

SUMMARY OF INHERITED (GERMLINE) AND TUMOUR (SOMATIC) BRCA TESTING PROCESS FOR MEDICAL ONCOLOGISTS

Background

Germline and tumour BRCA (refers to BRCA 1 & BRCA 2) testing may now be requested by medical oncologists, to allow determination of likely response to the PARP inhibitor olaparib.

Eligible patients

- Have a diagnosis of
 - advanced (FIGO stages III and IV) high grade epithelial ovarian, primary peritoneal or fallopian tube cancer and are commencing first-line platinum based chemotherapy
 - high grade serous epithelial ovarian cancer (HGSC), 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
- Have no known contraindication to the use of olaparib as maintenance therapy
- Patients with a known BRCA (somatic or germline) mutation need not be referred for additional mutation testing
- Patients who have previously undergone full germline BRCA mutation screening* without detection of a pathogenic or likely pathogenic germline variant will not benefit from additional germline analysis and should be considered for tumour BRCA testing
- Patients who have previously undergone full germline BRCA mutation screening* and tumour analysis should not require additional testing

*Predictive BRCA testing is only used to exclude specific familial variants and is not equivalent to full BRCA mutation screening

Timing of testing

First Line Maintenance Treatment

If indicated, olaparib should be commenced as maintenance treatment within eight weeks of completion of platinum-based therapy (See Ovarian Chemotherapy Protocols). Note: Where debulking surgery is required last dose of platinum chemotherapy should be within 12 weeks of starting olaparib maintenance. Given the test turnaround time of up to 6¹ weeks, germline BRCA1/2 testing should be offered to potentially eligible patients at the time of commencement of first line platinum treatment.

¹ 90% of test results within this turnaround time of 6 weeks

SUMMARY OF INHERITED (GERMLINE) AND TUMOUR (SOMATIC) BRCA TESTING PROCESS FOR MEDICAL ONCOLOGISTS

Platinum Sensitive Relapsed Maintenance treatment

If indicated, olaparib should be commenced as maintenance treatment within eight weeks of completion of a second line course of platinum-based therapy. Given the test turnaround time of up to 6¹ weeks, germline and tumour BRCA testing should be offered to potentially eligible patients at the time of relapse following first-line treatment and treatment planning of the second-line course of platinum-based therapy.

Patient information and consent

The indication for testing is to determine likely response to olaparib therapy. Written consent must be provided for genetic testing and is incorporated in the test request form. Information materials to assist discussion are available on the NCCP website [here](#)².

Test request

An integrated test request form is available from the testing laboratory for both germline and tumour BRCA testing which includes details of sample and transport requirements and incorporates written patient consent.

SUMMARY OF INHERITED (GERMLINE) AND TUMOUR (SOMATIC) BRCA TESTING PROCESS FOR MEDICAL ONCOLOGISTS

Results

Results are sent to the ordering consultant by email. Note that this testing is limited to the germline and tumour BRCA gene and that a hereditary predisposition to ovarian cancer can occur in other genes.

Possible outcomes are as follows:

	Results	Olaparib treatment	Offer genetics referral
1.	Germline BRCA mutation identified	Eligible	Yes
2.	Tumour BRCA mutation identified	Eligible	No
3.	Both Germline and tumour BRCA mutation identified	Eligible	Yes
4.	Germline 'variant of uncertain (or unknown) significance' (VUS) identified	Not eligible	Yes
5.	Germline 'variant of uncertain significance' (VUS) plus tumour BRCA mutation identified	Eligible	Yes
6.	No mutation identified	Not eligible	If a strong family history

With the patient's agreement, a referral should be made to Cancer Genetics Services, to discuss the implications of the results for the patient and their family.

Cancer Genetics Services

- Cancer Genetics service , St James's Hospital, Dublin 8 Tel:- 01 4103759

2. See <http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/sactguidance/BRCA%20testing%20for%20olaparib.html> for test request/consent form, patient information materials & treatment regimen

3. All public and voluntary hospitals and some private hospital emails are connected securely to healthmail. To check if a particular institution is healthmail connected, please go to: <https://www.ehealthireland.ie/A2I-HIDs-Programme/Healthmail>. Note that personal email accounts or those related to academic postings are not connected to healthmail and should not be used for return of results.