BRCA2 Targeted Analysis

NCCN Guidelines
When BRCA1 and BRCA2 results are negative, additional testing may be helpful for some patients with breast, ovarian, and pancreatic cancer. Guidelines from the National Comprehensive Cancer Network® (NCCN®) recommend considering germline genetic testing for high-penetrance breast and/or ovarian cancer genes (including, but not limited to, BRCA1/2, CDH1, PALB2, PTEN, and TP53) in patients with any of the criteria in the table below. To discuss comprehensive genetic testing for breast, ovarian, and pancreatic cancer genes, an Integrated Genetics’ Genetic Coordinator is available at 800-345-4363.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>NCCN Guidelines</th>
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<td>Breast cancer diagnosed ≤ age 45</td>
<td>OVarian cancer at any age&lt;/p&gt;</td>
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| Male breast cancer at any age                                             |Pancreatic cancer at any age</p> |<p> |<p>Triple negative breast cancer diagnosed ≤60                             |Metastatic prostate cancer at any age</p> |<p> |<p>Breast, ovarian, or pancreatic cancer at any age; and Ashkenazi Jewish ancestry |A first or second degree relative meeting any of the criteria in this table

The BRCA2 c.9812T>G (p.Leu3271Ser) targeted variant was NOT identified in this individual. This variant is also known as c.9812T. No pathogenic variants were identified.

Additional Clinical Information

NCCN Guidelines
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RECOMMENDATIONS

Genetic counseling is recommended to discuss the potential clinical and/or reproductive implications of these results, as well as recommendations for testing family members. To access Integrated Genetics Genetic Counselors please visit www.integratedgenetics.com/genetic-counseling or call (855) GC-CALLS (855-422-2557).

METHODS AND LIMITATIONS

Next-generation sequencing: Genomic regions of interest are selected using a custom capture reagent for target enrichment and sequenced via the Illumina(R) next generation sequencing platform. Regions of interest include all exons and intron/exon junctions (+/-20 nucleotides) of the BRCA1 (NM_007294.3) and BRCA2 (NM_000059.3) genes. Sequencing reads are aligned with the human genome reference GRCh37/hg19 build. Minimum mean coverage is 40X. Any segment failing minimum read depth coverage is rescued by bi-directional Sanger sequencing to complete sequence analysis. Variants, including SNVs and CNVs, are identified using a custom bioinformatics pipeline.

Reported variants: Pathogenic and likely pathogenic variants and variants of uncertain significance (VUS) are reported. Non-deletion variants are specified using the numbering and nomenclature recommended by the Human Genome Variation Society (HGVS, http://www.hgvs.org/). Benign variants are not reported. Variant classification and confirmation are consistent with ACMG standards and guidelines (Richards, PMID:25741868; Rehm, PMID:23887774). Detailed variant classification information is available upon request. A variant of uncertain significance (VUS) should not be used in clinical decision making; a VUS is classified based on inadequate or conflicting evidence regarding its pathogenicity or clinical relevance.

Limitations: Technologies used do not detect germline mosaicism and do not rule out the presence of large chromosomal aberrations, including rearrangements, gene fusions, or variants in regions or genes not included in this test, or possible inter/ intragenic interactions between variants. Variant classification and/or interpretation may change over time if more information becomes available. False positive or false negative results may occur for reasons that include: genetic variants, pseudogene interference, technical handling, blood transfusions, bone marrow transplantation, mislabeling of samples, or erroneous representation of family relationships. For heterozygous variants in the same gene the assay cannot determine whether they are on the same or a different chromosomes; to determine phase and clinical significance, rarely, parental testing may be required. Exact breakpoints of exon-level deletions/duplications are not determined. The presence of an inherited cancer syndrome due to a different genetic cause cannot be ruled out. Any interpretation should be clinically correlated with information about the patient's presentation and relevant family history.

REFERENCES


This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.