

### **First Visit – Second opinion example**

**Susie Woo, Metastatic triple negative breast cancer (weakly estrogen receptor positive), germline BRCA1 positive here to discuss second-line treatment options  
(Some comments in parentheses, not spoken)**

Patient: Good morning Doctor Lee.

Doctor: Good morning Susie. I apologise for the wait.

Patient: Oh its fine, I understand.

Doctor: So as you may know, I'm a medical oncologist here at this hospital who sees breast cancer patients. Your primary oncologist Dr. Aaron Chua and I spoke and I've had the chance to review your chart but I would very much like to hear from you about how you're doing with your current treatment.

Patient: I'm still a little fatigued from the chemotherapy but it was more tolerable than the first few rounds. Also doing ok with the injections to help with my bones.

Doctor: If the fatigue bothering your daily activities?

Patient: Oh, I get by. My husband has been handling more of the household so I can focus more recovery from treatments. He couldn't join today due to some errands he had to run for the family.

Doctor: Good to hear you've got support from family members. Is there anything we can help with in terms of general support at the moment?

Patient: I think we're ok. Dr. Chua has gotten a supportive care nurse and medical social worker to help with various miscellaneous logistical and financial support through this so far. I'm quite ok. Just hope to find good treatment options.

Doctor: Yes, and we will certainly do our best on that front. What has Dr. Chua shared with you so far?

Patient: He mentioned that there were options like other hormones and targeted therapies... I can't remember the name but its written here.. and chemotherapies that I could try. But that you would also explore if there were any clinical trials.

Doctor: Yes, that is my understanding as well. What have you heard about clinical trials?

Patient: That its kind of where doctors go to when they run out of options. I understand its more controlled and better than like... being a lab rat but I'm just hoping for a miracle so I get more time. As much time as I can with my family.

Patient: Sorry Doctor.

Doctor: Please don't apologise, you're going through a lot at the moment, it's normal to feel emotional about it.

Patient: Sorry I interrupted, please go on Doctor.

Doctor: Yes, as we were saying, actually I would like to say that clinical trials today are actually not always the last resort and as Dr. Chua alluded to, you still have available therapies. Exploring clinical trials at this point is really your medical team being comprehensive to help find you more options and choose the best one. Choosing the best option is really a shared decision that primarily centers around what's important to you. As doctors, we make recommendations based on what we know about the effectiveness of the drugs as well as their side effects. But we never want our treatment to be worse than the breast cancer. Our goal is to improve survival as well as quality of life and manage symptoms such that living with this cancer becomes almost like a long-term condition. So when one treatment doesn't work any longer, we change to another one to control it for a period of time and so on.

Patient: I get that Doctor.

Doctor: That's good. So with respect to the options so far. I would say lets break them up into 3 separate boxes to discuss: hormonal therapy, chemotherapy and clinical trials. With regards to fulvestrant and palbociclib, that would not be my first go-to option. Remember when you had that biopsy of the bone last year?

Patient: Yes

Doctor: Yea so that biopsy showed that the tumour is now entirely negative for estrogen, progesterone and HER2 receptors, what we call triple negative breast cancer. Although it was initially slightly positive for estrogen, the tumours can change over time. So currently, if its predominantly triple negative, hormonal therapies like fulvestrant as a backbone may not be as effective. Hormonal therapies generally

take time to work and although the tumour is just in your bones at the moment on scans, because it came back in a few months after you finished chemo and while you were on tamoxifen, I think you may need something "stronger".

Patient: I get what you're saying doctor.

Doctor: Yes so with regards to the second box which is chemotherapy, there are a number which are reasonable options. These would include Eribulin and capecitabine. Eribulin would be preferred between the two if we want to try something that is "stronger" as there was a study that showed patients with triple negative breast cancer appeared to respond better to it compared to some other chemotherapies. However, capecitabine which is an oral tablet compared to eribulin which is a drip infusion, is generally better from a side effect profile and most patients tolerate it fairly well.

Patient: What are the side effects doctor?

Doctor: Yes so Eribulin can have fatigue like what you're currently feeling

Patient: Ugh

Doctor: Yea, unfortunately. And also things like hair loss, nausea, constipation, diarrhoea. Capecitabine on the other hand has no hair loss. Mainly oral ulcers, dryness or rash of the hands or feet and diarrhoea. But all are very manageable with medications. I think both are reasonable options just how much we think we can manage the different side effects.

Patient: I understand.

Doctor: Ok, I'd like to pause at this point in case you have any further questions?

Patient: I think I'm good, please carry on.

Doctor: Ok, so for the last box, clinical trials. We know understanding more about triple negative breast cancer. Specifically, we know that there are actually different subtypes of triple negative breast cancer. One subtype, in particular, is called the AR positive subtype. AR stands for androgen receptor and this subtype of triple negative breast cancer has a lot of this AR receptor on its surface which means that it can be targeted with drugs that target the androgen receptor. We do have two such trials at the moment, one with a new compound called VT464 and another using an existing drug used in prostate cancer called bicalutamide. The big caveat for these trials, though, is that to qualify, your tumour needs to be AR+ or else the drugs are unlikely to be suitable for you. So we do need to test your tumour to find out.

Patient: Ah I see.

Doctor: Yes, so if you're agreeable we can arrange to retrieve your previous biopsy tissue for testing.

Patient: Yes I am.

Doctor: Good, there is just some paperwork which my nurse will guide you through later for consent.

Patient: No problem.

Doctor: Other than the AR trials, we also have another trial involving drugs that target PI3K, called PI3K inhibitors and your tumour mutation profile did show this mutation. So that could be another trial. The thing to note about this trial is that it is a Phase 1 trial, meaning this is the first time the drug is tested in patients. As opposed to the AR trials which are Phase 2 trials, meaning that there is already some early data in patients and now there are doing a larger trial to find the most effective dose. For Phase 1 trials, we have a specialized team to take you through the screening and monitoring which I would recommend meeting in a separate visit.

Patient: I got it so far doctor.

Doctor: Great. I know it's a lot to take in. Would you like me to continue or are there any questions?

Patient: No questions.

Doctor: Ok, so aside from the 2 AR trials and PI3K inhibitor trial, there are also clinical trials targeted another mutation that you have been found to carry, BRCA. Now this is a gene that is involved in repair of DNA damage and when it is mutated, patients tend to accumulate more mutations as they are unable to repair DNA damage, which is what led to the higher predisposition for cancer in your case. But at the same time, on the other hand, this also gives us a target and drugs have been developed specifically for patients with this mutation. We currently have 2 other Phase 1 clinical trials using a targeted drug called a PARP inhibitor that has been very successful in ovarian cancer patients with this mutation and combine them with other targeted drugs that block 2 other pathways ATM and ATR.

Patient: Wow ok, I didn't realise there were so many options. It's quite a bit to process.

Doctor: Yes I'm sorry it's a lot I know. And that's why don't worry we don't need to make any decisions today. In fact, what I would recommend is let's test the tissue first and screen your case with the Phase 1 clinical trials team to see which trials are actually ones that you can qualify for and then touch base again shortly to review them against the chemotherapy options.

Patient: Yes, I'm agreeable with that plan. I don't feel up for more chemotherapy at the moment given I've had so much of it and if there are new options that potentially provide something that's more effective, I would be open.

Doctor: Great. So let me be the liaison with the Phase 1 team to let them start the screening process. I'll put in an appointment with them in the meantime. However, if after screening you are not found to be eligible for all the Phase 1 trials, they will inform you beforehand and cancel the appointment so it's not a wasted trip.

Patient: I'd appreciate that doctor.

Doctor: Lastly, just to end of on the clinical trials, you may hear about this treatment called immunotherapy in triple negative breast cancer that uses the immune system to attack cancer cells. I just want to say that while this is an ongoing area of study, we don't have an open trial at this hospital at the moment on that front. I'm not aware if there are open studies at other hospitals but you're welcome to explore.

Patient: Ok doctor.

Doctor: Great so I know it's a lot of information but I think we have covered the ground we wanted to today for the 3 boxes: hormonal therapy – I don't think it's a go-to, chemotherapy – eribulin and capecitabine both reasonable, depends on the side effect profile you prefer mainly and quite a few clinical trial options but we need to get the tissue tested first and Phase 1 screening done.

Patient: Yes I think that sounds like a good plan doctor.

Doctor: Good, may I examine you?

Patient: Ok doctor.

Doctor: Ok all good. So I think we have our plan and work to follow up on. I'll go enter the orders and my nurse will come in to guide you through the forms for tissue retrieval as well as some reading material regarding the AR trials alright.

Patient: Thank you doctor.

Doctor: Nice to meet you, we will be in touch.

Patient: Thank you, bye bye

Doctor: Bye