Making Choices

Deciding whether to join the IBIS-II DCIS study
A Decision Aid for Women with DCIS
Making Choices

Deciding whether to join the IBIS-II DCIS study
A Decision Aid for Post-Menopausal Women with DCIS
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Introduction

A substantial number of women suffer from some kind of breast condition. Your doctor will have explained that you have just been treated for a breast condition called **Ductal Carcinoma In Situ (DCIS)**. DCIS occurs when abnormal cells grow but are confined to the milk ducts, in other words it is not an invasive breast cancer and it does not spread to other parts of your body. However, past investigations have shown that women who have had DCIS have an increased risk of developing invasive breast cancer in the same, or the other breast, sometime in the future.

Research continues to find ways of lowering this risk. You have been invited to consider taking part in the **International Breast Cancer Intervention Study-II (IBIS-II)** DCIS study investigating the role of **tamoxifen** and **anastrozole (also known as Arimidex®)** in reducing the risk of breast cancer in post-menopausal women who have been treated for DCIS. Both of these treatments already have an established role in the treatment of invasive breast cancer. This booklet is designed to assist you in deciding whether to take part in the IBIS-II study as one of your treatment options. We explain your current treatment options and offer advice on how to make the decision that best suits you.

At the back of the booklet you will find pages labelled “Your Notes” for you to write down questions to ask your doctor or research nurse. A glossary of medical terms and words used in clinical trials is also included. For more detailed information about any of the issues raised please see the Participant Information Sheet for the IBIS-II DCIS study.

*Whether or not you decide to participate in the IBIS-II DCIS study, you will receive the very best care.*
Understanding breast cancer risk

In this booklet, we use “risk” to mean the likelihood of developing future breast cancer. Everyone has some chance of developing breast cancer in their life (men too).

Increased risk of breast cancer

Some people are more likely than others to develop breast cancer for various reasons, and these people are said to be at an increased risk. There are two major risk factors known to increase the risk of breast cancer – being female, and being of an older age.

Other risk factors include:

- Having had one of certain previous breast conditions such as DCIS
- Having a family history of breast cancer
- Never having had children
- Being 30 years or older at the birth of their first child
- Going through menopause after the age of 55

While reading the entire booklet may help you to understand your risk management options, it is not essential. However, we think you will find the sections on potential benefits and risks of management options particularly useful. The diagrams are included to complement the text - it is not necessary to read both. The worksheets are optional; you do not have to complete them.
What is Ductal Carcinoma In Situ (DCIS)?

Ductal Carcinoma In Situ (or DCIS) refers to the most common type of non-invasive breast cancer in women.

The breast contains lobules (milk sacs or glands) that produce milk, and ducts that take the milk to the nipple. Sometimes the cells on the inside of the milk ducts become abnormal in size and shape, and begin to multiply in an uncontrollable way.

In **DCIS**, abnormal cells remain within the milk ducts of the breast and do not spread outside the ducts to other parts of the breast or body. In **invasive breast cancer** the abnormal cells spread into (invade) the breast tissue surrounding the ducts (see illustrations below).

**DCIS** is commonly described as ‘pre-cancerous’, ‘pre-invasive’ or ‘intra-ductal cancer’
General population breast cancer risk

In developed countries, close to 10 out of 100 women will develop breast cancer at some point in their life (these figures are averages).

What is your risk of developing future breast cancer after DCIS?

After DCIS, your risk of developing future breast cancer, either invasive or another DCIS, increases to about 20% or close to double the usual risk (these figures are averages).

Your precise risk will depend on features of your DCIS and the number of risk factors that apply to you. Your doctor can tell you more about your individual risk.

If invasive breast cancer develops, there is a very good chance that this can be detected early and treated effectively so the majority of women can be cured and return to their normal life.
What can you do to manage your risk of future breast cancer?

Following your surgery (and possibly radiotherapy) for DCIS, you may want to consider a number of options to manage the risk of developing breast cancer in the future. These options are:

**Option I**  
**STANDARD CARE**

**Option II**  
**CLINICAL TRIAL**

**RISK MANAGEMENT**

- a) without tamoxifen  
- b) with tamoxifen

**RISK MANAGEMENT**

- on the IBIS-II  
- DCIS study  
- (for 5 years)

This will be decided in consultation with your usual doctor. This is ultimately your choice.

Regardless of which option you choose, your doctor will ensure you get the best medical care.
Option I

Standard care

a) Risk management WITHOUT tamoxifen

Having had treatment for DCIS, you may now choose standard risk management with mammographic screening each year (rather than every second year) and regular clinical examinations of your breasts. This helps to ensure any further problems are identified as early as possible. Your doctor will discuss this with you in more detail.

What are some of the “PROS” of this option?

• Increased monitoring gives you a good chance of detecting any changes in breast tissue early

• You would not have side effects that may occur if taking tamoxifen or anastrozole

• There is no “daily reminder” of the threat of cancer by taking a pill

What are some of the “CONS” of this option?

• Mammograms and clinical examinations may alert you and your doctor to the fact that there is something wrong, but they do not prevent or reduce the risk of developing breast cancer

• You may feel that you have not done enough to maximise your chances of preventing breast cancer

• You may not have the reassurance of taking a daily pill to prevent breast cancer
Option 1

Standard care

b) Risk management WITH tamoxifen

Taking preventive treatment in the form of a drug called tamoxifen is another standard option you may consider. You will still have the same regular screening for breast changes as in the “risk management without tamoxifen” option.

What is tamoxifen?

Tamoxifen is a tablet whose effectiveness in treating early and advanced stages of breast cancer has been consistently proven and monitored for almost 30 years. In women at high risk of developing breast cancer, tamoxifen is known to reduce the chance of developing the disease. Recently, two large studies have explored the use of tamoxifen in women with DCIS and both have suggested that tamoxifen may be effective in reducing breast cancer risk. Further research is required to determine the role of tamoxifen in the treatment of women with DCIS.

How is it taken?

Tamoxifen is taken as a tablet once a day for 5 years. Tamoxifen is available for the treatment of breast cancer under the Pharmaceutical Benefit Scheme (PBS). The cost is for one prescription per 60 days.
Tamoxifen

How does it work?

Tamoxifen is an anti-oestrogen drug which blocks the action of oestrogen. Oestrogen is a female hormone which is produced mainly by the ovaries in women before menopause. After menopause, low levels of oestrogen continue to be produced in fat, liver, muscle and breast tissue itself. Oestrogen stimulates the growth of breast tissue and if the tissue contains cancerous cells then it will stimulate the growth of the cancerous tissue too.

Some cells have parts within them called oestrogen receptors. These are molecules that the oestrogen binds to, starting a chain reaction causing the cell to divide and grow. Breast cancer cells sensitive to oestrogen are called “oestrogen-receptor-positive” (ER positive or ER+) and those that are not sensitive are called “oestrogen-receptor-negative” (ER negative or ER-).

Tamoxifen is a drug that can mimic oestrogen. The easiest way to understand the way tamoxifen works is to liken the process to that of a lock and key. The oestrogen receptor is the lock and oestrogen is the key. When oestrogen comes into contact with the receptors, which are inside the cell, they unlock or activate the cancer cell to divide, and the tumour grows. Tamoxifen imitates the action of the oestrogen and fits into the lock but the key does not turn and the cells do not divide. The tamoxifen key remains in place and prevents the oestrogen from reaching the cancer cells so they either grow more slowly or stop growing altogether. 

Tamoxifen is only effective against cancers that are ER positive (ER+). You have been offered tamoxifen because tests have shown your DCIS tumour cells were oestrogen sensitive (ER positive).
Tamoxifen: Potential BENEFITS

Effective against breast cancer

In **women who have already had invasive breast cancer**, tamoxifen reduces the development of a new breast cancer by about half over 5 years (compared to women not receiving tamoxifen).

It is estimated that for every 1,000 **women diagnosed with invasive breast cancer** who then take tamoxifen for 5 years, more than 100 new diagnoses of hormone sensitive breast cancer will be prevented within the next 10 years.

In women like you, **who have been treated for DCIS**, tamoxifen reduces the risk of developing a new breast cancer by close to half over 5 years (compared to women not receiving tamoxifen).

It is estimated that for every 1,000 **women diagnosed with DCIS**, who then take tamoxifen for 5 years, 52 new diagnoses of breast cancer can be prevented.
Tamoxifen: Potential BENEFITS

Risk of invasive breast cancer

After DCIS your risk of developing future breast cancer is about 20% (20 in every 100 women).

If tamoxifen is taken for 5 years, the 20 in 100 women is reduced to 10 in 100 women. That is, 10 less women in every 100 will develop breast cancer in the future.

Taking tamoxifen for 5 years can reduce this risk from 20% back to the general population’s risk of 10% (10 in every 100 women).
Tamoxifen: Other potential BENEFITS

- **Maintains bone density**
  Tamoxifen has been shown to help maintain bone density in post-menopausal women with invasive breast cancer by preventing the loss of calcium from the bones. In some studies tamoxifen has been shown to increase bone density by a small amount. Therefore taking this treatment may reduce the risk of fractures caused by loss of bone density.

- **Lowers cholesterol levels**
  Tamoxifen can lower the level of cholesterol in the blood.

- **Reduces breast complaints**
  Tamoxifen appears to reduce breast complaints such as cysts, non-cancerous (benign) breast disease, soreness and tenderness, by blocking the effect of oestrogen on breast tissue.

- **Reduces breast tissue density**
  Dense breasts may appear foggy on a mammogram, making this test less sensitive. Tamoxifen has been shown to reduce breast density. Hence taking tamoxifen may make the mammogram a more sensitive test and allow breast cancer to be more easily seen and detected earlier.

Tamoxifen is likely to improve your bone density, and reduce your cholesterol level, breast complaints and breast tissue density.
Tamoxifen: SIDE EFFECTS and potential RISKS

Tamoxifen, like most medications, may cause unwanted side effects in some women. Each woman responds differently to this treatment; many have very few or no side effects. Whilst taking this medication, you are carefully monitored for any side effects and your doctor can discuss ways of lessening their impact. Please bear this in mind as you consider the following list of some known side effects of tamoxifen.

COMMON SIDE EFFECTS
(about 1 in 3 women may experience these)

- Menopausal-like symptoms
  *(Hot flushes, vaginal dryness, vaginal discharge and vaginal itchiness)*

Menopausal-like symptoms are fairly common but are usually mild and disappear when tamoxifen is no longer taken. Hot flushes can occur even in women who have already gone through menopause. Hormone Replacement Therapy (HRT) is usually avoided after the diagnosis of breast cancer, including DCIS (this can be discussed with your usual doctor). Alternative treatments to ease these side effects may be useful (e.g. herbal medication).
Tamoxifen: SIDE EFFECTS and potential RISKS

RARE but potentially serious SIDE EFFECTS

(about 1-2 in 1,000 women experience these)

- **Endometrial cancer (cancer of the womb)**
The uterus (womb), like the breast tissue, is also sensitive to stimulation by oestrogen. Tamoxifen may stimulate the uterus and cause cancer of the lining of the uterus, called endometrial cancer. Fortunately this is very rare. The risk of developing endometrial cancer after taking tamoxifen for 5 years increases 2-3 times, from 3-4 women in 10,000 per year (the general population risk) to 8-10 women in 10,000 per year. However, because of careful and frequent monitoring of gynaecological problems whilst on tamoxifen, most cancerous changes in the uterus are detected very early. These are usually successfully treated by a hysterectomy. If you have already had a hysterectomy, you cannot develop endometrial cancer, so for you there is no risk.

- **Blood clots (thrombosis)**
Tamoxifen may double the risk of blood clots, particularly in the veins of the legs. If these clots break loose, they can block smaller vessels in the heart, lungs and brain. This can be prevented to some extent by exercise and treatments prescribed by your doctor. Clots are most common at times when you are immobilised, such as for an operation, or a leg fracture. Talk to your doctor about stopping tamoxifen temporarily in these circumstances.

- **Changes in vision**
Women taking tamoxifen may be at a very slight increased risk of developing cataracts or retinopathy (a condition affecting the retina of the eye).

*Your doctor will discuss the side effects of tamoxifen with you in detail.*
Tamoxifen: SIDE EFFECTS and potential RISKS

Each diagram represents 100 women. The light-orange shaded area shows the number of women in the general population who may develop each of the presented symptoms over 5 years. The darker orange shaded area shows the number of additional women who may develop each of the presented symptoms over 5 years because they are taking TAMOXIFEN.

Compared to the general population, an additional 30 women taking TAMOXIFEN may experience one or more of the following menopausal-like symptoms:

- Hot flushes
- Vaginal dryness
- Vaginal discharge
- Vaginal itchiness

In addition, tamoxifen may very rarely cause blood clots and endometrial cancer (for the number of women who experience these side effects see diagram on page 19).
In the next 5 years for every 1,000 women who have had DCIS and do NOT take tamoxifen:

- **860 women** will not develop future breast cancer.
- **3 women** will develop blood clots anyway.
- **1 woman** will develop endometrial cancer anyway.
- **140 women** will develop future breast cancer within the 5 years.
In the next 5 years for every 1,000 women who have had DCIS and **TAKE tamoxifen:**

- **912 women** will **NOT** develop future breast cancer (i.e. 52 **fewer** women will be diagnosed with future breast cancer due to tamoxifen).

- **3 additional women** will develop blood clots due to tamoxifen.

- **1 - 2 additional women** will develop endometrial cancer due to tamoxifen.

- **70 women** will develop future breast cancer within the 5 years despite taking tamoxifen.
Summary of Risk management WITH tamoxifen

What are some of the “PROS” of this option?

- My doctor and I can make the choice to take a medication known to be effective against breast cancer
- I will be in control of the treatment I’ll be receiving (as opposed to being randomly assigned to a treatment in the clinical trial option)
- I will have more protection against breast cancer than with the “risk management without tamoxifen” option
- I will not have to fill in questionnaires or become involved in a more time-consuming treatment schedule, as I would in a clinical trial

What are some of the “CONS” of this option?

- Side effects of therapy may be too unpleasant and reduce my current quality of life
- I will have to pay for tamoxifen and this may be a financial cost for me and my family
- I am concerned about the slight possibility of developing endometrial cancer or blood clots as a result of taking tamoxifen
- I want to maximise my chances and with a clinical trial I may be allocated a newer drug that may be more effective than tamoxifen
Option II

IBIS-II DCIS Clinical Trial: tamoxifen or anastrozole

A further option is to participate in the IBIS-II DCIS clinical trial. This research study investigates whether a newer treatment (anastrozole) is as good as or better than tamoxifen in preventing women with DCIS from developing future breast cancer, and whether anastrozole has fewer side effects than tamoxifen. Anastrozole is described in more detail on page 25.

What is a clinical trial?

Clinical trials are a vital part of research into new and more effective medical treatments. Treatments used today (i.e. current standard treatments) have come from testing in clinical trials in the past. For some people, however, clinical trials raise fears of “experimentation” and “being a guinea pig”. Understanding more about clinical trials may reduce these concerns.

Strict controls govern how clinical trials are conducted. Each clinical trial must be approved by an ethics committee. This committee makes sure that the rights of the study participants are protected. New treatments are only assessed in clinical trials after years of extensive testing in laboratories where their safety and effectiveness have been proven. As a result much is already known about the benefits and risks of treatments offered within clinical trials. Sometimes the medication used in a clinical trial is not “new”, it is simply being used in a different way. In some cases, as with anastrozole, the drug may have already been shown to be effective for treating breast cancer, and safe for other groups of participants in earlier clinical trials.
What is a randomised double-blind study?

In a randomised clinical trial, the treatment each participant receives (either the standard or new treatment) is determined “by chance” (using a computer). If either participants or doctors choose which treatment will be received, participants who receive the new drug may be different (for example fitter, or younger) from participants who do not. Randomisation makes sure that the study groups are as similar as possible. This gives a more reliable picture of the effects of the treatments. The researchers know that the treatments used are both effective for the condition being treated. The clinical trial will help to find out which treatment is better.

In a randomised double-blind study (such as IBIS-II DCIS), neither the doctors nor the participants know who is receiving the standard treatment or the newer treatment. It is important that the side effects reported by participants and their doctors are not based on what they expect to happen. If participants know that they are taking the new treatment, they might expect it to work better. If they expect it to work well they may report hopeful signs and not report unpleasant effects. This would bias the trial by making the results of the new treatment look better than they really are. The study co-ordinating centre can find out who is receiving which treatment, so should there be a medical need, this information is readily available to the woman’s doctor. All participants are carefully monitored during the study. Any participant is free to withdraw from the study at any time.
Why do people not take part in a trial?

• They prefer to decide on a treatment with their own doctor.

• They do not want to take a treatment that is still being investigated.

• They do not like the uncertainty of not knowing which treatment they are receiving.

• They may think a trial takes too long.

Why do people take part in a trial?

• They may receive a newer treatment that is not yet available to the general public and that may be more effective than the treatments currently recommended.

• To benefit future generations.

• To give themselves the best chance of reducing the risk of cancer coming back.

• They appreciate the extra personalised care and attention given by research nurses and treating doctors. It has been shown that people receiving treatment on trials do just as well as, or better than those getting the same treatment outside of a clinical trial.
What is the IBIS-II DCIS Clinical Trial?

The IBIS-II (International Breast Cancer Intervention Study-II) DCIS clinical trial is investigating methods of preventing breast cancer. This trial is offered to post-menopausal women who have not had invasive breast cancer but have been treated for DCIS (non-invasive breast cancer). The study is being conducted internationally and will involve more than 4,000 women worldwide. The IBIS-I clinical trial has demonstrated the effectiveness of tamoxifen in the prevention of breast cancer. However, recent findings suggest that a newer drug (anastrozole) may be even more effective than tamoxifen in preventing breast cancer, whilst having fewer side effects overall.

The IBIS-II DCIS study will assess whether anastrozole is equally effective or more effective than tamoxifen in the prevention of breast cancer.

How the trial works

To test which treatment is more effective, women in the IBIS-II DCIS study, who have previously had DCIS, will have their treatment randomly allocated by a computer. One group of 2,000 women will be given tamoxifen and the other group of 2,000 women will receive anastrozole, so the effects of these drugs can be compared. Neither you, your doctors or the medical team will know which medication (tamoxifen or anastrozole) you are taking until after the study is completed. However, this information can be obtained from the coordinating centre, should there be a medical need or if you withdraw for any reason. You may withdraw from the study at any time you wish, or when a change in your condition suggests that it would be best. You can be assured that leaving the study will not influence your relationship with the medical/research staff or your future medical treatment(s).
Anastrozole  
(also known as Arimidex®)

What is it?
Anastrozole is a new type of treatment which has been successfully used to treat oestrogen sensitive (ER+) advanced breast cancers in post-menopausal women, during the last decade. Recent results from a research study (called ATAC - see pages 26-27), and other studies which have included women who had developed early invasive breast cancer, indicate that anastrozole is significantly more effective than tamoxifen in reducing the risk of the breast cancer coming back. Anastrozole was also about twice as effective as tamoxifen in preventing a new breast cancer developing in the opposite breast. Anastrozole seemed to produce fewer short-term side effects than tamoxifen. The IBIS-II DCIS study will assess whether anastrozole is of benefit to women like you who have been treated for DCIS. Longer-term benefits and side effects of anastrozole are being investigated in clinical treatment trials.

How is it taken?
Anastrozole is taken as a tablet once a day for 5 years. At the end of the 5-year study your treatment will stop, and your progress will be monitored for another 5 years. Participants in the study will receive their medication (anastrozole or tamoxifen) free of charge for the length of the treatment phase of the study (5 years).

How does it work?
Anastrozole is a treatment belonging to a group of drugs called aromatase inhibitors. It is designed to reduce the amount of oestrogen produced in post-menopausal women. Whilst tamoxifen binds to the oestrogen receptors in the cell, anastrozole blocks the production of oestrogen in the body, thus reducing oestrogen to almost undetectable levels. As a result it may stop existing breast cancers growing and the development of new oestrogen sensitive (ER+) breast cancers may be prevented.
Anastrozole: Potential BENEFITS

Potentially more effective against breast cancer than tamoxifen, with fewer side effects

The ATAC study compared the effects of anastrozole and tamoxifen in 9,366 post-menopausal women with early stage oestrogen-sensitive invasive breast cancer (women were monitored for more than 5 years). This study looked at how effective each treatment is in preventing breast cancer from returning, either in the breast where cancer developed originally, or in the other breast.

In this study, women who took anastrozole had fewer incidences of breast cancer returning and fewer side effects, compared to women who took tamoxifen. For example, out of 1,000 women allocated to 5 years of treatment with anastrozole or tamoxifen for early stage breast cancer, 130 women who received anastrozole had their cancer come back. In comparison, out of 1,000 women who received tamoxifen, 161 women had their cancer come back (see diagram on page 27).

Both tamoxifen and anastrozole are effective in reducing the risk of breast cancer coming back. The IBIS-II DCIS study will indicate whether anastrozole is more effective than tamoxifen in preventing breast cancer development in women at increased risk of breast cancer.
ATAC trial: Effectiveness of tamoxifen vs. anastrozole in women with early stage invasive breast cancer

1,000 women taking TAMOXIFEN for 5 years

1,000 women taking ANASTROZOLE for 5 years

161 130
Women whose cancer came back

839 870
Women whose cancer did not come back
Anastrozole: Potential BENEFITS

The previous page was about women who already had invasive breast cancer. How may anastrozole assist women diagnosed with DCIS to prevent the development of invasive breast cancer in the future?

Based on previous studies, it is hoped that anastrozole will be more effective than tamoxifen in the prevention of breast cancer, with fewer serious side effects. The IBIS-II DCIS study will determine if this is true.
Anastrozole: SIDE EFFECTS and potential RISKS

Although most women find anastrozole easy to tolerate, it can have some adverse side effects. These, however, are rarely serious.

COMMON SIDE EFFECTS
(Between 1 in 10 women and 1 in 100 experience these)

- **Menopausal-like symptoms: Hot flushes and vaginal dryness**
  Hot flushes are fairly common side effects but are usually milder than those experienced with tamoxifen. Vaginal dryness is a common side effect. HRT cannot be taken to ease these side effects whilst on the IBIS-II DCIS study. Alternative treatments such as herbal medicine can be used.

- **Joint/back pain or stiffness**
  Some women who have taken anastrozole have noticed that they felt mild to severe joint/back pain and stiffness in the morning but this disappeared after they started moving around.

- **Carpal Tunnel Syndrome**
  Some women may experience pressure on a nerve at the wrist causing pain, weakness or numbness. This condition, known as Carpal Tunnel Syndrome, can be treated.

These side effects are usually temporary and disappear when anastrozole is no longer taken.
Anastrozole: SIDE EFFECTS and potential RISKS

COMMON SIDE EFFECTS (cont.)

- Fractures
  Oestrogen is necessary to maintain bone density. Since anastrozole directly reduces oestrogen levels, it may lead to loss of bone density. As a result, the risk of fractures may increase whilst taking anastrozole, but will return to normal once anastrozole is no longer taken.

- Osteoporosis
  Osteoporosis affects 45 in every 100 women who are 50 years of age or older, during their lifetime. For some women taking anastrozole the risk of fractures and osteoporosis appears to increase and this is currently being investigated in a number of studies. If you choose to take part in the IBIS-II Prevention study, your bone density will be assessed, and if osteoporosis is detected treatment for this will be recommended.

VERY RARE but potentially SERIOUS SIDE EFFECTS

- Allergic skin reactions
  (less than 1 in 10,000 women experience this)

  Very rarely women develop a severe skin reaction in the form of lesions, blisters or ulcers. Contact your study doctor immediately if you develop any of these symptoms.
Anastrozole: SIDE EFFECTS and potential RISKS

Each diagram represents 100 women. The light-orange shaded area shows the number of women in the general population who may develop each of the presented symptoms over 5 years. The darker orange shaded area shows the number of additional women that may develop each of the presented symptoms over 5 years because they are taking ANASTROZOLE.

Compared to the general population, an additional 10 women taking ANASTROZOLE may experience:

- **Hot flushes**

Compared to the general population, an additional 7 women taking ANASTROZOLE may experience:

- **Joint pain or stiffness**
Anastrozole: SIDE EFFECTS and potential RISKS

What to do if side effects become too bothersome

It is not expected that taking part in this clinical trial should cause you undue discomfort. However, should the side effects become too unpleasant, it is strongly recommended that you discuss available treatment options with your study co-ordinator or doctor. If you become concerned about a symptom, a “treatment holiday” of up to three months may be possible. To protect your health, it is strongly advised that any changes to the treatment program are made by your study doctor.
## Summary of main BENEFITS & RISKS

### Breast cancer

<table>
<thead>
<tr>
<th>TAMOXIFEN</th>
<th>ANASTROZOLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ Known to reduce the risk of breast cancer coming back</td>
<td>+ + Known to reduce the risk of breast cancer coming back (slightly more effective than tamoxifen in doing this)</td>
</tr>
<tr>
<td>+ Known to prevent or delay breast cancer developing for the first time</td>
<td>? (+) Potential ability to prevent breast cancer developing for the 1st time; this needs confirmation</td>
</tr>
</tbody>
</table>

### Bone Density Loss

<table>
<thead>
<tr>
<th>TAMOXIFEN</th>
<th>ANASTROZOLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ Reduces the risk of bone density loss</td>
<td>- Increases the risk of bone density loss</td>
</tr>
</tbody>
</table>

### Endometrial cancer

<table>
<thead>
<tr>
<th>TAMOXIFEN</th>
<th>ANASTROZOLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Known to increase the risk of endometrial cancer</td>
<td>+ Does not increase the risk of endometrial cancer</td>
</tr>
</tbody>
</table>

### Blood clots

<table>
<thead>
<tr>
<th>TAMOXIFEN</th>
<th>ANASTROZOLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Known to increase the risk of blood clots</td>
<td>+ Does not increase the risk of blood clots</td>
</tr>
</tbody>
</table>

| + ---- Known benefit | ? (+) ---- Potential benefit |
| - ---- Known risk |
What is involved if you join the study?

If you join the IBIS-II DCIS study, your wellbeing will be closely monitored and all information regarding your condition will be carefully and confidentially recorded. You will have some additional examinations and tests at no financial cost to you. Although they can be inconvenient, these tests make sure you are thoroughly monitored throughout your treatment.

Screening mammograms and clinical examinations

Screening mammograms and clinical examinations will be done at least once a year. This is normal following the diagnosis of DCIS and would be carried out regardless of whether you join the IBIS-II DCIS study or not.

Medication

You’ll be given a 6-months supply of tablets in numbered containers. Extra tablets will be included to allow for some delay in the next appointment (e.g. due to travel or sickness). Whilst on the study, you will be asked to take 2 tablets a day, an active drug and a placebo tablet. A placebo tablet is a tablet that looks like the trial medication but contains no active ingredients. You’ll be taking a tamoxifen tablet and a placebo tablet; or an anastrozole tablet and a placebo tablet. The placebo tablet is used to ensure that neither you nor your doctor knows which treatment you are receiving. However, since the tablets you receive may contain lactose and gluten, you should not participate in the study if you suffer from lactose or gluten intolerance. You don’t have to change your diet or lifestyle whilst taking the medication.
Regular support

You will have access to a support team who can provide information on a regular basis during the study. This team includes your study doctor and your IBIS-II study co-ordinator. During the first year of the study, you will be asked to come to the clinic (at 6 months and 12 months), for a breast examination and to check your general health. After the first year of the study, your study co-ordinator will arrange your annual follow-up visits. With your permission, your GP will also be informed about the study and will be able to provide additional information should you need any.
Tests & Questionnaires whilst on the study

Bone density tests and advice for healthy bones

At the start of the study, you will have an x-ray of your spine and a bone mineral density test (DXA scan) to assess the condition of your bones (unless you have already had one during the past 2 years).

Throughout the study you will be offered advice on how to maintain healthy bones. This advice is the same as for similar women in the community not on the trial. This advice covers exposure to sunlight, weight bearing exercises, Calcium and Vitamin D supplements (you will need to pay for any supplements you use).

Blood samples

When you join the study a blood sample of 20ml (about 4 teaspoons) will be taken. A further 10ml blood sample (about 2 teaspoons) will be taken at years 1 and 5 of the study.

Questionnaires

After the 5th year of treatment, you will be asked to complete questionnaires once a year for another 5 years in order to monitor your health and wellbeing following the treatment.

You will be able to contact your study doctor or co-ordinator between your visits.
## Summary table of follow-up schedule whilst on the study

<table>
<thead>
<tr>
<th></th>
<th>0-1 years</th>
<th>2-5 years</th>
<th>6-10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Contact by IBIS-II study co-ordinator</strong>*</td>
<td>Every 6 months</td>
<td>Every 6 months or 12 months (your choice)</td>
<td>Once a year</td>
</tr>
<tr>
<td><strong>Clinical examination</strong></td>
<td>At study entry, 6 months and 1 year</td>
<td>Once a year</td>
<td>Will be discussed with study doctor</td>
</tr>
<tr>
<td><strong>Mammogram</strong></td>
<td>Possibly at study entry; At 1 year</td>
<td>Once a year</td>
<td>Once a year</td>
</tr>
<tr>
<td><strong>Blood sample</strong></td>
<td>At study entry and 1 year</td>
<td>At year 5</td>
<td>--</td>
</tr>
<tr>
<td><strong>Bone density tests</strong></td>
<td>At study entry (unless one done within last 2 years)</td>
<td>Only if recommended by your GP or study doctor</td>
<td>Only if recommended by your GP or study doctor</td>
</tr>
<tr>
<td><strong>Questionnaire</strong></td>
<td>--</td>
<td>--</td>
<td>Once a year</td>
</tr>
</tbody>
</table>

*You can contact your study co-ordinator at any time*
Summary of Option II
Risk management on clinical trial

What are some “PROS” of this option?

- I want to maximise my chances of preventing the development of breast cancer and by taking part in a clinical trial I may be allocated to the newer treatment (anastrozole), which may be more effective in this respect than the standard treatment (tamoxifen).

- I will be closely monitored on the trial and be supported by a research team. I will be contacted to arrange my screening follow up appointments. I will have any medical tests arranged for me. My bone density will be assessed.

- Irrespective of which drug I am given, I will be receiving excellent treatment and attention.

- I will not have to pay for whichever drug I receive whilst on the study.

- My observations will be helping scientific research worldwide, and other women in the future, and probably help to save lives.

What are some “CONS” of this option?

- I will not know which of the two drugs I am receiving.

- I may have to deal with side effects (see pages 15-17 and 29-32).

- I will have to complete questionnaires and have three additional blood tests.

- I cannot take Hormone Replacement Therapy (HRT) whilst on the study.

- I will need to visit an IBIS centre 6 monthly in the first year and thereafter annually for 5 years.
Making a decision

The previous pages have outlined the main risk management options available to you now. The following steps may help you to make the decision whether or not to join the IBIS-II DCIS study.

The decision-making process can be helped by following these 6 steps:

1. Understand your diagnosis and your future risk of breast cancer as fully as you can.

2. Understand your options for further management and the risks and benefits of these options.

3. Review the pros and cons of these options.

4. Assess how important the pros and cons are to you.

5. Prioritise the pros and cons of the study for you (and your family).

6. Get more information/clarification about any uncertain areas.

You have already gone through steps 1-3. To help you complete steps 4-6 and come to the decision that suits you best, we have included examples of how some women reached their decision. This information is presented in a work-sheet format that you can use (see overleaf).

You will receive excellent care whether you choose standard treatment or to take part in the clinical trial.
Worksheets

This worksheet starts with examples of how some women view the pros and cons of the standard treatment and the IBIS-II DCIS study (next 2 pages). This is followed by your own worksheet, where we invite you to list the pros and cons of the statements in the boxes and rate how important these are to you.

Each statement has three options underneath it, each describing a level of concern that you may have about the issue raised by the statement. By circling one of the options, you can indicate (and see at a glance) how important each issue is to you:

- Circling **Big Concern** => indicates that the issue is **very important** to you,
- Circling **Small Concern** => indicates that the issue is **somewhat important**,
- Circling **No Concern** => indicates that the issue is **not important** to you

The column with the least number of concern options circled may indicate that you are more inclined to choose that option. There is a space for you to add your own pros and cons and rate their importance.

**Example:**
One of the cons of participating in the IBIS-II DCIS study are the side-effects of anastrozole or tamoxifen. If a woman feels that she will be able to handle these (i.e. this issue is only a small concern to her), she circles “Small Concern” under this statement:

```
Side effects from anastrozole or tamoxifen, whichever I’m allocated

No Concern Small Concern Big Concern

“I think I’ll be able to handle that”

At the bottom of the worksheet you can indicate (by circling one of the 1-5 stars) which way you are leaning in your decision:

Participating in the study

Not participating in the study

By circling the 3rd star, this woman is showing she is still unsure whether or not to join the trial.
```
Anna’s worksheet: “Will the IBIS-II DCIS study suit me?”

<table>
<thead>
<tr>
<th>PROS of the study</th>
<th>CONS of the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>This may help future generations of women</td>
<td>I may get a drug not previously tested for DCIS</td>
</tr>
<tr>
<td>“I can make a difference. My daughter may benefit”</td>
<td>“This does not concern me”</td>
</tr>
<tr>
<td>No Benefit</td>
<td>No Concern  Small Concern  Big Concern</td>
</tr>
<tr>
<td>Small Benefit</td>
<td></td>
</tr>
<tr>
<td>Big Benefit</td>
<td></td>
</tr>
<tr>
<td>I will get excellent care on the trial</td>
<td>I won’t know which drug I’m getting</td>
</tr>
<tr>
<td>“It’s good to know I am getting cutting edge care”</td>
<td>“I understand why this is necessary”</td>
</tr>
<tr>
<td>No Benefit</td>
<td>No Concern  Small Concern  Big Concern</td>
</tr>
<tr>
<td>Small Benefit</td>
<td></td>
</tr>
<tr>
<td>Big Benefit</td>
<td></td>
</tr>
<tr>
<td>I might get access to a new and better drug which may reduce my chance of</td>
<td>Side effects from anastrozole or tamoxifen, whichever I’m allocated</td>
</tr>
<tr>
<td>getting breast cancer again</td>
<td>“I think I’ll be able to handle that”</td>
</tr>
<tr>
<td>“It’s good to know I’m getting every chance”</td>
<td>No Concern  Small Concern  Big Concern</td>
</tr>
<tr>
<td>No Benefit</td>
<td></td>
</tr>
<tr>
<td>Small Benefit</td>
<td></td>
</tr>
<tr>
<td>Big Benefit</td>
<td></td>
</tr>
<tr>
<td>Other:</td>
<td>Other:</td>
</tr>
<tr>
<td>No Benefit</td>
<td>No Concern  Small Concern  Big Concern</td>
</tr>
<tr>
<td>Small Benefit</td>
<td></td>
</tr>
<tr>
<td>Big Benefit</td>
<td></td>
</tr>
</tbody>
</table>

Any further questions? Will I get access to the tablets once the trial is over?

How is Anna leaning? Participating in the study (circle one star only) Not participating in the study

(Anna is leaning towards joining the study)
Dianne’s worksheet: “Will the IBIS-II DCIS study suit me?”

<table>
<thead>
<tr>
<th>PROS of the study</th>
<th>CONS of the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>This may help future generations of women</td>
<td>I may get a drug not previously tested for DCIS</td>
</tr>
<tr>
<td>“I’m more important right now”</td>
<td>“This does not concern me”</td>
</tr>
<tr>
<td>(Circle one star only)</td>
<td>(Circle one star only)</td>
</tr>
<tr>
<td>No Benefit</td>
<td>No Concern</td>
</tr>
<tr>
<td>Small Benefit</td>
<td>Small Concern</td>
</tr>
<tr>
<td>Big Benefit</td>
<td>Big Concern</td>
</tr>
</tbody>
</table>

| I will get excellent care on the trial | I won’t know which drug I’m getting |
| “I get excellent care from my doctor now” | “I’d prefer to know” |
| (Circle one star only) | (Circle one star only) |
| No Benefit | No Concern |
| Small Benefit | Small Concern |
| Big Benefit | Big Concern |

| I might get access to a new and better drug which may reduce my chance of getting breast cancer again | Side effects from anastrozole or tamoxifen, whichever I’m allocated |
| “But it might not be better” | “I don’t want to have hot flushes” |
| (Circle one star only) | (Circle one star only) |
| No Benefit | No Concern |
| Small Benefit | Small Concern |
| Big Benefit | Big Concern |

| Other: | Other: |
| “I don’t like blood tests” | “I don’t want to have hot flushes” |
| (Circle one star only) | (Circle one star only) |
| No Benefit | No Concern |
| Small Benefit | Small Concern |
| Big Benefit | Big Concern |

Participating in the study

Not participating in the study

Any further questions? Can I continue taking the drugs when the treatment is over?

How is Dianne leaning? Participating in the study ★ ★ ★ ★ ★ Not participating in the study

(circle one star only)

(Dianne is leaning towards NOT joining the study)
YOUR worksheet: “Will the IBIS-II DCIS study suit me?”

<table>
<thead>
<tr>
<th>PROS of the study</th>
<th>CONS of the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>This may help future generations of women</td>
<td>I may get a drug not previously tested for DCIS</td>
</tr>
<tr>
<td>No Benefit</td>
<td>No Concern</td>
</tr>
<tr>
<td>Small Benefit</td>
<td>Small Concern</td>
</tr>
<tr>
<td>Big Benefit</td>
<td>Big Concern</td>
</tr>
<tr>
<td>I will get excellent care on the trial</td>
<td>I won’t know which drug I’m getting</td>
</tr>
<tr>
<td>No Benefit</td>
<td>No Concern</td>
</tr>
<tr>
<td>Small Benefit</td>
<td>Small Concern</td>
</tr>
<tr>
<td>Big Benefit</td>
<td>Big Concern</td>
</tr>
<tr>
<td>I might get access to a new and better drug which may reduce my chance of getting breast cancer again</td>
<td>Side effects from anastrozole or tamoxifen, whichever i’m allocated</td>
</tr>
<tr>
<td>No Benefit</td>
<td>No Concern</td>
</tr>
<tr>
<td>Small Benefit</td>
<td>Small Concern</td>
</tr>
<tr>
<td>Big Benefit</td>
<td>Big Concern</td>
</tr>
<tr>
<td>Other:</td>
<td>Other:</td>
</tr>
<tr>
<td>No Benefit</td>
<td>No Concern</td>
</tr>
<tr>
<td>Small Benefit</td>
<td>Small Concern</td>
</tr>
<tr>
<td>Big Benefit</td>
<td>Big Concern</td>
</tr>
</tbody>
</table>

Any further questions?

What are YOU leaning towards?

<table>
<thead>
<tr>
<th>Participating in the study</th>
<th>★ ★ ★ ★ ★</th>
<th>Not participating in the study</th>
</tr>
</thead>
</table>

(circle one star only)
Further contacts

Many women seek information on the internet about breast cancer treatments, research, clinical trials and support services. However not all information reported is accurate or reliable.

Listed below are a number of websites that are prepared by cancer organisations. As the information can only be general and not specific to your situation, it is important to discuss any questions you have with your treating doctor.

Australia and New Zealand

Australian New Zealand Breast Cancer Trials Group  www.anzbctg.org
Breast Cancer Institute of Australia  www.bcia.org.au
IBIS-II co-ordinating centre, UK  www.ibis-trials.org
National Breast Cancer Centre, Australia  www.nbcc.org.au
The Cancer Council Australia  www.cancer.org.au

The IBIS-II DCIS Research Protocol, Decision Aid Booklet, and Questionnaires have been reviewed and endorsed by the ANZ BCTG Consumer Advisory Panel.
References


• The ATAC (Arimidex, Tamoxifen Alone or in Combination) Trialists’ Group. Results of the ATAC (Arimidex, Tamoxifen Alone or in Combination) trial after completion of 5 years’ adjuvant treatment for breast cancer. *The Lancet* 2005; 365:60-62.


Glossary of terms

**Advanced breast cancers**: Cancer cells have spread past the breast and armpit to other parts or organs of the body.

**Anastrozole (also known as Arimidex®)**: A new aromatase inhibitor therapy (tablets) for treating breast cancer which stops the body making female sex hormones (oestrogen).

**Aromatase inhibitors**: Drugs that block the enzyme aromatase in post-menopausal women. They lower the amount of oestrogen in your body.

**Bone density**: How closely compacted the substance is inside your bones. A measure of bone strength.

**Bone mineral density test**: An X-ray to determine the amount of calcium and other minerals in the bone, used to diagnose osteoporosis.

**Cancer**: A group of diseases in which malignant cells grow out of control and may spread to other parts of the body.

**Carpal Tunnel Syndrome**: Pressure on a nerve at the wrist causing pain, weakness or numbness. This condition can be treated.

**Cataract**: A disease of the eye, causing impaired vision or blindness.

**Cholesterol**: A substance found in fats in the bloodstream.

**Clinical trial**: A scientific test of the effectiveness and safety of a drug involving consenting human participants.

**Cyst**: An accumulation of fluid or semisolid material within a small sac.

**DCIS**: Non-invasive (early) breast cancer that has not spread to neighbouring tissue.

**Diagnosis**: Process of identifying a disease from symptoms & tests.

**Endometrial cancer**: A cancer of the lining of the uterus.
ER: Oestrogen receptor, a part of the cell where oestrogen attaches.

Hormone sensitive breast cancer: A breast cancer that grows in response to the female hormone oestrogen.

Gynaecological problems: Problems affecting the female reproductive organs.

HRT (Hormone Replacement Therapy): Medication containing one or more female hormones, often used to treat symptoms of menopause.

Hysterectomy: Surgical operation for removing the uterus.

Invasive breast cancer: Breast cancer which has spread beyond the tissue in which it developed and is growing into surrounding, healthy tissues.

Mammogram: A low-dose X-ray of the breast to check for any abnormal tissue.

Oestrogen: Female sex hormones produced primarily by the ovaries in pre-menopausal women and by the aromatase enzyme in post-menopausal women.

Osteoporosis: A condition that weakens bones, and makes them more prone to fracture.

Menopause: The time in a woman’s life when the ovaries cease to function and menstrual periods stop for at least 12 months.

Post-menopausal: The period in a woman’s life after the menopause.

Radiotherapy: Diagnosis and treatment of disease by X-rays.

Standard risk management: The current way to minimise your risk of breast cancer.

Tamoxifen: A long-established treatment for breast cancer, which stops the action of oestrogen on cancer cells.

Treatment holiday: Stopping the treatment for a period of time.
ACKNOWLEDGEMENTS

This Decision Aid was conceived and developed by a team from the Medical Psychology Research Unit at the University of Sydney, led by Professor Phyllis Butow and Dr Ilona Juraskova. Noteworthy contributors include Ms Anna-Lena Lopez and Mr Benaud Smith. Graphic design was undertaken by Ben Carew who can be contacted on +61 2 8307 3800.

We gratefully acknowledge the following people for their valuable input into the development of this resource:

- The women who participated in earlier breast cancer prevention studies who reviewed the Decision Aid
- The ANZ BCTG IBIS-II team, particularly Professor John Forbes, Mrs Margaret Seccombe, and Ms Rochelle Thornton
- The ANZ BCTG Consumer Advisory Panel
- The expert health care professionals: Associate Professor Fran Boyle, Dr Nicole McCarthy, Professor Alan Coates, Dr Simone de Morgan and Dr Kelly Phillips
- The Cancer Research UK team, particularly Professor Jack Cuzick

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