Cancer Association of South Africa (CANSA)

Research • Educate • Support

Fact Sheet
on
Tumour Markers

Introduction

A tumour marker is any cellular, molecular, chemical or physical change that can be measured and used to study a normal or abnormal process in the body which can be found in the blood, urine, or body tissues and can be elevated in cancer. There are many different tumour markers, each indicative of a particular disease process, and they are used in oncology to help detect the presence of cancer.

[Picture Credit: Tumour Marker Test]

An elevated level of a tumour marker is usually indicative of the presence of cancer, however, there can also be other causes of the particular elevation.

Tumour markers are assuming a growing role in all aspects of cancer care, starting from screening to follow-up after treatment, and their judicious application in clinical practice needs a thorough understanding of the basics of pathophysiology, techniques of identification or testing, reasons for out-of-range levels of tumour markers, as well as the knowledge of evidence of their role in any given malignancy. Tumour markers are, at the most, just an adjunct to diagnosis, and establishing a diagnosis on the basis of tumour markers alone (especially a single result) is fraught with associated pitfalls because of the problem of non-specificity. In reality an ideal tumour marker does not exist.

Some tumour markers are specific to one type of cancer, while others are related to several different types of cancer. Tumour markers may also become elevated as a result of the presence of non-cancerous conditions. Tumour markers can be produced directly by the tumour or by non-tumour cells as a response to the presence of a tumour. Most tumour markers are tumour antigens, but not all tumour antigens can be used as tumour markers.

Researched and Authored by Prof Michael C Herbst
[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]
Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

Xia, P. & Dubrovska, A. 2020.
"Coronavirus disease 2019 (COVID-19), the highly contagious illness caused by a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread across the globe, becoming one of the most challenging public health crisis of our times. SARS-CoV-2 can cause severe disease associated with multiple organ damage. Cancer patients have a higher risk of SARS-CoV-2 infection and death. While the virus uses angiotensin-converting enzyme 2 (ACE2) as the primary entry receptor, the recent experimental and clinical findings suggest that some tumor markers, including CD147 (basigin), can provide an additional entry for SARS-CoV-2 infection through binding to the viral spike (S) protein. In the absence of specific viral drugs, blocking of CD147 might be a way to prevent virus invasion. Identifying other target proteins is of high importance as targeting the alternative receptors for SARS-CoV-2 might open up a promising avenue for the treatment of COVID-19 patients, including those who have cancer."

Walk, E.E., Yohe, S.L., Beckman, A., Schade, A., Zutter, M.M., Pfeifer, J., Berry, A.B. & College of American Pathologists. 2020.
Context.—: Cancer immunotherapy provides unprecedented rates of durable clinical benefit to late-stage cancer patients across many tumor types, but there remains a critical need for biomarkers to accurately predict clinical response. Although some cancer immunotherapy tests are associated with approved therapies and considered validated, other biomarkers are still emerging and at various states of clinical and translational exploration.
Objective.—: To provide pathologists with a current and practical update on the evolving field of cancer immunotherapy testing. The scientific background, clinical data, and testing methodology for the following cancer immunotherapy biomarkers are reviewed: programmed death ligand-1 (PD-L1), mismatch repair, microsatellite instability, tumor mutational burden, polymerase δ and ε mutations, cancer neoantigens, tumor-infiltrating lymphocytes, transcriptional signatures of immune responsiveness, cancer immunotherapy resistance biomarkers, and the microbiome.
Data sources.—: Selected scientific publications and clinical trial data representing the current field of cancer immunotherapy.
Conclusions.—: The cancer immunotherapy field, including the use of biomarker testing to predict patient response, is still in evolution. PD-L1, mismatch repair, and microsatellite instability testing are helping to guide the use of US Food and Drug Administration-approved therapies, but there remains a need for better predictors of response and resistance. Several categories of tumor and patient characteristics underlying immune responsiveness are emerging and may represent the next generation of cancer immunotherapy predictive biomarkers. Pathologists have important roles and responsibilities as the field of cancer immunotherapy continues to develop, including leadership of translational studies, exploration of novel biomarkers, and the accurate and timely implementation of newly approved and validated companion diagnostics.

Limitations of Tumour Markers
Tumour markers are not fool proof. Other tests are usually needed to learn more about a possible cancer or recurrence.

Some of the limitations of tumour markers are listed below:

- A condition or disease, other than cancer, can elevate tumour marker levels
- Some tumour marker levels may be high in people without cancer
- Tumour marker levels may vary over time, making it hard to get consistent results

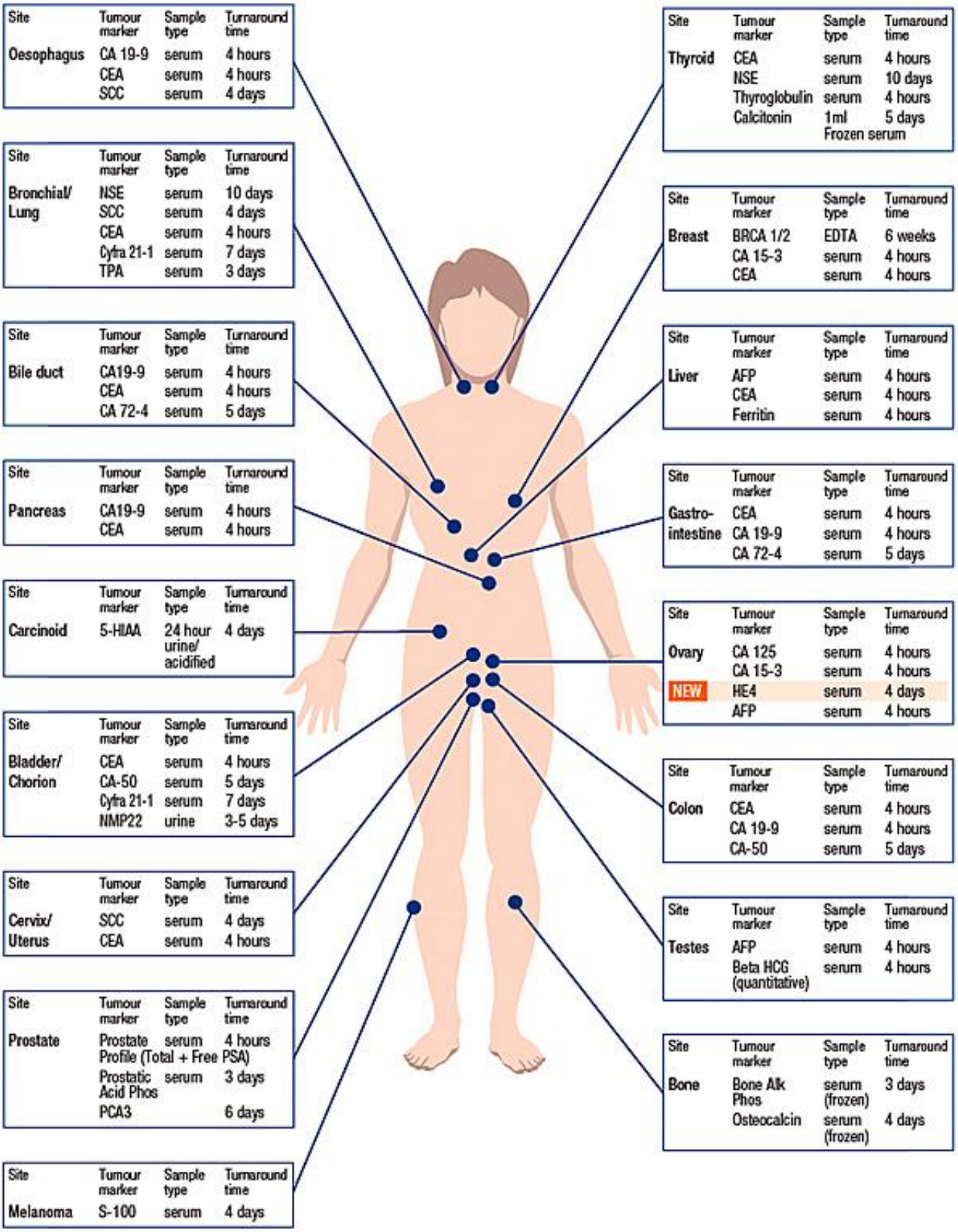
- The level of a tumour marker may not rise until a person's cancer worsens. This is not helpful for early detection, screening, or watching for recurrence
- Some cancers do not make tumour markers that are found in the blood. This includes cancers with no known tumour markers. Also, some patients do not have higher tumour maker levels even if the type of cancer they have usually makes tumour markers

Malhone, C & Longatto-Filho, A. 2019.
"Tumors markers can be described as molecular products expressed by neoplasia tissues (immunohistochemistry), or metabolized and secreted by tumor and characterized biochemically in body fluids such as blood and urine. They may have utility as indicators of tumor stage and grade as well useful for monitoring responses to treatment and predicting recurrence, progression, development of metastases, or even patient survival. Unfortunately, in some cases they may have no identified clinical potential. Several investigations have been carried out, especially in the last decade, using biotechnological methods, in order to identify new potential tumor markers. By translating these findings into clinical use one may facilitate accurate diagnosis and prognostic prediction, and contribute to individualized treatment. The objective of this review is to describe some biomarkers with potential use in clinical settings of uterine cervix, ovary, and endometrium carcinomas."

Araujo, D.V., Bratman, S.V. & Siu, L.L. 2019. Designing circulating tumor DNA-based interventional clinical trials in oncology. *Genome Med*, 11 (1), 22. 2019 Apr 19.
"Circulating tumor (ct) DNA is a powerful tool that can be used to track cancer beyond a single snapshot in space and time. It has potential applications in detecting minimal residual disease and predicting relapse, in selecting patients for tailored treatments, and in revealing mechanisms of response or resistance. "

Barzaman, K., Karami, J., Zarei, Z., Hosseinzadeh, A., Kazemi, M.H., Moradi-Kalbolandi, S., Safari, E. & Farahmand, L. 2020.
"During the past recent years, various therapies emerged in the era of breast cancer. Breast cancer is a heterogeneous disease in which genetic and environmental factors are involved. Breast cancer stem cells (BCSCs) are the main player in the aggressiveness of different tumors and also, these cells are the main challenge in cancer treatment. Moreover, the major obstacle to achieve an effective treatment is resistance to therapies. There are various types of treatment for breast cancer (BC) patients. Therefore, in this review, we present the current treatments, novel approaches such as antibody-drug conjugation systems (ADCs), nanoparticles (albumin-, metal-, lipid-, polymer-, micelle-based nanoparticles), and BCSCs-based therapies. Furthermore, prognostic and predictive biomarkers will be discussed also biomarkers that have been applied by some tests such as Oncotype DX, Mamm αPrint, and uPA/PAI-1 are regarded as suitable prognostic and predictive factors in breast cancer."

Tumour Markers at a Glance



(The Doctors Laboratory).

Tumour Markers in General Use

Tumour markers alone are not diagnostic for cancer; for some types of cancer, they provide additional information that can be considered in conjunction with a patient's medical history and physical examination as well as other laboratory and/or imaging tests.

Tumour markers that are generally used in oncology are dealt with in this Fact Sheet. They are listed in no particular order.

This Fact Sheet may not contain a comprehensive list of all tumour markers, however, the most used tumour markers are included.

Tumour Marker CA 19-9

Ca 19-9 is not sensitive or specific enough to use as a screening test for cancer, and it is not diagnostic of a specific type of cancer. Its main use is as a tumour marker:

- To help differentiate between cancer of the pancreas and other conditions, such as pancreatitis
- To monitor a person's response to pancreatic cancer treatment and/or cancer progression
- To watch for pancreatic cancer recurrence

Tumour Marker CEA

Carcinoembryonic antigen (CEA) is a protein found in many types of cells but associated with tumours and the developing foetus. It is used for staging of applicable cancers, to determine prognosis, and to monitor success of treatment and detect recurrence.

Tumour Marker BR-ABL

This tumour marker is associated with the following cancers:

- Chronic myeloid leukaemia (CML)
- BCR-ABL-positive acute lymphocytic leukaemia (ALL)

Tumour Marker SCC-Ag

Elevated expression of SCC-Ag has been used as a biomarker for aggressive squamous cell carcinoma (SCC) in cancers of the:

- Cervix
- Lung
- Head and Neck
- Liver

Tumour Marker NSE

The NSE (neuroenzyme-specific-enolase) is an enzyme only found is nervous tissue or in neuroendocrine tissue. At present, it is used in small cell lung cancer.

NSE: Neuron-specific enolase (NSE) is a substance that has also been detected in patients with certain tumours, namely:

- Neuroblastoma
- small cell lung cancer
- medullary thyroid cancer
- carcinoid tumours
- endocrine tumours of the pancreas
- melanoma.

Tumour Marker Cyfra 21-1

It is used in lung cancer, diagnosis. Cyfra can also be used in uterine cancer, oesophageal cancer, and bladder cancer.

Tumour Marker TPA

Tissue polypeptide antigen (TPA) is a differentiation and proliferation marker of non-squamous epithelium and derived neoplasms. TPA is a tumour marker in gastric and colorectal carcinoma.

Tumour Marker CA 72-4

CA 72-4 is of particular interest, not only for its capabilities in diagnosing and monitoring certain neoplastic diseases, but also for its excellent specificity. Several studies focused on the potential clinical usefulness of CA 72-4 in gastrointestinal (GI) cancer, gynaecological cancer, colorectal and ovarian cancer.

Tumour Marker 5-HAA

Also known as: HIAA; Serotonin Metabolite.
Formal name: 5-hydroxyindoleacetic Acid.
Related tests: Serotonin; Chromogranin A.

The 5-hydroxyindoleacetic acid (5-HIAA) urine test is used to help diagnose and monitor carcinoid tumours.

Tumour Marker CA-50

CA-50 is not organ-specific and its elevated levels in serum can be observed in a variety of malignancies, especially gastrointestinal cancers.

Moderately high serum levels of CA 50 can also be seen in benign hepatobiliary diseases, especially in jaundice cases.

Tumour Marker Chromogranin A (CgA)

This tumour marker is associated with Neuroendocrine tumours (carcinoid tumours, neuroblastoma). It is one of the most sensitive tumour markers for carcinoid tumours.

Tumour Marker PSA

Tumour marker Prostate Specific Antigen (PSA) is a good marker, very well known, because of its high specificity: found in normal prostatic epithelioma and secretions, but not in other tissues. PSA is normally present, in low concentrations, in every male adult's blood. Produced by normal and abnormal cells of the prostate, it is highly sensitive to the presence of prostate cancer: its increasing is correlated to the tumour grade and its volume.

Prostate Serum Profile (Total + Free PSA)

Free PSA is a newer evaluation for prostate health. Most PSA in the blood is bound to serum proteins, but a small amount is not protein-bound and is called free PSA. In men with prostate cancer, the ratio of free (unbound) PSA to total PSA is decreased.

Prostatic Serum Acid Phos (PCA3)

PCA3 is a molecular diagnostic test performed on urine rather than blood and detects mRNA that is excreted into the urethra via the epithelial cells that line the prostatic ducts. Prostate cancer cells tend to produce this compound far more than normal cells do.

Tumour Marker S-100

S-100 protein continues to be an extremely useful marker especially for soft tissue and peripheral nervous system tumours.

Tumour Marker Thyroglobulin

The measurement of the protein Thyroglobulin (abbreviated Tg) in blood, is an important laboratory test for checking whether a patient still has some thyroid tissue present.

Tumour Marker AFP

Tumour marker AFP - the developing foetus normally produces the alpha-foetoprotein. Its level decreases fast after birth, and normally is not detectable in safe adult's blood (except during

pregnancy). Elevated results of the AFP strongly suggest the presence of primitive liver cancer, or a germinal ovarian or testicular cancer. The AFP's interest lies in cancers of the liver, then ovary and testicle.

Calcitonin Tumour Marker

Also known as: Human Calcitonin; Thyrocalcitonin
Formal name: Calcitonin
The calcitonin test is primarily used to help diagnose C-cell hyperplasia and medullary thyroid cancer, to evaluate the effectiveness of treatment, and to monitor those affected for recurrence. It is also ordered to screen for medullary thyroid cancer in family members of people with multiple endocrine neoplasia type 2 (MEN 2).

Tumour Marker DCP

Its full name is Des-gamma-carboxy prothrombin. It is associated with hepatocellular carcinoma (HCC).

ALK Gene Rearrangements

Transforming rearrangements of the ALK (anaplastic lymphoma kinase) gene have recently been described in non-small cell lung cancer (NSCLC).

BRCA 1 / 2 Tumour Marker

Also known as: BRCA; Breast Cancer Susceptibility Genes 1 and 2. Formal name: Breast Cancer Gene 1 and Breast Cancer Gene 2. Standard *BRCA1* and *BRCA2* tests are used to detect mutations that are known to increase the risk of breast and ovarian cancer development. If a *BRCA1* or *BRCA2* mutation has been identified in a family member with breast and/or ovarian cancer, then that specific mutation can be tested in other family members to assess their risk.

Tumour Marker CA 15-3

Its full name is Cancer Antigen 15-3 or Carbohydrate Antigen 15-3. CA 15-3 is not sensitive or specific enough to be considered useful as a tool for cancer screening. Its main use is to monitor a person's response to breast cancer treatment and to help watch for breast cancer recurrence. CA 15-3 is sometimes ordered to give a doctor a general sense of how much cancer may be present (the tumour burden). CA 15-3 can only be used as a marker if the cancer is producing elevated amounts of it, so this test will not be useful for all people with breast cancer.

This tumour marker is raised in:

- Breast Cancer (often not elevated in the early stages of breast cancer)
- Lung cancer
- Ovarian cancer

- Endometrial cancer
- Bladder cancer
- Gastrointestinal cancer

Tumour Marker 72-4

Tumour marker CA 72-4 - diagnosing gastric carcinoma is often complicated and can be extremely difficult due to presentation with vague, non-specific symptoms that are sometimes associated with non-malignant disease. It is used together with tumour markers CEA and CA 19-9.
(CancerSafe)

Tumour Marker CA 125

Tumour marker CA 125 is a marker for ovarian cancer : the CA 125 is the essential marker for this cancer. It's THE marker in serous adenocarcinomas.

Tumour Marker B2M (Beta-2 microglobulin)

Serum and plasma $beta_2$ microglobulin values have emerged as markers for the activation of the cellular immune system, as well as a tumour marker in certain haematologic malignancies. Urine $beta_2$ microglobulin values indicate renal filtration disorders.

Beta-2 microglobulin tumour marker is used to determine the prognosis and to monitor the success of treatment and to detect recurrence in:

- Multiple myeloma
- Chronic lymphocytic leukaemia (CLL
- Some lymphomas

Tumour Marker hCG

Its full name is Human chorionic gonadotropin, also called Beta-hCG. It is associated with:

- Testicular cancer
- Trophoblastic disease
- Germ cell tumours
- Choriocarcinoma

Tumour Marker JAK2 Mutation

It is associated with certain types of leukaemia. It is used to help diagnose leukaemias. It is also used to diagnose bone marrow disorders characterised by overproduction of one or more types of blood cells known as myelo-proliferativbe neoplasms (MPNs), especially Polycythaemia Vera (PV).

KRAS Mutation Tumour Marker

It is associated with the following cancers:

- Colorectal cancer
- Non-small cell lung cancer

Tumour Marker Lactate Dehydrogenase (LDH)

A lactate dehydrogenase (LD or LDH) test is a non-specific test that may be used in the evaluation of a number of diseases and conditions. LD is an enzyme that is found in almost all of the body's cells (as well as in bacteria) and is released from cells into the fluid portion of blood (serum or plasma) when cells are damaged or destroyed. Thus, the blood level of LD is a general indicator of tissue and cellular damage. The level of LD may also rise in other types of body fluids (e.g. cerebrospinal fluid, pleural fluid, etc.) in the presence of certain diseases.

An LD *blood* test may be used to help stage, determine prognosis, and/or monitor treatment (i.e., chemotherapy) of cancers, such as germ cell tumours (e.g., some types of testicular cancer and ovarian cancer), lymphoma, leukaemia, melanoma, and neuroblastoma

Tumour Marker SMRP

It full name is Soluble Mesothelin-related Peptides. It is associated with mesothelioma (a rare type of cancer associated with asbestos exposure).

T-cell Receptor Gene Rearrangement

This tumour marker is associated with T-cell lymphoma. It is used to detect characteristic changes (rearrangements) in specific genesis T-cells.

Tumour Marker HE 4

Human epididymis protein 4 (HE4) belongs to the family of whey acidic four-disulfide core proteins. HE4 has been shown to be overexpressed in 93% of serous, 100% of endometrioid, and 50% of clear cell ovarian carcinomas.

Beta HCG (Quantitiative) Tumour Marker

Tumour marker BHCG is normally produced by placenta during pregnancy. It is used as pregnancy test, since its level grows fast in first three months. Apart from this field, BHCG is used for testicular cancer, where high levels can be observed; less commonly, ovary, liver, and last, stomach, pancreas and lung.

Marijuana consumption leads to increased levels.

Osteocalcin Tumour Marker

Serum osteocalcin (OC) is derived largely from new cellular synthesis. It is a marker for bone formation and a non-invasive specific marker of osteoblastic activity. The clinical significance of OC is in monitoring prostatic cancer bone metastases.

Some Pathologies and Their Respective Tumour Markers

Breast	CA15-3, CEA, Cyfra 21-1.
Ovary	CEA, CA125, CA 19-9; AFP, BHCG.
Uterine	SCC, Cyfra 21-1 ; CEA, CA 19-9, CA 125.
Prostate	PSA, FPSA and ratio.
Testicle	BHCG, AFP.
Colorectal	CEA, CA 19-9, CA 125.
Pancreas	CEA, CA 19-9, CA 72-4.
Liver	AFP, CEA.
Stomach	CA 72-4, CEA, CA 19-9.
Oesophagus	CEA, Cyfra 21-1.
Thyroid	CEA, NSE.
Lung	NSE, CYFRA 21-1; CEA, CA 125, CA 19-9.
Bladder	TPA, CEA, Cyfra 21-1.

Values of Some Tumour Markers

Range – moderate to high values:

CEA	ng/ml <5 5-10 10->100 000
AFP	ng/ml <15 15-200 200-10 000
PSA	ng/ml <4 4-10 10-1 000
FPSA/PSA	ratio : >0.25 . <0.25 <0.10
CA 15-3	U/ml <40 40-60 60-30 000
CA 19-9	U/ml <35 35-100 100-5 000 000
CA 125	U/ml <35 35-50 50- 50 000
CA 72-4	U/ml <6.7 7-30 30-10 000
BHCG	UI/ml <5 >5 5-500 000
B2M	mg/l <2 >2 2-10
NSE	ng/ml <21 22-40 40-10 000
CYFRA 21	ng/ml <3,5 >3,5 3,5-1000.

Multiple Tumour Marker Tests

Tumour markers are not, by and large, useful diagnostic tests, but more often useful to find the origin of confirmed carcinoma of unknown primary (CUP) or to track the evolution of a confirmed tumour.

Multiple Tumour marker tests will give a more exact result; these are:

- Colorectal: M2-PK, if M2-PK is not available, so can test CEA, CA 19-9, CA 125
- Breast: CEA, CA 15-3, Cyfra 21-1
- Ovary: CEA, CA 19-9, CA 125, AFP, BHCG
- Uterine: CEA, CA 19-9, CA 125, Cyfra 21-1, SCC
- Prostate: PSA, FPSA and ratio
- Testicle: AFP, BHCG
- Pancreas/Stomach: CEA, CA 19-9, CA 72-4
- Liver: CEA, AFP
- Oesophagus: CEA, Cyfra 21-1
- Thyroid: CEA, NSE
- Lung: CEA, CA 19-9, CA 125, NSE, Cyfra 21-1 (Sensitivity at 95 percent percentile for Cyfra 21-1 is 79 percent, while for SCC and CEA are 41 and 31 percent respectively)
- Bladder: CEA, Cyfra 21-1, TPA

Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/ estate/heirs) relating to the use of any information contained in this Fact Sheet.

Whilst CANSA has taken every precaution in compiling this Fact Sheet, neither it, nor any contributor(s) to this Fact Sheet can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet.

Sources and References Consulted or Utilised

Abbou, S.D., Shulman, D.S., DuBois, S.G. & Crompton, B.D. 2019. Assessment of circulating tumor DNA in Pediatric solid tumors: the promise of liquid biopsies. *Pediatr Blood Cancer*, 66 (5), e27595. May 2019.

American Family Physician
http://www.aafp.org/afp/2003/0915/p1075.html

Arai, Y., Takeuchi, H., Oishi, K. & Yoshida, O. 1992. Osteocalcin: is it a useful marker of bone metastasis and response to treatment in advanced prostate cancer? *Prostate*. 1992; 20(3):169-77.

Araujo, D.V., Bratman, S.V. & Siu, L.L. 2019. Designing circulating tumor DNA-based interventional clinical trials in oncology. *Genome Med*, 11 (1), 22. 2019 Apr 19.

Barzaman, K., Karami, J., Zarei, Z., Hosseinzadeh, A., Kazemi, M.H., Moradi-Kalbolandi, S., Safari, E. & Farahmand, L. 2020. Breast cancer: biology, biomarkers, and treatments. *Int Immunopharmacol*. 2020 Jul;84:106535.

Bunworasate, U. & Voravud, N. 1995. CA 50: a tumor marker for gastrointestinal malignancies. *J Med Assoc Thai*. 1995 May;78(5):255-70.

Canadian Cancer Society
http://www.cancer.ca/en/cancer-information/diagnosis-and-treatment/tests-and-procedures/tumour-markers/?region=on

Cancer.Net
http://www.cancer.net/navigating-cancer-care/diagnosing-cancer/tests-and-procedures/tumor-marker-tests

CancerSafe
http://www.cancersafe.com/screening/index.asp

Guadagni,F., Roselli, M., Cosimelli, M., Ferroni, P., Spila, A., Cavaliere, F., Casaldi, V., Wappner, G., Abbolito, M.R. & Greiner, J.W. 1995. CA 72-4 serum marker: a new tool in the management of carcinoma patients. Cancer Invest. 1995. 13(2):227-38.

Lab Tests Online
https://labtestsonline.org/understanding/analytes/ca19-9/tab/test/
https://labtestsonline.org/understanding/analytes/tumor-markers/start/1
https://labtestsonline.org/understanding/analytes/tumor-markers/start/2
https://labtestsonline.org/understanding/analytes/5hiaa/tab/test/
https://labtestsonline.org/understanding/analytes/calcitonin/tab/test/
https://labtestsonline.org/understanding/analytes/brca/tab/test/
https://labtestsonline.org/understanding/analytes/ca15-3/tab/test/
https://labtestsonline.org/understanding/analytes/ldh/tab/test/

LifeExtension
http://www.lifeextension.com/magazine/2013/12/prostate-diagnostic-and-assessment-tests/page-01

Maděrka, M., Pilka, R., Neubert, D. & Hambálek, J. 2019. New serum tumor markers S100, TFF_3 andAIF-1 and their possible use in oncogynecology. *Ceska Gynekol*, 84 (4), 303-308. Summer 2019.

Malhone, C & Longatto-Filho, A. 2019. Cervical, ovarian and endometrial tumor markers: potential clinical value. *Semin Ultrasound CT MR*, 40 (4), 350-357. Aug 2019.

Mayo Clinic
http://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/62137
http://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/88878

Medical Dictionary
http://medical-dictionary.thefreedictionary.com/Tumor+Markers

MedicineNet.Com
http://www.medicinenet.com/script/main/art.asp?articlekey=8722
http://www.medicinenet.com/script/main/art.asp?articlekey=8732

Medscape
http://emedicine.medscape.com/article/2087513-overview#a2
http://emedicine.medscape.com/article/1953022-overview
http://emedicine.medscape.com/article/2086864-overview
http://www.medscape.com/viewarticle/711023_5

National Cancer Institute
http://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis/tumor-markers-fact-sheet

NovaTec
http://www.novatec-id.com/products/tumor-markers/ferritin/

OncoLink.Org
http://www.oncolink.org/treatment/article.cfm?id=296
http://www.oncolink.org/treatment/article.cfm?id=296

Plos.Org
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0019096

Sharma, S. 2009. Tumor markers in clinical practice: general principles and guidelines. *Indian J Med Paediatr Oncol*. 2009 Jan-Mar, 30(1):1-8. Doi: 10.41009756328.13

Schmitt, F.C. & Bacchi, C.E. 1989. S-100 protein: is it useful as a tumour marker in diagnostic immunocytochemistry? Histopathology, 1989. Sep: 15(3):281-8.

Solomon, B., Varella-Garcia, M. & Camidge, D.R. 2009. ALK gene rearrangements: a new therapeutic target in a molecularly defined subset of non-small cell lung cancer. *J Thorac Oncol.* 2009 Dec;4(12):1450-4. doi: 10.1097/JTO.0b013e3181c4dedb.

The Doctors Laboratory
http://www.tdlpathology.com/about-tdl/publications/lab-report-newsletter/spring-2010/tumour-markers

Thyca.Org
http://www.thyca.org/pap-fol/more/thyroglobulin/

Tumour Marker Test
http://www.thesilverpen.com/breast-cancer-information-facts/breast-cancer-diagnosis/tumor-markers/

van Poppel, H., Billen, J., Goethuys, H., Elgamal, A.A., Gerits, M., Mortelmans, L., Blanckaert, N. & Baert, L. 1996. Serum tissue popypeptide antigen (TPA) as tumor marker for bladder cancer. *Anticancer Res*. 1996. Jul-Aug. 16(4B):2205-7.

Walk, E.E., Yohe, S.L., Beckman, A., Schade, A., Zutter, M.M., Pfeifer, J., Berry, A.B. & College of American Pathologists. 2020. The cancer immunotherapy biomarker testing landscape. *Arch Pathol Lab Med*. 2020 Jun;144(6):706-724.

Wikipedia
https://en.wikipedia.org/wiki/Tumor_marker

Wiley Online Library
http://onlinelibrary.wiley.com/doi/10.1111/j.1445-2197.1982.tb05282.x/abstract

Xia, P. & Dubrovska, A. 2020. Tumor markers as an entry for SARS-CoV-2 infection? *FEBS J*. 2020 Sep;287(17):3677-3680.