OCRF talking research webinar:

The path to hope on World Ovarian Cancer Day

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Host: Loretta Hart

Panel:

- **Professor David Bowtell**, Peter MacCallum Cancer Centre and the University of Melbourne
- **Dr Rachel Delahunty,** Peter MacCallum Cancer Centre, The Mercy Hospital for Women and Geelong University Hospital
- **Olivia Curtis**, OCRF ambassador living with ovarian cancer.

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Robin Penty 00:00

Hello everyone and welcome. My name is Robin Penty, and I'm the CEO of the Ovarian Cancer Research Foundation. It's a great pleasure to host you today on world Ovarian Cancer Day. And to introduce you to some amazing people we'll hear from shortly. I'm just going to make a few introductory remarks and then hand you over to our our facilitator journalist Loretta Hart. So I'll start by acknowledging the traditional owners of the lands on which we meet today and pay my respects to elder's past and present and to all Aboriginal and Torres Strait Islander people joining us this afternoon. So for a bit of background, most of you on the call will be quite aware really of the current state of the nation for ovarian cancer research. But as a general reminder, five year survival rates for ovarian cancer have remained unchanged for 30 to 50 years. The current five year survival rate is 49%. And of course, the subtle nature of symptoms means that more often women and girls and people with ovaries are diagnosed at late stage where survival is 29%. It is a complex disease and it's chemo resistant. And as a result, recurrence is very high. Around 80% of women experienced recurrence of this cancer. There is no early detection method. And as mentioned, Treatment and Diagnosis hasn't much changed. However, hope does lie and research. We feel very strongly about this. And that's what we're here to talk about today. So research has revolutionized outcomes for other cancers, notably breast and melanoma. And it's the community awareness raising that has also assists in this area. For

example, survival rates from breast cancer have shifted from 84% to 92%, in just the last 25 years in Australia, and that's through growing awareness, growing engagement across all pillars of society, including charitable foundations like ours. It's also a fact that To date, the Commonwealth Government has funded ovarian cancer research research at less than 0.7% of total grant distribution. The world Ovarian Cancer Coalition just recently announced that if nothing changes, the incidence of ovarian cancer in Oceania and Australia will increase by 81% by 2050, which is not long away. So this day is an important opportunity to change that. So on behalf of the PCRF, I thank you for tuning in the path to hope on world Ovarian Cancer Day. And I thank our amazing panel in advance. Thank you for your time, your expertise and your knowledge. So here's an introduction to Loretta, Loretta Hart is a passionate broadcaster and communicator and the driving force behind weekly news and current affairs radio program, the pulse, just strong focus on women's health, their stories and issues that affect them. As a mantra for women in business and life. Loretta is an advocate for supporting positive change for individuals and the community through the sharing of stories. And I thank you, Loretta, and hand over to you now.

Loretta Hart 03:29

Thanks, Robin. So very pleased to be facilitating this really important conversation today. So yes, we'll be spending the next hour together exploring this path to hope. We're going to begin with a panel discussion with our three guests. And I'll introduce them all in a moment. And then there's going to be time after our panel discussion for you to ask questions. And I want to thank those who've already submitted questions through prior to the event, we've got those. So you're very welcome to submit questions using the q&a function down the bottom of your screen as we go along. So feel free to pop the question in as it occurs to you, you don't have to wait until the section arrives. And there's actually a feature where you can see questions that have been popped in. And if there's something that you feel really passionate about, as well, please vote for that. And that'll pop it up to the top of the list, so that we're really, you know, answering questions that are really being engaged in one from this audience today. Our focus today is about research. And that's what we really would love to receive your questions about. And just remember that we actually cannot answer personal medical questions. We have a chat function is also available for you today. Feel free to comment as the conversation happens, but also be mindful and considerate of others on the call with comments that you're making. We also appreciate that some of the topics that we talked about today And might be quite emotional. And at the end of the event, we will share some contact details for some support services. If you're feeling that you need them to take care of yourself today. Today's webinar will be recorded and is being recorded right now. And it will be made available through the Ovarian Cancer Research Foundation website in the coming weeks. So I know that you probably got pen and paper you write things down, you will have access to a recording of this. So you can just enjoy the conversation as it flows. Okay, so to our panel discussion for today. Firstly, I'd like to welcome Professor David Bowtell, Professor Bowtell is from the Peter McCallum Cancer Center and the University of Melbourne and is an internationally recognized expert in ovarian cancer research and pioneer in genomics and personalized medicine. He is the principal investigator for the Australian ovarian cancer study, one of the largest population based cohort study of ovarian cancer in the world involving over 3000 women. David is a fellow of the Australian Academy of Health and Medical Sciences and the Australian Academy of Science and he was director of research at Peter Mac for the decade of 2000 to 2009. Professor Bowtell's research

has made major contributions to molecular classification of ovarian cancer, the identification of therapeutic targets including cyclinE1 acquired drug resistance, the genomics of hybrid serious ovarian cancer and long term long term survival. His current research is focused on exceptional survivors and early stage clinical trials in ovarian cancer. David, you have a very long bio, but we're really pleased to have you joining us today. Also on the panel, we have Dr. Rachel Delahunty. Dr. Delahunty is a medical oncologist at the Peter MacCallum Cancer Center, the Mercy Hospital for Women and Geelong University Hospital. She's a specialist and got gynecological oncology and transitional research and completed her PhD through the University of Melbourne and the Peter MacCallum Cancer Center. Dr. Delahunty is principal investigator on the traceback study. This is the identification of women can their germline BRCA-1 /2 mutations through retrospective analysis of patient diagnosis with high grade serous ovarian cancer, and Rachel it's wonderful to have you joining us as well today. Now, a third panel member waiting patiently to be introduced is Olivia Curtis. In 2020, as COVID pandemic took hold, mother of three, Olivia was diagnosed with stage four low grade serous carcinoma, an uncommon, but less aggressive form of ovarian cancer. Olivia, we're really grateful that you're here with us today to share your story with us. And if it's okay, we may actually start our panel discussion with you and your story. As I mentioned, your diagnosis was in 2020. Are you able to share with us what led to his diagnosis?

Olivia Curtis 08:24

Sure. Thanks so much for having me, everyone. My road to diagnosis probably started about 18 months before, I really thought there was something wrong. And I think I've pinpointed this to a trip to the centre of Australia that I took with my husband. We were sleeping and slag and rooftop tent and driving up to 1200k's a day. And I thought, Oh, that'd be a fantastic adventure. So much fun. IIt was the biggest drag. I mean, I was, we had to stop on people's properties for me to go to the bathroom several times an hour. It was really, it was exhausting. And I wasn't enjoying myself and we were getting in fights. And I it's only now that I reflect and think, wow, I had cancer, and all of those things that I was putting down to being Oh, you know, I've just had too much to drink because I'm bored and I'm drinking too much in the car or, you know, maybe I'm just a bit tired or I'm bit conscious of my bladder after having three children. So I kind of put it to the back of my mind until I started working from home in lockdown. These niggling little things continued to really get in the way of my day, but women tend to make excuses and so frequent urination, just that niggling discomfort, thinking, oh gee, might my ovaries feel a bit twitchy today, I'm really tired. I was able to go about my day, but only just, and I allowed it to get to the point where I was falling asleep at six o'clock in the evening, and surviving on a handful of nuts. And I thought, Okay, this is really weird. Now, I think I'd better go and talk to someone. And it was a couple of days after that, that I was laying in bed, and I put my hand on my stomach. And I thought, oh, there's something hard there. Better go and get that checked out. And I said to my husband, you know, what does it feel like? And he said, it kind of feels like when you were pregnant. And I thought, Oh, God, I hope not. I've got three kids. And I'm too old for this. And I can't have another pregnancy. And so I went to the doctor the next day, and I said, but we need to do a pregnancy test. This is so weird. These are my symptoms. It feels like I'm pregnant. And he put his hands on my stomach. And he said, Yeah, it feels like you've got a term baby in there. And I went, Oh, God, no. Anyway, we did the pregnancy test. And very sadly, I was not pregnant, a pregnancy would have been fantastic in comparison. So the next step was to do some scans. He said, look, something's not right. But you're too young for cancer. So don't worry too much.

My mom has a history of very large fibroids. And so I thought, yeah, I've just got some fibroids like mum might have to have a hysterectomy. So he sent me for an MRI the next day, they said, yeah, you've got something in there. It's it's pretty big. And I remember thinking, I just don't, I really want to speed this along. And I remember ringing my friend who is an obstetrician, and she was training in ultrasound at the Sydney Adventist Hospital at the time. And so I said, you know, what's going on. And it really wasn't until that chat with the doctor that had read my ultrasound, that I really started to think, gee, you know, having discomfort during intimate moments and feeling so exhausted, and having diarrhea and going to the toilet 30 times a day, that had become normal to me, because it's so slow, and it's so sneaky that way it happens. And it really wasn't until we were sitting in that quiet room. And I was being told, you know, we think this is what's going on that I reflected, and I joined all the dots and I thought, yeah, okay, that's not just what happens to a mum of three when she gets pre menopausal. That's not normal.

Loretta Hart 12:55

Like, yeah, and I think you know, so many things. You've just said, there'll be women who are on this call and watching the replay later nodding and saying, Yeah, too busy put it back in my mind. There are so many reasons why this could be until we, we find that we, what what we're actually experiencing is not normal, and and not right. So what did the diagnosis mean for you in terms of your treatment options?

Olivia Curtis 13:19

I got I was very lucky. So between going to the GP and having a preliminary diagnosis, which is really all they can give you because you don't know about, you don't know that ovarian cancer is ovarian cancer until you test it and look them under a microscope. And so they were pretty confident that once I'd had this scan, this is what we were looking at. I was basically led down the hall by the woman that read my ultrasound, and she said, Look, if anyone was going to look at this, I would go to this guy. And so very, very fortunately, I was introduced to Professor Russell Hogg, who saw me the very next day. So it was, it was five days, and I had an idea of what was going on. Which is just amazing. I'm so fortunate. And I really think that the series of events that I'm going to tell you about has put me in that 29% that lucky 29% of us that get to stick around. So when I saw Russell, he said, Look, I've got some mates, and I thought, okay, right, cool. And he said, I think I can take it out. And he started making phone calls. And he started calling people on their mobile and saying, I've got this lovely, you know, 35 year old lady and she's got three kids and, you know, I think that we can do it and so he started assembling a team. And part of that team was a urologist. He got a specialist in isa test especially as general surgeon and also a caller rectal surgeon. And he said, Look, this is going to take some time. I'm really sorry, I'm gonna need about four weeks to coordinate and get a theater and you know, organize everything and up up to four weeks. That's like, that's a lifetime. Why can't we do this today? But as I've come to learn, there are so many things that go into this. I mean, he kept ringing me and saying, I just want to do one more MDT. And for people that don't know what that is. That's a multidisciplinary team meeting. And all of these really amazing people probably like the two that we have with us today are on phone calls, talking about you giving their best guess about what to do giving their thoughts and I'll maybe you should operate this way. And maybe you can

get all that in one if you do this, this and this. And so there were four or five of those before I got to surgery. And many, many, many scans and and to be very clear, before they operated, they wanted pictures from every angle and they were colonoscopies and endless endless endoscopies. And it just kind of seemed like it was a lifetime, but it with every single step. They were getting, I think ready to throw the kitchen sink at me.

Loretta Hart 16:23

Olivia I might just jump in, and just really bring David into the conversation to this point if that's okay, just because, David, we're listening to Olivia's story and her story I know is similar and different to everyone's story is different. But the similarities, there's a complexity here. Obviously, there's a team of surgeons, they're working together, there's there's ongoing meetings, there's not a one way fits all approach. Is this because of ovarian cancer in itself is a complex thing. Can you Can we just break it down? What is ovarian cancer?

Prof. David Bowtell 16:56

Thankfully, right, I think Liv's story is really illustrative of so many things, to be honest. And as you suggest, ovarian cancer is not just one disease, it's many diseases. I guess one way to think about this is a bit like an proportioner doll, and you just start, you know, dividing it and dividing it. And the first division is based on histology. So her's is a low grade, serious cancer, this is a diagnosis that the pathologist make. The most common type of ovarian cancer is high grade serous ovarian cancer, they sound kind of like the same thing. But they're absolutely completely different. There's different there's breast cancer and kidney cancer, in terms of the way they're put together, their wiring, how they behave clinically how they respond to treatment, the genes that drive them the possibility of inherited risk, all those things are very different. And what we've come to understand over the last decade or more, is that the term ovarian cancer is really quite sort of deflating. It sounds like a single disease, but it's actually many different diseases. And until you sort of really appreciated that, while we treated it as a kind of a one size fits all, then that really impeded progress. But by understanding the subtle differences or not so subtle, sometimes differences between these diseases, then we can really start to trade as individual entities that they are. Oops, you've been muted, I think

Loretta Hart 18:34

I was being respectful and quiet my end. And so as we have, as you say, these babushka dolls, and these these layers or onion layers, I've heard you also speak about them. This is where the complexity and detection comes from.

Prof. David Bowtell 18:48

Yeah, it certainly adds to it. I mean, there are other reasons why early detection, I think that's what you're getting at is so difficult for this disease. You know, that's a very common question. People ask, you know, we've got mammagraphy screening, and we've got cervical cancer screening and bowel cancer screening, why don't we have it for ovarian cancer, we hear over

and over again, that outcomes are better, and the disease is diagnosed earlier. I think the first thing to say is that it's not from the lack of trying. There have been many researchers around the world that have worked very hard on this. And in fact, Australia has been a significant player in this space, particularly supported by OCRF, which have made early detection, one of the major areas of investment. It's the biology of the disease, and as you suggest, that makes it so difficult the diversity of different types of ovarian cancer. So for example, one test might only detect one type, but not the other type. But there are other aspects of it as well. It's something that's buried deep inside. I mean, these other screens that I described for breast, cervical cancer or bowel cancer are not particularly comfortable, but in a sense, they're more accessible as opposed to an old organ that sort of brought inside your tummy. And the the nature of the way these cancers arise mean that there's, we think a fairly short period of time between when they first arise and when they spread. And, and to contrast that, say with bowel cancer the the period of time, there's probably several years between when you can when a doctor can see something that is, you know, concerning and when it actually becomes a malignant cancer, there's probably several ideas for that. Whereas in the case of ovarian cancer that's much shorter. So your chances of getting it right at that point between when it arises, and when it becomes a problem is much less likely. So there's a whole there's a whole slew of reasons why early detection is is particularly difficult. But given that it's such an important and attractive thing, it's something that, you know, there's ongoing investment in very wise men.

Loretta Hart 21:02

Rachel, if I can come to you, you thanks for for being patient with how the conversation I can see you nodding there with many things that is that David's saying? This is, as I was explaining, it's a complex field. And there seems to be, you know, many challenges, many hurdles you work in this day to day with patients, and also in research. What is it that you are finding is promising about researching ovarian cancer at the moment, there's gonna be something promising around, you know, we're going to talk about hope today, where are the promising pieces, and I'm sure David will also have something to say about this.

Dr Rachel Delahunty 21:40

Yeah, so I think the statistics in my mind are, you know, they're not really reflective in some ways of of the amazing progress that's been made. And I really do believe that the statistics will improve based on some of the most recent developments and the things that are happening now. So I feel really fortunate to be in the clinic now, rather than, you know, 20 years ago, when this was a really difficult disease. And, you know, just even the last few years, we've seen some amazing completely practice changing things. So I think for me, personally, the fact that we are now been through the developments in understanding, say, for example, if I take highgrade serous cancer, which David mentioned, you know, only fairly recently, it's been recognized that it actually doesn't even come from the ovary, that it starts in the fallopian tube, and that the first changes that lead to that development actually occur really long time before the cancer develops and sets David said, you know, the time from spread short, but that's that particular change happens a long time before. So that's already told us that, you know, perhaps some of our screening, or early detection or screening has failed because of, you know, this particular thing, that's not the first change happened so much earlier, and that we really need to be able to

detect that first change. So even understanding the basic biology of this has been really fundamental in and being able to get in and do something about it. So from that, we know that prevention, so is so important, for example, so if we can get the tubes and ovaries removed from women before that actual cancer develops, that, you know, people can that can be avoided, cancer can be avoided. So understanding the biology has been a really important step forward, through work that David's lab has led, there's been some really important developments in the risk factors as well. So genetics, which I'm really passionate about, and I'm really, I think all of us in the clinic are working really hard to make sure that all of our women that are eligible for genetic testing, get that. And that's really important, not only because it's a pathway to prevention for their family members, but because it's really, really important for everyone's treatment. So so I can recommend one thing for the women that are listening is that no matter what your cancer is your ovarian cancer is talk to your doctor about whether there could be a genetic component. And there may not be because they're not all cancer, as we alluded to, you know, that's rare and cancer is very different. But ask that question, because it is important for your treatment as well. And it's so exciting. We now have we can actually personalize treatment in the clinic. So David mentioned earlier, and that was, you know, this is starting to be not one size fits all but digging down deeply into the gene changes and so many of the women would have heard of PARP inhibitors. So they've been really revolutionary. And it's just amazing to see women doing well. And we are always nervous about using the C word for cure. But I think now we are we are getting there where we actually believe some of these women are being cured. So PARP inhibitors have been a game changer. I know not all women do have them, you know only 15 to 20% Depending on your actual type of ovarian cancer. That's the sort of high grade mucinous cancers but there's also been amazing developments in understanding something like low grade serous cancer. So the genes that are driving that, and we now have trials that are looking at at those and I think we could, you know, talk a lot, I think the big thing is that just the excitement of being able to to give personalized medicine, which can really make a big difference and avoid excess side effects from treatments that might be non effective.

Loretta Hart 25:23

Thanks, Rachel and David Rachel's covered a fair bit of ground there, can I have come to you and ask the same question. What do you what are you most excited about? What are where are the promising areas of research at the moment?

Prof. David Bowtell 25:37

Well, obviously PARP inhibitors, something very important for that group of patients that I think they really illustrate very nicely. A broader point that, that if you understand the biology of the cancer, then you can start to deal with it in a more specific way. And, you know, in lives case, she's certainly benefiting from that. And this is the whole concept of personalized medicine, that you sort of understand the wiring of the, of the cancer, and you know, you know that you've got to cut the blue wire, not the red wire kind of thing. So I think that that's, that's something that's still evolving, it's, it's important that more women can access that. And that's something that we're working on very hard things that are on the horizon. You know, I think this is a very probably a very educated audience here. So they'll be very familiar with things like popping

evidence inside, but probably more recent things, I think, called One thing is an antibody drug conjugates ADCs. So the idea here is that you haven't had a body which we all make and fight infections, but these are antibodies that are raised and, and cloned and made and manufactured, and they are linked to very cytotoxic drugs. But the reason that they're effective is that the antibodies homed in on the tumor, they're made, you choose antibodies that are directed to the tumor, and, and they carry with them, the cytotoxic drug, and that allows a more specific targeting of the cancer. And so there's been some very interesting trials with a drug called Nova toxin, which targets the fallout receptor on many of these cancers. And that looks very interesting. I think lots of people will be familiar with the mRNA vaccines are the result of the last five years. And one of the companies one of the two companies that really pioneered that is bionic, bio Entech. And they actually started out not working, not intending to work on COVID, but came along, but in fact, personalized cancer vaccines. So they've now now that we're sort of post COVID, hopefully, they're really returned to that question, as have other mRNA companies. And the idea behind those is that individuals, a person's cancer, often hairy, carries many mutations in it, that subtly change the nature of the normal proteins. And, and that that's something that the immune system can recognize. And so the kind of the clever part of mRNA technology is that you can identify those mutations and then replicate those at an industrial scale to make a personal vaccine that is hoped, and there's evidence that this is likely to be the case that will amplify the body's immune response against the cancer. And so there's been some just in the last 12 months and very interesting clinical trials in in other cancers, particularly in melanoma with personalized vaccines, but also in hard to treat cancers, small numbers. But there was a very interesting trial in pancreatic cancer, which is, you know, often has a very bleak outcome using a personalized vaccine. So I think that if I was sort of crystal ball gazing, I'd say, antibody drug conjugates are going to be very important and, and personalized vaccines are very important emerging area.

Loretta Hart 29:07

And, David, I'm wondering, you know, you said that you can, if you look on the horizon, how far away is his horizon?

Prof. David Bowtell 29:19

Yeah, I think we were talking the other day. And, you know, I, you know, there's a famous quote, the future is here, but it's just not evenly distributed. And, and so, actually, there are clinical trials currently in personalized vaccine. Australia is, in particularly in Victoria, there's been a lot of effort going into establishing that technology in Australia. So both Moderna and BioNTech, are establishing that technology and in fact, manufacturing technologies. So Rachel might be able to comment better than me, but I think that clinical trials in this space, for ovary uh, probably a year or two or less away? Rachel, I'm not sure. Were there any trials are actually active at the moment?

Dr Rachel Delahunty 01:40

There are some there has been some early phase sort of gyane vaccines, but again, I think it is, I think that timeline is probably right, David, the next year or two, and the antibody drug

conjugates are in trials at the moment. So we've had some great success in them or relapse setting for ovarian cancer with mapatumumab. And I'm really, I think David's completely correct. ADCs are a real game changer. And I believe in particularly the women that are going to be non BRCA mutant that I can really see those ones coming forward into care. And there's other antibody drug conjugates different targets, sort of similar, and cytotoxic, or chemotherapy backbone, or something slightly different. So they're really exciting. And I think that's absolutely, the next chapter.

Loretta Hart 31:00

Thank you, Olivia, if I can come back to you. We've been listening to David and Rachel speak about the exciting things, but that, that there are a lot of heavy, promising things that are emerging. You're also a part of, you know, you're furthering the research for your own cancer in the donation of your tumor to be able to, as David said, to find out more about that puzzle. How critical has the research been from your perspective?

Olivia Curtis 31:30

Well, in my situation in the situation of all women with low grade serous ovarian cancer, absolutely critical, because we tend to go through all of the standard therapies, extensive surgery, oftentimes, and in my own experience, further extensive surgeries, chemotherapy. And then we go on to the sort of hormone blocker type things, which were no good. In my case, they worked for about eight months, and then I was finding that I was having recurrences. So, you know, you can get to a stage with this, as I did, where the surgeon say, Look, we have really taken out everything that we can. And if we were to operate on you again, it would be too risky. And we may not be able to see you back together. You know, you can only take so much of of somebody's abdominal wall. I understand. Unfortunately, before you have to stop. So doors were closing for me. And because I had been asked to donate or not donate, he said, Can I have your tumor? And I said, Yeah, sure, you know, give me the paperwork, and I'll sign it. And I didn't really know what was what it was for at the time. I thought it was gonna get like divvied up and sent to places, you know, he said, Oh, it's gonna go into a tumor library or something like that. I thought, yeah, great. I don't care what you do with it. I don't want it. I don't know that I don't need it. That's right. It can be wherever it wants to be. And after, after my physical recovery, my mental recovery started to happen. I started to understand why he had asked for for that. So he had sent it off. Testing had been done on it. In my medical oncologist said to me, you know, there's been testing done on your tumor. Someone's contacted me now to do some blood testing, because, you know, they were interested in finding out whether there was any genetic link. Unfortunately, there was no genetic link, there was nothing of any. Well, there was no known genetic issue with my with my blood, nothing of significance for me now, that's not to say there won't be in the future. So I'm very glad they did that. But this has led me to this fantastic clinical trial that I'm part of now. I got a phone call from the Prince of Wales Hospital saying we think we may have a spot for you in this drug trial. It's a combination, targeted therapy, which we're finding has been very, very successful on low grade serous cancers, would you be interested and I thought, Oh, my goodness, you know, if every single woman had this kind of individualized care, outcomes would be so different. And it has given me so much hope, not

only for my own personal ideas of what my life will look like in the future, but the future of all women and ovarian cancer sufferers everywhere. I'm hugely hopeful, hugely.

Loretta Hart 35:00

Wonderful. We're going to go to some of the questions. Thank you. Yeah, goodness, are the questions from the floor? And, David, I've got one for you that I'm going to start with if that's okay. And the question is coming in and saying globally, where are the leading research institutions and clinical teams doing work on ovarian cancer?

Prof. David Bowtell 35:15

Yeah, it's a really good question. The short answer is that there in lots of places are very encounters complexities, as we've heard, and there are a number of different problems, identifying genetic risk development, early detection test, understanding drug resistance, one area that our lab is particularly interested in long term survivors and how women become long term survivors. And then there are clinical trials, very active clinical trials. And so, you know, I guess the first thing to say is, one of the countries is Australia, Australia, absolutely punches above its weight in this space. And we probably have the best and largest cohort study. By that I mean, a group of women who have consented to be part of biobanks, as we've described, and first collect that all that clinical information associated with their cancer journey, and use that to really drive the research. There's a wonderful collaborative spirit in Australia. That's not replicated, for example, in United States. So we have been able to do things in this country that I've really struggled to do, for example, in American. So So, I guess, behind the question was, I suspect, a question about particular areas of research, and, and one that will be very important, the audience, I think, will be clinical trials. So as some of you may be aware of Australia has an extremely effective, what's known as a cooperative group, it's called an afghan. It's the Australian New Zealand gynecological oncology group. And essentially, what that is, is that academic clinicians like Rachel, who are interesting, advancing clinical trials in this space, work collaboratively and cooperatively to coordinate their activities around clinical trials to make sure that the best trials go ahead and that they're funded and that they occur as quickly as possible. So there's a shorter time from starting the trial to recruiting patients in them so that patients can really benefit from that. Both Rachel and I were across the Wellington at the recent annual ANGOG meeting and there are over 1500 people who are members of ANZGOG, so, Australia has one of the best and largest clinical trial networks in the world, I think.

Loretta Hart 37:55

Gold meal for us. Awesome. That's music to my ears. It's wonderful to hear. Rachel, I'm gonna have another question come through it. I might direct it to you, and or David, but if you'd like to jump in together, the question is, are PARP inhibitors generally more effective when there are genetic mutations detected such as BRCA and not so effective when no known defective genes are detected?

Dr Rachel Delahunty 38:19

So that was the PARP inhibitors?

Loretta Hart 38:20

Yeah.

Dr Rachel Delahunty 38:21

Yeah. That's that is true. So we know that, I guess, David always comes back to the understanding the science and that you know of the biology of a disease. And then, you know that helps you treat it. And that's exactly the story with PARP inhibitors that it was understanding that the, you know, the genetic defects that some so women that have, for example, a mutation in BRCA one and two or another gene like red 51C, have defects in their ability to repair DNA. So that means that they're more susceptible to cancer, but it also means that something like a PARP inhibitor, which essentially induces other DNA breaks, and it means that that cancer cell can then not be repaired. We call that synthetic lethality. And that's why PARP inhibitors in a group of women that have an underlying genetic mutation in their their blood or their tumor, respond so well. And that's been shown fairly well in multiple clinical trials. Now, in Australia, we have access to olaparib and niraparib. But there's also some evidence for this thing called homologous recombination deficiency, which is just a very long term, which is hard. We call it HRD. So women that have a high grade non mucinous, ovarian cancer can now get that testing done in their tumor. And again, this is something for women to talk to their clinicians about it that can occur when it's not clear that there's a mutation in the blood or tumor. So somewhere in the pathway that there is an abnormality that would again show susceptibility to PARP inhibitors, so that it appears that the benefit is not quite as good as if you have a BRCA one or two mutation, but it's still quite good. And now we are lucky that in Australia as of fairly recently, we have access to PARP inhibitor in women that have ripped DNA repair defects as measured by the basically a scarring on a tumor test. People that don't have any deficiency, we call them HRP are efficient, the benefit is a lot less. We don't have access in Australia. And I actually, personally believe that's the right decision because the benefit was very small in this clinical trials that have been conducted. And there's this idea of resistance, which David has spoken about that we worry, you know, it does affect long term treatment. So in Australia at the moment we have access to PARP inhibitors, if your HR deficient, or you have a gene mutation. And I personally believe that's the right group of women. I don't know if David wants to add to that?

Prof. David Bowtell 40:29

100% that covers it really well I think.

Loretta Hart 40:31

Thank you. We have another question for the panel. It's a double banger. So there's two questions in one here. I like when people try and get the most out of the opportunity. So given that low grade serous carcinoma is rare, what research has been done to understand the cause

of this disease? And the second part is, how can this research be fast tracked to get better and more effective treatment?

Dr Rachel Delahunty 41:26

Yes, so I think for something like yeah low grade cancer, it is a rare cancer and actually many gynae cancers are so in the clinic, we often see a whole the whole clinic of rare cancers. So there is an there has been an international recognition that rare cancers are under studied, there really group a group of cancers that are difficult to study just purely by numbers. So the unfortunately, some of the progress has been plagued by an inability to recruit to study. So that's been seen for something like a sarcoma, or so forth that trials have had to shut early. So there has been international recognition of that. And that's led to collaborative groups that concentrate entirely on rare cancers. In we have now rare cancer, Australia and Claire Scott's been really pivotal to the rare cancer movement in Australia. And she's done wonderful work. And not only in getting recognition for rare cancers, but getting funding. So through organizations like the one that clears lead, there has been that has led to further genetic testing or genomic testing, which has now facilitated similar things to what to what leaves had so enabling genomic testing to then guide trials or guide access to drugs. So I think internationally, there has been recognition that it is a it is a difficult space, there are groups that are working on this now and low grade serous cancer you certainly there's people at Peter Mac that have an interest in that area, and how to fast track it further. I think that is that collaboration and getting funding, of course to support rare cancer research because it is difficult for pharma for example, if it's a relatively rare group, of course there at the end of the day that has to be has value for money. So if any through collaboration internationally, that's certainly a way that that can occur.

Loretta Hart 43:17

Is there anything else you'd like to add to that, David? Yeah,

Prof. David Bowtell 43:20

Maybe a couple of things I am so we know that. For example, BRCA one and DRC two are associated with a really substantial risk of developing ovarian in cancer, particularly BRCA one, so they're called high risk genes. Because if you carry one of those mutations, you're very substantially increased risk of developing, particularly high grade serous ovarian cancer. Because of the size of the studies in the way that they've been done, I think we can be pretty confident that, for example, for low grade serous cancer, if there was a high risk chain, or even a moderate risk chain that was associated with inherited risk, we would have found it by now. Now, that's not to say that we won't find some genes that have an impact in terms of inherited risk, but their impact is likely to be relatively small. Not small, if you happen to end up with low grade serious cancer, but reassuring in terms of other cancers in the family, I think that's probably a fair conclusion to, to make. What was the second thing I was thinking about? So in terms of risk, I think we know that I know, the second thing that I find very sort of curious and live actually illustrates this, unfortunately, is that, for most cancers, the risk of developing cancer just increases in time with time, it's a very much an age related disease. And that's certainly true for ovarian cancer. And for the most common type of ovarian cancer, the, I think the median age

of diagnosis is in the mid to late 50s. So what's unusual about low grade serous cancers is there's what's known as a bimodal distribution. So there's a sort of a peak in young women, and then there's sort of another peak in all the women. So that's, that's really unusual. And that might kind of give us a clue as to what might be initiating some of these cancers. And we also know when we look at the genes that are changed in the low grade serous cancers, there's one particular part on chromosome one that is often partially lost. And that, again, is providing a clue that that loss occurs in the cancer doesn't occur in the rest of the patient. But something has triggered it. And perhaps that's something that's in some way linked to puberty, maybe something happens during puberty, and then it takes a number of years for that to finally show up years later as a lump in someone's tummy like. So. I think it was Rachel really nicely outlined, the only way that we're going to crack a hard problem like this is working together. And there's, there's a very significant international consortium, both at the clinical level, but there's also consulted in the sort of world laboratory level, and Australia has a real, really significant leadership role in that place. Now, Anna DeFazio is based at Westmead in Sydney is one of the few members of the steering committee for that consortium.

Loretta Hart 46:30

That's fantastic. Thank you. And the next question, I would like to ask, and it'll probably go to both David and Rachel. It's a little complex. And so I'm just going to invite both David and Rachel to click on your little q&a box at the bottom of your screen so that you can help me with this. And the question came in at 1:22pm, you might need to scroll down to see that. I'm going to read it just for the benefit of the audience. But I think there's a there's quite complex. Rachel, can you seen that one? Now? The question from Nina Yeah. Well, Rachel, I might get you to read it. Because there's some big words in there that I think you'll do better with than me. Yeah. So I'm hoping for the two of you just to discuss that for Nina. Yep.

Dr Rachel Delahunty 47:00

So hi, ovarian cancer survivor stage one a low grade endometrial with proceeding significant endometriosis here. Can you talk a bit on the different ideologies of low and high grade epithelial ovarian cancer, eg high grade seems to arise from the fallopian tubes low grade appears to arise in a more stepwise progression from a borderline Shiva. Thank you. So yeah, thank you for the question. So yeah, you're highlighting really nicely this what we use the word heterogeneity, just meaning that ovarian cancer is just a broad term to describe a very, very different amount, number of diseases that occur at a similar location, and which I think has been part of, you know, hampered the the progress in the area, but through particularly through understanding or having access to genomic testing that has really revolutionized our understanding. So you say very nicely about high grade serous cancer coming from the fallopian tube, completely agree with that. And I think as we all people working in the field now appreciate that is that as well, and that's a particular cancer type that strongly associated with genetics. So, high grade serous ovarian cancers have some of the highest rate of gene changes in BRCA one and two and those other ovarian cancer genes compared to any other cancer type. So heritability is the greatest risk factor that is not a cancer that's particularly hormonally associated, its genetic risks that drives that, that development of that is disease and that why I'm so passionate about making sure that women are getting genetic testing. Because genetic

testing of women with high grade serous cancers an opportunity to find gene changes in families that may otherwise be unknown, and then give their family the opportunity to family members to the opportunity to have genetic testing and be prevented from having ovarian cancer if they do have a gene change. If you compare that to some of the low grade cancers, you've had a low grade, endometriosis associated cancer. So we know that young women with endometriosis that develop ovarian cancer tend to have a better outcome than, say, some of the other cancers. And endometriosis is a is quite a common condition in the community. And there's lots in place to say in the recent years, there's been lots of acknowledgment of this as a problem not only causing women impairment of their quality of life, but you know, potentially it's slightly increased risk of cancer. And that is now appreciated. The risk of cancer associated with endometriosis overall, is relatively low. But it's it is recognized now that there is there is a risk associated with that. And it can be a so at risk, slight risk factor for endometrioid or clear cell cancers. Endometriosis in itself is not an actual precursor for cancer, but it's certainly so it can occur endometriosis, and lots of women that don't go on to develop cancer. But I guess just if you have endometriosis making sure that it's adequately managed, which can include being on oral contraceptive pill, that sort, which is a great management strategy, and is important in making sure that you're getting adequate care. So just trying to think of like, in terms of other ideologies are five, they've all have slightly different. Basically, all those different cancers have their own risk factors there and different cells of origin. So we could probably talk about this for for a long time. So mucinous cancers are very different cancer again. So I think that's a very important thing to just recognize that they all develop slightly differently. So when we talk about genetics or endometriosis, it's not it's not directly applicable to all. I don't if you want to add anything to that, too, David?

Prof. David Bowtell 50:52

I think you've covered it really well.

Loretta Hart 50:56

Nicely done. Thank you. Thank you for all our people who had to ask questions today. We appreciate that. And I think that I also appreciate the fact that there was many votes for many of the questions that we've got to so obviously, we're covering topics that were really needed to be heard by our audience. We're coming to the end of our time together. And I'm mindful that, you know, our webinar series is entitled The path to hope. So I have a question just for each of our panelists to finish up with today. And I'm hoping they're hopeful sort of type questions. Rachel, I might come to you first, if that's okay. And and I am going to make it a tricky one. If you could pick one thing to change the stats of a ovarian cancer, what would you focus on in the short term?

Dr Rachel Delahunty 51:45

You picked one that's very close to my heart, that's easy. So genetic testing, because the best way to improve the survival for ovarian cancer for us women is for women to never get ovarian cancer in the first place. So my hope is that we can enable genetic testing for the women that

are at risk to make sure that we're not missing those genetic induced cancers. And I think that that's completely doable.

Loretta Hart 52:13

Thank you, David, five years from now, there's a big if, IF the funding is there. Where do you think we could be in terms of improved survival?

Prof. David Bowtell 52:27

Oh, that's a big question. I think that I think as Rachel mentioned earlier, the current stats are a little bit misleading. Because essentially, when you look at five year survival, you look at windows of time. And because of that, the way those that's put together, the data that we've got at the moment is probably from the early part of this early part of last decade, just get my decades right, or the mid part of last decade. So we're not really seeing the impact, for example of maintenance, PARP inhibitors after first line chemotherapy, and I think we're going to see a big uplift in that group. And I think we're also going to see, as we've suggested, a significant change around the use of antibody drug conjugates, particularly in women with relapse resistance is age. So I think it could improve. I don't have to put a figure on it. I'm kind of obviously shying away from that, but I think that we will see the benefit of what we're working in the stats of what we've already seen in the clinic in terms of PARP inhibitors. And I think we will certainly see that. I think we researchers are always very careful as, as Rachel said, you know, using the, the cure word and things like that, but I think that we will see significant benefit with the antibody drug conjugates. And further on the horizon with the the personalized vaccine inspect.

Loretta Hart 53:59

Thank you. Big question. Well, as you're a short period of time, you've done it done it. Well, David, I'll give you if I can come to you. How can patients, their loved ones, the wider community become involved in supporting ovarian cancer research and advocacy?

Olivia Curtis 54:15

That's an easy one. Talk about it. Have a conversation. You know, I I've been known to sit in cafes and overhear women saying, Oh, I've got this pain and go, Oh, have you heard of ovarian cancer? Have you been having trouble with your pools? Have you been doing this? You know, let's make it a conversation that isn't taboo. Let's, let's talk about it. But also, by a white shirt, go to witchery and buy a white shirt. Look Fabulous. Start a conversation that way. Donate to the OCRF anything you have, there's no donation too small. And share the information that we put out there on your social media. There are so many ways that you can you can make a difference. It doesn't need to be giving a million dollars, it can just be sitting next to the woman at the cafe that you overhear talking about something that think is setting off alarm bells and saying I you know, I heard this the other day, maybe go and see a doctor.

Loretta Hart 55:16

I love it. Absolutely. Especially love the piece about buy a white shirt and look fabulous. I think that's a fantastic way to get the conversation started. We've come to the end of our conversation today. And I know it's not going to be the end all these types of conversations. I'd like to thank our fabulous panelists Dr. David Bowtel. Professor David Bowtell sorry, Dr. Rachel Delahunty. Olivia Curtis thanks for your time. And thanks for your wisdom. I think its been really really generous sharing. It's been really wonderful. And I'm reading the comments in the chat section. And I, I know that so many of our attendees who are here live and all those who watched the recording, I'm sure also you get great benefit out of this conversation. So thanks very much. We promised you an insightful and informative conversation. I think we've done it. I think it's wonderful to David would you like to make a comment before we wrap.

Prof. David Bowtell 56:30

Oh, just one thing. I just wonder I mean, number of guests here have have taken the time to ask questions that we've not had time to address. I wondered whether there was an opportunity to sort of offline briefly address some of those. I don't know, if I'm asking something that's difficult to do or impractical at the moment, but I just am aware that people would not been able to get there to that question.

OCRF 56:43

Hi, David. It's Adel from the OCRF. We can definitely send you those questions and then circulate them to everyone who attended today, if that sounds okay.

Prof. David Bowtell 56:50

Yeah I think if we can try to collectively just briefly provide some responses, that would be great.

Loretta Hart 57:00

Yeah, that's a great idea. Wonderful. So thank you, thank you very much. That's a generous offer to make sure that everyone's questions get to be answered, to be conversation. And I know Adel may have a slide that we're going to pop up next. For those potentially, there might be some people who are feeling like, they might need a little support beyond this conversation with the emotions that maybe have been stirred up. And we've got some numbers on the screen for you. If you'd like to take those down, and please reach out to those services because they are fantastic in what they offer. As we said, this has been recorded, and it's going to be available on the Ovarian Cancer Research Foundation website, in the very, very short future. And we'll be in touch. There will be a survey that will follow this presentation that you'll get via email. And we would love feedback. We would love ideas on future events that that can be can be run future conversations. And I'm guessing then Adel that those questions might be answered and forwarded to that email as well. Because our end of our time together, I think we've got about 60 seconds before we get back to the rest of your day. Thanks again so much. From for all the panel for being here. Thanks for those who attended live thank you for those that from the Ovarian

Cancer Research Foundation that made today happen and we hope that you have a very happy world ovarian cancer day thanks so much.