INVITAE

INVITAE DIAGNOSTIC TESTING RESULTS

Patient name:	**Sample type:**	**Report date:**
DOB:	**Sample collection date:**	**Invitae #:**
Sex assigned at birth:	**Sample accession date:**	**Clinical team:**
Gender:		
Patient ID (MRN):		

Reason for testing

Family history

Test performed

Sequence analysis and deletion/duplication testing of the 70 genes listed in the Genes Analyzed section.

- Invitae Multi-Cancer Panel

RESULT: POSITIVE

One Pathogenic variant identified in BRCA2. BRCA2 is associated with autosomal dominant hereditary breast and ovarian cancer syndrome and autosomal recessive Fanconi anemia.

Additional Variant(s) of Uncertain Significance identified.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
BRCA2	c.2808_2811del (p.Ala938Profs*21)	heterozygous	PATHOGENIC
POLE	c.407A>T (p.Lys136Ile)	heterozygous	Uncertain Significance

About this test

This diagnostic test evaluates 70 gene(s) for variants (genetic changes) that are associated with genetic disorders. Diagnostic genetic testing, when combined with family history and other medical results, may provide information to clarify individual risk, support a clinical diagnosis, and assist with the development of a personalized treatment and management strategy.

Next steps

- This is a medically important result that should be discussed with a healthcare provider, such as a genetic counselor, to learn more about this result and the appropriate next steps for further evaluation, treatment and/or management. This result should be interpreted within the context of additional laboratory results, family history and clinical findings.
- Please see NCCN (www.nccn.org) and PMID: 33414132 for management guidelines regarding BRCA2-related condition(s).
- Consider sharing this result with relatives as they may also be at risk. Details on our Family Variant Testing program can be found at www.invitae.com/family.
- Register your test at www.invitae.com/patients to download a digital copy of your results. You can also access educational resources about how your results can help inform your health.

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Clinical summary

A Pathogenic variant, c.2808_2811del (p.Ala938Profs*21), was identified in BRCA2.

- The BRCA2 gene is associated with autosomal dominant hereditary breast and ovarian cancer (HBOC) syndrome (MedGen UID: 151793) and autosomal recessive Fanconi anemia, type D1 (FA-D1) (MedGen UID: 325420).
- This result is consistent with a predisposition to, or diagnosis of, autosomal dominant BRCA2-related conditions.
- Females with a pathogenic BRCA2 variant have a 44-80% lifetime risk of breast cancer (PMID: 32676552, 33471974). The risk for contralateral breast cancer 10 years after primary diagnosis is 10-30% (PMID: 26700119). The lifetime risk for ovarian, fallopian tube, or peritoneal cancer is 13-29% (PMID: 32676552, 28632866, 23628597). Males have a 7-8% risk of breast cancer (PMID: 18042939) and a 19-61% risk of prostate cancer (PMID: 28448241, 31495749). Both males and females have an increased risk of pancreatic cancer (4-9% lifetime risk) (PMID: 29922827, 27306910) and melanoma (lifetime risks not established) (PMID: 10433620).

  Biallelic pathogenic variants in BRCA2 are associated with a particularly severe form of Fanconi anemia (PMID: 16825431) characterized by bone marrow failure, short stature, abnormal skin pigmentation, developmental delay, and malformations of the thumbs, skeletal, and central nervous systems (PMID: 20417588, 8986277). Risks of leukemia and early onset solid tumors are significantly elevated (PMID: 20507306, 12393424, 12393516), with up to a 97% risk of malignancy by 5 years of age (PMID: 16825431).
- Biological relatives have a chance of being at risk for autosomal dominant BRCA2-related conditions and have a chance of being carriers for autosomal recessive BRCA2-related conditions. Those at risk should consider testing.

A Variant of Uncertain Significance, c.407A>T (p.Lys136Ile), was identified in POLE.

- The POLE gene is associated with autosomal dominant PPAP (polymerase proofreading–associated polyposis) (MedGen UID: 767374) and autosomal recessive FILS syndrome (facial dysmorphism, immunodeficiency, livedo, and short stature) (MedGen UID: 767490).
- Not all variants present in a gene cause disease. The clinical significance of the variant(s) identified in this gene is uncertain. Until this uncertainty can be resolved, caution should be exercised before using this result to inform clinical management decisions.
- Complimentary familial VUS testing is not offered. Details on our VUS Resolution and Family Variant Testing Programs can be found at https://www.invitae.com/family.

Variant details

BRCA2, Exon 11, c.2808_2811del (p.Ala938Profs*21), heterozygous, PATHOGENIC

- This sequence change creates a premature translational stop signal (p.Ala938Profs*21) in the BRCA2 gene. It is expected to result in an absent or disrupted protein product. Loss-of-function variants in BRCA2 are known to be pathogenic (PMID: 20104584).
- This variant is present in population databases (rs80359351, gnomAD 0.003%).
- This premature translational stop signal has been observed in individual(s) with female breast cancer, male breast cancer, ovarian cancer, prostate cancer, and pancreatic cancer (PMID: 9585613, 12955716, 21952622, 23929434).
- This variant is also known as 2807del4, 3034del4, 3036del4, 3034delAAAC, 3036delACAA, and 3036_3039del4.
- ClinVar contains an entry for this variant (Variation ID: 9322).
- For these reasons, this variant has been classified as Pathogenic.

POLE, Exon 5, c.407A>T (p.Lys136Ile), heterozygous, Uncertain Significance

- This sequence change replaces lysine, which is basic and polar, with isoleucine, which is neutral and non-polar, at codon 136 of the POLE protein (p.Lys136Ile).
- This variant is present in population databases (no rsID available, gnomAD 0.002%).
- This variant has not been reported in the literature in individuals affected with POLE-related conditions.

- ClinVar contains an entry for this variant (Variation ID: 850323).
- Advanced modeling of protein sequence and biophysical properties (such as structural, functional, and spatial information, amino acid conservation, physicochemical variation, residue mobility, and thermodynamic stability) performed at Invitae indicates that this missense variant is expected to disrupt POLE protein function with a positive predictive value of 80%.
- In summary, the available evidence is currently insufficient to determine the role of this variant in disease. Therefore, it has been classified as a Variant of Uncertain Significance.

Genes analyzed

This table represents a complete list of genes analyzed for this individual, including the relevant gene transcript(s). If more than one transcript is listed for a single gene, variants were reported using the first transcript listed unless otherwise indicated in the report. An asterisk (*) indicates that this gene has a limitation. Please see the Limitations section for details. Results are negative unless otherwise indicated in the report. Benign and Likely Benign variants are not included in this report and in specific scenarios variants of uncertain significance in the requisitioned gene(s) may not be included in this report.

GENE	TRANSCRIPT
AIP	NM_003977.3
ALK	NM_004304.4
APC*	NM_000038.5
ATM*	NM_000051.3
AXIN2	NM_004655.3
BAP1	NM_004656.3
BARD1	NM_000465.3
BLM	NM_000057.3
BMPR1A	NM_004329.2
BRCA1	NM_007294.3
BRCA2	NM_000059.3
BRIP1	NM_032043.2
CDC73	NM_024529.4
CDH1	NM_004360.3
CDK4	NM_000075.3
CDKN1B	NM_004064.4
CDKN2A (p14ARF)	NM_058195.3
CDKN2A (p16INK4a)	NM_000077.4
CHEK2	NM_007194.3
CTNNA1	NM_001903.3
DICER1*	NM_177438.2
EGFR	NM_005228.3
EPCAM*	NM_002354.2
FH*	NM_000143.3
FLCN	NM_144997.5
GREM1*	NM_013372.6
HOXB13	NM_006361.5
KIT	NM_000222.2
LZTR1	NM_006767.3
MAX*	NM_002382.4
MBD4	NM_003925.2
MEN1*	NM_130799.2
MET*	NM_001127500.1
MITF	NM_000248.3
MLH1*	NM_000249.3

GENE	TRANSCRIPT
MSH2*	NM_000251.2
MSH3*	NM_002439.4
MSH6*	NM_000179.2
MUTYH	NM_001128425.1
NF1*	NM_000267.3
NF2	NM_000268.3
NTHL1	NM_002528.6
PALB2	NM_024675.3
PDGFRA	NM_006206.4
PMS2*	NM_000535.5
POLD1*	NM_002691.3
POLE	NM_006231.3
POT1	NM_015450.2
PRKAR1A	NM_002734.4
PTCH1	NM_000264.3
PTEN*	NM_000314.4
RAD51C	NM_058216.2
RAD51D	NM_002878.3
RB1*	NM_000321.2
RET	NM_020975.4
SDHA*	NM_004168.3
SDHAF2	NM_017841.2
SDHB	NM_003000.2
SDHC*	NM_003001.3
SDHD	NM_003002.3
SMAD4	NM_005359.5
SMARCA4	NM_001128849.1
SMARCB1	NM_003073.3
SMARCE1	NM_003079.4
STK11	NM_000455.4
SUFU	NM_016169.3
TMEM127	NM_017849.3
TP53	NM_000546.5
TSC1*	NM_000368.4
TSC2	NM_000548.3

GENE	TRANSCRIPT
VHL	NM_000551.3

Methods

- Genomic DNA obtained from the submitted sample is enriched for targeted regions using a hybridization-based protocol, and sequenced using Illumina technology. Unless otherwise indicated, all targeted regions are sequenced with ≥50x depth or are supplemented with additional analysis. Reads are aligned to a reference sequence (GRCh37), and sequence changes are identified and interpreted in the context of a single clinically relevant transcript, indicated in the Genes Analyzed table. Enrichment and analysis focus on the coding sequence of the indicated transcripts, 20bp of flanking intronic sequence, and other specific genomic regions demonstrated to be causative of disease at the time of assay design. Promoters, untranslated regions, and other non-coding regions are not otherwise interrogated. For some genes only targeted loci are analyzed. Exonic deletions and duplications are called using an in-house algorithm that determines copy number at each target by comparing the read depth for each target in the proband sequence with both mean read-depth and read-depth distribution, obtained from a set of clinical samples. Markers across the X and Y chromosomes are analyzed for quality control purposes and may detect deviations from the expected sex chromosome complement. Such deviations may be included in the report in accordance with internal guidelines. Variants are reported according to the Human Genome Variation Society (HGVS) guidelines. Confirmation of the presence and location of reportable variants is performed as needed based on stringent criteria using one of several validated orthogonal approaches (PubMed ID 30610921). Sequencing is performed by Labcorp Genetics, Inc (1400 16th Street, San Francisco, CA 94103, #05D2040778). Confirmatory sequencing is performed by Labcorp Genetics, Inc (1400 16th Street, San Francisco, CA 94103, #05D2040778). RNA sequencing is performed by Labcorp Genetics, Inc (1400 16th Street, San Francisco, CA 94103, #05D2040778).

  The following additional analyses are performed if relevant to the requisition. For PMS2 exons 12-15, the reference genome has been modified to force all sequence reads derived from PMS2 and the PMS2CL pseudogene to align to PMS2, and variant calling algorithms are modified to support an expectation of 4 alleles. If a rare SNP or indel variant is identified by this method, both PMS2 and the PMS2CL pseudogene are amplified by long-range PCR and the location of the variant is determined by Pacific Biosciences (PacBio) SMRT sequencing of the relevant exon in both long-range amplicons. If a CNV is identified, MLPA or MLPA-seq is run to confirm the variant. If confirmed, both PMS2 and PMS2CL are amplified by long-range PCR, and the identity of the fixed differences between PMS2 and PMS2CL are sequenced by PacBio from the long-range amplicon to disambiguate the location of the CNV. For C9orf72 repeat expansion testing, hexanucleotide repeat units are detected by repeat-primed PCR (RP-PCR) with fluorescently labeled primers followed by capillary electrophoresis. Interpretation Reference Ranges: Benign (Normal Range): <25 repeat units, Uncertain: 25-30 repeat units, Pathogenic (Full Mutation): >=31 repeat units (PMID: 21944779, 22406228, 23111906, 28689190, 31315673, 33168078, 33575483). A second round of RP-PCR utilizing a non-overlapping set of primers is used to confirm the initial call in the case of suspected allele sizes of 22 or more repeats. For RNA analysis of the genes indicated in the Genes Analyzed table, complementary DNA is synthesized by reverse transcription from RNA derived from a blood specimen and enriched for specific gene sequences using capture hybridization. After high-throughput sequencing using Illumina technology, the output reads are aligned to a reference sequence (genome build GRCh37; custom derivative of the RefSeq transcriptome) to identify the locations of exon junctions through the detection of split reads. The relative usage of exon junctions in a test specimen is assessed quantitatively and compared to the usage seen in control specimens. Abnormal exon junction usage is evaluated as evidence in the Sherloc variant interpretation framework. If an abnormal splicing pattern is predicted based on a DNA variant outside the typical reportable range, as described above, the presence of the variant is confirmed by targeted DNA sequencing.

- A PMID is a unique identifier referring to a published, scientific paper. Search by PMID at **http://www.ncbi.nlm.nih.gov/pubmed**.
- An rsID is a unique identifier referring to a single genomic position, and is used to associate population frequency information with sequence changes at that position. Reported population frequencies are derived from a number of public sites that aggregate data from large-scale population sequencing projects, including ExAC (**http://exac.broadinstitute.org**), gnomAD (**http://gnomad.broadinstitute.org**), and dbSNP (**http://ncbi.nlm.nih.gov/SNP**).
- A MedGen ID is a unique identifier referring to an article in MedGen, NCBI's centralized database of information about genetic disorders and phenotypes. Search by MedGen ID at **http://www.ncbi.nlm.nih.gov/medgen**. An OMIM number is a unique identifier referring to a comprehensive entry in Online Mendelian Inheritance in Man (OMIM). Search by OMIM number at **http://omim.org/**.
- Invitae uses information from individuals undergoing testing to inform variant interpretation. If "Invitae" is cited as a reference in the variant details this may refer to the individual in this requisition and/or historical internal observations.

Limitations

Based on validation study results, this assay achieves >99% analytical sensitivity and specificity for single nucleotide variants, insertions and deletions <15bp in length, and exon-level deletions and duplications. This test detects insertions and deletions larger than 15bp but smaller than a full exon but sensitivity for these may be marginally reduced. Deletion/duplication analysis for this test determines copy number at a single exon resolution at virtually all targeted exons. However, in rare situations, single-exon copy number events may not be analyzed due to inherent sequence properties or isolated reduction in data quality. Certain types of variants, such as structural rearrangements (e.g. inversions, gene conversion events, translocations, etc.) or variants embedded in sequence with complex architecture (e.g. short tandem repeats or segmental duplications), may not be detected. Additionally, it may not be possible to fully resolve certain details about variants, such as mosaicism, phasing, or mapping ambiguity. Unless explicitly guaranteed, sequence changes in the promoter, non-coding exons, and other non-coding regions are not covered by this assay. Please consult the test definition on our website for details regarding regions or types of variants that are covered or excluded for this test. This report reflects the analysis of an extracted genomic DNA sample. While this test is intended to reflect the analysis of extracted genomic DNA from a referred patient, in very rare cases the analyzed DNA may not represent that individual's constitutional genome, such as in the case of a circulating hematolymphoid neoplasm, bone marrow transplant, blood transfusion, chimerism, culture artifact or maternal cell contamination. Interpretations are made on the assumption that any clinical information provided, including specimen identity, is accurate. RNA analysis is not designed for use as a stand-alone diagnostic method and cannot determine absolute RNA levels. Results from the RNA analysis may not be informative for interpreting copy number events. Additionally, sensitivity to detect RNA splicing events may be reduced for variants in the first donor site of each gene.

APC: Sequencing analysis for exons 5 includes only cds +/- 10 bp. ATM: Sequencing analysis for exons 6, 24, 43 includes only cds +/- 10 bp. DICER1: Sequencing analysis for exons 22 includes only cds +/- 10 bp. EPCAM: Sequencing analysis is not offered for this gene. FH: Sequencing analysis for exons 9 includes only cds +/- 10 bp. GREM1: Promoter region duplication testing only. MAX: Sequencing analysis for exons 2 includes only cds +/- 10 bp. MEN1: Sequencing analysis for exons 2 includes only cds +/- 10 bp. MET: Sequencing analysis for exons 12 includes only cds +/- 10 bp. MLH1: Sequencing analysis for exons 12 includes only cds +/- 10 bp. MSH2: Analysis includes the exon 1-7 inversion (Boland mutation). Sequencing analysis for exons 2, 5 includes only cds +/- 10 bp. Deletions restricted to only the EPCAM gene will not be detected unless EPCAM analysis is requested. MSH6: Sequencing analysis for exons 7, 10 includes only cds +/- 10 bp. NF1: Sequencing analysis for exons 2, 7, 25, 41, 48 includes only cds +/- 10 bp. PMS2: Sequencing analysis for exons 7 includes only cds +/- 10 bp. POLD1: Sequencing analysis for exon 22 includes only cds +/- 10 bp and exon 27 includes only cds +-0 bp. PTEN: Sequencing analysis for exons 8 includes only cds +/- 10 bp. RB1: Sequencing analysis for exons 15-16 includes only cds +/- 10 bp. SDHA: Deletion/duplication analysis is not offered for this gene and sequencing analysis is not offered for exon 14. Sequencing analysis for exons 6-8 includes only cds +/- 10 bp. SDHC: Sequencing analysis for exons 2, 6 includes only cds +/- 10 bp. TSC1: Sequencing analysis for exons 21 includes only cds +/- 10 bp. MSH3: Sequencing analysis of the repeat region of exon 1 (5:79950697-79950765) is not offered.

Disclaimer

DNA studies do not constitute a definitive test for the selected condition(s) in all individuals. It should be realized that there are possible sources of error. Errors can result from trace contamination, rare technical errors, rare genetic variants that interfere with analysis, recent scientific developments, and alternative classification systems. This test should be one of many aspects used by the healthcare provider to help with a diagnosis and treatment plan, but it is not a diagnosis itself. This test was developed and its performance characteristics determined by Labcorp Genetics. It has not been cleared or approved by the FDA. The laboratory is regulated under the Clinical Laboratory Improvement Act (CLIA) as qualified to perform high-complexity clinical tests (CLIA ID: 05D2040778). This test is used for clinical purposes. It should not be regarded as investigational or for research.

This report has been reviewed and approved by:

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Clinical Molecular Geneticist

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This document is not part of the Invitae® clinical report and does not represent medical advice. These are general guidelines that are not specific to your result and may not represent all relevant international recommendations. You can use this guide to talk to your healthcare provider about your test results, clinical history, and the most current guidelines. This guide may not be appropriate for results that are suspected to be blood-limited, possibly mosaic, or suggestive of a larger imbalance of genetic material. Invitae recognizes that individuals have diverse gender and sexual identities. In this guide, the terms female, male, women, and men refer to sex assigned at birth.

What is a positive BRCA2 result?

A positive test result means that a genetic change (variant) was found in the BRCA2 gene. A positive BRCA2 variant is considered "pathogenic" or "likely pathogenic" because it is associated with hereditary breast and ovarian cancer (HBOC) syndrome.

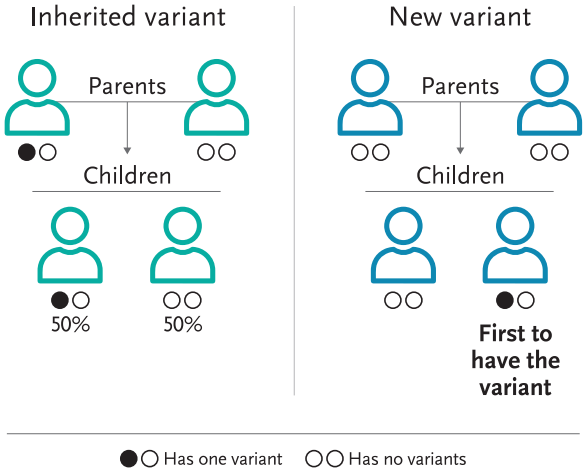
What does this mean?

Individuals with positive variants in BRCA2 are more likely to get certain cancers compared to the average person. There is an increased chance for female breast cancer (44-80% and a 10-30% chance of developing a second breast cancer within 10 years), male breast cancer (7-8%), ovarian cancer (13-29%), pancreatic cancer (4-9%), and prostate cancer (19-61%). There is also an increased chance for melanoma, however, lifetime risks are not clear. Types of cancer and age of onset can vary, and some individuals may never develop cancer. Individuals may have different conditions or symptoms depending on whether they inherit one or two variants in BRCA2. Some people inherit two BRCA2 variants, which may cause a rare condition called Fanconi anemia. See the table later in this guide for ways to manage HBOC.

What does this mean for family members?

Relatives should be informed about these results. It is recommended that family members talk with their own healthcare provider about a plan for genetic testing and/or health screening. Genetic testing is a personal choice and some individuals may choose not to have genetic testing. Laws protecting employment and health insurance may apply to individuals undergoing genetic testing (for example, the Genetic Information Nondiscrimination Act in the United States).

Will family members have the same variant(s)?
The image shows where a BRCA2 variant may have come from. Any individual can inherit and pass on a BRCA2 variant, regardless of sex.



BRCA2 variants are usually inherited from a parent. Siblings, children, and other relatives may also have this BRCA2 variant. Being the first person in the family to have a new BRCA2 variant is rare. HBOC usually does not affect children. Genetic testing for a BRCA2 variant is not typically indicated until age 18 or older.

For individuals who are planning a family, reproductive options may be available to help lower the chance of passing on a variant to children.

Create a plan with a healthcare provider

These options are a guide for an individual and their healthcare provider. They are meant to be used along with an individual's genetic test results and other health information as part of a discussion to make a personalized care plan. Each option may or may not be right for an individual. A positive test result on its own cannot predict how a condition may affect an individual. This guide may not be appropriate for results that are suspected to be blood-limited, possibly mosaic, or suggestive of a larger imbalance of genetic material.

Options to consider

TOPIC	OPTION	MORE INFORMATION
General BRCA2 management	• Education regarding signs and symptoms of cancer, especially those associated with positive BRCA2 variants. (1)	
Breast cancer (female)	• Breast awareness starting at age 18 (1)	• Women should be familiar with their breasts and report changes to a healthcare provider. (1)
	• Clinical breast exam every 6-12 months starting at age 25 (1)	
	• Breast MRI with and without contrast (or mammogram, only if MRI is unavailable) every year starting at age 25 (1) • Screening may be considered earlier than age 25 if there is a family history of breast cancer diagnosed before age 30. (1)	
	• Mammogram and breast MRI with and without contrast every year starting at age 30 (1) • For women age 76 or older, management should be considered on an individual basis. (1)	• Women treated for breast cancer who have not undergone a bilateral mastectomy should continue these breast screening recommendations. (1)
	• Consider risk-reducing mastectomy (surgery to remove the breasts). (1)	• Degree of protection, reconstruction options, risks, family history, and residual breast cancer risk should all be considered when discussing this option. (1)
	• Consider risk reduction agents (chemoprevention). (1)	• This should include a discussion of risks and benefits. (1)
Breast cancer (male)	• Chest self-exam starting at age 35 (1)	
	• Clinical chest wall exam every year starting at age 35 (1)	
	• Consider mammogram every year starting at age 50, or 10 years before the earliest known male breast cancer in the family (whichever comes first). (1)	
Ovarian cancer	• Recommend risk-reducing salpingo-oophorectomy (RRSO) (surgery to remove the ovaries and fallopian tubes) between the ages of 35-40. (1) • It is reasonable to delay RRSO until age 40-45 unless there is a specific family history of an earlier onset ovarian cancer. (1) • Salpingectomy (surgery to remove the fallopian tubes) is an option for premenopausal patients who are not yet ready for oophorectomy. (1)	• Counseling should include a discussion of reproductive desires, extent of cancer risk, degree of protection for breast and ovarian cancer, management of menopausal symptoms, hormone replacement therapy, and related medical issues. (1)
	• Consider risk reduction agents (chemoprevention). (1)	• This should include a discussion of risks and benefits. (1)
Prostate cancer	• Prostate-specific antigen (PSA) screening starting at age 40. This can be considered every year rather than every other year. (2)	• Personal and family history can inform when to begin shared decision-making regarding prostate cancer screening. (2)

TOPIC	OPTION	MORE INFORMATION
	• Consider digital rectal examination when PSA testing is done. (2)	
Pancreatic cancer	• Screening should be considered for individuals with a family history of pancreatic cancer (exocrine) in a first- or second-degree relative on the same side (or presumed to be on the same side) of the family as the BRCA2 variant. (1) • For these individuals, consider pancreatic imaging with contrast-enhanced MRI/magnetic resonance cholangiopancreatography (MRCP) and/or endoscopic ultrasound (EUS) every year starting at age 50, or 10 years before the earliest known pancreatic cancer in the family (whichever comes first). (1)	• This screening should be performed in an experienced high-volume center. (1)
Melanoma	• There are currently no formal screening recommendations for melanoma in individuals with a positive BRCA2 variant. However, following general population recommendations for melanoma risk management is encouraged, including skin exam (full body) every year and reducing UV exposure. (1)	• When outdoors, wear sunscreen, sun-protective clothing, hats, and sunglasses. (3) • Avoid tanning beds, excessive sun exposure, and sunburns. (3) • Education on the skin changes to look for and self-exams can help find suspicious lesions. (3)
Family planning	• Discuss reproductive risks. (4) • Individuals with a BRCA2 variant have a 50% chance to pass on the variant to a child.	• Preconception and prenatal reproductive options are available and could be discussed in more detail with a reproductive specialist.
	• Individuals with certain BRCA2 variants may have an increased chance to have a child with Fanconi anemia, if their reproductive partner also has a positive BRCA2 variant.	• Fanconi anemia is a condition characterized by bone marrow failure, short stature, abnormal skin pigmentation, developmental delay and malformations of the thumbs, skeletal and central nervous systems. The risks for leukemia and early onset solid tumors are significantly elevated.
	• An individual's reproductive partner can consider genetic testing to help determine the risk of a child inheriting two BRCA2 variants and having Fanconi anemia. (4)	• If an individual's reproductive partner also has a positive BRCA2 variant, there may be a 25% chance to have a child with Fanconi anemia.

These options include recommendations from NCCN (1,2), PMID: 33414132 (3), and PMID: 28225426 (4). Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic Version 3.2024 (1). © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed 02/12/2024. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer Early Detection Version 1.2024 (2). © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed 01/02/2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. More information about genetics and disease continues to be available, so please always refer to the current guidelines and recommendations when considering surveillance and treatment options. Information on this document may not include all relevant international recommendations and acts as a supplement to the Invitae result report. This information is not meant to replace a discussion with an individual's healthcare provider and should not be considered or interpreted as medical advice. Additional resources provided within this document do not indicate or imply any endorsement by Invitae with respect to any third party or any website or the products or services offered by any third party.

Resources

Genetic counseling can help individuals understand their genetic test results and options for next steps. Reviewing test results with a genetic counselor or other healthcare provider is recommended. Local or telehealth genetic counselors can be identified using the Find a Genetic Counselor search tool at nsgc.org (US and Canada). Individuals who had genetic testing through Invitae can also log in to their patient portal (invitae.com) to view their results, contact a genetic counselor, or join Invitae's Patient Insights Network (PIN) (pin.invitae.com), an online platform where individuals can share information about their health and experiences to help advance research and drug development.

Notes for personalized assessment