

Cancer Association of South Africa (CANSA)

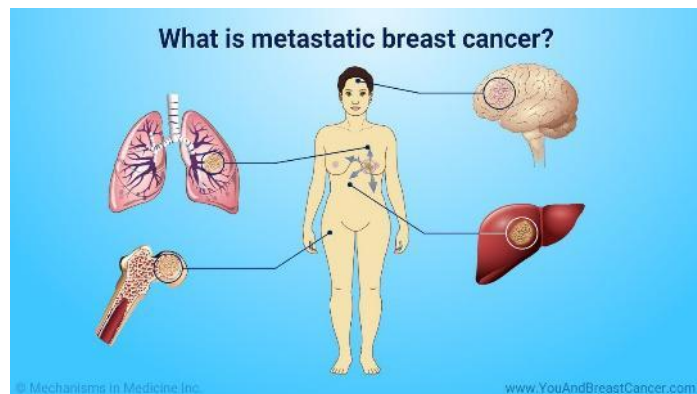


CANSA Fact Sheet on Metastatic Breast Cancer

Introduction

Metastatic breast cancer is cancer that has spread beyond the breast and lymph nodes under the arm. It occurs in both men and women. The most common sites where breast cancer spreads to are the bones, lungs, liver and brain.

[Picture Credit: Metastatic Breast Cancer]



Cancer cells can break away from the original tumour in the breast and travel to other parts of the body through the bloodstream or the lymphatic system, which is a large network of nodes and vessels that works to remove bacteria, viruses, and cellular waste products from the body.

The metastatic tumour in a different part of the body is made up of cells from the breast cancer. For instance, if breast cancer spreads to the bone, the metastatic tumour in the bone is made up of breast cancer cells, not bone cells.

Breast cancer can be "metastatic at diagnosis". This means that the cancer in the breast was not detected before it spread to another part of the body. It is also known as cancer of unknown primary (CUP).

No one dies from breast cancer that remains in the breast. The lump itself is not what kills. The spread of cancerous cells to a vital organ is what kills. This is called metastasis. Metastasis refers to the spread of the cancer to distant organs. When the cancer does so, it is known as metastatic, or stage IV, disease.

Research shows that in about 6 -10 % of all breast cancer patients, the cancer has spread to distant organs and is classified as Stage IV at the time of the first diagnosis. In the majority of patients with metastatic breast cancer, the metastasis is diagnosed after a cancer has already been treated at an earlier stage.

Metastatic breast cancer is also known as 'MBC', stage IV or Advanced Breast Cancer. (National Breast Cancer Foundation, 2025).

Giugliano, F., Giordano, E., Gilardi, L., Salimbeni, B.T., Zagami, P., Esposito, A., Marra, A., Trapani, D., Berton Giachetti, P.P.M., Malagutti, B., Henry, T., Deandreis, D., Curigliano, G., Ceci, F. & Criscitiello, C. 2025.

"Radioligand therapy (RLT) represents a promising advancement in precision oncology and enables the targeted delivery of radiation to cancer cells. This approach has shown success in other tumor types, such as prostate cancer and neuroendocrine tumors. Its potential in metastatic breast cancer (mBC) is currently under investigation. This review discusses RLT mechanism of action, therapeutic potential, and integration into the existing therapeutic landscape of mBC. While clinical trials have shown promising results, challenges remain regarding target heterogeneity, implementation, and optimizing treatment strategies. Further research is essential to integrate RLT into clinical practice and improve patient outcomes fully."

Conflict of interest statement

Declaration of competing interest FG is supported by the ESMO Translational Fellowship 2024-2025. BTS reports personal fees for speaker's bureau from Lilly and for travel from AstraZeneca. AM has received honoraria as a consultant, advisor or speaker from Roche, Eli Lilly and Menarini/Stemline; has received travel and accommodation support from AstraZeneca, and is supported by the ESMO José Baselga Fellowship for Clinician Scientists sponsored by AstraZeneca 2023–2025. GC reports consulting or advisory roles with AstraZeneca, Celucity, Daiichi Sankyo, Ellipsis, Exact Sciences, Gilead, Lilly, MBS, Menarini, Merck, Pfizer, Roche and Veracyte; institutional research funding from Astellas, AstraZeneca, Blueprint Medicine, BMS, Daiichi Sankyo, Kymab, Merck, Novartis, Philogen, Relay Therapeutics, Roche and Sanofi; speaker fees from AstraZeneca, Daiichi Sankyo, Novartis, Pfizer and Roche; and writing engagement with Pfizer. CC reports personal fees for consulting, advisory role and speakers' bureau from Lilly, Roche, Novartis, MSD, Seagen, Gilead and Pfizer. All the competing interests were outside the submitted work. All the other authors declare no potential conflict of interest.

Corti, C., Rugo, H.S. & Tolaney, S.M. 2025.

"The art of sequencing therapy in the management of breast cancer is a multifaceted challenge that demands the careful integration of clinical trial data, real-world evidence, and individualized patient factors to guide treatment decisions. As the therapeutic landscape evolves rapidly with new agents and combinations, clinicians are confronted with critical decisions on how best to order treatments to maximize benefit, minimize toxicity, and preserve future options. For patients with estrogen receptor-positive (ER+) disease, this review discusses how emerging resistance patterns after cyclin-dependent kinase 4 and 6 inhibitors require careful re-evaluation of subsequent endocrine and targeted therapies, as well as chemotherapy, emphasizing the need for evidence-based strategies and ethical crossover designs in clinical trials. In addition, for both ER+ and ER- metastatic breast cancer (MBC) with nonoverexpressed human epidermal growth factor receptor 2 (HER2), this review highlights pivotal trials investigating antibody-drug conjugates (ADCs)-including trastuzumab deruxtecan, sacituzumab govitecan, and datopotamab deruxtecan-and the challenges related to control arm selection and crossover that may affect outcome interpretation. Finally, for patients with HER2-positive disease, the review explores first-line and maintenance strategies-including insights from landmark trials like CLEOPATRA and PATINA-and addresses the impact of brain metastases on

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sequencing decisions. By critically appraising current data and identifying gaps in biomarker-guided and sequencing-specific strategies, this review provides practical insights to inform clinical practice and optimize personalized treatment plans for patients with MBC.”

Tumour Grade vs Tumour Stage

A cancer’s grade describes how abnormal the cancer cells and tissue look under a microscope when compared to healthy cells. Cancer cells that look and organise most like healthy cells and tissue are low grade tumours. Doctors describe these cancers as being well differentiated. Lower grade cancers are typically less aggressive and have a better prognosis.

While a grade describes the appearance of cancer cells and tissue, a cancer’s stage explains how large the primary tumour is and how far the cancer has spread in the patient’s body.

There are several different staging systems. Many of these have been created for specific kinds of cancers. Others can be used to describe several types of cancer.

One common system that many people are aware of puts cancer on a scale of 0 to IV.

- Stage 0 is for abnormal cells that haven’t spread and are not considered cancer, though they could become cancerous in the future. This stage is also called “in-situ.”
- Stage I through Stage III are for cancers that haven’t spread beyond the primary tumour site or have only spread to nearby tissue. The higher the stage number, the larger the tumour and the more it has spread.
- Stage IV cancer has spread to distant areas of the body.

(University of Texas, MD Anderson Cancer Center. 2025).

The International Classification of Disease 10th Version (ICD-10)

The International Classification of Diseases (ICD) is designed to promote international comparability in the collection, processing, classification, and presentation of mortality statistics. This includes providing a format for reporting causes of death on the death certificate.

ICD serves a broad range of uses globally and provides critical knowledge on the extent, causes and consequences of human disease and death worldwide via data that is reported and coded with the ICD. Clinical terms coded with ICD are the main basis for health recording and statistics on disease in primary, secondary and tertiary care, as well as on cause of death certificates. These data and statistics support payment systems, service planning, administration of quality and safety, and health services research. Diagnostic guidance linked to categories of ICD also standardizes data collection and enables large scale research.

For more than a century, the International Classification of Diseases (ICD) has been the basis for comparable statistics on causes of mortality and morbidity between places and over time. Originating

in the 19th century, the latest version of the ICD, ICD-11, was adopted by the 72nd World Health Assembly in 2019 and came into effect on 1st January 2022.

The ICD-10 Code for secondary malignant neoplasm of breast – C79.81.
(World Health Organization, 2025).

Incidence of Metastatic Breast Cancer in South Africa

According to the latest edition of the National Cancer Registry (2024) the following number of breast cancer cases in women was histologically diagnosed during 2024:

Group	Actual Number of Cases	Estimated Lifetime Risk	Percentage of All Cancers
2024			
All females	11 262	1:28	23,05%
Asian females	509	1:22	37,22%
Black females	5 305	1:46	22,53%
Coloured females	1 643	1:19	29,69%
White females	3 805	1:11	20,21%

Frequency of Histologically Diagnosed Cases of Breast Cancer

According to the latest edition of the National Cancer Registry (2024), the frequency of histologically diagnosed cases of breast cancer in women in South Africa is as follow:

Group	0 to 19 Years	20 to 29 Years	30 to 39 Years	40 to 49 Years	50 to 59 Years	60 to 69 Years	70 to 79 Years	80 + Years
2024								
All females	6	155	1 094	2 314	2 666	2 517	1 737	773
Asian females	0	8	35	84	129	131	91	31
Black females	4	113	761	1 393	1 316	996	494	226
Coloured females	1	18	113	307	424	407	262	111
White females	1	16	185	530	795	983	890	405

The Role of BRCA Gene Mutation

BRCA is an abbreviation originating from Br(east) Ca(ncer) and are tumour suppressor genes. Every cell in a human body contains them. There are two types: BRCA1 and BRCA2. Their main function in the body is to repair DNA, keep other genes healthy, and prevent cancerous changes. These genes can become mutated.

A mutation is a change in the gene which makes the gene stop doing its main function, therefore, no longer keeping abnormal cell growth in check. These changes (mutations) can be inherited or passed on from parents, grandparents, and great grandparents.

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If someone has a gene mutation, their risk of cancer increases.

Anyone can have a BRCA gene mutation. Though, they are more commonly found in certain ethnic groups, including Ashkenazi Jews, Afrikaners, French Canadians, and people of Icelandic backgrounds.

The most common cancers that can result from BRCA gene mutations are breast cancer, ovarian cancer, and prostate cancer. The full list includes.

WOMEN

BRCA1

Breast cancer
Ovarian cancer
Pancreatic cancer

BRCA2

Breast cancer
Ovarian cancer
Pancreatic cancer
Melanoma

MEN

BRCA1

Breast cancer
Prostate cancer
Pancreatic cancer

BRCA2

Breast cancer
Prostate cancer
Melanoma
Pancreatic cancer

If someone has a BRCA mutation, they may pass the mutation to their children. Each child has a 50% chance of inheriting their parents' BRCA gene mutation. One's siblings may also have inherited the BRCA gene mutation.
(National Cancer Institute, 2022)

Signs and Symptoms of Metastatic Breast Cancer

Signs and symptoms of metastatic breast cancer can include:

- Constant fatigue
- Numbness and weakness in various body parts
- Loss of appetite
- Nausea and vomiting
- Unplanned loss of weight
- Severe headaches
- Seizures
- Loss of balance
- Confusion

(Renew Cure, 2026; Breastcancer.org, 2026).

Diagnosis of Metastatic Breast Cancer

A metastatic tumour is always caused by cancer cells from another part of the body.

In most cases, when a metastatic tumour is found first, the primary cancer can also be found. The search for the primary cancer may involve laboratory tests, X-rays, computed tomography (CT) scans, magnetic resonance imaging (MRI) scans, positron emission tomography (PET) scans, and other procedures.

However, in some patients, a metastatic tumour is diagnosed but the primary tumour cannot be found, despite extensive tests, because it either is too small or has completely regressed. The pathologist knows that the diagnosed tumour is a metastasis because the cells do not look like those of the organ or tissue in which the tumour was found. Doctors refer to the primary cancer as unknown or occult (hidden), and the patient is said to have cancer of unknown primary (CUP).

Some women have metastatic breast cancer when they are first diagnosed, but this is not common (approximately five percent of diagnoses). More commonly, metastatic breast cancer arises months or years after a person has completed treatment for early or locally advanced (stage I, II or III) breast cancer. This is sometimes called distant recurrence.

Some people with metastatic tumours do not have symptoms. Their metastases are found by X-rays or other tests.

When symptoms of metastatic cancer occur, the type and frequency of the symptoms will depend on the size and location of the metastasis. For example, cancer that spreads to the bone is likely to cause pain and can lead to bone fractures. Cancer that spreads to the brain can cause a variety of symptoms, including headaches, seizures, and unsteadiness. Shortness of breath may be a sign of lung metastasis. Abdominal swelling or jaundice (yellowing of the skin) can indicate that cancer has spread to the liver.

Sometimes a person's original cancer is discovered only after a metastatic tumour causes symptoms.

Diagnosis of metastatic breast cancer may include:

- biopsy of any suspicious area
- Blood tests which may include tumour markers
- bronchoscopy, if the patient has a constant cough or trouble breathing
- Computed Tomography (CT) scans (chest, abdomen, pelvis, and/or brain)
- Magnetic resonance imaging (MRI) of the spine or brain
- Positron Emission Tomography (PET) scan
- X-ray or ultrasound of the abdomen or chest

(Johns Hopkins Medicine, 2026; Breast Cancer.org, 2026; National Breast Cancer Foundation, 2025).

Treatment of Metastatic Breast Cancer

Treatments for metastatic and earlier-stage breast cancer are very different. For earlier-stage breast cancer - particularly for women who are relatively young and healthy - doctors will often advise a very

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aggressive, rigorous course of treatment aimed at getting rid of the cancer completely. The side effects can be difficult, but there is a finish line in sight: initial breast cancer treatment usually lasts no more than six to nine months.

With metastatic cancer, some form of treatment will be a fact of life, more or less, as from the date of commencement of treatment. This means the treatment philosophy changes. The aim of treatment changes to gain maximal control of the tumour at the lowest possible cost in terms of toxicity.

Research shows that Metastatic Breast Cancer is best treated by a team of specialists. The medical team may include:

- surgeon: performs biopsies and other procedures and removes single metastatic cancers
- medical oncologist: specialises in chemotherapy, hormonal therapy, targeted therapies, pain medications, and nutritional support
- radiation oncologist who is a person that specialises in radiation therapy
- radiologist: takes and interprets mammograms, ultrasounds, bone scans, CT scans, MRIs, PET scans, and other tests to determine the location and size of the cancer and to help determine how the cancer is responding to treatment
- pathologist: examines the biopsy sample and conducts special tests on cancer tissue to determine the characteristics of the cancer such as hormone-receptor status and HER2 status.

It may seem logical to assume that metastatic breast cancer has the same hormone-receptor status and HER2 status as the original cancer. Research has shown that the "personality" of the recurrent or metastatic cancer may be different than the original cancer. For example, the hormone-receptor status may change from hormone-receptor-positive to hormone-receptor-negative or *vice versa*. The HER2 status also may be different than the original breast cancer. If either of these factors have changed, they can affect the treatment plan.

A mutation in the oestrogen receptor 1 (*ESR1*) gene portends a worse prognosis among patients with oestrogen receptor (ER)-positive, metastatic breast cancer. A mutation in this gene may confer resistance to aromatase inhibitor (AI) therapy.

(Dana-Faber Cancer Institute, 2025; Breast Cancer.org, 2026; Cleveland Clinic, 2023; Mayo Clinic, 2025).

Pain Control and Palliation for Metastatic Breast Cancer

With metastatic breast cancer, pain can be related to treatment or the cancer itself. Pain is not the same for everyone. Even among people at a similar stage of disease, pain can vary. Some people have more intense and more frequent pain than others.

One should never feel pain is simply a part of one's treatment or that one should be strong and endure it. Even when pain is mild, it can interfere with daily life and make other side effects, such as fatigue,

seem worse. Let the health care provider(s) know about any pain or discomfort that may be experienced.

Pain is usually easier to treat when one first has it. Waiting until the pain is severe before getting relief can make it harder to control and may require more medication. That is why it is so important to talk with one's health care provider about pain. Sometimes, treatment plans can be changed to reduce painful side effects.

Every visit with one's health care provider should include a discussion of pain. The health care provider can change the type and dose of pain medication throughout one's care in response to specific needs.

A health care provider may also suggest other types of pain control as needs change. This ensures one is getting the most benefit from available therapies and is as comfortable as possible.

Palliative care and pain specialists (physicians, nurse practitioners and nurses) treat pain from cancer or other causes. They can treat people with early breast cancer as well as those with metastatic cancer.

Palliative medicine is a medical specialty, just like oncology. Palliative care specialists give extra care to help people maintain the best quality of life possible. They have special training in pain management and symptom management.

Be sure to ask the oncologist for a referral if pain is not controlled or in the event of having side effects from the pain medications. The provider should be able to follow the specialist's recommendations and carry out the pain management. If the treatment is effective, one should not need to see the specialist again.

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: <https://pactr.samrc.ac.za/>

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Summary for the Average Reader

Metastatic breast cancer (MBC), also known as Stage IV or advanced breast cancer, occurs when cancer cells from the breast travel through the bloodstream or lymphatic system to form new tumours in distant organs. While it is currently considered incurable, it is highly treatable, and medical advances allow many people to manage it as a chronic illness for years.

Key Sites and Symptoms

Symptoms vary based on where the cancer has spread. The most common locations include:

- **Bones:** Progressive bone pain, joint swelling, or fractures that occur without injury.
- **Liver:** Jaundice (yellowing of skin/eyes), abdominal pain, nausea, and loss of appetite.
- **Lungs:** Constant dry cough, shortness of breath, or persistent chest pain.
- **Brain:** Persistent headaches, vision changes, seizures, or personality shifts.

Diagnosis and Subtypes

Diagnosis typically involves imaging (CT, PET, MRI) and a biopsy of the new tumour. This is critical because the cancer's characteristics—such as Hormone Receptor (HR) status and HER2 status—can change from the original diagnosis, which directly impacts treatment options.

Treatment Strategies

Treatment focuses on controlling tumour growth and maintaining quality of life.

- **Systemic Therapies:** These travel throughout the body and include chemotherapy, hormone therapy, immunotherapy, and targeted therapies (like CDK4/6 or PARP inhibitors).
- **Local Treatments:** Surgery or radiation may be used specifically to relieve symptoms, such as radiating a bone lesion to prevent fractures or reduce pain.
- **Palliative Care:** Often started alongside active treatment to manage side effects and emotional well-being.

Survival and Outlook

The 5-year relative survival rate is approximately 31-32%. However, outcomes are highly individual. Some patients, particularly those with HR+ and HER2-negative subtypes, may live 10 years or more. For personalized support, organizations like the National Breast Cancer Foundation and Susan G Komen offer dedicated resources and support groups. (AID Overview, 2026).

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.

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