

The evolution of BRCA testing: treatment & prevention opportunities



Mutation of the BRCA genes (BRCA1 and BRCA2) is associated with response to PARP inhibitors such as olaparib and rucaparib. PARP inhibitors are currently approved in four cancer types: breast (HER2 negative), ovarian, pancreatic and prostate.

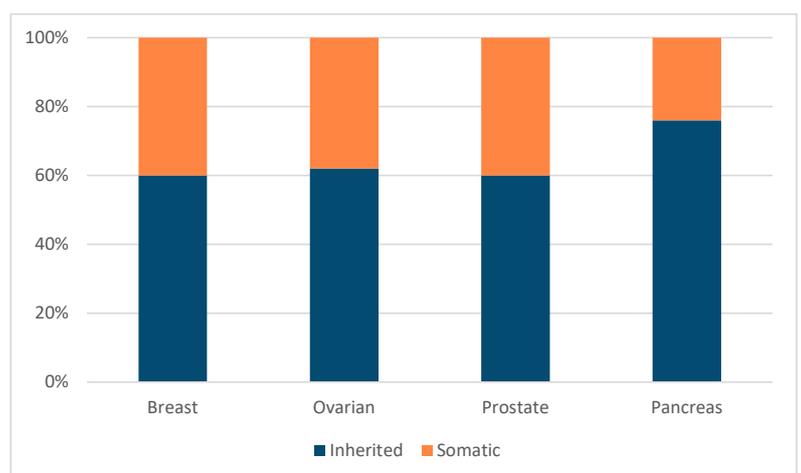
BRCA mutations can be inherited or somatic (see figure). Current PARP inhibitor approvals for breast and pancreatic cancer are restricted to patients with inherited mutations, whereas approvals in prostate and ovarian cancer cover both inherited and somatic mutations. Of note, PARP inhibitors appear to show similar activity against tumours with inherited or somatic mutations¹.

The success of PARP inhibitor therapy mandates a new approach to BRCA mutation testing. All patients with advanced breast, ovarian, pancreatic or prostate cancer should have access to BRCA mutation testing. BRCA testing can be performed as part of a comprehensive biomarker test using DNA from the tumour, as both inherited and somatic mutations will be present in the tumour cells. In a recent study, however, nearly 10% of inherited mutations were missed by tumour only analysis, due to either errors in mutation classification or technical limitations of the tumour assay².

In an ideal world, all patients potentially eligible for PARP inhibitors would receive genetic counselling prior to biomarker testing. In reality, however, this is rarely feasible, and so a pragmatic approach is required. As a minimum, the clinical team should discuss the risks and benefits of testing with the patient, including the potential to detect inherited mutations.

Working closely with Clinical Genetics can avoid misclassification of mutations in tumour samples³ and establish appropriate referral pathways for those with mutations^{4,5}. It is worth noting that family history is not a useful predictor of inherited mutations in those with cancer⁶.

Most important of all, the possibility of detecting an inherited mutation should not deter oncologists from testing for BRCA mutations in those diagnosed with breast, ovarian, pancreatic or prostate cancer⁷.



¹ BMC Cancer. 2020 Jun 3;20(1):507

² JAMA Netw Open. 2020 Oct 1;3(10):e2019452

³ JNCI Cancer Spectr. 2020 Mar 5;4(3):pkaa018

⁴ JAMA Oncol. 2020 Jun 1;6(6):815-816.

⁵ NCI Cancer Spectr. 2019 Nov 11;4(1):pk2095

⁶ JAMA Oncol. 2020 Oct 30. doi: 10.1001/jamaoncol.2020.6252

⁷ https://www.linkedin.com/posts/european-society-for-medical-oncology_map2020-precisiononcology-activity-6725429856491982848-clfT