

## FAQS FOR NON-GENETICS HEALTH CARE PROFESSIONALS ON

### INFORMED CONSENT FOR INHERITED (GERMLINE) BRCA TESTING

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

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

BRCA germline testing should be considered in those who have HER2-negative locally advanced or metastatic breast cancer. Patients should have been previously treated with an anthracycline and/or a taxane in the (neo)adjuvant, locally advanced or metastatic setting unless patients were not suitable for these treatments. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine-based therapy or be considered unsuitable for endocrine-based therapy

If the patient has previously undergone germline BRCA 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.

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

BRCA germline testing should be offered to potentially eligible patients with locally advanced or metastatic breast cancer who have been previously treated with an anthracycline and/or a taxane in the (neo)adjuvant, locally advanced or metastatic setting unless patients were not suitable for these treatments. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine-based therapy or be considered unsuitable for endocrine-based therapy.

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

Approximately 5-10% of all breast cancers and 20-25% of hereditary breast cancers are associated with mutations in breast cancer susceptibility genes 1 and 2 (BRCA1 and BRCA2)<sup>1</sup>

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<sup>1</sup> Easton DF. How many more breast cancer predisposition genes are there? Breast Cancer Res. 1999;1(1):14-7.

4. What are the **implications for my patient with breast cancer** of identifying a germline BRCA mutation?

The implications in relation to personal cancer risk are an increased risk of other cancers, particularly ovarian cancer. There can also be an increased risk of melanoma, pancreatic and other BRCA related cancers.

As it is an inherited cancer predisposition, there are implications for biological (blood) male and female relatives who may also carry the gene.

A woman with a BRCA1 gene mutation has a lifetime risk (to 80yrs) of breast cancer of up to 90% and a lifetime risk of ovarian cancer of up to 60%. A woman with a BRCA2 mutation has a lifetime risk of breast cancer of up to 85% and a lifetime risk of ovarian cancer of up to 30%. There are other cancers that may arise in individuals with variants (mutations) in these genes but the lifetime risk of developing these is much lower<sup>3</sup>.

The measures that can be taken to reduce these risks include prophylactic surgery (bilateral mastectomy and/or bilateral salpingo-oophorectomy (surgery to remove fallopian tubes and ovaries). Breast surveillance with MRI +/- mammography is recommended for women with a BRCA mutation who have not had prophylactic surgery. There is currently no recommended ovarian surveillance.

With your patient's agreement referral to genetic services (enclosing a copy of the genetic result) is recommended, and the effect of a BRCA mutation on personal cancer risk and the approach to informing relatives would be addressed in more detail at the cancer genetics consultation.

5. What are the **implications for my patient's family** of finding a germline BRCA mutation and how is this managed?

If your patient is found to have a germline BRCA mutation, then it is likely that this has been inherited and that biological (blood) relatives – both males and females, could also carry the BRCA variant (mutation) and be at risk of BRCA associated cancers (including those referred to above and male breast and prostate cancer). Those currently unaffected by cancer could still harbour the BRCA variant (mutation).

During the consent process, sharing results with family members will have been discussed and recorded, (most patients are happy to do so). The patient should be reminded of this when results are communicated. The patient should firstly share the genetic BRCA test result with her first degree relatives (parents, siblings, children), given the implications this may have for both male and female relatives who may wish to be tested. Typically, during her consultation with the clinical genetics service, disclosure to relatives will be discussed and the patient may be given a 'to whom it may concern' letter that she may use to disseminate the information to her first degree relatives if she prefers.

The patient's relatives should **not** be offered testing through the talazoparib testing pathway and should be offered genetic counselling by the Cancer Genetics Service in advance of testing. This

testing of unaffected relatives is known as predictive or cascade screening and must be preceded by genetic counselling by a qualified genetic counsellor or genetic consultant.

#### 6. 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 germline mutation in BRCA genes, which would predict likelihood of response to talazoparib.
- Patients should be told the test may yield three possible results:
  - A germline BRCA mutation is identified
  - A germline 'variant of uncertain (or unknown) significance' (VUS) identified
  - No germline BRCA mutation identified
- Discuss the benefits, risks, implications and limitations of the test e.g test sensitivity and specificity and impact on blood relatives.
- Discuss consent that the genetic test may be used for the benefit of other family members and made available for use in genetic counselling of other family members attending genetic centres, if requested.
- Discuss consent to communicate the genetic result to the GP and/or other healthcare professionals involved in the patient's care.
- Discuss consent that DNA may be stored indefinitely at the testing laboratory and/or other testing centres.
- Discuss consent that the DNA may be used confidentially for quality assurance purposes.
- Under the provisions of Part 4 of the Disability Act 2005, an insurer cannot request, take into account or process the results of genetic tests.

#### 7. Is **written consent** required?

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

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

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

9. Who will give my patient **the results**?

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 talazoparib eligibility, and recommendation for referral to the Cancer Genetics Service if indicated.

Patients with an identified germline mutation, or a germline “variant of uncertain significance” (VUS), should be referred with the patient’s agreement to the cancer genetics service, where they will be prioritised for review. Those in whom no germline mutation is found should still be offered a referral to the genetics service if there is a separate indication e.g. a patient with multiple primary cancers, young age of cancer onset or a strong family history such as a number of first degree relatives with breast/ovarian and /or pancreatic cancer.

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

The germline test 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.

11. Can the test result be **inconclusive**? What are the implications of an inconclusive result?

Yes, it is possible that a germline ‘variant of uncertain significance’ is identified, meaning the implication of the mutation in their BRCA gene is unclear. In this case the patient is not eligible for talazoparib. The patient should be offered a referral to the Cancer Genetics Service to discuss their result.

12. What are the implications of a finding of **no germline BRCA mutation** in my patient?

If no germline mutation has been identified, the patient is not eligible for talazoparib. A referral to genetics services should be considered if you have concerns for inherited predisposition to cancer on the basis of the patient or family characteristics such as, a patient with young age of onset, a patient with multiple primary cancers or a strong family history of cancer, such as male breast cancer, or a number of first degree relatives with breast/ovarian and /or pancreatic cancer.

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

If a patient has multiple primary cancers, young age of cancer onset or a strong family history of cancer, e.g. a number of first degree relatives with breast/ovarian or bowel 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 breast cancer.

If you need to discuss a patient, please contact the Cancer Genetics Services, St James's Hospital, Dublin 8, Tel 01 4103759