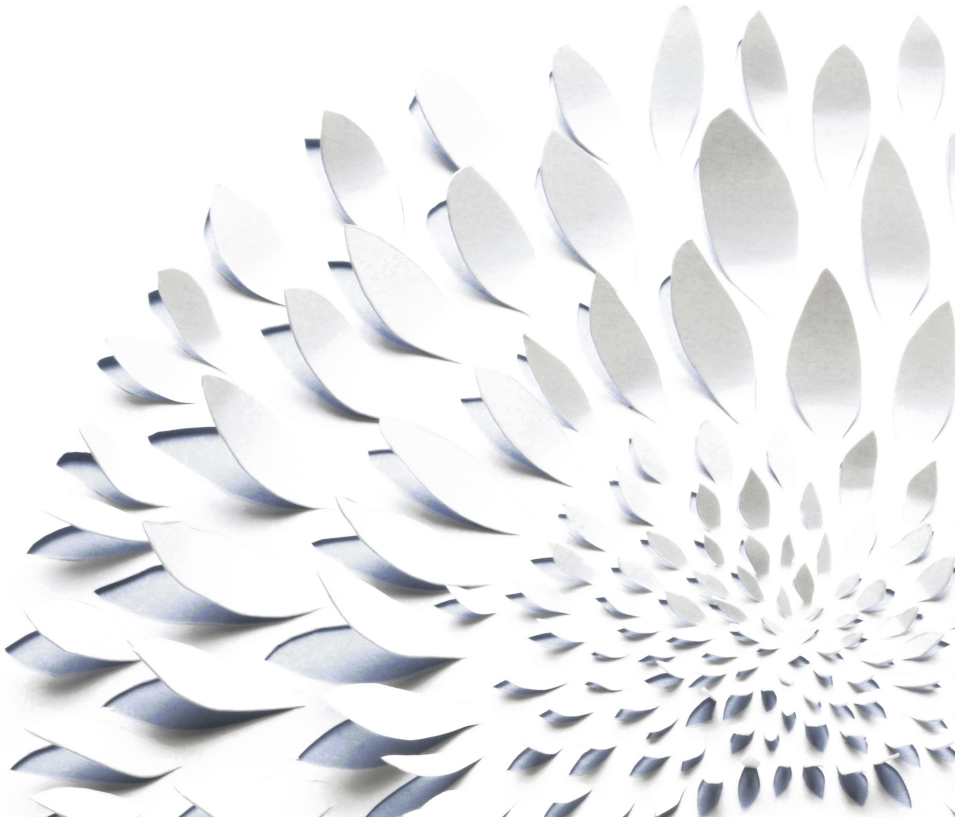
Triple negative metastatic breast cancer

hope &hurdles



Contents

Introduction

In this booklet you will find information about the treatment recommendations for your subtype of metastatic breast cancer — **triple negative metastatic breast cancer**.

> *It has taken me a while to get my head around the diagnosis and the fact that nearly every case is different in its state and treatment options. People need simpler, clearer explanations in the initial diagnosis phase around why their cancer is being treated in a certain way. If we had more personalised information it would go a long way to helping to absorb the facts and come to terms with what is ahead.* — Leanne

There have been significant advances in the treatment of metastatic breast cancer in recent years, due to a deepening understanding of breast cancer biology. This has led to the recognition of three main breast cancer 'subtypes' which are now the main guide for treatment recommendations. Many treatments target specific features of the breast cancer subtype and are already making a real difference for many people with metastatic breast cancer. As a result, cancer can be controlled for longer and longer periods, leading to improvements in quality of life.

Subtypes of breast cancer

Three main subtypes of breast cancer have been identified, although in the future it is expected that these will be further divided as understanding of the inner ('molecular') workings of each subtype of breast cancer expands. Consequently, treatment will become more and more specific to an individual cancer. Developing this 'personalised' treatment is the main goal of current research.

The three subtypes of breast cancer that guide treatment options are:

1. Hormone receptor positive metastatic breast cancer

Hormone receptor (HR) positive cancers have what are called Oestrogen Receptors (ER) and/or Progesterone Receptors (PR) on the surface of the cancer cells. This means that hormones (mainly oestrogen) and hormone blocking treatments can directly influence the activity of these cancer cells via these receptors. When oestrogen attaches, or binds, to the receptors this signals the cell to grow and divide, producing new cells. Hormone treatments work either by attaching to the receptors and blocking oestrogen from binding to them, or by preventing the production of oestrogen in the body. Both of these effects prevent oestrogen from stimulating growth of the cancer cells.

Around 70% of metastatic breast cancers are hormone receptor positive, with 10 per cent of these also being HER2-positive.

2. HER2-positive metastatic breast cancer

HER2-positive cancers have what are called HER2 receptors in excess of normal on the surface of the cancer cells. These receptors allow growth factors to stimulate the growth of the cancer cells. Treatments that block the HER2 receptors prevent this growth stimulation, in turn controlling the cancer.

Around 20% of metastatic breast cancers are HER2-positive. Around half of these cancers are also hormone receptor positive.

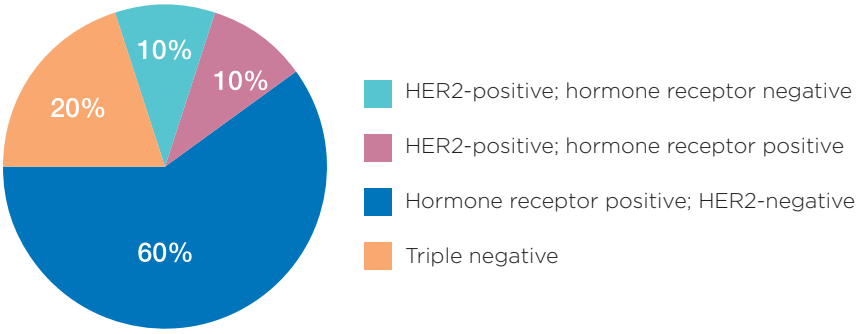
3. Triple negative metastatic breast cancer

Triple negative breast cancers have none of these receptors (oestrogen, progesterone or HER2) on the surface of the cancer cells. This means that they do not respond to treatments that block these receptors. However, they are particularly responsive to chemotherapy, and this is the backbone of treatment for these cancers.

Research is focusing on identifying receptors and other targets in these triple negative breast cancer cells to create additional treatment options; some of these are just beginning to become available.

Around 20% of metastatic breast cancers are triple negative.

Subtypes of metastatic breast cancer



Identifying the different subtypes of breast cancer

A pathologist will test your breast cancer in the laboratory to determine whether it has hormone receptors and whether it is HER2-positive.

These tests will have been done on your original breast cancer, if you had an early breast cancer prior to the diagnosis of your metastatic breast cancer. If it is possible however, a biopsy of the metastatic breast cancer will be done to confirm whether the receptor results have remained the same as originally or not. Sometimes a biopsy is not possible, and the results from the initial cancer will be used.

If you have presented with metastatic breast cancer without a previous early breast cancer, this is called 'de novo' metastatic breast cancer. A biopsy will need to be performed, both to confirm that the diagnosis is metastatic breast cancer and to check the receptor results.

For more information about having **metastatic disease as your first diagnosis** see Section 7 of the *Hope & Hurdles Information Guide*.

Talking with your treating team about the pathology of your breast cancer can be a complex discussion, especially if metastatic breast cancer is your first diagnosis of breast cancer. It is okay to keep asking questions about the type of cancer you have.

These booklets are designed to help guide your understanding and help you to think about the questions you can ask your specialists. You are not expected to understand all of the

treatment pathways that may be available to you, particularly when you are first diagnosed. Over time you are likely to have a much better understanding of your subtype of metastatic breast cancer. As you read through the information in this booklet you may want to take notes and add them to the back section of this booklet. You can then take those notes along to your specialist to answer your questions.

What does it all mean and how will the subtype of breast cancer influence my prognosis?

One of the first things that people often ask when told the news that their breast cancer has spread is, 'How long do I have to live?' You may wonder how the subtype of your breast cancer might influence your prognosis.

It is very common for people who are diagnosed with metastatic breast cancer to be fearful of their prognosis and believe that their lifespan will be very short. Friends and family often want to know about prognosis and ask questions that lead to a lot of stress and anxiety for everyone. Regardless of the subtype of breast cancer, it is often the case that reality is so much better than what people predict for themselves.

Although metastatic breast cancer is not currently considered curable it is very treatable, and for some people it may be controlled for several years. There have been a small number of women whose metastatic breast cancer has been in remission so long, it is thought they may be cured. It is hoped that with increasingly effective treatments in coming years, this will not be such a rare occurrence.

The prognosis in metastatic breast cancer varies widely based on many individual factors and characteristics of the disease. If you wish, an estimate can be made for you based on the details of your case but it is important to remember it is just an estimate. The most useful way to look at a prognosis is to understand what the average is for your situation, as well as the worst and the best case scenarios. Whether (and when) you want to discuss this with your doctor is entirely up to you.

However, it is important that you understand in broad terms what your doctor expects for you, so you are able to be realistic — and in particular not imagine the very worst.

You may find survival figures quoted for the different subtypes of breast cancer, but such figures are generalisations and will be unlikely to accurately describe your situation.

> *My psychologist advocates to learn to 'live in the moment' which has helped me to enjoy what each new day brings instead of living in fear of what might be taken from me in the future.*

> *After being diagnosed with metastatic breast cancer, I thought my life was over. But now I see things very differently. I've been living with this diagnosis for over two years now and with the wonderful support of family and friends, my medical team, and the team from BCNA, I'm beginning to accept what I have and move forward a little bit everyday.* — Sonia

Aim of treatment

The aim of treatment for metastatic breast cancer is both to lengthen survival and improve quality of life. These aims are equally important and the best way to achieve them is to control the cancer.

Treatments may include:

- anti-cancer therapies, including:
    - localised treatments, such as radiotherapy and surgery
    - systemic treatments, such as chemotherapy and targeted treatments (currently in development), which treat the cancer wherever it is in the body
- treatments to control symptoms
- other supportive care measures to improve quality of life.

This booklet focuses only on the systemic anti-cancer treatments that are appropriate for triple negative metastatic breast cancer.

For more information on **localised cancer treatments**, see BCNA's booklets on the specific sites of metastatic breast cancer.

For information on **symptom management** and supportive care, see the **Treatment and side effects** section of the *Hope & Hurdles Information Guide*.

Treatment for triple negative metastatic breast cancer

Chemotherapy

The backbone of systemic treatment for triple negative metastatic breast cancer is chemotherapy. There are at least ten different chemotherapy drugs that may be effective in triple negative metastatic breast cancer. It is most common to use these treatments individually, as single agents, although occasionally two may be used together in combination.

Initial treatment (first line)

An initial course of chemotherapy will be recommended, called 'first line' treatment, which will usually start within a few weeks of the diagnosis of triple negative metastatic breast cancer. It may be delayed a short time if radiotherapy or surgery is required. Chemotherapy is usually given in cycles of three to four weeks, or other sequences such as every two out of three weeks, depending on the drug/s used. Chemotherapy will continue until it is thought to be either causing excessive side effects or it is no longer beneficial in controlling the cancer. Usually between four and eight cycles of chemotherapy are given to make up a single course of treatment.

Second and subsequent lines of treatment

You may be able to have a break when a treatment is completed, or it may be necessary to start another treatment at that time. Either way you will be recommended to proceed with the next treatment when it is clear that the cancer is

active and worsening in terms of symptoms, scans or findings on physical examination. This next treatment is called 'second line' treatment and will proceed just as for first line treatment.

When second line treatment is exhausted, you may proceed to 'third', 'fourth', 'fifth' line etc. treatment, as considered appropriate by your medical oncologist and you. This decision will depend on how well the cancer responds to treatment, how well you tolerate the treatment and, importantly, your wishes about treatment.

In summary, you will receive a sequence of treatments over time, each adding a period of cancer control. Where possible, you will have chemotherapy-free periods between different treatments and the choice of chemotherapy schedules will take possible side effects into account.

Tests and monitoring

Throughout your treatment you will be monitored carefully and will have regular appointments with your medical oncologist. When you are receiving chemotherapy, monitoring will be more intense. You will see your medical oncologist before each cycle of chemotherapy (every three or four weeks depending on the chemotherapy course). Your doctor will assess how you are getting on at each visit in terms of:

- how you are coping with the chemotherapy
- any side effects you are experiencing
- whether the cancer is responding to the treatment.

Sometimes at these visits your doctor may recommend a change in chemotherapy dose, a change in medication to control side effects, a break in treatment to help with side

effects, or a change in chemotherapy if it is causing you excessive side effects or if it is not working. You can also discuss with your doctor having a rest from treatment for a while, or a break if you have a holiday or special event planned.

> *I have given myself permission to take a break from treatment. I have finally acknowledged that it is going to be ok to take that break; that my oncologist is right, my cancer won't get worse and I can have a rest for a while.*
> — Wendy

The types of test you may have include:

Blood tests will usually be done every few weeks when you are receiving chemotherapy to check your blood count levels (white blood cells that help fight infection, red blood cells that carry oxygen and platelets for clotting), liver function and kidney function.

Tumour marker blood tests (if above normal) will usually be done with each cycle. Tumour markers are proteins found in the blood, such as CA 15-3 and CEA, which are produced in the body in response to cancer or by the cancer itself. They can be useful in monitoring response to the treatment, although they are not always helpful.

Scans such as CT scans and bone scans will be done every two to three cycles to help assess the response of the cancer to treatment.

Times that additional tests might be needed

It is always important to consider making an earlier appointment to see your medical oncologist if you are not feeling well and especially if you develop symptoms that make you think the cancer is becoming more active again. You might like to see your GP to help decide if you need an early appointment with your oncologist.

Tests and monitoring during breaks between chemotherapy courses

Visits to your medical oncologist may be able to be reduced in frequency. However, a blood test is likely to be ordered before each visit and scans done every few months.

Assessing how well treatment is working

Sometimes it can be difficult to determine if your cancer has worsened or progressed, because scans cannot show everything.

Your medical oncologist will base their assessment on a combination of factors:

- how you are feeling generally
- whether you have any specific symptoms
- results of your blood tests, including tumour markers if they are useful in your case
- findings on physical examination
- X-rays and scans.

If after careful assessment your oncologist considers the cancer has progressed, a new treatment will be recommended.

Length of the chemotherapy course

How long you continue with a chemotherapy course depends on:

- how well it is controlling the cancer
- how well you are coping with side effects
- whether there are side effects that might cause longer term problems e.g. nerve ending damage
- how you feel about continuing the course
- whether there are any specific commitments you have — such as a planned holiday or special event.

In other words, it is a very open-ended decision and involves some discussion between you and your medical oncologist. Generally, however, as long as the cancer is responding to treatment, aiming for six cycles of treatment in the first instance is appropriate. Although there is evidence that longer overall duration of treatment can prolong the benefit of treatment, it is important not to continue in the face of side effects that interfere with your ability to live well. Some chemotherapies, especially oral ones, can sometimes be continued for long periods (12 months and more) with good cancer control and have the added benefit of avoiding many hospital visits for IV drip treatments.

Factors that influence which chemotherapy treatment is recommended

There is no definite right and wrong about which chemotherapy to receive or when. It is expected that most people with metastatic breast cancer will receive a sequence of treatments as described above and your medical oncologist will work with you regarding the best choice of treatment for you at any given time. It is quite common to find, when talking

with other women who have a similar diagnosis to you, that they have received a very different chemotherapy treatment. However there are some guiding principles and government regulations that influence choices. Your oncologist is the best person to discuss this with.

Deciding on the right chemotherapy for you

- what chemotherapy, if any, you received previously. For instance, treatment you were given for early breast cancer in the past. Usually these chemotherapies will not be repeated, although if more than 12 months has elapsed, a taxane chemotherapy may be re-used with good results
- which chemotherapy has the best chance of working
- any ongoing side effects from previous treatment, such as nerve ending damage, skin problems, effects on the heart etc.
- your preference for oral or intravenous chemotherapy and any opinions you have about other side effects such as hair loss
- whether you carry a BRCA gene mutation. If you have not been tested for BRCA mutations it is worth discussing this with your medical oncologist, as triple negative breast cancer is more commonly associated with these mutations than other subtypes of breast cancer. Carboplatin, a platinum based chemotherapy, has been shown to be particularly effective for this subtype of metastatic breast cancer. There are also other targeted treatments that may be considered for BRCA-related metastatic breast cancer.

Pharmaceutical Benefits Scheme (PBS) regulations also influence which chemotherapy you may be recommended to receive. The PBS is the Australian Government scheme which subsidises the cost of most drugs used in the treatment of metastatic breast cancer. For certain chemotherapies to be covered by the PBS they can only be used after other chemotherapies have been used. Fortunately these restrictions only apply to a small number of chemotherapy drugs currently.

At the end of this booklet is a list of chemotherapy options that may be used for triple negative metastatic breast cancer. It has been provided for those who want more information on the types of drugs that may be recommended and when they may be used.

Making a decision to stop chemotherapy altogether

Provided chemotherapy is working well for you and you are coping okay with it, it is reasonable to continue to have successive lines of treatment. Some people may have more than six lines of treatment.

However, what is appropriate is very individual. Although stopping chemotherapy and active treatment is a big decision, it is important that you feel free to have this discussion with your medical oncologist, and your family if that is important to you, and make this decision when it feels right for you.

Your oncologist may also at some point suggest this to you if they feel the chance of responding to another line of treatment is remote, if they feel your wellbeing is suffering excessively from treatment or if they consider you are not well enough to receive treatment.

Chemotherapy side effects and their management

Side effects of chemotherapy

Each chemotherapy drug is a little different in its side effects. Not all treatments cause nausea or vomiting, nor do all cause hair loss. Some cause nerve ending damage (pins and needles/numbness of fingers and toes), others redness/soreness of hands and feet and others body aches and pains.

All chemotherapy treatments affect your blood counts making you more susceptible to infection. It is very important that you seek urgent medical attention for signs of infection, especially a temperature over 38°C.

Your medical oncologist and chemotherapy nurse will help you manage any side effects you are experiencing. There are also helpful information sheets about each chemotherapy treatment on the eviQ website which your team should provide you with. EviQ is an evidence-based national information resource for cancer treatments. You can find out more on the eviQ website at eviq.org.au.

Please also see the **Treatment and side effects** section of the *Hope & Hurdles Information Guide*.

Targeted treatments for triple negative breast cancer

There are no targeted treatments available for triple negative breast cancer at the time of writing (2017), except in clinical trials. It is already known that triple negative breast cancer is made up of a number of subtypes, with different molecular characteristics, each with different targets for treatment. It is likely that additional subtypes of triple negative metastatic breast cancer will be identified as research continues.

The good news is that there are treatments under development for some of these targets and it is expected that over the next few years there will be a major growth in this area with new treatments becoming available for triple negative metastatic breast cancer.

New targeted treatments on the horizon for triple negative metastatic breast cancer

The treatments closest on the horizon are:

- **PARP inhibitors: olaparib (Lynparza):** PARP inhibitors are effective for BRCA mutation-related metastatic breast cancer and may be used alone or in combination with chemotherapy. Olaparib is an oral medication that is well tolerated. It is not yet available in Australia.

  A PARP (poly ADP-ribose) inhibitor is a medication that blocks an enzyme in cells called PARP. PARP helps repair DNA when it becomes damaged. In cancer treatment, blocking PARP may help keep cancer cells from repairing their damaged DNA, causing them to die.

- **Androgen blocking therapies:** some cases of triple negative breast cancer have been shown to have Androgen Receptors (AR), much like other breast cancers have Oestrogen Receptors (ER). Trials are currently investigating the use of androgen blocking treatments in this subtype of breast cancer.

- **Immune stimulating therapies:** the development of immune therapies for cancer has taken off in recent times, especially in the treatment of melanoma skin cancers. It appears triple negative breast cancer is one of the subtypes of breast cancer most likely to respond to these treatments. Trials are underway with pembrolizumab (Keytruda) and related drugs for triple negative breast cancer testing positive for PDL-1.

Role of clinical trials

With the focus on developing new targeted treatments for triple negative breast cancer, you may have the opportunity to enrol in a clinical trial. At the time of writing (2017), all of the new treatments described as being closest on the horizon are only available in Australia in clinical trials. Whether to participate in a clinical trial is an individual decision, and it is important that you understand the benefits and risks involved as well as the required time and practical commitments before making a decision.

Your participation in research will certainly benefit future patients with triple negative breast cancer, and although participation may benefit you personally, this is not always the case. However, patients on clinical trials are monitored very carefully, so any risk to you is minimised, and there is research

that suggests that just participating in a clinical trial results in improved outcomes for the individuals involved. Your medical oncologist would not offer you trial enrolment if they did not think this could be of value to you.

For more information on **clinical trials** see page 58 of the *Hope & Hurdles Information Guide*.

More information

Metastatic breast cancer is a complex disease and there is no single standard of care. Every woman's experience is different, meaning treatment is individualised based on multiple factors. A big part of treatment decision-making will be the subtype of breast cancer that you have and the ability to be prescribed treatments that target specific features of that cancer. Many other factors will influence treatment decision making including your personal preferences, your life stage and general health and wellbeing.

This booklet has been developed to give you specific information about medical treatment that your medical oncologist will discuss with you. We know that many other health professionals and supporters in your life will also be important to how you manage your cancer.

For more information on **practical, emotional and financial supports** available, refer to BCNA's *Hope & Hurdles Information Guide*.

You can order a copy online from bcna.org.au or phone **1800 500 258**.

Chemotherapy: Treatment options

This section is a guide for those people who want to know more about the types of drugs that may be recommended and when they are most likely to be used. The order that you may be recommended these treatments will be individualised, however, there are several common patterns that are listed at the end of this section that you may find helpful. If you want to know more about anything listed here, or if you have additional questions, talk to your medical oncologist.

*__adjuvant__ treatment is treatment that is given in addition to a primary therapy such as surgery for early breast cancer.

Drug name ***Generic***	**Drug name** ***Trade*** ***(Abbreviation)***	**Class of chemotherapy**	**Combinations used**	**When used** 'Line' of treatment	**Comments**
doxorubicin	Adriamycin (A)	Anthracycline	AC	• Commonly used as adjuvant treatment in early breast cancer* • May be used as single agent or in combination with cyclophosphamide (AC)'as 1st or later line treatment in: • 'de novo' metastatic breast cancer • for those who have not received anthracycline chemotherapy as adjuvant treatment	There is a limit to the total amount of anthracycline chemotherapy that can be safely given due to effects on heart muscle.
epirubicin	Epirubicin (E)	Anthracycline	EC	As for doxorubicin	As for doxorubicin

Drug name ***Generic***	**Drug name** ***Trade*** ***(Abbreviation)***	**Class of chemotherapy**	**Combinations used**	**When used** 'Line' of treatment	**Comments**
docetaxel	Taxotere (D)	Taxane		• Commonly used as adjuvant treatment in early breast cancer* • Commonly used as a 1st line treatment in: • 'de novo' metastatic breast cancer • for those who have not received a taxane as adjuvant treatment • for those who completed adjuvant taxane more than 12 months previously • May be used as 2nd line treatment when other drugs are used as 1st line treatment	
paclitaxel	Taxol (P)	Taxane	PC	• As single agent, used as for docetaxel • May be used in combination with carboplatin, often as 1st line treatment	
nab-paclitaxel	Abraxane (nab-P)	Taxane		• Used as for docetaxel	
capecitabine	Xeloda (X)	Anti-metabolite		• Commonly used as 1st, 2nd or 3rd line treatment for metastatic breast cancer	This is an oral treatment Due to low level of side effects for many patients treatment may be able to continue for long periods (more than a year)

Drug name ***Generic***	**Drug name** ***Trade*** ***(Abbreviation)***	**Class of chemotherapy**	**Combinations used**	**When used** 'Line' of treatment	**Comments**
cyclophos-phamide	Cytoxan (C)	Alkylator	AC, EC, CMF, low dose CM	• Not used as a single agent • Used in combination with doxorubicin or epirubicin as above • May be used in combination as a later line treatment: CMF or low dose CM	Cyclophosphamide can be given orally or intravenously. The low dose CM is an oral treatment.
methotrexate	(M)	Anti-metabolite	CMF	• May be used in CMF or CM as a later line treatment	
5 Fluorouracil	(F)	Anti-metabolite	CMF	• May be used in CMF as a later line treatment	
vinorelbine	Navelbine	Vinca-alkaloid		• Commonly used as a later line treatment, usually as a single agent	May be given orally or intravenously. **PBS restriction:** oral vinorelbine can only be used if an anthracycline has previously been given
eribulin	Halaven	Micro-tubule inhibitor		• Commonly used as a 3rd line treatment after a taxane and capecitabine	**PBS restriction:** Must have received at least two prior chemotherapy treatments for metastatic disease
carboplatin	(Carbo)	Platinum	Carbo-Gem Carbo-P	• May be used as single agent or in combination as 1st line treatment in those who have received adjuvant anthracyclines and taxanes, especially if BRCA mutation carrier • May be used as later line treatment as single agent or in combination	This chemotherapy may be especially effective in BRCA mutation related metastatic breast cancer, but is also effective in other cases

Drug name ***Generic***	**Drug name** ***Trade*** ***(Abbreviation)***	**Class of chemotherapy**	**Combinations used**	**When used** 'Line' of treatment	**Comments**
gemcitabine	(Gem)	Anti-metabolite	Carbo -Gem	• Rarely used as single agent • May be used in combination with carboplatin (see above)	
liposomal doxorubicin	Caelyx	Anthracycline		• May be used as a later line treatment	Although an anthracycline it has much less effect on the heart muscle and therefore can be used after other anthracyclines used earlier in treatment **PBS restriction:** Must have received previous taxane and capecitabine

Notes

More information

More information is available in the *Hope & Hurdles Information Guide* and in the *Hope & Hurdles* booklets:

- *Metastatic breast cancer in the bone*
- *Metastatic breast cancer in the liver*
- *Metastatic breast cancer in the lung*
- *Metastatic breast cancer in the brain*
- *Hormone receptor positive metastatic breast cancer*
- *HER2-positive metastatic breast cancer*
- *Planning ahead (formerly called Getting your affairs in order)*

hope &hurdles

March 2017

This booklet was developed by Associate Professor Jacquie Chirgwin in collaboration with BCNA, women living with metastatic breast cancer and the *Hope & Hurdles* Advisory Group.

About Breast Cancer Network Australia

Breast Cancer Network Australia (BCNA) is the peak national organisation for Australians personally affected by breast cancer. We work to ensure that people diagnosed with breast cancer and their families receive the very best information, treatment, care and support possible.

Breast Cancer Network Australia

bcna.org.au
1800 500 258
beacon@bcna.org.au