OCRF Talking research webinar: The path to hope on World Ovarian Cancer Day unanswered audience questions

The Ovarian Cancer Research Foundation (OCRF) would like to thank Professor David Bowtell and Dr Rachel Delahunty for generously sharing their expertise and providing answers to questions we ran out of time to address during the webinar.

I lost my mother to HGSOC 6 yrs ago at age 62. Extensive genetic testing showed no known risks, despite significant cancer history on the maternal side. What preventative actions can/should be considered by those of us likely to be at some level of increased risk we simply doesn't understand yet?

In the setting of a strong family history where the risk is undefined/unexplained – for an affected family member like yourself, risk reducing surgery can absolutely be considered- eg removal of the tubes and ovaries. The optimal timing will depend on factors like the family history age of onset of cancer, your age and childbearing wishes/status.

I would recommend attending a risk management clinic to discuss this and other risk management considerations. If there is no risk management clinic available locally, attending a gynaecologist would be worthwhile. Also just addressing lifestyle issues like a healthy weight and exercising regularly are important.

Also just to flag that science is dynamic and understanding of risk is changing all the time. Eg- we now test for 12 ovarian cancer genes, 6ish years ago (depending on the location of the hospital) it was only two, and new things are coming eg- polygenic risk scores …. So, might be worth talking to an FCC down track to see if there is anything new.

Also, for women with cancer like your mum with a strong family history but no variant found – they can consider the ViP study

https://www.petermac.org/research/clinical-research/clinical-research-by-centre/familial-cancer-research-centre/variants-in-practice-vip

Is there a high risk of Ovarian cancer if you have Stage 4 endometriosis and adenomyosis or can you explain more on the connection, if there has been further research into it?

I think answered this in part but essentially there is only small increased absolute risk of OC with ovarian endometriosis – about extra 2 cases/10000 women years of follow up for women with ovarian endometriosis compared to without. Not all endo the same eg- peritoneal endo likely different risk to ovarian endo.

Having higher stage or deeply infiltrate not clearly linked to higher risk.
There has been research into understanding endo particularly in genetics but further research is needed

I have HGSOC Stage 3. Why can we not continue using Lynparza after the 2-year mark? Will there be any new treatments going forward to prolong our lives?

Really clear data from large trials to show that it can be safely ceased after two years. Many women achieve long term remission -maybe cure with this. The field wonder if two years is even needed… With extended courses come increased risks eg- MDS/AML which are very low with two years of first line maintenance.

Yes, definitely new drugs coming – eg ADCs. Also other work underway looking at re-challenge with PARPi or PARPi combinations if the cancer was to come back after initially having the two years of maintenance therapy.

My sister was diagnosed with stage 4 ovarian cancer last year, high grade serous carcinoma. Has proven chemo resistant, can patients seek options outside of their treatment teams & how?

Yes absolutely. As clinicians we encourage patients to seek second opinions and go elsewhere. Best to be honest with to your/your sister's doctor- eg say I would really to go xyz centre to see if they have anything to offer me. Clinicians will not be offended and understand it's important for people to feel like all options have been explored.

What research is being conducted to understand the cause of LGSOC? What sort of research is being done regarding treatment options for the 'rarer' OC subtypes, e.g. low-grade endometrioid, and clear cell. Is there individualised treatment on the horizon for these types?

This is covered in the recording but yes personalised options in trials for rare cancers like low grade serous cancer and clear cell. If you have a recurrent rare ovarian cancer—seek out genomic testing (testing of the tumour). Now available through CaSP with no charge – chat to you doctor about it. Also worth speaking to rare cancer groups like The Stafford Fox Rare Cancer's program and Rare Cancers Australia.

In view of the OCRA Hope trial showed that there was no great benefit to the majority of women in early intervention/diagnosis where do you think the majority of research money should be directed rather than towards multiple centres looking at early detection tests:

David Bowtell is co-Chair of a conference in the UK in October that aims to explore this very question, and identify Grand Challenges for the field. This meeting will focus on high grade serous cancer as this is the most common, but the meeting may be a template for other rarer ovarian cancers as well as possible additional international coordination of research and funding efforts. The meeting will bring together ~40 of the world leaders in ovarian cancer research including early, mid and late career to get a spectrum of insights. OCRF will also participate in the meeting. Watch this space!

With regard to research of long term survivors, what aspects are looked at? Does it include consideration of lifestyle factors that changed after the survivors' diagnosis such as diet, exercise, mental health, supplement use. or other non-mainstream therapies? If not, what do you explore?

To support members of the Armed Services, US Department of Defense has a very extensive research program, which includes an important and impactful focus on ovarian cancer (https://cdmrp.health.mil/ocrp/default). Following an international competition, in 2016 OCRP funded two large-scale international consortia of researchers to study long term survivors. David Bowtell is one of the principal investigators of the MOCOG consortium, leading the genetic and genomic (gene changes in the cancer itself) part of the study. Australia, through the Australian Ovarian Cancer Study and the Westmead Gyne bank has been by far the largest single contributor of samples to the study, reflective of the collaborative strength of Australian ovarian cancer research. The MOCOG study has 3 main areas of focus: the immune response of the patient against the cancer, genomics and genetics, and epidemiology which includes the

possible impact of diet, lifestyle, supplements, other medications. This is a very important part of the study as patients are keen to know what else they might do to improve their chances, and we have sought the views of long-term survivors. One of our first papers in this space can be found here: https://pubmed.ncbi.nlm.nih.gov/31706666/ and the work is ongoing. A major paper from the Bowtell lab on the impact of genetic changes in the cancer on long term survival was published recently: https://pubmed.ncbi.nlm.nih.gov/36456881/