

Genetic Testing of *BRCA1* and *BRCA2* in a person with ovarian cancer

Cancer in the general population

Cancer is a common condition which will affect up to 1 in 2 people in the general population in their lifetime. In the UK around 2 in 100 (2%) women develop ovarian cancer. The majority (85 out of 100, or 85%) of ovarian cancer cases are due to a combination of increasing age, environmental, lifestyle, and low risk genetic factors.

Why am I being offered a genetic test?

You have been given this leaflet because you have been diagnosed with ovarian cancer. Genetic testing of your tumour will help your oncologist plan the best treatment for you. Genetic testing of your blood may help guide your future care and provide you with information on future cancer risk. It may also give us information to help your relatives to manage their future cancer risk.

What are genes?

Genes are our cells' instruction manuals. We each have around 20,000 pairs of genes which are present in almost every single cell of our bodies. Our genes tell our cells how to function normally. Different genes have different roles in the body. The genetic test we are offering you looks to see if there are changes in two genes associated with ovarian cancer.

What are cancer-causing genetic variants called?

Many different words are used to describe cancer-causing genetic changes. "Mutation," "disease-causing alteration or variant," "pathogenic mutation," or "pathogenic variant" are all terms you may come across. We will use the term "pathogenic variant" to describe a variant in a gene which is known to cause cancer.

How do changes in genes cause cancer?

Most of the time cancer-causing genetic changes are found **ONLY** in the cancer cells (in the tumour). In this case the changes are called "**somatic** pathogenic variants".

A smaller number of women with ovarian cancer have inherited a genetic change which means they are more at risk of cancer. This is called a "**constitutional** or **germline** pathogenic variant".

Which genes are associated with ovarian cancer?

The two main genes we test for in ovarian cancer are called *BRCA1* and *BRCA2*. We all have two copies of these genes, as we inherit one copy from each of our parents. We can look at the *BRCA1* and *BRCA2* genes in the ovarian cancer cells (the tumour) to see if there is a **somatic** pathogenic variant. To see if this variant is also present in other cells in the body we can also look at the *BRCA1* and *BRCA2* genes in the blood cells. If the variant is also present in the blood cells this means it is an inherited **germline** pathogenic variant.

How do we test for genetic variants?

There are two tests to look for genetic changes that may have contributed to you developing cancer.

1. Tumour testing to look for **somatic** variants. Your oncologist will send a sample of your tumour onto a specialist laboratory to test it for variants in *BRCA1* and *BRCA2*. These results will take around 5 weeks to be reported.
2. A blood test to look for **germline** variants. Your treating team will take a blood sample from you and ask you to sign a consent form to have this sample stored. A member of the genetics team will contact you to explain more about testing your blood sample for variants in *BRCA1* and *BRCA2*. The results may take around 6-8 weeks to be reported.

What are the outcomes of testing? (1)

1. Somatic testing (from your tumour)

a) A *BRCA1* or *BRCA2* pathogenic variant is detected in your tumour sample which we know is associated with ovarian cancer. Your oncologist may use this information to guide your treatment. We would need to check to see if the variant is also present in your blood sample.

b) No *BRCA1* or *BRCA2* pathogenic variant is detected in your tumour sample. In this case it would be unlikely that your cancer was caused by a *BRCA* pathogenic variant. We would still check your blood test results to confirm this.

What are the outcomes of testing? (2)

1. Germline testing (from your blood sample)

(a) A BRCA1 or BRCA2 pathogenic variant is detected in your blood sample which we know is associated with ovarian cancer. This is often called being a “BRCA carrier.” This will likely explain why you developed cancer.

In this case you would meet with a member of the genetics team to discuss what this means for your future management and for your relatives. We know that germline BRCA carriers are at increased risk of breast cancer as well as ovarian cancer. Although treating your ovarian cancer takes priority, we can also assess your future breast cancer risk and offer personally tailored advice about managing this risk.

The chance that a first degree relative (parent/sibling/child) of a person with a pathogenic variant will also carry that variant is 1 in 2 (50%). We can support families to share this information with relatives so they can be tested.

(b) No BRCA1 or BRCA2 pathogenic variant is detected in your blood sample. In this case it would be less likely that your cancer was due to an inherited condition. You will still have a full review of your personal and family history to check no further genetic testing or screening is needed.

(c) A Variant of Uncertain Significance is detected (VUS). In rare cases we may identify a BRCA1 or BRCA2 variant, but we do not know if it is affecting the way the gene is working to cause cancer. This is known as a ‘variant of unknown significance.’ Most of these are likely to be harmless and we would usually manage you as if you had no variant identified. Sometimes we may wish to perform additional tests to clarify the significance of the variant which we will discuss with you. As our knowledge about genetic variation increases, we may decide this variant is pathogenic or harmless and change your management if needed.

How will finding a pathogenic variant in BRCA1 or BRCA2 affect my treatment?

Your oncologist may use this information to help decide the best treatment for your cancer. In particular, they may suggest prescribing a medication called a PARP Inhibitor. PARP Inhibitors have been shown to improve response to cancer treatment in BRCA carriers.

What can be done if I decide not to undergo testing?

If you do not have either tumour or blood testing, your oncologist will not be able to use the test information in your treatment plan and Genetics would make a risk assessment for family members based on the family history alone.

Sometimes, although someone does not wish to pursue a blood test at that time, they may decide to have a blood sample stored for either their own future use or for that of their family members. This is something we can discuss with you. You could still have your tumour tested to help make decisions about your treatment if you wish.

Family history information

The genetics team will take a family history to make sure we have offered you all the tests you need. They will also use this information to give screening advice in the family, even if a genetic test is negative. You can fill out your family history information in advance of your appointment at www.fhqs.org or by scanning the QR code below.



Websites for further information

Breast awareness (Macmillan):

<http://www.macmillan.org.uk/Cancerinformation/Testscreening/Breastscreening/Breastawareness.aspx>

Ovarian symptoms (Ovarian Cancer National Alliance):

<http://www.ovariancancer.org/about-ovarian-cancer/symptoms/>

Details regarding your test

- Date of test:
- Contact person:
- Results expected:

To provide feedback on this leaflet please go to <https://www.surveymonkey.co.uk/r/DHX7HQN>