

## **Weston Park Cancer Charity Podcast**

### **Episode 5 – Breast Cancer – Dr Penelope Ottewell**

**Ruby Osborn:** Hello and welcome to the Weston Park Cancer Charity Podcast, sharing stories about our work, what we do, and the people we support. From funding life-saving research to providing practical help and emotional support, it's our job to care in every sense for our patients and their families. I'm Ruby, and October is Breast Cancer Awareness Month, so today I'm talking to one of our research grant holders who is working on breast cancer and how it spreads to the bone.

**Penelope Ottewell:** Hello everybody, my name is Dr Penelope Ottewell, I'm a senior lecturer based at the University of Sheffield. My primary role is to carry out research, so I run a research team, and we look at breast cancer, mainly we look at secondary breast cancer and the spread to bone. My research team are focused on trying to identify better ways to treat this to help patients ultimately in the clinic, and we also do have some involvement in teaching of some of the medical students and collaboration with the clinical colleagues over at Weston Park Cancer Hospital.

We know that one in eight women will develop breast cancer at some time in their life, and this condition doesn't just affect women, it also affects men. The good news is that because of research we know more about the disease which has enabled us to develop better and more targeted treatments. These targeted treatments mean that, now, about 80 to 90% of patients who are diagnosed with early breast cancer will make full recovery. However, unfortunately the majority of those 10 to 20% of people who do not make a full recovery, they will experience some kind of relapse where their tumour will grow back. In most cases this tumour recurs within the bone. When tumour cells start to grow in the bone, they cause destruction of the bone and this makes holes within the bone which is incredibly painful for the patient.

At the moment when a patient presents in a clinic we don't know which of those patients are going to develop tumour growth in bone and which ones aren't, and this is actually quite important because we don't want to over-treat people so we only want to be targeting treatment for those people who are likely to develop tumour growth in bone, because we know that cancer therapies, they're not nice things for people to take, so we only want to give those to people if necessary. So normally we don't know that a patient has tumour growth in the bone until they present in the clinic with extreme bone pain or even with fractures.

Unfortunately at this point we then run out of curative treatments for these patients. Currently within the clinic, a patient with bone metastases are treated with drugs to control their disease rather than to cure it. So they are given a drug known as a bisphosphonate and this drug is to control the tumour destruction of

the bone, so it preserves the bone. Now this treatment strategy is incredibly important because it increases the quality of life for the patient, however it's not curative. And once a patient has tumour growth in their bone their life expectancy decreases to about two to three years, so we really need to do something better for this patient population.

So there was some research that was carried out by my team in collaboration with other people's team, which was supported by Weston Park Cancer Charity, which appeared to indicate that if we gave these same treatments but we gave them earlier so when the tumours were very small or before they'd spread, that this might be able to actually stop the tumours from spreading at all. This led to a large number of clinical trials, the biggest of which was carried out here in Sheffield, again with the support of Weston Park Cancer Charity. What we found is that patients who work more than five years postmenopausal when they got this treatment did really well, so they had prolonged life, they had less tumour in their bone and less tumour in other sites.

However patients who were premenopausal when they got the same treatment did worse, so although they got less tumour their bone they got more tumour growing in other sites. The research that we're doing in the laboratory at the moment is focusing on why do these bisphosphonates appear to have anti-tumour effects when given to women who are postmenopausal, but pro-tumour effects when given to women who are premenopausal. So the idea of being here that if we can identify why this is, we might be able to help those premenopausal women in the same way that we've been able to help the postmenopausal women.

**Ruby:** Okay, so if you know that there's something different you could maybe develop an extra drug to give to those patients to correct for that?

**Penny:** Well this is what we're thinking at the moment. At the moment we think that this is due to changes in the immune system. So we know that patients who are postmenopausal have very low concentrations of this hormone called oestrogen, and we know that patients who are premenopausal have high levels of oestrogen, so we think that oestrogen affects the immune system. Because of this, we think that we can give some of these new immunotherapies and these will be able to overcome the effects of oestrogen, and therefore if we give immunotherapies along with the bisphosphonate to premenopausal women, we might also be able to increase the anti-tumour effects seen with the bisphosphonate.

**Ruby:** Is there a way to just reduce the levels of oestrogen, would that have the same effect, or are there nasty side effects from that?

**Penny:** We can reduce oestrogen, and in fact with patients who have the certain type of breast cancer that responds to oestrogen, these patients are routinely given treatments that reduce their oestrogen levels, and these patients do do well when given a bisphosphonate. But as you said Ruby, correctly, anti-oestrogens do have effects on the bone and the immune system, so it is an

option but it might not be the best option, so we're just trying to weigh up what's the best thing to do for these patients.

**Ruby:** Do we know why breast cancer likes to move into the bone?

**Penny:** We know that the bone, it contains lots of factors that tumours need to survive. So if you imagine a tumour as a group of people, when you have too many people, or tumour cells, all squashed together in an environment then it becomes uncomfortable for them, they don't have enough food to eat, they don't have enough resources. Your bone is full of marrow and it's full of lots of chemicals that act as food for other cells. These chemicals then get spread into the circulation so the tumours in the primary site, in the breast, can sense this. And they think, okay, I haven't got enough food here, I'm hungry, where can I go and live that's a nice environment for me. And bone seems to be an ideal environment for tumour cells to go to, so it's not just breast cancer cells that go to bone, lots of other cancer types going to bone as well.

**Ruby:** What could your research mean for patients in the future?

**Penny:** We're hoping that in the future that our research can lead to patients either not developing metastases at all or not developing tumours spread to the bone, or indeed to any other site. This might be an idealistic thing, because we know that in things such as breast cancer that the tumour cells tend to spread to places like bone even before we know that the primary tumour is there. So what we really are hoping is that we'll be able to stop tumours that are in the bone from growing.

There was a grant that was recently funded by Weston Park Cancer Charity where we found that breast cancers themselves make a molecule that called IL-1 $\beta$ . This molecule helps the tumour cells spread around the body and particularly grow in the bone. This molecule is only found in cancer cells that spread; it's not found in the cancer cells that don't spread. So we think that we might be able to use this in a future as a biomarker, so we might be able to take a biopsy from a patient, look at it, see whether it makes this molecule IL-1 $\beta$ . If it does then these patients are probably those who are going to get bone metastases or tumour growth in their bone, and therefore these are the patients that we would need to treat. That's really quite a step forward.

The other important thing that we found from this particular study was that, we know that IL-1 $\beta$  is produced during inflammatory diseases such as arthritis, and because things like arthritis are so frequent there are drugs available in the clinic that target this particular molecule. Using our preclinical models in the laboratory we found that if we use these IL-1 $\beta$ -targeted drugs, we can stop tumour cells spreading to the bone and even when the tumour cells are in the bone we can stop them growing in this site. So this is really exciting for us and we've been collaborating now with our clinical colleagues over at Weston Park Hospital and at the Christie in Manchester, and we're now putting this into a clinical trial so hopefully we should have the first clinical trial here in Sheffield to help Sheffielders, where we are looking to see whether this anti-IL-1 $\beta$  drug can prevent or treat bone metastasis.

**Ruby:** Well that leads me on to, what makes Sheffield such a good place to do research?

**Penny:** Well Sheffield's a great place, particularly for breast cancer and bone metastases. We are a centre of excellence for bone metastasis and we are the biggest centre in Europe. And I think actually it's such a good place to carry out research because we have really good links between preclinical researchers, such as myself and my team, and the clinical colleagues at Weston Park Hospital, so we work in collaboration. We have multiple teams within the University that are working on different forms of tumour growth in bone as well, so we have a wealth of knowledge here and we can bounce ideas off each other. And we also have the opportunity to work with wonderful charities such as yourself which help drive our research forward. I mean I do say that but it's true, if we don't have the funding we can't do the research. We're at a really good point here at Sheffield, we have all of those magic ingredients all together to help drive things forward.

**Ruby:** What led you to being a researcher and what keeps you going?

**Penny:** I've always wanted to do some kind of science and when I was at university I had a really inspirational lecturer who happened to teach on cancer, and because of him I decided to do a year out at university and I went to the Christie in Manchester to do a year's research, and it was while I was there that I could actually see that research was ongoing in the lab could be translated directly into patient benefit. That was something that I wanted to be involved in, I wanted to be at that cusp of doing work that was going to directly impact upon people. It's when you do something that either gets ultimately fed into a clinical trial and you can see the benefit for the patients, or even those small things where you produce a bit of data which then leads into somebody else's research. It's that collaborative work that really keeps me going.

**Ruby:** Why is it important that we keep doing research? Because we've been studying cancer for a long time, and there keep being all these news headlines about "oh we've made this breakthrough" but there's still a huge amount of research going on.

**Penny:** Survival rates for breast cancer increased from 64% to 82% from 1975 to 2002 and this is all because of research. But we're still not there yet, so even in some parts of the world with the best care possible, this doesn't go above 90%. And things like breast cancer and all cancers, because of our lifestyle now, incidences are going up. And we still lose unfortunately around 2000 people a year in the UK alone just because of breast cancer. There's a long way to go and the more research we do, the more we know about the disease, and these huge advances come because of leaps forward in science.

We have now learnt that actually cancers are not just specific to their type of cancer but they are also very specific to individuals, so I think those next steps that we need to make are going to be really looking at personalised medicine and what's best for that individual. And this is going to take a considerable amount of research because you've not just got the cancers to think about but you've got to

think about that person as an individual, how their tumours develops in them, how this fits in with their lifestyle et cetera.

And I think what's also important to point out is that, as patients are living longer with things like breast cancer because their treatments are getting better, things like tumour relapse in other sites including bone is occurring more and more. Patients aren't dying because of their primary tumour anymore, they're living a long life and then tumours are coming up later on say 10, 15 years later, then they're starting to get tumour growth in the bone. And because this is something that is becoming more and more prevalent now, it's something that hasn't really been researched until relatively recently, so we're a bit behind the curve when it comes to treatments for tumour growth in bone. Now we're starting to chip away at the edges because of better treatment options. What we need to do now is we need to basically have the revolution that we've had for primary breast cancer, where we've got really good targeted treatments for that, so we can have good targeted treatments for tumour growth at other sites, so that patients can live a normal life expectancy and a normal healthy life expectancy.

**Ruby:** That's all for this episode of the Weston Park Cancer Charity Podcast, thank you for listening. That was Dr Penelope Ottewell, senior lecturer and researcher at the University of Sheffield. Please join us next time when I'll be speaking to another of our breast cancer researchers.

**Dean Andrews:** Cancer changes everything, but so can we.