Hereditary Breast/Ovarian Cancer – OMIM 604370, 612555

Background

Breast and ovarian cancers are among the most common cancers worldwide affecting around 10% of women in their lifetime. 5-10% of all breast cancers and ovarian cancers are hereditary and are mostly linked to pathogenic variants in *BRCA1* (OMIM 113705) or *BRCA2* (OMIM 600185) genes. However, pathogenic variants in other genes can also be responsible and the routine screen for patients with a suitable family history now also includes the genes *TP53* (OMIM 191170), *PTEN* (OMIM 601728), *STK11* (OMIM 602216) and *PALB2* (OMIM 610355). If a pathogenic variant is found in one of these genes then other family members can be tested. The pattern of inheritance is autosomal dominant, therefore there is a 50% chance of an affected adult passing the disease allele onto his/her child (although breast cancer is rare in men, males with a pathogenic variant are at increased risk of some cancers and can pass the pathogenic variant on to their children).

Recommended Clinical Referral Criteria

- **Family history of breast and/or ovarian cancer**: Requests for testing for this reason are only accepted from the clinical genetics service. The guidelines for referral to clinical genetics are available here: http://www.wales.nhs.uk/sites3/Documents/525/Cancer%20-%20Ref%20Guidlines%202016.pdf

Genetic testing will only be offered by the clinical team where appropriate according to the following criteria:

- **Personal history of high grade serous ovarian cancer at any age:** mainly referred from oncologists. *BRCA1* and *BRCA2* tested. When a pathogenic variant is found treatment with PARP-inhibitors may be appropriate. It is recommended that a blood sample is tested initially. However tumours with an acquired pathogenic variant may also be suitable for treatment with PARP-inhibitors therefore if no pathogenic variant is identified in a blood sample then analysis of a tumour sample can be requested.

- **Triple negative breast cancer diagnosed at age <50:** may be referred from oncologists or genetics.

Molecular Analysis

Variant screen on blood samples: Next generation sequence (NGS) analysis of *BRCA1* and *BRCA2* (any gaps will be filled by Sanger sequencing) and, where relevant of *TP53, PTEN*, *STK11* and *PALB2* (gaps not filled, percentage coverage stated on report). NGS or MLPA dosage analysis of *BRCA1* and *BRCA2*. Pathogenic variants are found in 15-20% of patients referred from genetics.

Variant screen on FFPE tissue: NGS analysis of *BRCA1* and *BRCA2* (gaps not filled, percentage coverage stated on report and no dosage analysis).
Common variant analysis: Testing for three common Ashkenazi Jewish pathogenic variants: c.68_69delAG and c.5266dupC in *BRCA1* and c.5946delT in *BRCA2*.
Familial follow-up: Testing for known familial pathogenic variants in *BRCA1*, *BRCA2*, *TP53*, *PTEN, STK11, PALB2* genes.

Turnaround Times (TAT)

Prices available on request, please contact the laboratory using details below.

Test	TAT (working days)
Test for known familial mutations in genes listed above	20
Test for three common Ashkenazi Jewish mutations in *BRCA1* and *BRCA2*	20
Next generation sequencing and dosage analysis (*BRCA1* and *BRCA2*)	40

Contact Details

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lab.genetics@wales.nhs.uk
www.wales.nhs.uk/AWMGS/
Accredited to ISO 15189:2012 (8988)

Sample Requirements

Blood – 5ml in EDTA
Please label samples with three identifiers and date of collection.
Please contact lab prior to sending a prenatal sample.
All samples must be accompanied by request form
Consent for testing & DNA storage is assumed when request for test received

Links

Orphanet: http://www.orpha.net/
EDDNAL: http://www.eddnal.com/
OMIM: http://www.omim.org/
Genetic Test Registry: http://www.ncbi.nlm.nih.gov/gtr/

Support

http://www.macmillan.org.uk/information-and-support/diagnosing/causes-and-risk-factors/genetic-testing-and-counselling/inherited-cancers-breast-ovarian.html