FAQS FOR NON-GENETICS HEALTH CARE PROFESSIONALS ON
INFORMED CONSENT FOR BRCA GERMLINE TESTING

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**Which patients** should be considered for BRCA germline testing in relation to the PARP inhibitor olaparib?

BRCA germline testing should be considered in those who have a diagnosis of serous epithelial ovarian, primary peritoneal or fallopian tube cancer AND have previously responded to platinum-based therapy AND have relapsed and are commencing a second or subsequent line platinum based treatment. They should have no contraindication to the use of olaparib as maintenance therapy.

If they have previously undergone germline BRCA1/2 testing, there is no need for that to be repeated. If you have a query regarding the result of a BRCA test carried out in the past, e.g. if there is no record of the result or the test found a variance of unknown significance, you should contact the cancer genetics service to discuss this. Note in a patient who has previously undergone a bone marrow transplant, a blood sample cannot be used for germline testing. They should be referred to the genetics service to arrange appropriate testing.

**When** should I discuss the test with my patient?

If indicated, olaparib should be commenced as maintenance treatment within eight weeks of completion of a second line course of platinum-based therapy. As the test result may take up to 12 weeks, BRCA1/2 testing should be offered to potentially eligible patients at the time of relapse.

A number of patients may subsequently not respond to their platinum-based therapy, in which case they will not proceed to olaparib maintenance therapy, regardless of their BRCA test result.

**What is the likelihood of finding a germline BRCA mutation in my patient?**

The frequency of germline BRCA1 and BRCA2 mutations is up to 38% in patients with platinum-sensitive recurrent high-grade serous ovarian cancer.

**What are the implications for my patient of identifying a germline BRCA mutation?**

A patient with a germline BRCA mutation is more likely to respond to PARP inhibitor therapy and is eligible for maintenance treatment with olaparib.

The implications in relation to personal cancer risk are an increased risk of other cancers, particularly breast cancer. As it is an inherited cancer predisposition, there are implications for blood relatives who may also carry the gene (see below). If identified, the effect of a BRCA mutation on personal

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cancer risk and the approach to informing relatives would be addressed in more detail at a cancer genetics consultation.

A woman with a BRCA1 gene mutation has a lifetime risk of breast cancer of 70% and a 45% chance of developing ovarian cancer. A woman with a BRCA2 mutation also has a lifetime risk of breast cancer of about 70% and a 15% chance of developing ovarian cancer. The measures that can be taken to reduce this risk include prophylactic surgery (bilateral mastectomy and bilateral salpingo-oophorectomy) and chemoprevention (for breast cancer risk). Breast surveillance with MRI +/- mammography is recommended for women with a BRCA mutation who have not had prophylactic surgery.

What are the implications for my patient’s family and how would this be managed?

If your patient is found to have a germline BRCA mutation, then it is possible that this has also been inherited by their blood relatives – including males and females, and those unaffected by cancer themselves. A first degree relative would have a 50% chance of carrying the mutation.

The cancer genetics service will discuss this issue with your patient and advise on invitation for genetic testing. Relatives should not be offered testing through the olaparib testing pathway and should be offered genetic counselling by the cancer genetics service in advance of testing.

What are the issues I should discuss with my patient as part of the informed consent process?

In summary, the following issues should be discussed: the purpose of the test in relation to their choice of treatment; the possibility that they may be found to have an inherited cancer predisposition and if so, that it could have been inherited by other family members also; the protections offered by Irish law in relation to use of genetic results; the possibility that a test may be inconclusive.

- The purpose of the test is to check for a significant alteration in a BRCA gene, which would predict likelihood of response to olaparib. Only a small number of patients with ovarian cancer have a tumour that can be treated in this way.
- There are implications to knowing that you have an inherited predisposition to cancer - including the need to consider sharing the test result with relatives who may have inherited it also. The sharing of their test result with relatives can only take place with their consent.
- Under Irish law, genetic test results cannot be used for insurance, pension, mortgage or employment purposes.
- It is possible for the result of the test to be inconclusive – that a change in a gene is identified, but we do not know if it is a significant change. In this situation, olaparib treatment would not be recommended but we would advise patients to discuss their result with a cancer geneticist.
Is **written consent** required?

Yes, written consent is a legal requirement for genetic testing. Evidence of written consent must accompany the sample and is therefore incorporated into the order request form. A copy of the test request-consent form should also be held locally in the patient’s medical record.

What **patient information** materials are available for my patient?

An information leaflet specific to Irish patients offered BRCA testing via this pathway is available on the NCCP website [www.hse.ie/nccpchemoregimens](http://www.hse.ie/nccpchemoregimens) or direct link [here](http://www.hse.ie/nccpchemoregimens). This should be provided to all patients offered the test. Other useful resources for patient information include:

- Irish Cancer Society: [https://www.cancer.ie/content/do-you-have-questions-about-inherited-breast-cancer-and-brca1-and-brca2-here-are-some#sthash.wQAitWzP.dpbs](https://www.cancer.ie/content/do-you-have-questions-about-inherited-breast-cancer-and-brca1-and-brca2-here-are-some#sthash.wQAitWzP.dpbs)

Who will give my patient the **result**?

The result will be emailed to you, the ordering clinician, at the email address you provide on the test request form. You should explain the result to the patient, its implications for olaparib eligibility, and offer to refer them to the cancer genetics service if indicated.

Patients with an identified mutation, or a variance of unknown significance, should be offered a referral to the cancer genetics service, where they will be prioritised for review. Those in whom no mutation was found should still be offered a referral to the genetics service, if they have a strong family history.

**Who else** will have access to the result?

The clinical cancer genetics service will have access to the result if the patient is referred to them. The result (including if no mutation has been found) can be used by genetics health care professionals dealing with their relatives, if the patient has consented to this. This is therefore included in the test request-consent form.
Can the test result be inconclusive? What are the implications of an inconclusive result?

Yes, it is possible that a ‘variant of unknown significance’ is identified, meaning the implication of the mutation in their BRCA gene is unclear. In this case the patient is not eligible for olaparib. However, they should still be offered a referral to the cancer genetics service to discuss their result.

What are the implications of a finding of no BRCA mutation in my patient?

If the result is that no mutation has been identified, the patient is not eligible for olaparib. A referral to genetics services is not indicated unless there is a separate indication, e.g. a patient with multiple primary cancers or a strong family history of cancer, such as a number of first degree relatives with breast or ovarian cancer.

Are there other cancer predisposition genes I should consider in my patient?

If a patient has multiple primaries or a strong family history of cancer, e.g. a number of first degree relatives with breast or ovarian cancer, they should be referred to the genetics service for a more detailed risk assessment and possible further genetic testing. These additional test results would not affect choice of systemic therapy for their ovarian cancer.

Is it possible to test my patient for a somatic BRCA mutation?

A test for somatic BRCA mutation is under development and will be incorporated into the testing pathway once accredited. It is possible for a somatic BRCA mutation to be identified in tumour tissue, in a patient who does not have an inherited/germline mutation. Olaparib is licensed for use in either situation.

Where can I access additional information on cancer genetics?

If you need to discuss a patient, please contact the cancer genetics services at: Dr David Gallagher, St James’s Hospital, Dublin 8, Tel 01 4103759

Additional useful resources on cancer genetics include:

NHS Mainstreaming Cancer Genetics BRCA toolkit http://www.mcgprogramme.com/brcatoolkit/