DOUGLASS HANLY MOIR PATHOLOGY

Information for Doctors

Ovarian cancer

Genetic testing to inform treatment decisions

PARP inhibitors, such as olaparib, are effectve in cancers with mutated BRCA1 or BRCA2 genes. Immunotherapy is potentially effective in patients with a mutated mismatch repair (MMR) gene and missing MMR protein.

Rebated testing of BRCA and MMR genes

When using tumour tissue, Sonic Genetics provides rebated sequence analysis of the BRCA1 and BRCA2 genes and immunohistochemistry for loss of proteins encoded by the DNA MMR genes, MLH1, MSH2, MSH6, and PMS2, when requested by a medical specialist.

When using a blood sample, Sonic Genetics provides rebated sequence analysis of these genes (plus deletions/duplications as specified overleaf), when requested by a medical specialist.

Once a disease-causing variant in any of these genes has been identified, rebated testing for that variant is available to relatives on request by a medical specialist.

When possible, start by testing tumour tissue

Start by testing a sample of tumour tissue. Sequence analysis of the BRCA genes will detect 90% of targetable mutations, whether they be germline (present in normal and tumour tissue) or somatic (limited to tumour tissue). Absence of an MMR protein can also be due to germline or somatic mutations in MMR genes. The distinction between mutation types is immaterial in selecting targeted therapies.

Test blood sample if tumour tissue is not available

If tumour tissue is not available, Sonic Genetics provides rebated sequence and deletion/duplication analysis of the BRCA1 and BRCA2 genes; testing of the MMR genes is available for a private fee. This analysis will not detect somatic mutations and so will fail to identify those patients with targetable somatic mutations.

Test blood sample if mutation is found in tumour

If the tumour tissue has a BRCA mutation or loss of an MMR protein, we offer rebated sequencing with deletion/duplication analysis of a blood sample to determine whether the mutation is germline or somatic. This clarifies the risk of cancer for relatives rather than informing decisions regarding the patient's chemotherapy. We also offer rebated testing for germline mutations in relatives (genetic counselling provided at no additional cost).

> If the patient has a family history or personal history suggestive of a familial cancer syndrome,[1] rebated testing is available for germline mutations. Non-rebated testing attracts a private fee.

Information for Doctors

Testing for BRCA1 and BRCA2 mutations

Fifteen to twenty-five per cent (15–25%) of high-grade serous papillary cancers have mutated BRCA1 or BRCA2 genes and are potentially sensitive to PARP inhibitors.

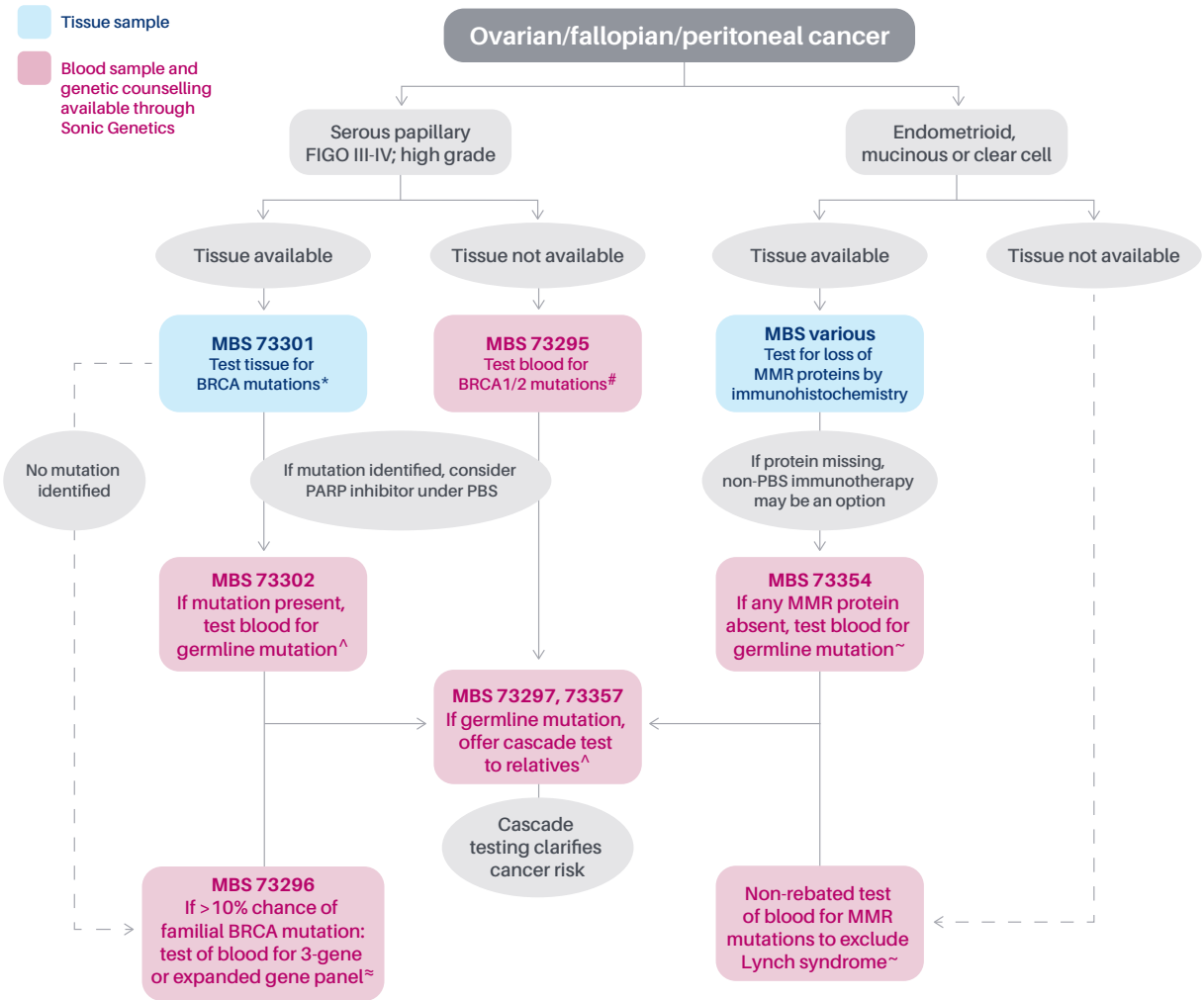
If a mutation is identified in the tissue sample, approximately 70% of these are germline, that is familial, and represent a significant cancer risk for relatives.

Testing for abnormal DNA mismatch repair (MMR) genes

Five per cent (5%) of ovarian cancers have loss of one or more MMR proteins due to MMR gene mutations. Such tumours are potentially sensitive to immunotherapy; immunotherapy for ovarian cancer is not listed on the Pharmaceutical Benefits Scheme (PBS).

If loss of an MMR protein is identified in the tissue sample, approximately 50% of patients have a germline mutation in an MMR gene; this finding represents a significant cancer risk for relatives.

Testing pathways, MBS Item numbers and therapeutic implications



* Sequence analysis of BRCA1/2
\# Sequence and deletion/duplication analysis of BRCA1/2
^ Sequence or deletion/duplication analysis of specific gene (as indicated)
~ Sequence and deletion/duplication analysis of MMR genes plus del/dup of EPCAM
≈ Sequence and deletion/duplication analysis of BRCA1/2 and PALB2, +/- sequence analysis of MMR genes plus others

For further information, including how to arrange a test, please refer to sonicgenetics.com.au/somaticbrca

Reference

1. Ovarian cancer (epithelial) - panel testing [Internet]. eviQ. <eviQ.org.au/p/3783>

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For further information, please refer to our website, sonicgenetics.com.au or call us on 1800 010 447

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