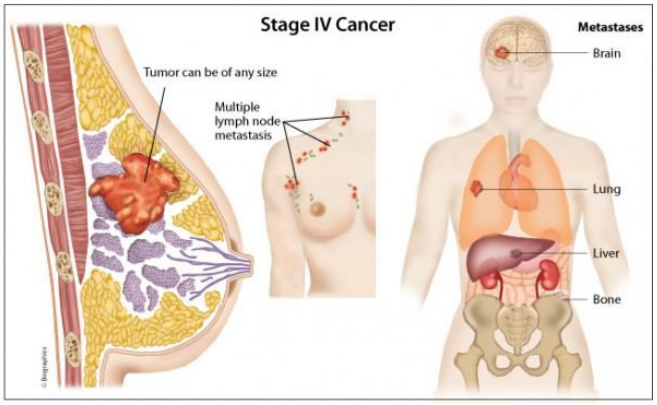
Cancer Association of South Africa (CANSA)

Research • Educate • Support

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: Stage IV]

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. (Metastatic Breast Cancer Network).

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Incidence of Metastatic Breast Cancer in South Africa
The South African National Cancer Registry (2012) does not provide information about metastatic breast cancer.

According to the National Cancer Registry (2012) the following number of breast cancer cases in women was histologically diagnosed during 2012:

Group 2012	Actual Number of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	8 203	1 : 26	22,79%
Asian females	446	1 : 16	41,07%
Black females	3 415	1 : 45	20,68%
Coloured females	1 158	1 : 17	27,76%
White females	3 184	1 : 12	10,06%

Frequency of Histologically Diagnosed Cases of Breast Cancer
According to the National Cancer Registry (2012), the frequency of histologically diagnosed cases of breast cancer in women in South Africa is as follow:

Group 2012	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
All females	4	59	646	1 567	1 958	1 873	1 289	375
Asian females	0	6	32	70	101	116	71	21
Black females	3	37	377	804	842	596	411	213
Coloured females	1	4	74	216	296	269	180	97
White females	0	10	155	453	689	866	610	334

It must be noted that correct cancer figures will only be available as from the 2012 statistics because it only became an obligation to report all cases of cancer to the National Cancer Registry during 2011.

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.
(National Cancer Institute; Susan G Komen).

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 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.
(WebMD).

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: 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 "personality" of the cancer (characteristics 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.
(BreastCancer.Org).

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. Therapeutic strategies that appear to confer an advantage in at least some of these patients may include the addition of palbociclib or everolimus to standard treatment regimens.

The prevalence of the Y537S and D538G mutations in *ESR1* in patients with advanced, ER-positive breast cancer is more common than previously appreciated.
(MedPage Today).

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Preferred Single Agents[1]

NOTE: All recommendations are category 2A unless otherwise indicated.

REGIMEN	DOSING
Doxorubicin[2,3]	**Day 1:** Doxorubicin 60–75mg/m^2 IV.Repeat cycle every 21 days. **or** **Day 1:** Doxorubicin 20mg/m^2 IV. Repeat cycle weekly.
Pegylated liposomal doxorubicin[4]	**Day 1:** Pegylated liposomal doxorubicin 50mg/m^2 IV. Repeat cycle every 28 days
Paclitaxel[5,6]	**Day 1:** Paclitaxel 175mg/m^2 IV. Repeat cycle every 21 days. **or** **Day 1:** 80mg/m^2 IV. Repeat cycle weekly.
Capecitabine[7]	**Days 1–14:** Capecitabine 1,000–1,250mg/m^2 orally twice daily. Repeat cycle every 21 days.
Gemcitabine[8]	**Days 1, 8, and 15:** Gemcitabine 800–1,200mg/m^2 IV. Repeat cycle every 28 days.
Vinorelbine[9]	**Day 1:** Vinorelbine 25mg/m^2 IV. Repeat cycle weekly.
Eribulin[10]	**Days 1 and 8:** Eribulin 1.4mg/m^2 IV. Repeat cycle every 21 days.

Other Single Agents[1]

Cyclophosphamide[11]	**Days 1–21:** Cyclophosphamide 50mg orally daily. Repeat cycle every 28 days.
Carboplatin[12]	**Day 1:** Carboplatin AUC 6mg • min/mL IV. Repeat cycle every 21–28 days.
Docetaxel[13-15]	**Day 1:** Docetaxel 60–100mg/m^2 IV. Repeat cycle every 21 days. **or** **Day 1:** Docetaxel 35mg/m^2 IV. Repeat cycle weekly for 6 weeks followed by a 2-week rest, then repeat.

Albumin-bound paclitaxel[16,17]	**Days 1, 8, and 15:** Albumin-bound paclitaxel 100mg/m^2 or 125mg/m^2 IV. Repeat cycle every 28 days. **or** **Day 1:** Albumin-bound paclitaxel 260mg/m^2 IV. Repeat cycle every 21 days.
Cisplatin[18]	**Day 1:** Cisplatin 75mg/m^2 IV. Repeat cycle every 21 days.
Epirubicin[19]	**Day 1:** Epirubicin 60–90mg/m^2 IV. Repeat cycle every 21 days.
Ixabepilone[20]	**Day 1:** Ixabepilone 40mg/m^2 IV. Repeat cycle every 21 days.
Chemotherapy Combinations[1]	
CAF[21]	**Days 1–14:** Cyclophosphamide 100mg/m^2 orally **Days 1 and 8:** Doxorubicin 30mg/m^2 IV **Days 1 and 8:** 5-fluorouracil 500mg/m^2 IV. Repeat cycle every 28 days.
FAC[22]	**Days 1 and 8 OR 1 and 4:** 5-fluorouracll 500mg/m^2 IV **Day 1:** Doxorubicin 50mg/m^2 IV (or by 72-hour continuous infusion) **Day 1:** Cyclophosphamide 500mg/m^2 IV. Repeat cycle every 21 days.
FEC[23]	**Days 1 and 8:** Cyclophosphamide 400mg/m^2 IV **Days 1 and 8:** Epirubicin 50mg/m^2 IV **Days 1 and 8:** 5-fluorouracil 500mg/m^2 IV. Repeat cycle every 28 days.
AC[24]	**Day 1:** Doxorubicin 60mg/m^2 IV **Day 1:** Cyclophosphamide 600mg/m^2 IV. Repeat cycle every 21 days.
EC[25]	**Day 1:** Epirubicin 75mg/m^2 IV **Day 1:** Cyclophosphamide 600mg/m^2 IV. Repeat cycle every 21 days.
CMF[26]	**Days 1–14:** Cyclophosphamide 100mg/m^2 orally **Days 1 and 8:** Methotrexate 40mg/m^2 IV **Days 1 and 8:** 5-fluorouracll 600mg/m^2 IV. Repeat cycle every 28 days.
Docetaxel + capecitabine[27]	**Day 1:** Docetaxel 75mg/m^2 IV **Days 1–14:** Capecitabine 950mg/m^2 orally twice daily. Repeat cycle every 21 days.
GT[28]	**Day 1:** Paclitaxel 175mg/m^2 IV **Days 1 and 8:** Gemcitabine 1,250mg/m^2 IV (following paclitaxel on day 1). Repeat cycle every 21 days.
Gemcitabine + carboplatin[29]	**Days 1 and 8:** Gemcitabine 1,000mg/m^2 **Days 1 and 8:** Carboplatin AUC 2mg • min/mL IV. Repeat cycle every 21 days.
Paclitaxel + bevacizumab[30]	**Days 1, 8, and 15:** Paclitaxel 90mg/m^2 by 1-hour IV **Days 1 and 15:** Bevacizumab 10mg/kg IV days 1 and 15. Repeat cycle every 28 days.

Preferred First-Line Agents for HER2-Positive Disease[1]	
General treatment note: All trastuzumab-containing regimens require cardiac monitoring at baseline and at 3, 6, and 9 months.[1]	
Pertuzumab + trastuzumab + docetaxel (Category 1)[31]	**Day 1:** Pertuzumab 840mg IV followed by 420mg IV **Day 1:** Trastuzumab 8mg/kg IV followed by 6mg/kg IV **Day 1:** Docetaxel 75–100mg/m^2 IV. Repeat cycle every 21 days.
Pertuzumab + trastuzumab + paclitaxel[32,33]	**Day 1:** Pertuzumab 840mg IV followed by 420mg IV cycled every 21 days, **plus** **Day 1:** Trastuzumab 4mg/kg IV followed by 2mg/kg IV weekly **OR**trastuzumab 8mg/kg IV followed by 6mg/kg IV cycled every 21 days, **plus** **Day 1:** Paclitaxel 80mg/m^2 IV weekly **OR** paclitaxel 175mg/m^2 cycled every 21 days.
Other First-Line Agents For HER2-Positlve Disease[1]	
Ado-trastuzumab emtansine (T-DM1)[34]	**Day 1:** Ado-trastuzumab emtansine 3.6mg/kg IV. Repeat cycle every 21 days.
Paclitaxel + carboplatin + trastuzumab[33,35]	**Day 1:** Carboplatin AUC 6mg • min/mL IV **Day 1:** Paclitaxel 175mg/m^2 IV cycled every 21 days, **plus** **Day 1:** Trastuzumab 4mg/kg IV followed by 2mg/kg IV weekly **OR** **Day 1:** Trastuzumab 8mg/kg IV followed by 6mg/kg IV every 21 days.
Weekly paclitaxel + carboplatin + trastuzumab[33,36]	**Days 1, 8, and 15:** Paclitaxel 80mg/m^2 IV **plus** carboplatin AUC 2mg •min/mL cycled every 21 days, **plus** **Day 1:** Trastuzumab 4mg/kg IV followed by 2mg/kg IV weekly **OR** **Day 1:** Trastuzumab 8mg/kg IV followed by 6mg/kg IV every 21 days.
Trastuzumab + paclitaxel[33,37,38]	**Day 1:** Paclitaxel 175mg/m^2 IV cycled every 21 days **OR** **Day 1:** Paclitaxel 80–90mg/m^2 IV weekly, **plus** **Day 1:** Trastuzumab 4mg/kg IV followed by 2mg/kg IV weekly **OR** **Day 1:** Trastuzumab 8mg/kg IV followed by 6mg/kg IV every 21 days.
Trastuzumab + docetaxel[33,39,40]	**Day 1:** Docetaxel 80–100mg/m^2 IV cycled every 21 days **OR** **Days 1, 8, and 15:** Docetaxel 35mg/m^2 IV weekly, **plus** **Day 1:** Trastuzumab 4mg/kg IV followed by 2mg/kg IV weekly **OR** **Day 1:** Trastuzumab 8mg/kg IV followed by 6mg/kg IV every 21 days.
Trastuzumab + vinorelbine[33,41]	**Day 1:** Vinorelbine 25mg/m^2 IV weekly **OR** **Days 1 and 8:** Vinorelbine 30-35mg/m^2 IV cycled every 21 days, **plus** **Day 1:** Trastuzumab 4mg/kg IV followed by 2mg/kg IV

	weekly **OR** **Day 1:** Trastuzumab 8mg/kg IV followed by 6mg/kg IV every 21 days.
Trastuzumab + capecitabine[33,42,43]	**Days 1–14:** Capecitabine 1,000–1,250mg/m^2 orally twice daily cycled every 21 days, **plus** **Day 1:** Trastuzumab 4mg/kg IV followed by 2mg/kg IV weekly **OR** **Day 1:** Trastuzumab 8mg/kg IV followed by 6mg/kg IV every 21 days.
Agents for Trastuzumab-Exposed HER2-Positive Disease[1]	
Lapatinib + capecitabine[44]	**Days 1–21:** Lapatinib 1,250mg orally daily **Days 1–14:** Capecitabine 1,000mg/m^2 orally twice daily. Repeat cycle every 21 days.
Trastuzumab + capecitabine[33,37,43,45]	**Days 1–14:** Capecitabine 1,000–1,250mg/m^2 orally twice daily cycled every 21 days, **plus** **Day 1:** Trastuzumab 4mg/kg IV followed by 2mg/kg IV weekly **OR** **Day 1:** Trastuzumab 8mg/kg IV followed by 6mg/kg IV every 21 days.
Trastuzumab + lapatinib[33,46]	Lapatinib 1,000mg orally daily, **plus** **Day 1:** Trastuzumab 4mg/kg IV followed by 2mg/kg IV weekly **OR** **Day 1:** Trastuzumab 8mg/kg IV followed by 6mg/kg IV every 21 days.

(Cancer Therapy Advisor).

How Cancer Kills

Not all cancers kill. Overall, more than 50% of people diagnosed with cancer live for more than 5 years. Some cancers have survival rates of more than 90%.

Early stage cancer also does not kill. It is for this reason that early diagnosis is so important – it is during early stage cancer that treatment is likely to work best.

Cancers can cause death in more than one way. There is, therefore, no single answer to the question of how cancer kills. It really depends on the type of cancer one has and which parts of the body are affected. There are some examples below.

Some types of cancer can spread to take over part of the body that does something essential for life. For example, if a cancer is growing in part of the digestive system, it can block it so that food cannot go through the intestines. If food cannot pass through, then the food cannot be absorbed.

If cancer affects the lungs, then eventually there is not enough healthy lung tissue to allow one to absorb enough oxygen and give off carbon dioxide. The cancer can also block off part of the lung. This part then collapses and often becomes infected. If one has advanced

cancer, one may not have the strength to fight off an infection, even with strong antibiotics. So the infection can eventually lead to death.

The human body has very finely balanced limits of certain body salts and chemicals. A cancer that has spread to the liver or bones can upset this chemical balance. The liver is the chemical factory of the body. It carries out many different tasks and is very important in maintaining the balance of body chemicals.

Cancer in the bones can affect the calcium balance of the body. If calcium levels go up or down in the blood, it upsets the whole chemical balance. Cancer in the bones can cause a lot of calcium to be released into the bloodstream. Normally the body has systems to correct this sort of imbalance. But when the imbalance becomes too great the systems do not work anymore. There is treatment to bring calcium levels back to normal, but these only work for a limited time. Then unfortunately the calcium levels will rise in the blood. If calcium continues to go up, it will cause the patient to become unconscious and eventually die.

If cancer cells take over the bone marrow, eventually the person will not have enough healthy bone marrow to make blood cells. In this event the person will not have enough red blood cells and will not have enough oxygen circulating around the body.

A drop in white blood cells means the patient has less resistance to infection. A drop in platelets means the patient is at greater risk of abnormal bleeding. If a blood vessel in a vital part of the body is damaged it can be life threatening. For example bleeding in the brain is a stroke, which can be fatal if the body cannot control it.

Some cancers make particular substances which upset the body balance. This can cause problems such as severe weight loss or dehydration, which will eventually overwhelm the natural balancing systems of the body.

Many treatments can control cancer for a long time, even if they cannot cure it. But if a cancer continues to grow, then unfortunately it can become too much for the body to cope with.
(Cancer Research UK).

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.
(Susan G Komen).

Living With Cancer

The first few months of cancer treatment are a time of change. But when one is living with cancer that does not go away it may feel like one is stuck in this change – not knowing what to expect or what is going to happen next.

Living with cancer is not so much about 'getting back to normal' as it is learning what is 'normal' now. People often say that life has new meaning or that they look at things differently now. Every day takes on new meaning.

One's new 'normal' may include making changes in the way one eats, the things one does, and one's sources of support. It may mean fitting cancer treatments into one's work and vacation schedule. It will mean making treatment part of everyday life – treatments that one may be getting for the rest of one's life.

Repeated recurrences, often with shorter time periods in between remissions, can become discouraging and exhausting. It can be even more discouraging if the cancer never goes away at all. The question of whether to keep treating cancer that does not go away or comes back again and again is a valid one. One's choices about continuing treatment are personal and based on own needs, wishes, and abilities. There is no right or wrong decision on how to handle this phase of the illness.

Still, it is important to know that even those who are not cured of cancer may go on living for months or years, even though there may be changes in their lives. Many families adjust to this kind of treatment schedule.

Having a cancer that cannot be cured does not put one beyond hope or help; it may merely be living with a disease that can be treated and controlled for a fairly long time.
(American Cancer Society).

Psychological Intervention
Psychological symptoms are associated with metastatic breast cancer.

The researchers identified ten randomised control trials (RCTs) involving 1 378 women. Of the seven RCTs on group psychological interventions, three were on cognitive behavioural therapy and four were on supportive-expressive group therapy. The remaining three studies were individual based and the types of psychological interventions were not common to either cognitive behavioural or supportive-expressive therapy.

A clear pattern of psychological outcomes could not be discerned as a wide variety of outcome measures and durations of follow-up were used in the included studies. The overall effect of the psychological interventions across six studies, on one-year survival, favoured the psychological intervention group with an odds ratio (OR) of 1.46 (95% confidence interval (CI) 1.07 to 1.99). Pooled data from four studies did not show any survival benefit at five-years follow-up (OR 1.03, 95% CI 0.42 to 2.52). There was evidence of a short-term benefit for some psychological outcomes and improvement in pain scores.

Psychological interventions appear to be effective in improving survival at 12 months but not at longer-term follow-up, and they are effective in reducing psychological symptoms only in some of the outcomes assessed in women with metastatic breast cancer.

Findings of the review should be interpreted with caution as there is a relative lack of data in this field, and the included trials had reporting or methodological weaknesses and were heterogeneous in terms of interventions and outcome measures.
(Mustafa, *et al*., 2013).

Living With Uncertainty
Here are some ideas that have helped others feel more hopeful and deal with the uncertainty and fear of cancer that does not go away:

- Be informed. Learn what can be done for one's health now and about the services available to self and loved ones. This can give a greater sense of control.
- Be aware that one does not have control over some aspects of one's cancer. It helps to accept this rather than fight it.
- Be aware of own fears, but practice letting them go. It is normal for these thoughts to enter one's mind, but do not keep them there. Some people picture them floating away, or being vaporised. Others turn them over to a higher power to handle. However it is done, letting them go can free one from wasting time and energy needlessly worrying.
- Express feelings of fear or uncertainty with a trusted friend or counsellor. Being open and dealing with emotions helps many people feel less worried and better able enjoy each day. People have found that when they express strong feelings, like anger and fear, they are better able to let go of these feelings. Thinking and talking about feelings can be hard. If it feels like cancer is taking over one's life, it may be helpful to find a way to express one's feelings.
- Enjoy the present moment rather than thinking of an uncertain future or a difficult past. If one can find a way to be peaceful inside oneself, even for a few minutes a day, one can start to recall that peace when other things are happening – when life is busy, scary, and confusing.

- Make time for what one really wants. One may find oneself thinking about all the things one has always wanted to do but never made time for. It is OK to pursue these things, and do not forget to enjoy everyday pleasures and have fun, too.
- Work toward having a positive attitude, which can help one feel better about life even if a cure is out of reach. Nearly everyone can find things to feel grateful for or hopeful about. But do not try to be upbeat or positive all the time – no one is! One needs to pay attention to one's feelings, even the so-called "negative" ones. Bad days are allowed - feel sad or angry - or grieve whenever there is a need to.
- Use energy to focus on what one can do now to stay as healthy as possible. Try to make smart choices in what to eat. If smoking, this is a good time to quit, and encourage others to quit as well.
- Find ways to relax and enjoy time alone and with others.
- Exercise and be as active as possible. Talk with the cancer care team about what is realistic.

Control what can be controlled. Some people say that putting their lives in order makes them feel less fearful. Being involved in one's health care, trying to find a 'new normal', and making changes in one's lifestyle are among the things one can control. Even setting a daily schedule can give more power. And while no one can control every thought, some say they have resolved to not dwell on the fearful ones.
(American Cancer society).

About Clinical Trials
Clinical trials are research studies that involve people. These studies test new ways to prevent, detect, diagnose, or treat diseases. People who take part in cancer clinical trials have an opportunity to contribute to scientists' knowledge about cancer and to help in the development of improved cancer treatments. They also receive state-of-the-art care from cancer experts.

Types of Clinical Trials
Cancer clinical trials differ according to their primary purpose. They include the following types:

Treatment - these trials test the effectiveness of new treatments or new ways of using current treatments in people who have cancer. The treatments tested may include new drugs or new combinations of currently used drugs, new surgery or radiation therapy techniques, and vaccines or other treatments that stimulate a person's immune system to fight cancer. Combinations of different treatment types may also be tested in these trials.

Prevention - these trials test new interventions that may lower the risk of developing certain types of cancer. Most cancer prevention trials involve healthy people who have not had cancer; however, they often only include people who have a higher than average risk of developing a specific type of cancer. Some cancer prevention trials involve people who have had cancer in the past; these trials test interventions that may help prevent the return (recurrence) of the original cancer or reduce the chance of developing a new type of cancer.

Screening - these trials test new ways of finding cancer early. When cancer is found early, it may be easier to treat and there may be a better chance of long-term survival. Cancer screening trials usually involve people who do not have any signs or symptoms of cancer. However, participation in these trials is often limited to people who have a higher than

average risk of developing a certain type of cancer because they have a family history of that type of cancer or they have a history of exposure to cancer-causing substances (e.g., cigarette smoke).

Diagnostic - these trials study new tests or procedures that may help identify, or diagnose, cancer more accurately. Diagnostic trials usually involve people who have some signs or symptoms of cancer.

Quality of life or supportive care - these trials focus on the comfort and quality of life of cancer patients and cancer survivors. New ways to decrease the number or severity of side effects of cancer or its treatment are often studied in these trials. How a specific type of cancer or its treatment affects a person's everyday life may also be studied.

Where Clinical Trials are Conducted

Cancer clinical trials take place in cities and towns in doctors' offices, cancer centres and other medical centres, community hospitals and clinics. A single trial may take place at one or two specialised medical centres only or at hundreds of offices, hospitals, and centres.

Each clinical trial is managed by a research team that can include doctors, nurses, research assistants, data analysts, and other specialists. The research team works closely with other health professionals, including other doctors and nurses, laboratory technicians, pharmacists, dieticians, and social workers, to provide medical and supportive care to people who take part in a clinical trial.

Research Team

The research team closely monitors the health of people taking part in the clinical trial and gives them specific instructions when necessary. To ensure the reliability of the trial's results, it is important for the participants to follow the research team's instructions. The instructions may include keeping logs or answering questionnaires. The research team may also seek to contact the participants regularly after the trial ends to get updates on their health.

Clinical Trial Protocol

Every clinical trial has a protocol, or action plan, that describes what will be done in the trial, how the trial will be conducted, and why each part of the trial is necessary. The protocol also includes guidelines for who can and cannot participate in the trial. These guidelines, called eligibility criteria, describe the characteristics that all interested people must have before they can take part in the trial. Eligibility criteria can include age, sex, medical history, and current health status. Eligibility criteria for cancer treatment trials often include the type and stage of cancer, as well as the type(s) of cancer treatment already received.

Enrolling people who have similar characteristics helps ensure that the outcome of a trial is due to the intervention being tested and not to other factors. In this way, eligibility criteria help researchers obtain the most accurate and meaningful results possible.

National and International Regulations

National and international regulations and policies have been developed to help ensure that research involving people is conducted according to strict scientific and ethical principles. In

these regulations and policies, people who participate in research are usually referred to as "human subjects."

Informed Consent

Informed consent is a process through which people learn the important facts about a clinical trial to help them decide whether or not to take part in it, and continue to learn new information about the trial that helps them decide whether or not to continue participating in it.

During the first part of the informed consent process, people are given detailed information about a trial, including information about the purpose of the trial, the tests and other procedures that will be required, and the possible benefits and harms of taking part in the trial. Besides talking with a doctor or nurse, potential trial participants are given a form, called an informed consent form, that provides information about the trial in writing. People who agree to take part in the trial are asked to sign the form. However, signing this form does not mean that a person must remain in the trial. Anyone can choose to leave a trial at any time—either before it starts or at any time during the trial or during the follow-up period. It is important for people who decide to leave a trial to get information from the research team about how to leave the trial safely.

The informed consent process continues throughout a trial. If new benefits, risks, or side effects are discovered during the course of a trial, the researchers must inform the participants so they can decide whether or not they want to continue to take part in the trial. In some cases, participants who want to continue to take part in a trial may be asked to sign a new informed consent form.

New interventions are often studied in a stepwise fashion, with each step representing a different "phase" in the clinical research process. The following phases are used for cancer treatment trials:

Phases of a Clinical Trial

Phase 0. These trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer. Phase 0 trials are also called micro-dosing studies, exploratory Investigational New Drug (IND) trials, or early phase I trials. The people who take part in these trials usually have advanced disease, and no known, effective treatment options are available to them.

Phase I (also called phase 1). These trials are conducted mainly to evaluate the safety of chemical or biologic agents or other types of interventions (e.g., a new radiation therapy technique). They help determine the maximum dose that can be given safely (also known as the maximum tolerated dose) and whether an intervention causes harmful side effects. Phase I trials enrol small numbers of people (20 or more) who have advanced cancer that cannot be treated effectively with standard (usual) treatments or for which no standard treatment exists. Although evaluating the effectiveness of interventions is not a primary goal of these trials, doctors do look for evidence that the interventions might be useful as treatments.

Phase II (also called phase 2). These trials test the effectiveness of interventions in people who have a specific type of cancer or related cancers. They also continue to look at the safety of interventions. Phase II trials usually enrol fewer than 100 people but may include as many as 300. The people who participate in phase II trials may or may not have been treated previously with standard therapy for their type of cancer. If a person has been treated previously, their eligibility to participate in a specific trial may depend on the type and amount of prior treatment they received. Although phase II trials can give some indication of whether or not an intervention works, they are almost never designed to show whether an intervention is better than standard therapy.

Phase III (also called phase 3). These trials compare the effectiveness of a new intervention, or new use of an existing intervention, with the current standard of care (usual treatment) for a particular type of cancer. Phase III trials also examine how the side effects of the new intervention compare with those of the usual treatment. If the new intervention is more effective than the usual treatment and/or is easier to tolerate, it may become the new standard of care.

Phase III trials usually involve large groups of people (100 to several thousand), who are randomly assigned to one of two treatment groups, or "trial arms": (1) a control group, in which everyone in the group receives usual treatment for their type of cancer, or 2) an investigational or experimental group, in which everyone in the group receives the new intervention or new use of an existing intervention. The trial participants are assigned to their individual groups by random assignment, or randomisation. Randomisation helps ensure that the groups have similar characteristics. This balance is necessary so the researchers can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups.

Randomisation is usually done by a computer program to ensure that human choices do not influence the assignment to groups. The trial participants cannot request to be in a particular group, and the researchers cannot influence how people are assigned to the groups. Usually, neither the participants nor their doctors know what treatment the participants are receiving.

People who participate in phase III trials may or may not have been treated previously. If they have been treated previously, their eligibility to participate in a specific trial may depend on the type and the amount of prior treatment they received.

In most cases, an intervention will move into phase III testing only after it has shown promise in phase I and phase II trials.

Phase IV (also called phase 4). These trials further evaluate the effectiveness and long-term safety of drugs or other interventions. They usually take place after a drug or intervention has been approved by the medicine regulatory office for standard use. Several hundred to several thousand people may take part in a phase IV trial. These trials are also known as post-marketing surveillance trials. They are generally sponsored by drug companies.

Sometimes clinical trial phases may be combined (e.g., phase I/II or phase II/III trials) to minimize the risks to participants and/or to allow faster development of a new intervention.

Although treatment trials are always assigned a phase, other clinical trials (e.g., screening, prevention, diagnostic, and quality-of-life trials) may not be labelled this way.

Use of Placebos

The use of placebos as comparison or "control" interventions in cancer treatment trials is rare. If a placebo is used by itself, it is because no standard treatment exists. In this case, a trial would compare the effects of a new treatment with the effects of a placebo. More often, however, placebos are given along with a standard treatment. For example, a trial might compare the effects of a standard treatment plus a new treatment with the effects of the same standard treatment plus a placebo.

Possible benefits of taking part in a clinical trial

The benefits of participating in a clinical trial include the following:

- Trial participants have access to promising new interventions that are generally not available outside of a clinical trial.
- The intervention being studied may be more effective than standard therapy. If it is more effective, trial participants may be the first to benefit from it.
- Trial participants receive regular and careful medical attention from a research team that includes doctors, nurses, and other health professionals.
- The results of the trial may help other people who need cancer treatment in the future.
- Trial participants are helping scientists learn more about cancer (e.g., how it grows, how it acts, and what influences its growth and spread).

Potential harms associated with taking part in a clinical trial

The potential harms of participating in a clinical trial include the following:

- The new intervention being studied may not be better than standard therapy, or it may have harmful side effects that doctors do not expect or that are worse than those associated with standard therapy.
- Trial participants may be required to make more visits to the doctor than they would if they were not in a clinical trial and/or may need to travel farther for those visits.

Correlative research studies, and how they are related to clinical trials

In addition to answering questions about the effectiveness of new interventions, clinical trials provide the opportunity for additional research. These additional research studies, called correlative or ancillary studies, may use blood, tumour, or other tissue specimens (also known as 'biospecimens') obtained from trial participants before, during, or after treatment. For example, the molecular characteristics of tumour specimens collected during a trial might be analysed to see if there is a relationship between the presence of a certain gene mutation or the amount of a specific protein and how trial participants responded to the treatment they received. Information obtained from these types of studies could lead to more accurate predictions about how individual patients will respond to certain cancer treatments, improved ways of finding cancer earlier, new methods of identifying people who have an increased risk of cancer, and new approaches to try to prevent cancer.

Clinical trial participants must give their permission before biospecimens obtained from them can be used for research purposes.

When a clinical trial is over

After a clinical trial is completed, the researchers look carefully at the data collected during the trial to understand the meaning of the findings and to plan further research. After a phase I or phase II trial, the researchers decide whether or not to move on to the next phase or stop testing the intervention because it was not safe or effective. When a phase III trial is completed, the researchers analyse the data to determine whether the results have medical importance and, if so, whether the tested intervention could become the new standard of care.

The results of clinical trials are often published in peer-reviewed scientific journals. Peer review is a process by which cancer research experts not associated with a trial review the study report before it is published to make sure that the data are sound, the data analysis was performed correctly, and the conclusions are appropriate. If the results are particularly important, they may be reported by the media and discussed at a scientific meeting and by patient advocacy groups before they are published in a journal. Once a new intervention has proven safe and effective in a clinical trial, it may become a new standard of care.
(National Cancer Institute).

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