab Clin Med.* 2004;143:241-254.
4. Hatton MW. Relationships among tumor burden, tumor size, and the changing concentrations of fibrin degradation products and fibrinolytic factors in the pleural effusions of rabbits with VX2 lung tumors. *J Lab Clin Med.* 2006; 147:27-35.
5. Ieko M, Nakabayashi T, Tarumi T, Naito S, Yoshida M, Kanazawa K, Mizukami K, Koike T. Soluble fibrin monomer degradation products as a potentially useful marker for hypercoagulable states with accelerated fibrinolysis. *Clin Chim Acta.* 2007;386(1-2):38-45.
6. Blackwell K, Hurwitz H, Lieberman G, Novotny W, Snyder S, Dewhirst M, Greenberg C. Circulating D-dimer levels are better predictors of overall survival and disease progression than carcinoembryonic antigen levels in patients with metastatic colorectal carcinoma. *cancer.* 2004;101(1):77-82.
7. Kilic M, Yoldas O, Keskek M, Ertan T, Tez M, Gocmen E, Koc M. Prognostic value of plasma D-dimer levels in patients with colorectal cancer. *Colorectal Dis.* 2008;10(3):238-41.
8. Oya M, Akiyama Y, Yanagida T, Akao S, Ishikawa H. Plasma D-dimer level in patients with colorectal cancer: its role as a tumor marker. *Surg Today.* 1998;28(4):373-8.
9. Xu G, Ya-Li Zhang, Wen Huang. Relationship between plasma D-dimer levels and clinicopathologic parameters in resectable colorectal cancer patients. *World J Gastroenterol.* 2004;10(6):922-923.
10. Rucker P, Antonio SM and Braden B. Elevated Fibrinogen-Fibrin Degradation Products (FDP) in Serum of Colorectal Cancer Patients. *Analytical Letters.* 2004;37:2965-2976.
11. Kerber A, Trojan J, Herrlinger K, Zgouras D, Caspary WF, Braden B. The new DR-70 immunoassay detects cancer of the gastrointestinal tract: a validation study. *Aliment Pharmacol Ther.* 2004;20:983-098.
12. Small-Howard A, Harris H. Advantages of the AMDL-ELISA DR-70 (FDP) Assay over Carcinoembryonic Antigen for Monitoring Colorectal Cancer Patients. *J Immunoassay Immunochem.* 2010;31(2):131-147.
13. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. *J Immunoassay* 1998;19(1):63-72.
14. Lee KH, Cho DH, Kim KM, et al. Meaning of the DR-70 immunoassay for patients with the malignant tumor. *Immune Network* 2006;6(1):43-51.
15. Charalabopoulos K. CEA levels in serum and BAL in patients suffering from lung cancer: correlation with individuals presenting benign lung lesions and healthy volunteers. *Med Oncol.* 2007;24:219-225.
16. Graffner H, Hultberg B, Johansson B, Moller T, Petersson BG. Detection of recurrent cancer of the colon and rectum. *J Surg Oncol.* 1985;28:156-159.
17. Ladenson JH, McDonald JM, Landt M, Schwartz MK. Colorectal carcinoma and carcinoembryonic antigen (CEA). *Clin Chem.* 1980;26:1213-1220.
18. Wang JY, Tang R, Chiang JM. Value of carcinoembryonic antigen in the management of colorectal cancer. *Dis Colon Rectum.* 1994;37:272-277.
19. Wang WS. Preoperative carcinoembryonic antigen level as independent prognostic factor in colorectal cancer. Taiwan experience. *Jpn J Clin Oncol.* 2000;30:12-16.
20. Kantrowitz M. False Positives and False Negatives in Tumor Marker Blood Tests. *Cancer Points.* <http://www.kantrowitz.com/cancerpoints/tumormarkerfalsepositives.html>[01/06/2010 11:59:54 PM].
21. Shimwell NJ, Wei W, Wilson S, et al. Assessment of novel combinations of biomarkers for the detection of colorectal cancer. *Cancer Biomark.* 2010;7(3):123-132.
22. Cordero OJ, Imbernon M, De Chiara L. Potential of soluble CD86 as a serum marker for colorectal cancer detection. *World J Clin Oncol* 2011;2(6):245-261.
23. Hundt S, Haug u, Brenner H. Blood markers for early detection of colorectal cancer: A systematic review. *Cancer Epidemiol Biomarkers Prev* 2007;16:1935-1953.

ONKO-SURE[®] BACKGROUND

<p>1. What is the clinical utility of Onko-Sure[®]?</p>	<ul style="list-style-type: none"> • Onko-Sure[®] is the first new cancer test cleared by the US FDA for monitoring of the treatment and recurrence of colorectal cancer since 1982 when Carcinoembryonic Antigen (CEA) was approved. • Onko-Sure[®] is more sensitive at detecting lower levels of tumor marker compared to CEA in lower stages of colorectal cancer.
<p>2. What does the Onko-Sure[®] assay detect?</p>	<ul style="list-style-type: none"> • Onko-Sure[®] measures Fibrin and Fibrinogen Degradation Products (FDP). • FDP are over produced in cancer patients because cancer cells release activators for the proteolytic enzymes that cleave fibrin and fibrinogen to form FDPs.
<p>3. Who can benefit the Onko-Sure[®] test?</p>	<ul style="list-style-type: none"> • Patients previously diagnosed for CRC should be tested to be monitored during treatment and post-treatment for reoccurrence of CRC.
<p>4. Can Onko-Sure[®] diagnose cancer?</p>	<ul style="list-style-type: none"> • The Onko-Sure[®] assay has been US FDA cleared to monitor colorectal cancer patients for treatment and post-treatment cancer recurrence. The Onko-Sure[®] assay has been cleared for expanded uses in other countries.

MECHANISM OF ACTION OF ONKO-SURE[®]

<p>1. Does Onko-Sure[®] detect other coagulation-related diseases?</p>	<ul style="list-style-type: none"> Onko-Sure[®] has not been cleared in the US to be marketed for the detection of other coagulation-related diseases.
<p>2. How do physicians use Onko-Sure[®] for monitoring CRC?</p>	<ul style="list-style-type: none"> Initial measurement is used to establish a patient-specific baseline post-operatively. A series of serial measurements should follow every 3-4 months to compare the tumor marker level with the original measurement (this is based on the attending doctor's advice). By comparing the later measurement with the baseline, the doctor can tell if the treatment is useful or not: <ul style="list-style-type: none"> - An increase of 15% or more in DR-70 compared to the baseline (ratio of measurement to the baseline equal or larger than 1.15): The treatment is not working and the tumor is growing. - The level of reading is within 15% of the baseline (ratio of measurement to the baseline is between 0.85 and 1.15): The tumor has not shrunk yet is not growing. - The level of reading is less than 15% of the baseline (ratio of measurement to the baseline lower than 0.85): The tumor is shrinking and the treatment is working. A combination of other biomarkers or imaging techniques is recommended to be used with DR-70[®].
<p>3. How much is the kit detection limit?</p>	<ul style="list-style-type: none"> The limit of the kit detection is 0.06 ug/ml.
<p>4. What kind of antibody is used in the kit?</p>	<ul style="list-style-type: none"> The kit uses a polyclonal antibody that detects all FDP breakdown particles including X, Y, L, D, and D-dimer.
<p>5. What is the Onko-Sure[®] test?</p>	<ul style="list-style-type: none"> Onko-Sure[®] is a simple, non-invasive and regulatory-approved in vitro diagnostic (IVD) blood test used for detection of fibrin/fibrinogen products (FDP) in the serum of patients. It is an ELISA-based assay that measures the accumulation of FDP in the serum using a polyclonal antibody against the DR-70[®] tumor marker. Onko-Sure[®] is used as a blood test for cancer detection, treatment monitoring and post-treatment recurrence monitoring in Europe (CE Mark certified), India, Taiwan, Korea, Vietnam; cleared in the US for the monitoring of colorectal cancer (CRC) treatment and post-treatment recurrence; approved by Health Canada in Canada for lung cancer detection and lung cancer treatment and recurrence monitoring. For more information on the test, contact Radient Pharmaceuticals Corp., in Tustin, California by calling 714-505-4460, or send an email to: info@radient-pharma.com, or go to their website at http://onko-sure.com. We are attempting to get information on the accuracy of this test.

MECHANISM OF ACTION OF ONKO-SURE® (CONT.)

6. I was wondering if OnkoSure DR 70 has a chemotherapy application. like monitoring patients etc.

- Onko-Sure® is also applicable to treatment monitoring as well as recurrence monitoring. One of the major applications for our test, which is equally important compared to cancer detection, is monitoring of cancer treatment and monitoring of post-surgery recurrence.
- So normally, they test the serum after surgery once with Onko-Sure®, and keep it as the base measurement. Then they will test the patient regularly, every 3-4 months to check the level of DR-70 in their serum. If they see more than 15% increase between different DR-70 levels, cancer has clinically progressed. Of course, other conventional means or markers also should be used to check the cancer progress or recurrence but Onko-Sure®, will help to get a more complete perspective of the situation.
- It has a US FDA clearance for monitoring of colorectal cancer treatment and recurrence:
 - For colorectal cancer, early identification of recurrence with prompt treatment can lead to a better survival rate and quality of life for the patients. For the last 25 years, Carcino-Embryogenic Antigen (CEA) has been the only routine tumor marker for colorectal cancer (CRC) monitoring; however, similar to any other tumor marker, it has its own limitations. DR-70® is the most recent available biomarker cleared by the US FDA for the monitoring of colorectal cancer treatment.
 - CEA, an adhesion molecule, is firmly attached to cancer cells. 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. Approximately half of all CRC patients have low CEA values not detectable by CEA test. Likewise, half of the CRC patients will experience recurrence. For this very reason, Onko-Sure® is advantageous over CEA in detecting lower levels of tumor marker leading to an early diagnosis of recurrence. Also, CEA has approximately a 20% chance of false positive in smokers while Onko-Sure® measurements are not affected by smoking.
 - In general, a combination of several tumor markers provides more accurate information about CRC monitoring. Therefore, it is recommended that both CEA and Onko-Sure® are used in combination for the monitoring of colorectal cancer treatment and post-treatment recurrence.
- It also has a Health Canada clearance for lung cancer detection as well as monitoring of treatment and monitoring of recurrence.
 - For lung cancer, early diagnosis and early identification of recurrence with prompt treatment can lead to a better survival rate and quality of life for the patients. The biological tumor markers available for lung cancer include: Carcinoembryonic antigen (CEA), Neuron specific enolase (NSE), and cytokeratin 19 fragment antigen 21-1 (CYFRA21-1). However, the assays for all of them have low sensitivity and are of a limited use for the lung cancer diagnosis. Being simple and non-expensive, they can be used for patients that have been diagnosed with non small cell lung cancer needing additional tests for more exact staging or exclusion of remote metastases.
 - Onko-Sure® is a simple, non-invasive, in vitro diagnostic (IVD) blood test used for screening, treatment and recurrence monitoring of lung cancer and it was cleared by health Canada as of 1995. Clinical data supports the medical utilization of Onko-Sure® for the screening and monitoring of lung cancer.
- Note: Onko-Sure® is an ELISA-based test that uses DR-70® polyclonal antibody against the full array of FDP.

ONKO-SURE[®] ASSAY FORMAT

<p>1. What is the variation expected in the results?</p>	<ul style="list-style-type: none"> • Variation depends on the concentration of serum (the more concentration, the less variation) • Overall intra-assay variation is 15% <ul style="list-style-type: none"> • In 80% of the cases: 0.5-10% • In 20% of the cases: 0.2-0.4% (below the linear range of the assay) • The linear range of the assay is 0.65-10 ug/ml
<p>2. What is the linear range of the assay?</p>	<ul style="list-style-type: none"> • The linear range of the assay is 0.65-10 ug/ml
<p>3. What is the kit shelf life?</p>	<ul style="list-style-type: none"> • About 9-18 months
<p>4. How do you interpret the test score?</p>	<ul style="list-style-type: none"> • Levels between 0-0.8 ug/ml: <ul style="list-style-type: none"> • No further testing (Negative zone) • Test annually for follow up • Levels between 0.8-1.2 ug/ml: <ul style="list-style-type: none"> • Repeat the test every 3 months (Intermediate zone) • Levels higher than 1.2 ug/ml: <ul style="list-style-type: none"> • Further detailed evaluation by a physician/oncologist (Positive zone)
<p>5. What is the cut off for this kit?</p>	<p>The cut off is at the level of 1-1.3 ug/ml and is different for different cancers:</p> <ul style="list-style-type: none"> • In Canada for its intended Health Canada approved use (lung cancer detection and treatment/recurrence monitoring) the cut-off of 1.2 ug/ml is used. However, the product insert states that all clinical diagnostic labs must evaluate their own cut-off due to variations between performance of lab equipment and technicians in different labs. • In all other international uses of the kit (they use a range such that below 0.8 ug/ml values are considered not concerning, values between 0.8 ug/ml and 1.2 ug/ml are tested in 3 months, and values greater than 1.2 ug/ml are tested with other diagnostic tools to rule out cancer). • In the US a cut-off value is not used for its intended FDA-cleared use (colorectal cancer treatment/recurrence monitoring); instead clinical significance is determined based on a change of 15% in the test value when comparing the current test results to the previous result in the monitoring series. • In two US studies in 2011 focusing on detection of colorectal cancer, the cut-off was 1.2 for lung cancer and 1.3 for colorectal cancer.

FALSE POSITIVE RESULTS

1. What are other conditions that cause elevated Onko-Sure® levels in some patients?

This is a list of the conditions that might affect the FDP level in the blood and so the DR-70 test results. If these conditions are present, please use multiple consequent measurements of DR-70 level along with another marker applicable depending on the tumor type.

Note: A good part of the conditions in the list is also affecting CEA test and that is why it is always good to use a panel of few biomarkers and multiple consequent measurements to be able to cover those conditions.

- Pregnancy
- Undergoing pregnancy-related complications:
 - o abruptioe placenta
 - o eclampsia
 - o pre-eclampsia
 - o intrauterine fetal death
- Inflammatory/autoimmune disease:
 - o Addison's
 - o Celiac disease
 - o Grave's disease
 - o Good pasture's syndrome
 - o HIV
 - o Hashimoto's Thyroiditis
 - o Lupus, Multiple Sclerosis
 - o Polymyalgia
 - o Raynaud's
 - o Scleroderma
 - o Sjogren's disease
- Surgery
- Trauma
- Burns
- Cirrhosis
- Renal disease/insufficiency
- Acute & Chronic Infections:
 - o bacteremia
 - o septicaemia (sepsis)
 - o Cellulitis
- Thrombotic problems:
 - o pulmonary embolism (PE)
 - o Disseminated intravascular coagulation (DIC)
 - o Deep Vein Thrombosis (DVT)
 - o myocardial infarction (MI)
 - o congenital heart disease
 - o peripheral vascular disease
 - o portacaval shunt
- Massive blood transfusion
- Therapy for coagolopathic conditions:
 - o Aspirin (ASA)
 - o Aggrenox
 - o Coumadin (Warfarin)
 - o Heparin
 - o Lovenox (Enoxaparin)
 - o Palvix
 - o Ibuprofen (Nurofen, Advil, Mortin, Nuprin)
- Hypercholesterolemi

ONKO-SURE[®] & CEA

<p>1. What are the advantages of Onko-Sure[®] over CEA for CRC monitoring?</p>	<ul style="list-style-type: none"> • CEA is not an optimal target for a blood test because CEA molecule is firmly attached to cancer cells because of its role as an adhesion molecule. In contrast, the DR-70[®] (FDP) antigen used in Onko-Sure[®] is freely diffusible in the blood. • Onko-Sure[®] has an advantage over CEA for CRC monitoring, especially in patients with low CEA values as it is more sensitive to lower levels of tumor marker compared to CEA. More than 30% of the CRC patients develop recurrence and more than half of all CRC patients with recurrence have low CEA values. • Onko-Sure[®] is not affected by smoking unlike CEA with 20% false positive in smokers
<p>2. What is the advantages of combining Onko-Sure[®] and CEA in order to monitor for CRC treatment and/or recurrence?</p>	<ul style="list-style-type: none"> • Shimwell et al from the UK published a paper in 2010 in “Cancer Biomarker”. The results of their study showed that combining CEA and Onko-Sure[®] increased the sensitivity of the test. • A collaborative study with Mayo Clinic in 2010 also showed that combining CEA and Onko-Sure[®] increased the sensitivity to 55% higher than that of CEA alone.

GENERAL

<p>1. What if I still have questions about Onko-Sure[®] test?</p>	<ul style="list-style-type: none"> • More information about the test is available online at www.onko-sure.com or you can email info@radient-pharma.com or call: 714-505-4460
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COMPETITORS

<p>1. What are the competitors of Onko-Sure®?</p>	<ul style="list-style-type: none"> • FDP-based ELISA Kits (Not approved for Cancer detection): <ul style="list-style-type: none"> • <i>Assearachrom D-DI</i> manufactured by Diagnostica Stago (only measures D-dimer) • <i>Imuclone D-dimer ELISA</i> manufactured by American Diagnostica (only measures D-dimer) • Non-FDP-based Tumor Marker ELISA Kits (Approved for cancer detection): <ul style="list-style-type: none"> • <i>Cancer Antigen 19-9 (CA-19-9):</i> <ul style="list-style-type: none"> • Cleared for: <ul style="list-style-type: none"> • Gastrointestinal malignancies: <ul style="list-style-type: none"> • Pancreatic cancer • Colorectal cancer • Gastric Cancer • Hepatic Cancer • Disadvantages: <ul style="list-style-type: none"> • Low sensitivity (23-65%) • Not cancer-specific • <i>Carcino-Embryonic Antigen (CEA):</i> <ul style="list-style-type: none"> • Cleared for several malignancies: <ul style="list-style-type: none"> • Colorectal cancer • Ovarian cancer • Lung cancer • Breast Cancer • Pancreas cancer • Stomach cancer • Disadvantages: <ul style="list-style-type: none"> • Affected by the following factors: <ul style="list-style-type: none"> • Inflammation • Cirrhosis • Peptic ulcer • Ulcerative colitis • Rectal polyps • Emphysema • Benign breast diseases • Smoking • Low sensitivity (38-69%) • Low specificity (55-95%) • Not cancer-specific
<p>2. How is Onko-Sure® different than a D-dimer or other FDP tests?</p>	<ul style="list-style-type: none"> • Onko-Sure® detects the initial plasmin degradation products (IPDP) and therefore it will recognize all of the fibrin and fibrinogen breakdown products including X, Y, D, L, D-dimer fragments, and a unique IPDP cancer-related breakdown product. • D-dimer is not approved for detecting or monitoring cancer and D-dimer values alone would greatly under-estimate cancer and miss some monomers altogether. • Other FDP tests only measure one or two of the selected degradation products. This does not give the complete picture of the total FDP produced by a cancer cell and would greatly under-estimate cancer and miss some altogether.

CLINICAL DATA

Publications

<p>1. Are there published clinical studies that support the use of Onko-Sure® in tongue cancer?</p> <p><u>2 Studies:</u></p> <ul style="list-style-type: none"> - 1 for DR-70 (Bold) - 1 for FDP 	<ol style="list-style-type: none"> 1. Ghosh M, Aroor AR, Raghavan MR. Clinical utility of serum fibrinogen degradation products (FDP) in the diagnostic and prognostic evaluation of oral cancer. <i>Ann Dent.</i> 1990 Winter;49(2):11-2, 45. 2. Li X, Zhi Q, Long X, et al. Serum concentration of AMDL DR-70 for the diagnosis and prognosis of carcinoma of the tongue. <i>British J Oral Maxil Surg</i> 2005;43:513-515.
<p>2. Are there published clinical studies that support the use of Onko-Sure® in CRC monitoring?</p> <p><u>12 Studies:</u></p> <ul style="list-style-type: none"> - 6 for DR-70 (Bold) - 6 for FDP 	<ol style="list-style-type: none"> 1. Okholm M, Iversen, LH, Thorlacius-Ussing O, Ejleron E, Boesby S. Fibrin and fibrinogen degradation products in plasma of patients with colorectal adenocarcinoma. <i>Dis Colon Rectum.</i> 1996;39:1102-1106. 2. Oya M, Akiyama Y, Yanagida T, Akao S, Ishikawa H. Plasma D-dimer level in patients with colorectal cancer: its role as a tumor marker. <i>Surg Today.</i> 1998;28(4):373-8. 3. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. <i>J Immunoassay</i> 1998;19(1):63-72. 4. Blackwell K, Hurwitz H, Lieberman G, Novotny W, Snyder S, Dewhirst M, Greenberg C. Circulating D-dimer levels are better predictors of overall survival and disease progression than carcinoembryonic antigen levels in patients with metastatic colorectal carcinoma. <i>cancer.</i> 2004;101(1):77-82. 5. Xu G, Ya-Li Zhang, Wen Huang. Relationship between plasma D-dimer levels and clinicopathologic parameters in resectable colorectal cancer patients. <i>World J Gastroenterol.</i> 2004;10(6):922-923. 6. Rucker P, Antonio SM and Braden B. Elevated Fibrinogen-Fibrin Degradation Products (FDP) in Serum of Colorectal Cancer Patients. <i>Analytical Letters.</i> 2004;37:2965-2976. 7. Kerber A, Trojan J, Herrlinger K, Zgouras D, Caspary WF, Braden B. The new DR-70 immunoassay detects cancer of the gastrointestinal tract: a validation study. <i>Aliment Pharmacol Ther.</i> 2004;20:983-098. 8. Lee KH, Cho DH, Kim KM, et al. Meaning of the DR-70 immunoassay for patients with the malignant tumor. <i>Immune Network</i> 2006;6(1):43-51. 9. Gieseler F, Luhr L, Kunze T, et al. Activated coagulation factors in human malignant effusions and their contribution to cancer cell metastasis and therapy. <i>Thromb Haemost</i> 2007;97(6):1023-1030. 10. Kilic M, Yoldas O, Keskek M, Ertan T, Tez M, Gocmen E, Koc M. Prognostic value of plasma D-dimer levels in patients with colorectal cancer. <i>Colorectal Dis.</i> 2008;10(3):238-41. 11. Shimwell NJ, Wei W, Wilson S, et al. Assessment of novel combinations of biomarkers for the detection of colorectal cancer. <i>Cancer Biomark.</i> 2010;7(3):123-132. 12. Small-Howard A, Harris H. Advantages of the AMDL-ELISA DR-70 (FDP) Assay over Carcinoembryonic Antigen for Monitoring Colorectal Cancer Patients. <i>J Immunoassay Immunochem.</i> 2010;31(2):131-147.
<p>3. Are there studies that support the use of Onko-Sure® in trophoblast cancer?</p> <p><u>1 Studies:</u></p> <ul style="list-style-type: none"> - 1 for DR-70 (Bold) - 0 for FDP 	<ol style="list-style-type: none"> 1. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. <i>J Immunoassay</i> 1998;19(1):63-72.

CLINICAL DATA

Publications

<p>4. Are there published clinical studies that support the use of Onko-Sure® in lung cancer detection and monitoring?</p> <p><u>11 Studies:</u></p> <ul style="list-style-type: none"> - 7 for DR-70 (Bold) - 4 for FDP 	<ol style="list-style-type: none"> 1. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. <i>J Immunoassay</i> 1998;19(1):63-72. 2. Wu DF, Zhou X, Anderson G et al. Sensitivity and specificity of DR-70 lung cancer immunology. <i>Anal Lett</i> 1999;32(7):1351-1362. 3. Ding L, Ping S, Jingmei Y. Application of tumor marker of DR-70 in the diagnosis of malignant tumors. <i>Chong Quing Med J</i> 1999;28(5). 4. Hatton MW. Fibrinogen catabolism within the procoagulant VX-2 tumor of rabbit lung in vivo: Effluxing fibrin(ogen) fragments contain antiangiogenic activity. <i>J Lab Clin Med.</i> 2004;143:241-254. 5. Adonis M, Martinez V, Marin P et al. Smoking habit and genetic factors associated with lung cancer in a population highly exposed to arsenic. <i>Toxicol Lett</i> 2005;159(1):32-37. 6. Adonis M, Martinez V, Marin P et al. CYP1A1 and GSTM1 genetic polymorphisms in lung cancer populations exposed to arsenic in drinking water. <i>Xenobiotica</i> 2005;35(5):519-530. 7. Hatton MW. Relationships among tumor burden, tumor size, and the changing concentrations of fibrin degradation products and fibrinolytic factors in the pleural effusions of rabbits with VX2 lung tumors. <i>J Lab Clin Med.</i> 2006; 147:27-35. 8. Antoniou D, Pavlakou G, Stathopoulos GP et al. Predictive value of d-dimer plasma levels in response and progressive disease in patients with lung cancer. <i>Lung Cancer</i> 2006;53(2):205-210. 9. Gieseler F, Luhr L, Kunze T, et al. Activated coagulation factors in human malignant effusions and their contribution to cancer cell metastasis and therapy. <i>Thromb Haemost</i> 2007;97(6):1023-1030. 10. Motamed-Khorasani A, Grimes R, Weber DF. The validation of DR-70 efficiency in early detection of lung cancer. <i>Lung Cancer</i> 2011;71(Supplement 2):S29. 11. Adonis M, Chahuan M, Urzua U, et al. Detection of preneoplastic lesions using biological and genomic lung cancer biomarkers in a high risk Chilean population. <i>Journal of Thoracic Oncology</i> 2011;6(6)(Supplement 2):S980.
<p>5. Are there published clinical studies that support the use of Onko-Sure® in stomach cancer?</p> <p><u>7 Studies:</u></p> <ul style="list-style-type: none"> - 4 for DR-70 (Bold) - 3 for FDP 	<ol style="list-style-type: none"> 1. Abbasciano V, Tassirari D, Sartori S, et al. Usefulness of coagulation markers in staging of gastric cancer. <i>Cancer Detect Prev</i> 1995;19(4):331-336. 2. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. <i>J Immunoassay</i> 1998;19(1):63-72. 3. Ding L, Ping S, Jingmei Y. Application of tumor marker of DR-70 in the diagnosis of malignant tumors. <i>Chong Quing Med J</i> 1999;28(5). 4. Kerber A, Trojan K, Herrlinger D, et al. The new DR-70 immunoassay detects cancer of the gastrointestinal tract: A validation study. <i>Aliment Pharmacol Ther</i> 2004;20:983-987. 5. Lee KH, Cho DH, Kim KM, et al. Meaning of the DR-70 immunoassay for patients with the malignant tumor. <i>Immune Network</i> 2006;6(1):43-51. 6. Gieseler F, Luhr L, Kunze T, et al. Activated coagulation factors in human malignant effusions and their contribution to cancer cell metastasis and therapy. <i>Thromb Haemost</i> 2007;97(6):1023-1030. 7. Kovacova E, Kinova S, Duris I, et al. Local changes in hemostasis in patients with gastric cancer. <i>Bratisl Lek Listy</i> 2009;110(5):280-284.

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<p>6. Are there published clinical studies that support the use of Onko-Sure® in ovarian cancer?</p> <p><u>12 Studies:</u></p> <ul style="list-style-type: none"> - 4 for DR-70 (Bold) - 8 for FDP 	<ol style="list-style-type: none"> 1. Astedt B, Svanberg L, Nilsson IM. Fibrin degradation products and ovarian tumors. <i>Br Med J</i> 1971;4:458-459. 2. Svanberg L, Astedt B, Gynning I, et al. Fibrin degradation products during postoperative radiotherapy of ovarian carcinoma. <i>Acta Obst Gyn Scand</i> 1973;52(2):141-145. 3. Rella C, Coviello M, Defreza N, et al. Plasma D-dimer measurement as a marker of gynecologic tumors: Comparison with CA-125. <i>Tumori</i> 1993;79(5):347-351. 4. Rose PG, Terrien JM, Baker S. Plasma D-dimer and peritoneal CA-125 levels as predictors of disease status in ovarian carcinoma. <i>J Surg Oncol</i> 1994;56(3):168-171. 5. Gadducci A, Baicchi U, Marrai R, et al. Preoperative evaluation of D-dimer and CA-125 levels in differentiating benign from malignant ovarian masses. <i>Gynecol Oncol</i> 1996;60(2):197-202. 6. Den Ouden M, Ubachs JM, Stoot JE, et al. Thrombin, antithrombin III and D-dimer plasma levels in patients with benign or malignant ovarian tumors. <i>Scand J Clin Lab Invest</i> 1998;58(7):555-559. 7. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. <i>J Immunoassay</i> 1998;19(1):63-72. 8. Ding L, Ping S, Jingmei Y. Application of tumor marker of DR-70 in the diagnosis of malignant tumors. <i>Chong Qing Med J</i> 1999;28(5). 9. Koh SC, Tham KF, Razvi K, et al. Hemostatic and fibrinolytic status in patients with ovarian cancer and benign ovarian cysts: Could D-dimer and antithrombin III levels be included as prognostic markers for survival outcome? <i>Clin Appl Thromb Hemostat</i> 2001;7(2):141-148. 10. Schaffrath M, Harter P, Wulgaris S, et al. Ovarian carcinoma: Clinical validity by simultaneous determination of fibrin degradation products with the DR-70 immunoassay and CA-125. <i>German J Obst Gyn</i> 2006;66:68-75. 11. Koh SC, Khalil R, Lim FK, et al. The association between fibrinogen, Von Willebrand Factor, antithrombin III, and D-dimer levels and survival outcome by 36 months from ovarian cancer. <i>Clin Appl Thromb Hemost</i> 2006;12(1):3-8. 12. Lee KH, Cho DH, Kim KM, et al. Meaning of the DR-70 immunoassay for patients with the malignant tumor. <i>Immune Network</i> 2006;6(1):43-51.
<p>7. Are there published clinical studies that support the use of Onko-Sure® in liver cancer?</p> <p><u>7 Studies:</u></p> <ul style="list-style-type: none"> - 5 for DR-70 (Bold) - 2 for FDP 	<ol style="list-style-type: none"> 1. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. <i>J Immunoassay</i> 1998;19(1):63-72. 2. Ding L, Ping S, Jingmei Y. Application of tumor marker of DR-70 in the diagnosis of malignant tumors. <i>Chong Qing Med J</i> 1999;28(5). 3. Ma J, Gong Q, Lin M, et al. Combined five tumor marker in detecting primary hepatic carcinoma. <i>Zhonghua Wai Ke Za Zhi</i> 2000;38(1):14-16. 4. Tseng CS, Lo HW, Chen PH, et al. Clinical significance of plasma D-dimer levels and serum VEGF levels in patients with hepatocellular carcinoma. <i>Hepatogastroenterology</i> 2001;51(59):1454-1458. 5. Kerber A, Trojan J, Herrlinger K, Zgouras D, Caspary WF, Braden B. The new DR-70 immunoassay detects cancer of the gastrointestinal tract: a validation study. <i>Aliment Pharmacol Ther.</i> 2004;20:983-098. 6. Lee KH, Cho DH, Kim KM, et al. Meaning of the DR-70 immunoassay for patients with the malignant tumor. <i>Immune Network</i> 2006;6(1):43-51. 7. Spadaro A, Tortorella V, Morace C, et al. High circulating D-dimers are associated with ascites and hepatocellular carcinoma in liver cirrhosis. <i>World J Gastroenterol</i> 2008;14(10):1549-1552.

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<p>8. Are there published clinical studies that support the use of Onko-Sure® in bladder cancer?</p> <p><u>5 Studies:</u></p> <ul style="list-style-type: none"> - 0 for DR-70 (Bold) - 5 for FDP 	<ol style="list-style-type: none"> 1. McCabe RP, Lamm DL, Haspel MV, et al. A diagnostic-prognostic test for bladder cancer using a monoclonal antibody-based enzyme-linked immunoassay for detection of urinary fibrin (ogen) degradation products. <i>Cancer Res</i> 1984;44:5888-5893. 2. Tsihlias J, Grossman HB. The utility of fibrin/fibrinogen degradation products in superficial bladder cancer. <i>Urol Clin North Am.</i> 2000 Feb;27(1):39-46. Review. 3. Oeda T, Manabe D. The usefulness of urinary FDP in the diagnosis of bladder cancer: comparison with NMP22, BTA and cytolog Nippon Hinyokika Gakkai Zasshi. 2001 Jan;92(1):1-5. Japanese. 4. Siemens DR, Morales A, Johnston B, Emerson L. A comparative analysis of rapid urine tests for the diagnosis of upper urinary tract malignancy. <i>Can J Urol.</i> 2003 Feb;10(1):1754-8. 5. Dey P. Urinary markers of bladder carcinoma. <i>Clin Chim Acta.</i> 2004 Feb;340(1-2):57-65. Review.
<p>9. Are there published clinical studies that support the use of Onko-Sure® in brain cancer?</p> <p><u>3 Studies:</u></p> <ul style="list-style-type: none"> - 1 for DR-70 (Bold) - 2 for FDP 	<ol style="list-style-type: none"> 1. Eclache V, Vu T, Le Roux G, et al. D-dimer levels in the cerebrospinal fluid: A marker of central nervous system involvement in neoplastic disease. <i>Nouv Rev Fr Hematol</i> 1994;36(4):321-324. 2. Goh KY, Tsoi WC, Feng CS, et al. Haemostatic changes during surgery for primary brain tumors. <i>J Neurol Neurosurg Psychiatry</i> 1997;63(3):334-338. 3. Ding L, Ping S, Jingmei Y. Application of tumor marker of DR-70 in the diagnosis of malignant tumors. <i>Chong Quing Med J</i> 1999;28(5).
<p>10. Are there published clinical studies that support the use of Onko-Sure® in pancreatic cancer?</p> <p><u>4 Studies:</u></p> <ul style="list-style-type: none"> - 3 for DR-70 (Bold) - 1 for FDP 	<ol style="list-style-type: none"> 1. Abbasciano V, Graziano L, Guerra S, et al. Coagulation disorders and tumor markers in the diagnosis of pancreatic cancer. <i>Oncology</i> 1991;48(5):377-382. 2. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. <i>J Immunoassay</i> 1998;19(1):63-72. 3. Kerber A, Trojan J, Herrlinger K, Zgouras D, Caspary WF, Braden B. The new DR-70 immunoassay detects cancer of the gastrointestinal tract: a validation study. <i>Aliment Pharmacol Ther.</i> 2004;20:983-098. 4. Ward DG, Wei W, Buckels J, et al. Detection of pancreatic adenocarcinoma using circulating fragments of fibrinogen. <i>Eur J Gastroenterol Hepatol</i> 2010 (Epub; PMID:20555269).
<p>11. Are there published clinical studies that support the use of Onko-Sure® in esophageal cancer?</p> <p><u>3 Studies:</u></p> <ul style="list-style-type: none"> - 2 for DR-70 (Bold) - 1 for FDP 	<ol style="list-style-type: none"> 1. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. <i>J Immunoassay</i> 1998;19(1):63-72. 2. Kerber A, Trojan J, Herrlinger K, Zgouras D, Caspary WF, Braden B. The new DR-70 immunoassay detects cancer of the gastrointestinal tract: a validation study. <i>Aliment Pharmacol Ther.</i> 2004;20:983-098. 3. Tomimaru Y, Yano M, Takachi K, et al. Correlation between pretherapeutic D-dimer levels and response to neoadjuvant chemotherapy in patients with advanced esophageal cancer. <i>Dis Esophagus</i> 2008;21(4):281-287.

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<p>12. Are there published clinical studies that support the use of Onko-Sure® in hematological cancer?</p> <p><u>3 Studies:</u></p> <ul style="list-style-type: none"> - 0 for DR-70 (Bold) - 3 for FDP 	<ol style="list-style-type: none"> 1. Cielinska S, Urbaniak-Kujda D, Kielbinski M, et al. Observation of D-dimer levels in serum of patients with acute leukemia. <i>Pol Arch Med Wewn</i> 2000;103(1-2):7-14. 2. Rość D, Kremplewska-Nalezta E, Gadomska G, Zastawna E, Michalski A, Drewniak W. Plasminogen activators (t-PA and u-PA) and plasminogen activators inhibitors (PAI-1 and PAI-2) in some myeloproliferative syndromes. <i>Med Sci Monit</i>. 2000 Jul-Aug;6(4):684-91. 3. Negaard HF, Irsen PO, Ostenstand B, et al. Hypercoagulability in patients with haematological neoplasia: No apparent initiation by tissue factor. <i>Thromb Haemost</i> 2008;99(6):1040-1080.
<p>13. Are there published clinical studies that support the use of Onko-Sure® in uterine cancer?</p> <p><u>1 Studies:</u></p> <ul style="list-style-type: none"> - 0 for DR-70 (Bold) - 1 for FDP 	<ol style="list-style-type: none"> 1. Rella C, Coviello M, Defreza N, et al. Plasma D-dimer measurement as a marker of gynecologic tumors: Comparison with CA-125. <i>Tumori</i> 1993;79(5):347-351.
<p>14. Are there published clinical studies that support the use of Onko-Sure® in breast cancer?</p> <p><u>8 Studies:</u></p> <ul style="list-style-type: none"> - 3 for DR-70 (Bold) - 5 for FDP 	<ol style="list-style-type: none"> 1. Mitter CG, Zielinski CC. Plasma levels of D-dimer: A cross linked fibrin degradation product in female breast cancer. <i>J Cancer Res Clin Oncol</i> 1991;117(3):259-262. 2. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. <i>J Immunoassay</i> 1998;19(1):63-72. 3. Ding L, Ping S, Jingmei Y. Application of tumor marker of DR-70 in the diagnosis of malignant tumors. <i>Chong Quing Med J</i> 1999;28(5). 4. Blackwell K, Haroon Z, Broadwater G, et al. Plasma D-dimer levels in operable breast cancer patients correlate with clinical stage and axillary lymph node status. <i>J Clin Oncol</i> 2000;18:600-608. 5. Dirix LY, Salgado R, Weytjens R, et al. Plasma fibrin D-dimer levels correlate with tumor volume, progression rate and survival in patients with metastatic breast cancer. <i>Br J Cancer</i> 2002;86(3):389-395. 6. Kim HK, Song KS, Lee KR, et al. Comparison of plasma D-dimer and thrombus precursor protein in patients with operable breast cancer as a potential predictor of lymph node metastasis. <i>Blood Coagul Fibrinolysis</i> 2004;15(1):9-13. 7. Lee KH, Cho DH, Kim KM, et al. Meaning of the DR-70 immunoassay for patients with the malignant tumor. <i>Immune Network</i> 2006;6(1):43-51. 8. Gieseler F, Luhr L, Kunze T, et al. Activated coagulation factors in human malignant effusions and their contribution to cancer cell metastasis and therapy. <i>Thromb Haemost</i> 2007;97(6):1023-1030.

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<p>15. Are there published clinical studies that support the use of Onko-Sure® in prostate cancer?</p> <p><u>4 Studies:</u></p> <ul style="list-style-type: none"> - 0 for DR-70 (Bold) - 4 for FDP 	<ol style="list-style-type: none"> 1. McCabe RP, Lamm DL, Haspel MV, et al. A diagnostic-prognostic test for bladder cancer using a monoclonal antibody-based enzyme-linked immunoassay for detection of urinary fibrin (ogen) degradation products. <i>Cancer Res</i> 1984;44:5888-5893. 2. Geenen RW, Delaere KP, Van Wersch JW. Coagulation and fibrinolysis activation markers in prostatic carcinoma patients. <i>Eur J Clin Chem Clin Biochem</i> 1997; 35(2):69-72. 3. Kohli M, Fink LM, Spencer HJ, et al. Advanced prostate cancer activates coagulation: A controlled study of activation markers of coagulation in ambulatory patients with localized and advanced prostate cancer. <i>Blood coagul fibrinolysis</i> 2002;13(1):1-5. 4. Langer F, Chun FK, Amirkhosravi A, et al. Plasma tissue factor antigen in localized prostate cancer: Distribution, clinical significance and correlation with haemostatic activation markers. <i>Thromb Haemost</i> 2007;97(3):464-470.
<p>16. Are there published clinical studies that support the use of Onko-Sure® in cervical cancer?</p> <p><u>3 Studies:</u></p> <ul style="list-style-type: none"> - 1 for DR-70 (Bold) - 2 for FDP 	<ol style="list-style-type: none"> 1. Gadducci A, Baicchi U, Del Bravo B, et al. Evaluation of some hemostatic parameters in patients with cervical carcinoma. <i>Eur J Gynecol Oncol</i> 1990;11(3):215-218. 2. Gadducci A, Baicchi U, Marrai R, et al. Pretreatment plasma levels of fibrinopeptide A (FPA), D-dimer (DD), and Von Willebrand Factor (VWF) in patients with operable cervical cancer: Influence of surgical-pathological stage, tumor size, histologic type, and lymph node status. <i>Gynecol Oncol</i> 1993;49(3):354-358. 3. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. <i>J Immunoassay</i> 1998;19(1):63-72.
<p>17. Are there published clinical studies that support the use of Onko-Sure® in thyroid cancer?</p> <p><u>3 Studies:</u></p> <ul style="list-style-type: none"> - 2 for DR-70 (Bold) - 1 for FDP 	<ol style="list-style-type: none"> 1. Sagripanti A, Carpi A, Baicchi U. The measurement of plasma D-dimer in the follow-up after thyroidectomy for cancer: Preliminary data. <i>Thyroidology</i> 1991;3(1):31-35. 2. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. <i>J Immunoassay</i> 1998;19(1):63-72. 3. Lee KH, Cho DH, Kim KM, et al. Meaning of the DR-70 immunoassay for patients with the malignant tumor. <i>Immune Network</i> 2006;6(1):43-51.
<p>18. Are there published clinical studies that support the use of Onko-Sure® in lymphoma?</p> <p><u>2 Studies:</u></p> <ul style="list-style-type: none"> - 2 for DR-70 (Bold) - 0 for FDP 	<ol style="list-style-type: none"> 1. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. <i>J Immunoassay</i> 1998;19(1):63-72. 2. Ding L, Ping S, Jingmei Y. Application of tumor marker of DR-70 in the diagnosis of malignant tumors. <i>Chong Quing Med J</i> 1999;28(5).

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Publications	
<p>19. Are there published clinical studies that support the use of Onko-Sure[®] in general cancer screen?</p>	<ol style="list-style-type: none"> 1. Wu D, Zhou X, Yang G, et al. Clinical performance of the AMDL DR-70 immunoassay kit for cancer detection. <i>J Immunoassay</i> 1998;19(1):63-72. 2. Ding L, Ping S, Jingmei Y. Application of tumor marker of DR-70 in the diagnosis of malignant tumors. <i>Chong Quing Med J</i> 1999;28(5). 3. Kerber A, Trojan J, Herrlinger K, Zgouras D, Caspary WF, Braden B. The new DR-70 immunoassay detects cancer of the gastrointestinal tract: a validation study. <i>Aliment Pharmacol Ther.</i> 2004;20:983-098. 4. Lee KH, Cho DH, Kim KM, et al. Meaning of the DR-70 immunoassay for patients with the malignant tumor. <i>Immune Network</i> 2006;6(1):43-51. 5. Gieseler F, Luhr L, Kunze T, et al. Activated coagulation factors in human malignant effusions and their contribution to cancer cell metastasis and therapy. <i>Thromb Haemost</i> 2007;97(6):1023-1030.
<p>1. What was the sensitivity and specificity of the DR-70 in all the studies published?</p>	<ul style="list-style-type: none"> • The sensitivity range: 50-95% • The specificity range: 57-100%

CLINICAL DATA	
<p>1. Has Onko-Sure[®] been clinically tested?</p>	<ul style="list-style-type: none"> • Studies have demonstrated similar sensitivity using the Onko-Sure[®] assay compared to CEA for CRC. However Onko-Sure[®] has been shown to indicate risk of recurrence specifically when CEA levels are still low. • Two recent 2010 (UK) and 2011 (US) studies showed that combining CEA and Onko-Sure[®] increased the sensitivity of the test to 55% higher than that of CEA alone. Therefore, we recommend combining these two biomarkers in order to get a better sensitivity compared to either alone.

REIMBURSEMENT (US SPECIFIC)	
<p>1. Is there reimbursement for the Onko-Sure[®] test?</p>	<ul style="list-style-type: none"> • There is no specific assigned CPT code for Onko-Sure[®] yet, but it is FDA approved for CRC monitoring similar to CEA. The recommendation is to submit using any of the following: <ul style="list-style-type: none"> • General immunoassay code (83520) • Fibrinogen Degredation Products code (85370)

FDA APPROVAL

1. What is the status of FDA Approval?	<ul style="list-style-type: none">• This test was cleared by US FDA in July 2008.• The intended use:<ul style="list-style-type: none">• Monitoring of colorectal cancer treatment• Monitoring of colorectal cancer recurrence
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HEALTH CANADA APPROVAL

1. What is the status of Health Canada Approval?	<ul style="list-style-type: none">• This test was cleared by Health Canada since 1998.• The intended use:<ul style="list-style-type: none">• Detection of lung cancer• Monitoring of lung cancer treatment• Monitoring of lung cancer recurrence
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