Genomic Testing (Secondary Findings) ACT Sheet

BRCA1 and BRCA2 Pathogenic Variants (Hereditary Breast and Ovarian Cancer)

Pathogenic or likely pathogenic heterozygous variants (mutations) in the BRCA1 or BRCA2 gene are associated with a significantly increased risk for female breast and ovarian cancer, and less often, for other cancers (e.g., male breast, prostate, and pancreatic cancer, and melanoma).

YOU SHOULD TAKE THE FOLLOWING ACTIONS:

- Inform the individual (or parent/guardian) of the result of the genomic screening result and that there is a high lifetime risk of developing cancer.
- Obtain and review family and medical history.
- Refer for genetic consultation and counseling.

Clinical Considerations:
Females with a heterozygous pathogenic BRCA1 or BRCA2 gene variant have a lifetime risk of 38% - 87% for breast cancer and 16% - 63% for ovarian cancer (includes fallopian tube and primary peritoneal cancers). Males with a pathogenic variant in BRCA1 or BRCA2 have a lifetime risk of 1% - 9% for breast cancer. Such males also have a higher risk for prostate cancer (9-15% by age 65). Those with pathogenic/likely pathogenic BRCA2 variants from both sexes have a higher risk for other cancers such as pancreatic and melanoma. Earlier, frequent, and more comprehensive cancer screening is necessary in these patients. Certain medications have been shown to prevent breast cancer in the high-risk population. For individuals with pathogenic variants, risk-reducing mastectomy and salpingo-oophorectomy can substantially lower the risk of cancer.

Prevalence: About 1 in 300 in the general U.S. population, 1 in 40 in the Ashkenazi Jewish population.

Mode of Inheritance: Hereditary cancer predisposition due to a pathogenic variant in the BRCA1 or BRCA2 gene is inherited as an autosomal dominant disorder with incomplete penetrance and variability in disease expression. Immediate and extended family members should be offered genetic testing for at least the familial pathogenic variant in the BRCA1 or BRCA2 gene. More extensive genetic testing for family members might be appropriate, depending on personal and family history. Note, carriers of a pathogenic BRCA2 gene variant are at risk of having a child with Fanconi anemia if their partner is also a carrier.

Additional Information:
- NCI Fact Sheet (BRCA I and II)
- GeneReviews
- Genetics Home Reference

Referral (local, state, regional and national):
- Testing
- Find Genetic Services
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**APPENDIX: Resources with Full URL Addresses**

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- Gene Reviews  

- Genetics Home Reference  

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- Testing  

- Find Genetic Services  
  [www.acmg.net/gis](www.acmg.net/gis)