



1-800-533-1710

Hereditary Breast/Gyn Cancer Panel

BRGYP

PATIENT NAME TESTRNV, IMPLEMENTATION					ORDER NUMBER L001000439
PATIENT ID X100366937	DATE OF BIRTH 02/19/1968	AGE 53 Y	SEX Female	REQUESTED BY CLIENT TEST	
COLLECTED 9/1/2021, 7:33 AM	RECEIVED 9/3/2021, 1:57 PM	REPORTED 9/9/2021, 6:12 PM			
The collected, received, and reported dates and times on the report are in the time zone of the performing location.				CLIENT ORDER NUMBER X100366937	
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TEST DESCRIPTION

Evaluation of 20 genes associated with hereditary breast and gynecologic cancers

SPECIMEN

WB Whole Blood

RESULT SUMMARY

Pathogenic Variant Detected

RESULT

Gene (Transcript)	Variant	Zygosity	Classification
BRCA1 NM_007294.4	p.E23Vfs*17 p.Glu23Valfs*17 c.68_69del Chr17(GRCh37):g.41276045	heterozygous	PATHOGENIC

The following heterozygous PATHOGENIC variant was detected:

BRCA1 (NM_007294.4), p.E23Vfs*17 (p.Glu23Valfs*17), c.68_69del, Chr17(GRCh37):g.41276045

No additional reportable variants were detected within all other tested genes. See the Genes Analyzed section for a complete list of genes evaluated by this assay.

INTERPRETATION

BRCA1 c.68_69del (p.E23Vfs*17), PATHOGENIC

The heterozygous c.68_69del (p.E23Vfs*17) frameshift variant in the BRCA1 gene (MIM:113705) is an established pathogenic variant. Variants in the BRCA1 gene have been associated with autosomal dominant hereditary breast and ovarian cancer (HBOC) syndrome and autosomal recessive Fanconi anemia (1). This result is supportive of a diagnosis of hereditary breast and ovarian cancer (HBOC) syndrome for this individual. This result is also supportive of carrier status for Fanconi anemia. Clinical correlation is recommended. Individuals with certain cancers and pathogenic or likely pathogenic variants in genes involved in the homologous recombination repair pathway may show sensitivity to poly(ADP-ribose) polymerase inhibitors (PARPi) and may be eligible for targeted treatments (2)(3)(4)(5)(6).

This result should be interpreted in the context of clinical findings, family history, and other laboratory testing.

Consultation with a genetics professional is recommended for interpretation of this result and to determine whether reproductive risk assessment and familial testing may be of benefit to this family. Genetic testing for family members is

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available by ordering FMTT / Familial Mutation, Targeted Testing for the specific variant(s) detected. Please contact the laboratory at 1-800-533-1710 or the online test catalog at www.mayocliniclabs.com for information about FMTT.

REFERENCES:

- 1) GeneReviews: BRCA1- and BRCA2-Associated Hereditary Breast and Ovarian Cancer (<https://www.ncbi.nlm.nih.gov/books/NBK1247/>) (PMID: 20301425)
- 2) Kaufman B, Shapira-Frommer R, Schmutzler RK, et al. Olaparib monotherapy in patients with advanced cancer and a germline BRCA1/2 mutation. J Clin Oncol. 2015;33(3):244-250. doi:10.1200/JCO.2014.56.2728 (PMID 25366685)
- 3) Litton JK, Rugo HS, Ettl J, et al. Talazoparib in Patients with Advanced Breast Cancer and a Germline BRCA Mutation. N Engl J Med. 2018;379(8):753-763. doi:10.1056/NEJMoa1802905 (PMID 30110579)
- 4) Moore KN, Secord AA, Geller MA, et al. Niraparib monotherapy for late-line treatment of ovarian cancer (QUADRA): a multicentre, open-label, single-arm, phase 2 trial [published correction appears in Lancet Oncol. 2019 May;20(5):e242]. Lancet Oncol. 2019;20(5):636-648. doi:10.1016/S1470-2045(19)30029-4 (PMID 30948273)
- 5) Robson M, Im SA, Senkus E, et al. Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation [published correction appears in N Engl J Med. 2017 Oct 26;377(17):1700]. N Engl J Med. 2017;377(6):523-533. doi:10.1056/NEJMoa1706450 (PMID 28578601)
- 6) Swisher EM, Lin KK, Oza AM, et al. Rucaparib in relapsed, platinum-sensitive high-grade ovarian carcinoma (ARIEL2 Part 1): an international, multicentre, open-label, phase 2 trial. Lancet Oncol. 2017;18(1):75-87. doi:10.1016/S1470-2045(16)30559-9 (PMID 27908594)

METHOD

Next generation sequencing (NGS) and/or Sanger sequencing is performed to test for the presence of variants in coding regions and intron/exon boundaries of the genes analyzed, as well as some other regions that have known pathogenic variants. The human genome reference GRCh37/hg19 build was used for sequence read alignment. At least 99% of the bases are covered at a read depth over 30X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for indels less than 40 base pairs (bp), above 95% for deletions up to 75 bp and insertions up to 47 bp. NGS, multiplex ligation-dependent probe amplification (MLPA), and/or a polymerase chain reaction (PCR)-based quantitative method is performed to test for the presence of deletions and duplications in the genes analyzed. PCR and gel electrophoresis is performed to test for the presence of the 10 Mb inversion of coding exons 1-7 of the MSH2 gene. See the Genes Analyzed field for a list of genes tested.

There may be regions of genes that cannot be effectively evaluated for sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high GC content, and repetitive sequences. Confirmation of select reportable variants was performed by alternate methodologies based on internal laboratory criteria. See www.mayocliniclabs.com BRGYP for details regarding genes with regions not routinely covered.

GENES ANALYZED

ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM (copy number variants only), MLH1, MSH2, MSH6, NBN, NF1, PALB2, PMS2, PTEN (including promoter), RAD51C, RAD51D, STK11, and TP53

DISCLAIMER

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Clinical Correlations

If testing was performed because of a clinically significant family history it is often useful to first test an affected family member. Detection of a reportable variant(s) in an affected family member would allow for more informative testing of at risk individuals.

To discuss the availability of further testing options or for assistance in the interpretation of these results, Mayo Clinic Laboratory genetic counselors can be contacted at 1-800-533-1710.

Technical Limitations

Next generation sequencing may not detect all types of genomic variants. In rare cases, false negative or false positive results may occur. The depth of coverage may be variable for some target regions, but assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.

There may be regions of genes that cannot be effectively evaluated for sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high GC content, and repetitive sequences. Confirmation of select reportable variants was performed by alternate methodologies based on internal laboratory criteria.

Additionally, low level mosaic variants may not be detected.

This test is not designed to differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.

Genes may be added or removed based on updated clinical relevance. Please refer to the Targeted Genes and Methodology Details for the Hereditary Breast/Gyn Cancer Panel in the Special Instructions section of the Test Catalog for the most up to date list of genes included in this test.

Reclassification of Variants Policy

See www.mayocliniclabs.com BRGYP for information regarding the laboratory's policy for reclassification of variants.

Variant Evaluation

Variant curation is performed using published ACMG-AMP recommendations as a guideline. Other gene-specific guidelines may also be considered. Variants classified as benign or likely benign are not reported.

Results from in silico evaluation tools may change over time and should be interpreted with caution and professional clinical judgment.

TEST CLASSIFICATION

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

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