Transcript from Webinar: Tuesday 14 March 2017

Topic: **Learning to love Tamoxifen and Aromatase Inhibitors**

Panelists: **Chanda Warren**

Dr David Porter

Dr Helen Warren

NZBCF: **Adele Gautier**

AG Hello and welcome. My name's Adele Gautier and tonight we're talking about learning to love Tamoxifen and Aromatase inhibitors. Before we get started, some housekeeping. If you have any technical issues there should be a phone number in the chat box at the bottom left of your screen, and you'll need to enter the pass code. Or you can enter details of the problem in the chat box and our support team will get in touch. You can use the chat box during the Webinar to ask questions which hopefully we'll be able to get to later, and you can also chat to other people there. Don't worry about missing out, the webinar's being recorded and it will be available on our website in the next few days. We have 3 panellists who are going to share with you tonight. Chanda is about to tick 5 years on Tamoxifen. David Porter is an oncologist at Auckland Hospital. And Helen Warren is a professor and doctor with a special interest in menopausal symptoms. But first we're going to hear from Chanda. And thank you so much for being here tonight. How about I just let you get started and you can share all your lovely information with Tamoxifen.

PowerPoint slide 1:

- **Diagnosed at 45**
- **Surgery and treatment marathon**
- **Reconstruction**

CW Thank you. And thank you to the Breast Cancer Foundation for hosting this evening. Hello to everybody that's joining us this evening. The first thing I wanted to say was that my specialist has continued to tell me that my side effects are high on the spectrum. So I just wanted to say to our listeners that, especially those that are new to Tamoxifen that what has happened to me won't necessarily happen to you.

So I often think of us breast cancer patients as quite similar to marathon runners. If you think about it, diagnosis is marathon one. Surgery marathon two. Chemo and radiation, another marathon. Reconstruction if you have it, marathon four. And then after you've done all of that you then enter the longest, and what can be the most difficult part of the marathon which is Tamoxifen and hormone therapy. And this is the time when so many of us aren't making it to the finish line because Tamoxifen and hormone therapy can be so disruptive and so life changing.

The evidence does tell us that it remains the best drug available for many of us to prevent a recurrence, and to protect us now and into the future.

So a little bit about my breast cancer marathon. I was diagnosed when I was 45 with invasive lobular breast cancer. A few days after the diagnosis I had a mastectomy. Not long after my oncologist started me on Tamoxifen with instructions to start monthly injections after radiation was completed. 18 months later I had a trans flap reconstruction which was a great success and I continue to be delighted with it every day. Certainly it's silver lining for me.

So, well what happened when I started Tamoxifen? I immediately understood why nearly half of women taking it give it up. In fact I was so bad that just a few weeks into my radiation therapy my radiation oncologist asked me to stop Tamoxifen because the side effects were so difficult for me. I remember talking to her in her office. I felt very brain foggy. She said it was almost as if my personality had been changed. And I remember that discussion just so clearly. I was hopelessly tired, but worst of all I had absolutely no motivation to do anything. So I stopped the Tamoxifen and restarted once I had completed radiation. That seems a long time ago now because in April I will be celebrating my halfway mark with Tamoxifen and 5 years cancer free. But for lots of us Tamoxifen is extraordinarily difficult and very disruptive, and the side effects can be a real problem to manage.

PowerPoint slide 2:
Tamoxifen and me

- **Halfway there – celebrating 5 years**
- **Extraordinarily difficult and disruptive**
- **Cognition/ memory problems**
- **Hot flushes**
- **Fatigue**
- **Weight gain**

CW So, side effects. When I first started as I said my brain was very foggy. And when I was looking back in my journal preparing for this evening I saw that I had written the times that I felt as though I had been knocked unconscious, had woken up with some kind of brain injury. The change was enormous. The things that I struggle the most with are remembering things and processing information. I find it very difficult to multi-task and organise. I find it very difficult to pay attention, which is you know not great. I have difficulty shifting focus from one thing to another. And I just seem to have a much lower tolerance for stressful situations. I've got a much lower initiative and I do have far less motivation than what I used to have. And I have to say despite having every alarm known to man, reminders, notebooks, oven clock, txts from friends and family I still manage to forget so many things. And if I wasn't relying on bullet points tonight which you've probably noticed I'm reading we would be here probably until tomorrow night if I was relying on my brain. So yeah, that's a generalised view.

So with that in mind I think you also have to take things with a little bit of humour. Now one of the funniest things that was ever said to me, I was talking to somebody complaining about all of these problems. About not being able to multi task. Not being able to concentrate. Short attention span. And this person replied and looked at me and said well basically Chanda what's happening is that by removing all of the oestrogen out of your body you are now starting to behave like a man. Now I thought that was really funny.

So back to the actual side effects. So hot flushes and sweats and fatigue. I think that we probably would agree that these are just so disruptive. They cause sleeplessness, fatigue and they're very difficult to manage. I think that the fatigue that I experience is partly due to these hot flushes which wake me up through the night every night.

The fatigue comes on instantly and there is no way you can manage fatigue other than to rest. I stop what I'm doing, and sometimes it happens when I'm driving and that's particularly disruptive and annoying. Weight gain. Right. This is a constant issue for me and I didn't used to be, but I'm continually hungry. I have to work really hard to control my weight. Most of us put on weight from diagnosis. It's a hot topic on all of the social media groups and support groups that I'm part of. We're all in the same boat. I try to eat healthily and I keep up to date with the research around nutrition but it's a daily battle as my appetite really just gets the best of me. But once again I know this is to do with not having enough oestrogen in my body and so I just as I say have to try and keep on top of that.

I've also had a problem with uterine thickening. I've had 2 surgeries because of this and it can be a side effect of Tamoxifen. Okay. So let's talk about now the things that have worked for me.

PowerPoint slide 3:
What has worked for me

- **Sleep hygiene**
- **Your medical team – critical relationship 5+ years**
- **Family and friends – must share your goals**
- **Support groups and online community (mybc)**
- **Knowing what to expect helps acceptance**
- **Professional counselling**

CW Well I'm absolutely certain that having a supportive medical team has been critical to me in getting through my Tamoxifen treatment this far. My Oncologist Dr Mike McCrystal. My GP Dr Erica Lauder, and my breast surgeon Dr Erica Whineray Kelly together support me to continue and complete my treatment. They've talked honestly about side effects from the outset and we have a collaborative relationship and I think that is just so important for us. I urge you all to ensure that your medical team share your goals and understand you, not just as a cancer patient but as mother, partner, and daughter and so on. When I visit my oncologist and my GP I am the one doing most of the talking to start with. They listen and I know without a shadow of a doubt when I leave that they really actually care about me. And I hope all of you have similar relationships with your medical team because I know what a difference they have made to this whole experience of hormone therapy and treatment. But having said that, oncologists and GPs are not mind readers. And so as patients we have a very high level of responsibility to communicate very clearly with these people about how we're feeling. And you have to trust them 100%.

Now if you are having any trouble at all with communication or you don't feel that for some reason that they don't understand you then I would recommend you look at making some changes because these relationships with your oncologist, GP and breast surgeon are critical for your wellbeing.

So sleep hygiene. Is really important. I try not to use a device before going to bed because we all hear constantly that it's not good for sleep patterns. So I try really hard not to do that. I do have Egyptian cotton sheets and I cannot recommend them enough

because just the fact that they're cool and they are really nice to sleep on when you're suffering with terrible hot flushes and sweats etc.

I tried Melatonin which has worked in the past but it does have its limitations with me. Sometimes it works, sometimes it doesn't. I do use Zopiclone but really only in case of an emergency because I just don't want to panic about something on the next day. So I did have one last night. I try not to drink coffee after midday.

Okay. So family and friends and support groups. This is really important. The goal for all of us is to get through our treatment. But it's hard to do it on your own and we need support and encouragement from friends and family. And I hope that we've got some friends and family listening in tonight so that they can learn about Tamoxifen and hormone therapy. Try and involve friends and family in treatment so that they can get a little bit of understanding about the side effects.

Knowing what to expect. Well it's not just our lives that change. The lives of those close to us do as well and it can be a big adjustment. It certainly was for my family and I. Everybody in your life needs to be ready for this and it's never too late to start involving them. I took family members with me to my appointments and it helped us all enormously. It's so important that we are supported and encouraged to complete the hormone therapy. So invite them to see the webinars like we're having tonight. Let them look at the breast cancer online community which I found to be so useful and helpful. And professional counselling. Well this has been really useful for me and helpful as well. You can access free counselling through the New Zealand Breast Cancer Foundation and I have friends at mybc.care and other breast cancer support groups. And I can honestly say that being part of a community that completely understands each other is beyond words.

Exercise. Well we all know that exercise has got to be good. Everything I've read says exercise is good for physical health but it's also really great for our brains. My problem is I really struggle with motivation and I do try and walk 30 minutes every other day. I was doing dragon boating a few years ago which I loved, but I did have to stop that because I had blood pressure problems. But I highly recommend dragon boating for fitness and pure joy. Bone training exercises also help but the research says that you have to be very consistent and you must look at increasing your effort on these particular exercises. I'm currently on Escitalopram for hot flushes. I did try Effexor but couldn't tolerate it. I also take Vitamin D monthly. I'm going to retry magnesium once the results of this new trial are out. I did take it for some cramping problems but I had issues with nausea. And I never have grapefruit because it interferes with Tamoxifen. And I'm also going to try some yoga next week.

PowerPoint slide 4:
The future

- **Expect treatment to work, and focus on the benefits**
- **Expect side effects and accept that things have changed**
- **Know your limits**
- **Power regained through knowledge and choices**
- **The biggest fight of your life**

CW So the future. Well I have to say I don't exactly like Tamoxifen but I love that it is keeping me cancer free now and will continue to protect me into the future. Also I expect the Tamoxifen treatment to work. With Tamoxifen my future is cancer free and I try hard to focus on the benefits rather than on the side effects.

Okay. Expecting side effects and knowing what your limits are. Being able to accept that things have changed has meant re-assessing what my limits are. What I can and cannot do. It can be overwhelming just to get through the marathon of breast cancer I talked about in the beginning. Things that changed, some were immediate. Others took a little longer but nothing will ever be the same for me, but I'm okay with that now. Know what your limits are and work towards staying within those limits because that really is the best place to be.

Power. Well one of the most frustrating feelings is that of powerlessness. I think all of us know that feeling. Suddenly we have the diagnosis and then forever we are told what to do. I find being informed about breast cancer in general has really helped me regain some of that lost power. I want to know about the latest research and I want to be able to talk about it with my medical team. This has been something that has really helped me through this entire process and there are loads of websites where you can get this information from, but stick with the trusted resources. There are quite a few including New Zealand Breast Cancer mybc.care.

So just to finish, tolerating the hormone therapy side effects is not easy but you can do it, but you need support and encouragement. Of course I struggle at times with acceptance about the way things have changed for me and my family, but I know my limits and thankfully so do they. There is far less likelihood of disappointment for myself and others now, and that is a really good space for all of us to be in. Making choices has helped me regain some power over Tamoxifen too. So be strong. This marathon is a long one, but you can do it. And I hope that everyone listening will make it to the finish line with their Tamoxifen therapy –because your life is worth it. Thank you.

AG: Great. Thank you so much Chanda. We're going to hear now from David Porter. David is a medical oncologist at Auckland Hospital who specialises in breast cancer. His interests include supportive care to people with chemotherapy and Tamoxifen. David tell us a bit about how these drugs work, what the side effects are and what you recommend.

Dr David Porter, Oncologist Auckland City Hospital

PowerPoint Slide 1:
What is hormone therapy?

- **Tamoxifen – blocks the action of oestrogen and is effective in women both before and after the menopause**
- **Aromatase inhibitors (Letrozole, Anastrozole, Exemestane) – reduce non-ovarian production of oestrogen, so are effective only in women after the menopause. Can only be used in combination with ovarian suppression/ surgical removal in younger women.**

DP: So I haven't got a human story to tell like the one I've just heard but that sets a very important scene for all of us. I must say when I first heard the title of this talk and endocrine therapy I thought well that's a bad romance.

So to start off what is hormone therapy or endocrine therapy, there are basically 2 choices. Tamoxifen is the older choice. It is 50 years old. It was first proposed in 1966. It blocks the action of oestrogen and is effective both before and after the menopause. The alternative aromatase inhibitors of which there are currently 3 on the market. These reduce non ovarian production of oestrogen and so effective in women who have been through the menopause. They can only be used in pre-menopausal women as ovarian function is also suppressed.

PowerPoint Slide 2:
How do we choose:

1. **Most effective**
2. **Least harm**

Factors in that decision:

- **Risk, size, grade, node involvement and ER/PR status**
- **Genomic information**
- **Contraindications (reasons not to)**
- **Tamoxifen: DVTs/ pulmonary emboli, risk of endometrial cancer**
- **AIs: joint pains, osteoporosis risk**

Generic information is more really about choosing chemotherapy although that could be important in the future about endocrine therapy. What the contraindications, well the reason not to use a particular treatment, so Tamoxifen might be a past history of clots or risk of endometrial cancer. For aromatase inhibitors the main one's joint pain and osteoporosis is really the side effect.

So how do we choose between them? Ideally we don't. Ideally the person who we're talking to with breast cancer actually makes that decision based on how we put the case to them. But there are 2 parameters really that are important. One is what's the most effective? And which is the least harm? Putting the tenet that if you have 2 treatments that are exactly as effective as each other you choose the one that does the least damage. If you have one that's more effective, then you choose that. I think the truth is somewhere between those 2. It is possible to do better as far as the breast cancer goes, but also introduce greater actual risk to the whole person. And I think it's important we see people as whole people, not just cases of breast cancer. So there are some factors in that decision. The first is the pathology information which tells us just how high risk that is.

Second question is once you've chosen a drug how long do we use it for? Well that's a controversial area. And people have conferences that go on for 4 days about that. As we currently sit, my personal view is that if you have a low risk breast cancer I tend to use Tamoxifen for 5 years as my starting point. For higher risk women now I use aromatase inhibitor with or without ovarian function for younger women. I use that for 5 years too. And the reason for that is that there are 4 studies presented last year. One of them has more benefit of prolonged aromatase inhibition beyond 5 years. The other 3 don't show anything at all.

So what are the other standard options? Well in the past particular in Auckland we've studied Tamoxifen switching to an aromatase inhibitor after 2 to 3 years on a 5 year course. The advantage of that being that we split the side effect profile because of osteoporosis and endometrial cancer in particular are reduced. But for younger women a 5 year course then switching over to aromatase inhibitor once the person has been through the menopause is something that can be done, although as time goes on people for whom that is the right thing to do are getting smaller.

One thing I quite like which isn't done much is to start off with the aromatase inhibitor first, and then changing to Tamoxifen after a couple of years. And the other option is Tamoxifen for 10 years. Again there will be a select group of people for whom this is a good decision, but not necessarily what I think of now as what I prefer to do.

PowerPoint Slide 3:

- **Tamoxifen -> AI ("Switch"/"extended)**

- **AI -> tamoxifen**
- **Tamoxifen for 10 years**
- **What can be tolerated, or made to be tolerable, for as long as possible (up to max effective duration) if a non-standard approach is needed.**

BUT
…50% of patients do not complete their treatment, mostly due to side effects.

DP But the important thing is to say that's great as long as Plan A works. So Plan B has to be what can the person put up with? What can be made to be bearable for as long as possible up to the maximum of effective duration. And that may not be the drug that they start off on. In those circumstances a non-standard approach is important because 50% of people roughly do not complete a course of endocrine therapy. If we had that level of people stopping treatment of chemotherapy there'd be hell to pay. But we were simply accepting it with hormone therapy. I mean know that those women who have stopped early have a high risk of dying. So sometimes I think that the duration of treatment is actually more important than the particular choice of agent by the person as well. And if we have to deviate from what we started with if it's getting too hard.

PowerPoint Slide 4:
Side-effects

- **Hot flushes**
- **Vaginal discharge/itch/bleeding**
- **Mood swings**
- **Cognition**
- **Weight gain**
- **DVT**

So what are the side effects? Well main ones that I've seen in clinic and I spend all my day dealing with the hot flushes. To a certain extent vaginal itch and bleeding. Mood swings, I just heard a fantastic story about everything that you ever hear about Tamoxifen. Cognition, there are quite compelling data now that any form of endocrine therapy does affect brain function. Sometimes joking you say that men's brains run on testosterone and women's run on oestrogen. But these for some women can be quite significant problems. I remember seeing one woman whose mood swings were so great that her marriage was in threat and she had to stop treatment because she just had such violent tempers. And these are things that are becoming increasingly recognised. I've been involved recently in a trial piloting magnesium as a way of managing cognition. We don't know the results of that yet, but what amazed me when we put this out was just the sheer number of women for whom this suddenly became an apparent problem. Whereas before they weren't telling us about it at all. Weight gain is an issue. That's a bit controversial on Tamoxifen. The average weight gain is the same on Tamoxifen as the placebo but some women just seem to put weight on on it.

PowerPoint Slide 5:
Management

- **Mood swings**
- **Cognition**
- **Weight gain**
- **Joint aches**
  - **Anti-inflammatories**

    - **Activity**
    - **Change medicines**
- **Bone mineral loss:**
    - **Use Tamoxifen in low risk cases**
    - **Bone density monitoring**
    - **Prophylactic bisphosphonate**
        - **May also reduce cancer risk**
        - **Preventative dentistry recommended**
- **Duration of treatment is important and may be more important than which drug is used.**

For aromatase inhibitors the main one is joint aches. And I think in clinical practice what we see is about 80% of women get joint aches and pain. Whereas the clinical trial is much lower than that. And we found in a study that we did a few years back that about 15% of the women that start aromatase inhibitors stop them within a few weeks because of that particular side effect. The more insidious one is bone mineral loss or osteoporosis which can be a major problem in the future, possibly under recognised in its importance. Again cognition. It's not clear whether these drugs are better than Tamoxifen in that regard. Hair loss or hair thinning can be an issue with these drugs and vaginitis, also a problem with Tamoxifen but more controversial how you deal with it in women on an aromatase inhibitor. The main one is mood swings, if they're bad enough there's actually only one thing you can do which is stop the treatment and try something else. Cognition we're trying magnesium as a pilot, but there are data again that say that cognition improves when women stop treatment. Weight gain, the usual standard exercise. Diet. They can be difficult to manage. I do occasionally change people from Tamoxifen to an aromatase inhibitor because of this side effect. Joint aches is a major for us. Again often the treatment does involve stopping treatment because people want to be mobile and we want them to have happy lives. And if they're stuck in a chair because they can't move then that's unacceptable. But things that we can do are to use anti inflammatories in the short term. Activity has been shown to improve on the joint aches. And change of medicine to Tamoxifen. Tamoxifen is much less likely to be associated with these problems. Bone and mineral loss, well my approach is to use Tamoxifen on a patients because it is good for bone in pre and post-menopausal women. You can do bone density monitoring for women on aromatase inhibitors and with the idea being that if the bone density starts to fall away then you add in a bisphosphonate or a bone strengthening agent. This has always struck me as being shutting the gate after the horse has bolted to a degree, and with the data that came out last year that suggested that using bisphosphonate for a 2 year course might reduce the risk of breast cancer. That's what we're doing now is giving a 2 year course of bisphosphonate. You do have to be careful about some complications in the bones particularly damage to the jaw after dental work. So we do ask for women to have their dental work up to date before they start that course of treatment.

I would just like to re-emphasise the duration of treatment is important and maybe more important in which drug is used. And what I say to a lot of my patients is trying to use drugs is sometimes like going to the shopping mall and trying on a new blouse or a particular item of clothing. If you don't like it, change it. Choose another one. And in the theme of the talk you know serial monogamy might actually be a good thing in this case.

Menopausal symptoms after breast cancer
Dr Helen Roberts, MB, MPH, FAChSHM
Associate Professor Women's Health

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AG Thank you so much David. Our last speaker tonight is Helen Roberts, a doctor at the Obstetrics centre who has had a lot of involvement with breast cancer patients with menopausal symptoms. Helen, you're a menopause guru. What are some of the most common menopausal side effects from cancer and how do patients get to these.

Powerpoint slide 1:
Possible treatments for hot flushes

- **No hormones – not Estrogen, not Progesterone, not Tibilone – research has shown that women on HRT and Tibilone have an increased risk of breast cancer recurrence**
- **You could try:**
  - **Antidepressants – SSRI/SNRI –1.13 flushes per day**
  - **Clonidine - -0.95 flushes per day**
  - **Gabapentin - -2.05 flushes per day**
- **Cognitive behaviour therapy may reduce menopausal symptoms.**
- **Overall, research hasn't proved other interventions help (including acupuncture, homeopathy, vitamin E, or magnetic devices) for hot flushes after breast cancer.**
- **Studies have showed mixed results, but some research has found that black cohosh may be effective for menopausal symptoms.**

HR Yeah I think we've really heard about that earlier on through yourself. I mean I think the very common menopausal symptoms are things like hot flushes and the most debilitating one of having hot flushes at night, which are night sweats. Because that's going to really interrupt sleep patterns which means the next day you just feel lousy, you can't think straight and your mood is really, really low. So that would be the commonest menopausal symptom. And then of course there are the vaginal symptoms and sometimes also the urinary symptoms. The vaginal symptoms being the ones we've heard about from David. Vaginal dryness, pain if you're sexually active and you're having sex. The urinary symptoms are recurrent urinary tract infections and perhaps also urgency, really feeling the need to go to the toilet really quickly. And sometimes losing urine before you actually get there. So those are the sort of symptoms that we're thinking are really due to menopause. And they happen for various reasons. We've just heard and I don't think we need to repeat that, they happen because of the treatment you're on. They happen if you have to have your ovaries removed obviously because that's going to put you into premature surgical menopause. And they happen if you're on Tamoxifen you get various symptoms and if you're on your aromatase inhibitors. So often your menopausal symptoms are due to what your treatment is. If you're on your aromatase inhibitors.

We would say there are for some women quite a lot of triggers for hot flushes, I mean for menopausal women who are around 50 triggers are things like hot spicy foods. We just had a gorgeous Thai curry before we came so you know all about that. Alcohol is a trigger. Many women will actually try and have layered clothing so when they go into a building when they feel really hot they can actually take off articles of clothing. And sometimes actually it's kind of useful to keep a hot flush diary to see what your triggers are, if you can kind of avoid them. And that's a very basic thing that can be really, really helpful.

Just moving on to the next slide and we're looking what sort of treatments we would offer women if they came to our clinics. And I think there's general agreement

internationally that you wouldn't be looking at using hormones. At least not for a very long period of time. So no oestrogen, no progesterone, no Tibolone which is another type of replacement, not available in New Zealand but available in Australia. But we do have a series of modalities that we can use to treat hot flushes. And we actually don't really know how they work. In fact we actually don't really know what causes hot flushes yet. All we can tell you is that these 3 things that we're going to talk about, if you have a study compared to placebo that hasn't got anything in it they have hot flushes tested in placebos so we know there's evidence that they kind of work.

The 3 things that we're talking about are the anti-depressants and you've heard about those and that's certainly one we would use. Benefits for placebo with those. And they're actually, you see it on that slide. You can see it's only helping 1 to 1½ flushes a day and you're thinking to yourself oh crikey that's not very much. But if you're up 5 or 6 times a night with your night sweats and now you're only waking actually 4 times a night that really can be actually helpful, because your sleep pattern's a wee bit better.

Clonidine's another one. Clonidine's used for migraines. It's used for blood pressure. It's less helpful than anti-depressants but it can be given trans-dermally and that can be quite a nice way to take it.

The one that really has the best evidence to be as near hormone replacement therapy in reducing flushes is Gabapentin. It's used for flushes, it's used for urogenic pain. In New Zealand we don't have it funded for hot flushes, but it will give sort of the same broad relief as if we're using oestrogen. So you might get a benefit for you know 2 less hot flushes per day.

There is evidence for if you see a health psychologist and looking at cognitive behaviour therapy that may be useful. A lot of women really want to know about, hey can you tell me about some other herbal things? Are there any of those that I can use. There's not a heck of a lot of evidence for those. Vitamin E doesn't seem to be very helpful. Acupuncture doesn't seem to be very helpful.

PowerPoint slide 2:
Black cohosh

- **Differing views on safety of black cohosh in women with previous breast cancer though**
- **NIH advise that only standard screening for recurrence needed with use**
- **Some concern also that product may cause liver damage but casual association not conclusive**

We've got a bit of mixed research for black cohosh, but some studies show that black cohosh may help with hot flushes. But then there's differing views on safety. I think so that if you look at some of the websites, for example the National Institute of Health in the States they only recommend standard screening during black cohosh, they're not particularly worried about women with breast cancer. There is concern about liver damage but the cause and effect whether the black cohosh caused the liver damage or not is still questionable.

So black cohosh is a maybe a possibility you're thinking about. standard

PowerPoint slide 3:
Phytoestrogens

- **Soy, red clover**
- **Natural aromatase inhibitors**
- **Cochrane review showed no benefit over placebo**

- **Need to be able to convert to equol**
- **Most Caucasian women non-convertors**
- **Mixed advice re safety from American and Canadian cancer societies**

So the phytoestrogens, can they be useful? Well Cochrane review that we did really showed that they probably don't have a lot of benefit over placebo. You need to be able to be a converter. You need to be able to convert the phytoestrogen into genistein diosteine and then to this equol. Caucasian women are not very good convertors. Asian women are much better convertors and so really it starts with how much help they're going to be and there's really mixed advice as to their safety from the American and Canadian cancer societies. I would think there would be a reasonably not too much of a worry but they've got to be helpful. I would probably doubt that there's a lot of evidence for that.

PowerPoint Slide 4:
Which SSRI/SNRI?

- **If you're on Tamoxifen**
  - **You shouldn't take paroxetine or fluoxetine**
  - **These may prevent Tamoxifen from working properly**
- **Instead use Citalopram or Venlafaxine**

So what you were talking about your anti-depressants and you're quite right Escitalopram is a really nice choice. It's well tolerated. It doesn't seem to cause the same sexual dysfunction. Because a lot of the anti-depressants can actually decrease libido. Venlafaxine's a little bit better than the others but Escitalopram has minimal side effects.

I'll be interested to hear from maybe later on but usually we'd say that you'll not benefit from your anti-depressants in 4 of 5 weeks you may not be able to get anything. We'd expect you to be feeling the benefits earlier as well. Then you have to be careful about if you're on Tamoxifen which ones you're going to use because some of them will actually interfere with how your Tamoxifen works. So if you're on Tamoxifen you may well be, suggestion would be to use Citalopram or Venlafaxine and not fluoxetine.

PowerPoint Slide 5:
SSRIs and SNRIs

- **Side-effects are usually mild and short-lived, but may include headache, nausea, reduced appetite, gastrointestinal disturbance, dry mouth, anxiety/agitation, sleep disturbance and sexual dysfunction**
- **The optimal length of treatment is unknown. Treatments should be stopped gradually to prevent withdrawal symptoms – mainly an issue with paroxetine and Venlafaxine.**

Side effects are rare. They're usually fairly mild and short lived. But sexual dysfunction is common with quite a lot of them. And how do you know how long to take these things for? Because you don't know. If you happen to be taking something that is actually really, really helping – I haven't got any flushes left at all which would be just a miracle wouldn't it. But when you don't know if your hot flushes have disappeared or because they are time limiting, or whether it's just the treatment. Every year or 2 or whatever you may be thinking of stopping what you're using. Seeing if your symptoms come back. And there's no rule of thumb – things like Gabapentin and <unclear>. It's probably a good idea to gradually reduce your dose, rather than stop abruptly.

PowerPoint Slide 6:
Clonidine

- **Clonidine is a drug usually used to treat high blood pressure.**
- **It can be taken orally or as a skin patch, and appears to have a mild to moderate success in treating hot flushes, reducing their frequency by up to 46%**
- **Tamoxifen users have less frequent and less severe hot flushes with 0.1mg/ day of transdermal clonidine or 0.1mg/ day oral clonidine.**
- **Side-effects are common with clonidine including dry mouth and insomnia or drowsiness.**
- **Doses used for treating hot flushes do not appear to affect blood pressure.**

And Clonidine we've talked about perhaps not quite as useful but it's quite nice if you can build it up and then use it transdermally.

The one that I seem to get lots of good feedback from women and lots of good feedback from research is Gabapentin. You do need to start it slowly. Randomised placebo control studies that were done into hot flushes used 300mg tablets 1, 3 times a day. And I've actually found that quite a few women will take 300mg at night and they'll actually be a lot better just on that. We always start slowly and build up if we need it for your day because you can sometimes get a little bit unsteady and a bit dizzy with them. So I have tried to get them funded in New Zealand for women with breast cancer and I cannot get them funded. And it's something that the breast Cancer Society may take up, it will be fantastic. There are Nupentin's probably the cheapest one. It's about $24 for the 3 tablets a day for 1 month. So that kind of thing would be smashing. The next slide covers the three things I've been talking about and pretty much repeats what I've said.

PowerPoint Slide 7:
Gabapentin

- **Unlike the SSRI/SNRI, Gabapentin has no known drug interactions, does not cause sexual dysfunction and appears to be well tolerated for hot flush relief.**
- **Further, it doesn't cause withdrawal symptoms like some SSRI/SNRI (Paroxetine and Venlafaxine)**
- **Side-effects (dizziness, unsteadiness and drowsiness) affect up to 20% of people, but appear to improve after the first week of treatment, are usually gone after four weeks and aren't severe enough for women to stop using the drug**
- **There's no benefit of adding Gabapentin to SSRI/SNRIs**
- **There's no benefit of adding Gabapentin to SSRI/SNRIs**
- **It is not funded for relief of flushes**
- **Nupentin (Gabapentin) costs $24.10 for 1 tab x 3 per day for 1 month**

PowerPoint Slide 8:
What about vaginal symptoms after breast cancer?

- **Women on aromatase inhibitors experience more vaginal dryness than those on Tamoxifen**
- **Tamoxifen may cause more flushes than AIs**
- **Use Replens first**
  - **If you haven't noticed a benefit after 2-3 months then try:**

- **Ovestin (Estriol) rather than Vagifem (Estradiol) as less estrogen is absorbed into the body on Ovestin.**

With vaginal symptoms that can be really difficult. You know if you're not sexually active your vagina can just feel like sandpaper. If you are sexually active it can be just impossible to have sex and it's just so dry and so uncomfortable. As David said you tend to get a wee bit more with AIs than you do with Tamoxifen. There is randomised placebo control studies to show that Replens can help vaginal symptoms, it won't help the urinary symptoms. Replens is not a hormone. We have a very good pharmacy here in Parnell in Gladstone Road and she has been bringing Replens in for many, many years. Specifically for women with breast cancer, and does a very good price range for Replens. Replens I think specifically vaginal moisturiser, it's not a lubricant. But you should use lube as well. But that's the first place to start. If that's not helpful, depending on what you're on I think that using a vaginal estrogen is something to be thinking about is Estriol, which is the best thing. You're not going to be thinking about Estradiol which is Vagifem. That's specifically because Estradiol is more for the vagina than Estriol which is hardly absorbed at all. So if you were going to be able to use it while you're on Tamoxifen or AIs Ovestin would be the thing to start with. And we have quite a lot of good studies to show that you could actually get really good relief and you don't even need to use one applicator. You can get away with a quarter of an applicator. Very, very, very low doses. The important thing is if your vagina is really, because it's really, really thin anything you put in is going to be really, really stingy. So I say to women if you're getting to the stage when your plans haven't helped. We've talked to your oncologist and we're going to use Ovestin, start with just some cream on your finger and very slowly over a period of weeks and weeks and weeks build that mucosa up. Once it's a little bit thicker things won't sting any more. So that's a way to kind of deal to that.

PowerPoint Slide 9:
Mirena for endometrial protection
Cochrane review

- **For those perimenopausal women using Tamoxifen**
- **Mirena IUD can decrease the risk of polyps and overgrowth (hyperplasia) of the lining of the womb (endometrium)**
- **Two year study – unable to tell whether Mirena use affected breast cancer recurrence**
- **BUT the O+G College in UK say No (UKMEC 3,4)**

Just very briefly have a talk, we've heard that one of the side effects of Tamoxifen is endometrial polyps or endometrial thickening. There's a lot of discussion about Mirena which is a sort of inter uterine system that has Levonorgestrel, which has progestin on the stem.

Now we know that Mirena can decrease the occurrence of endometrial polyps with Tamoxifen because we have studies on that. We know that it can decrease the endometrial building up. But we really don't know, the studies haven't been long enough to tell us whether it affects recurrence or not. And there's differing opinions worldwide about the use of Mirena. Some women would perhaps do what you were doing which was just having your endometrium looked at and doing an endometrial thickness assessment to make sure that it's okay. That's another way to do things there.

The last one is to talk about, and this is actually an Australian booklet from Cancer Australia. I think it's a really nice booklet and that's just the URL if you wanted to download it. There's other sub-pamphlets here on Tamoxifen and AIs as well on that last sheet. And that's kind of really all I can say.

PowerPoint Slide 10:
Pamphlets

- **Pamphlet for women with previous breast cancer**

- **Click to download BCFNZ Patient Sheets**
  Tamoxifen
  Aromatase Inhibitors

Q&A Session

AG Right, thank you Helen and thanks to all 3 of you that's great. We're now going to open up questions. There's a whole lot of questions sitting here. You can type your questions in the box. And we'll get to as many as we can with the time available.

First up Helen there are a couple of questions. You mentioned that hot flushes don't necessarily go on forever. People have asked how long they go on for.

HG That is the million dollar question. We have no way of telling if you have short term flushes. If you're a non-flusher, hey, some women actually come to my clinic go through all this and they don't get a single hot flush. And that's possible. But if you do get flushes we have no way of telling you. We can't do hormone levels and then say you're okay, you're a short term flusher or obviously you're going to be a long term flusher. We just don't know. If you keep going with everything that helps for a period of time and then you decided talking to whoever you see about oh maybe 2 or 3 years down the line I might try and withdraw a bit slowly and see what if my symptoms come back. And that's the normal kind of thing. But there's not an easy answer.

DP My sense is they're often about 12 to 18 months and they gradually resolve. But there's a lot of variation around that. Some people have terrible flushes that go on for 3 months and other people just carry on the whole time they're on treatment. There's no way of knowing that as well.

AG: There's a couple of questions that people have asked about what's high risk and what's low risk. Can you talk about how you categorise patients?

DP Oh yeah, I was hoping we weren't going to get asked that question. What I personally use to predominantly determine risk is the number of lymph nodes that are found in the axilla or the arm pit at the time of surgery. And the person I would categorise as definitely high risk if there are more than 4 nodes involved. If a person is node negative then most of the time I categorise them as low risk and in the middle ground, although I agonise over that. Because risk is not, you know can't easily be just defined into high risk or low risk. It's a continuum from low to very high. And there are other factors. And really the most important one for that group in the middle is to have a honest and open discussion. Well Chanda was talking before about being able to communicate with your oncologist or your doctors about you know, talk about the things that you're worried about. And I can't emphasise that enough as being incredibly important aspect of this. If you actually discuss it with them and settle on what you think is the right

strategy for you, for example to come to the clinic and be handed a prescription and be told here, take this.

AG Right, thanks David. And another one here, someone's asked how often should I be seeing an oncologist. I haven't seen one for 3 years and I've been on Tamoxifen for almost 4 years.

DP Again there's no one quick answer to that. The approach that I take to hormone therapy in my clinics is I like to see a person about once every 6 months or so as my default setting. The reason for that is that I'm interested in trying to make sure that the person's still taking the Tamoxifen. There's a lot of evidence that if we see a person simply because a certain length of time has gone past and they're well, they'll tell us they're well and we'll go yes, we agree with you that you're well. And it's not necessarily a great way of going about it. If we're talking about follow up for breast cancer concerns you're actually far better to see a person if they've got worries that they've got breast cancer, rather than seeing them say once a year. Chances of that being the right time if they do need help is actually quite small. So the main reason my follow with people is to check that their hormone therapy's going okay. The concept is the same as I have with chemotherapy every week. We spend a lot of time on chemotherapy trying to stop people from having more of these overwhelming side effects. And we've been successful in the last 20 years in getting the completion rates of chemotherapy up quite a lot. And I think that's a lot of the reason why breast cancer survivorship has improved over the last 2 decades. And that's a personal view, I can't quote a science for that. But I think you know we shouldn't necessarily accept that half the women get so frustrated with the side effects of not sleeping at night that they eventually say look I can't handle this any more, I'm going to stop. The measures that we've talked about are all designed to try and make it more bearable. And so if those things are happening, I'll often see people to just try and find something for that.

AG Helen, a question about libido and Tamoxifen. Any suggestions on how to improve libido while on Tamoxifen?

HR Well I think it's a difficult one because it's such a multi-faceted thing, libido. It's not just that your vagina may be dry and it's sore to have intercourse, and you can try and make that better if you're using lube. And I did say that some of the best lubes I think are Glide and Astroglide which are really a lot better than KY Jelly. And most pharmacies would have those. But it's not just that your vagina is sore. It's all about what's been happening with your and how you think of yourself. And how your body has changed. And maybe how your looks may have changed because of your treatment. How your relationship is affected. Your libido is a multi-faceted thing. I think it's really, really difficult to get something that's simple. Certainly making the vagina more comfortable with whatever you're going to use is a big one. I don't think anybody would be thinking of some randomised evidence that testosterone replacement helps libido for women, but I don't think any of us would be comfortable using that for breast cancer so that wouldn't be something that I would be comfortable with. What do you think David?

DP I think you want to be doing it in a clinical trial as we're doing rather than just introducing it. There would be concerns, particularly for women on aromatase inhibitors. Because the androgens are converted to oestrogen by the aromatase enzymes so I would be a little concerned about that.

HR And I would agree. So I think it's pretty much a relationship thing. We had some really, really good health psychologists that can often see partners together and talk through those issues. So it's not a simple easy answer.

DP I think a lot of oncologists are very happy with the idea of using topical oestrogen for the vagina. For women on Tamoxifen I think a lot of people have concern about using a vaginal oestrogen on a aromatase inhibitor because they're worried that the oestrogen that you've taken out of the system with your aromatase inhibitor is simply going to be replaced with absorption through the vagina. There are some preparations of Estriol overseas which are very low strength and have shown absolutely no absorption of Estriol into the system and work very well.

HR You're talking about Vagifem 10 micrograms?

DP There's an Estriol gel that I've seen reported overseas. And I also think that there are, have been clinical trials with people being on aromatase inhibitors and intermittently after the first 5 years and there's a thought that that actually could be better, but that's experimental. But my thought overall is if it comes to the crunch between a woman saying I can't handle this, I'm going to stop completely well we give them a couple of weeks of Estriol from time to time.

HR Sometimes the vagina oestrogen sometimes that always needs to be given, you have a loading dose of 2 or 3 weeks and then you do it twice weekly. And it often takes 4 to 6 weeks for the vagina mucosa to become better. But when you stop it and give it intermittently you're kind of losing a little bit of the benefit. Like you know that's certainly one idea. And to me it would be interesting to look at that Estriol gel. We don't use Vagifem in New Zealand any more. Vagifem 25 was available here but that's now been taken off the market internationally, it's now Vagifem 10. They've done that because we know that smaller doses of 17 β-estradiol help your vagina. If we want to get Vagifem here we would be getting it from Australia but in fact most of us would like to start with Estriol, a much weaker oestrogen, even less absorbed than 17 β-estradiol and let's fund it in New Zealand as well.

AG Sure, right. There's a couple of the side effects that you mentioned on the AIs including the joint pain and osteoporosis. People have asked about these.

DP Well Tamoxifen's a funny drug. It's an anti-oestrogen in breast tissue but it's pro-oestrogenic in the uterus which is why there's a small risk of endometrial cancer. But it's also pro-oestrogenic in bones. In post-menopausal women if you're using it by itself it actually increases bone density. In pre-menopausal women it's probably used by itself, slight negative impact upon the bones. Certainly not as much as an aromatase inhibitor does. The issue would be if you combined it with ovarian function suppression or oophorectomy which I think the evidence is not there to support the standard of care at the moment as a routine at least. In that situation primarily the ovarian function suppression is a problem and there's studies that show that you lose about 10% of bone density within the first 6 to 12 months of that sort of treatment. Although that is an issue for that sort of treatment. As far as joint aches and pains go if you asked me 5 years ago if people on Tamoxifen got bone and joint pain I'd say no, I've never seen it. But since we've started recognising it in aromatase inhibitors we do see an occasional person that comes in saying they're sore and they get miraculously better when you stop it.

HR One of the things, could I make a comment about bone density? Would that be all right? Because one of the things that's kind of nice to use is FRAX which looks at bone density guidelines. And you can actually just Google FRAX that comes up on your computer and you can see for women they can actually see where they are on a graph with bone density. I think we're changing how we're thinking about this. We're not in the business of preventing osteoporosis any more, we're in the business of preventing clinical fracture. So even now if you were 50, menopausal at 50 and your bone density T score is -2.5 which they would tell you that is osteoporosis. If you go to FRAX they wouldn't treat you because at 50 your risk of fracture is so low, your bone density is low that you wouldn't start treatment for quite a few years. So we need to really keep it in perspective. If it's fracturing we're preventing, so using treatments later on is probably the beneficial thing rather than preventing osteoporosis.

DP The studies of aromatase inhibitors say that an excess of fracture about 1% per annum over people on Tamoxifen has been shown to be fairly consistent and shown afterwards. And what has also been shown is that bone density actually isn't a terribly good predictor of new fractures. So that's all part of the reason why we've moved more toward using bisphosphonate as I say. Also the evidence suggests that there's no reduced factor and benefit.

AG A couple of questions from pre-menopausal women. One is why not just remove my ovaries, rather than using Tamoxifen and if you are pre-menopausal how do you know when you should switch to an AI?

DP Okay. So I'll talk about my thoughts on the first question, why not go straight to an oophorectomy. Yes you can do that but it's not a reversible step. So if you are having really significant problems with the hormone therapy it's another way out. So for women who are considering this I'd say look an oophorectomy is about as effective as Tamoxifen as a single agent. There are some advantages of it. You don't have to take a pill every day, and remember to take a pill every day. If you're thinking about doing it what I tend to say to people I'm consulting is have Zoladex first because if it's terrible then you can stop it and it's exactly the same thing. And then if it's going okay rather than having a monthly injection, then talk about it. The second question was how do you know?

AG When to switch an AI if pre-menopausal.

DP That's a toughie. Look I think there are 2 reasons to switch. One is if you, the evidence is there that an aromatase inhibitor plus ovarian function is better. Also nastier. I remember seeing a woman who'd been in the soft trial who I was talking to at a consumer forum a couple of years back and she told me that she lost 30% of her bone density in 2 years on that study. And so it's something that if you do you have to be a little cautious about managing the side effects. It's certainly a good option for some women. How do you know if it's the right option for you? Well I think you have to talk to your oncologist. Say look if you're having lots of trouble with Tamoxifen consider a change, but you need to consider the pros and cons and that's actually quite a long conversation.

AG I've got a couple of questions about soy: is taking a soy supplement for menopause too risky? And also you mentioned European women can't convert phytoestrogens, does that make a big difference? Is there not much point for European women to take soy?

HR Well a lot of the studies that we looked at were actually not getting it in your diet. You have to take a heck of a lot of soy in your diet to get up to the level where it might be beneficial. So there are a lot of the studies were done because it was actually taken in tablet form. Yeah, you don't know if you're a convertor until you've tried it and I don't expect that there's any major harm, in fact Chinese studies show that there's some decreased recurrence of breast cancer with phytoestrogens. So I wouldn't expect there'd be an awful lot of harm but if you wanted to do it in your diet you'd be drinking a heck of a lot of soy milk. Or look at taking replacement tablets, soy tablets. But I think if you're not seeing any sort of benefit within a few months' time, you aren't a converter and isn't going to help you.

AG Okay a couple of questions on the cognition. David a question about what the dose of magnesium to take and can Tamoxifen cause dementia?

DP I don't think Tamoxifen can cause dementia. I think it can cause reversible cognition problems. In memory, poor attention the sort of things that we've been hearing about earlier on. But they get better when you stop. There's really good evidence around that. The dose of magnesium is one that we used in our study was 400mg elemental magnesium a day which is actually quite hard to get in most supplements. There is one brand that does it. I have to be careful not to promote a particular brand. But it is supported by on television by a famous New Zealander who's just been caught drunk driving. So that's a big hint. I have a theorem that if you get a better night's sleep it improves cognition. I think the hot flushes at night are actually quite a major thing and so historically I've been trying to get people to take Citalopram and having very little luck, but I'm having quite a lot more success having people try magnesium. There is some data that says it reduces hot flushes and it's pretty devoid of side effects. Unfortunately it's not a prescription item but it costs less than $20 for a bottle of 60 and that would last you 2 months. So I don't know that it works for cognition. We don't have those results yet. But I am using it a bit in general clinical practice now and some people come back saying it's great. Others saying it didn't make much difference can I try something else.

AG A couple of these comments that people have asked is that because of Tamoxifen. One is very dry eyes. And another person has said how do I stop fluid collecting on my limbs on Tamoxifen.

HR Well dry eyes is a sort of common menopausal symptom in a way. Some women who do get the hot flushes and night sweats do actually get, because of the lack of oestrogen, quite dry eyes, just use drops and that type of stuff. But I'm not specifically, is it a Tamoxifen side-effect that you have come across?

DP No.

HR It may be due to decreased oestrogen levels and that's a possibility. What was the other thing that they asked you?

AG Fluid collection.

DP Well I wouldn't have necessarily have thought that fluid collecting was in keeping with the Tamoxifen side-effect unless you're unlucky enough to have a clot in your calf vein in the past. Which you know should have been fairly obvious. The question that I have in my mind is how long after chemotherapy are you and particular if you had Taxotere because that's quite good for causing fluid retention. And if not, you know get yourself

checked out because there are some other reasons why you can retain fluid and nothing to do with those things. So I think I wouldn't necessarily attribute it to Tamoxifen.

AG Are there any foods or supplements that compromises the effectiveness of Tamoxifen. Chanda mentioned grapefruit before.

DP The 2 ones that I try to avoid are Prozac and Paxil or their generics so fluoxetine paroxetine. There is some evidence to say they may interfere with the activation of Tamoxifen. So Tamoxifen as you swallow it is actually not an active drug. It metabolises into the liver, into the thing that does the business. And if you inhibit that conversion then it doesn't work. You don't get hot flushes because you don't have the active product, but it's also not working. That's why. And there is less reasonable evidence to suggest that it might interfere with the activity of the drug. So where there's alternatives we prefer to use Citalopram or Venloflaxine if possible.
This is a question taking calcium supplements

AG We're low on time now, we have a question about calcium supplementation.

HR Are you going to quote the Auckland data?

DP I'd like to take the 5th amendment on that one.

HR I think there's quite a lot of data that came from the bone clinic here and also came from the WHI to suggest that long term calcium use in post-menopausal women actually increase cardio vascular stuff. And I know there's some disagreement with that but it's no longer, if you go and have your bone density done and you're a wee bit low that they'll say general lifestyle advice; they used to say calcium but they don't do it any more at the bone clinics. So maybe not.

DP To my mind the evidence is actually fairly poor.

AG We're out of time but we've got a few more questions. If you would like to ask some more questions send them by email so please do that. Thank you all so much for joining us tonight and a special thank you to our panel. If you need some advice from our breast care nurse feel free to call our breast nurse, the number's on your screen now and remember we do offer free counselling for breast cancer and if you join the online community you can get in touch with other people like you. We hope to see you all next time. Thanks, bye bye.

Support and information
Questions or concerns about what you've heard tonight?
You can talk to a breast nurse from 8am tomorrow – just call 0800 BC NURSE (0800 2268 773). Leave a message if you call outside office hours and someone will get back to you.

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