

MyRisk[™] Hereditary Cancer Test

MyRisk Genetic Result

RECEIVING HEALTHCARE PROVIDER

Test HCP, MD
Test Medical Center
6609 BLANCO RD STE 200
SAN ANTONIO, TX 78216

SPECIMEN

Specimen Type: Blood

Draw Date: Apr 22, 2024 Accession Date: Apr 22, 2024

Report Date: Apr 22, 2024

MyRisk[™] Hereditary Cancer Test

PATIENT

Legal Name: Pt Last Name,

Pt First Name

Date of Birth: Apr 22, 1985 Patient ID: Patient id

Sex at Birth: F

Accession #: 07283343-BLD Requisition #: 47624609

GENETIC RESULT: NEGATIVE - NO CLINICALLY SIGNIFICANT MUTATION IDENTIFIED

Note: "CLINICALLY SIGNIFICANT," as defined in this report, is a genetic change that is associated with the potential to alter medical intervention.

*

BREAST CANCER RISKSCORE®: REMAINING LIFETIME RISK 35.3%

This level of risk is at or above 20% threshold for consideration of modified medical management. See RiskScore Interpretation Section for more information.



CLINICAL HISTORY ANALYSIS: NO ADDITIONAL MANAGEMENT GUIDELINES IDENTIFIED BASED ON THE CLINICAL HISTORY PROVIDED

Other clinical factors may influence individualized management. This analysis may be incomplete if details about cancer diagnoses, ages, family relationships or other factors were omitted or ambiguous. If this patient also has a clinically significant mutation, the recommendations based on the clinical history analysis should be considered in light of the possibility that this mutation explains all or some of the cancer history in the family.

ADDITIONAL FINDINGS: NO VARIANT(S) OF UNCERTAIN SIGNIFICANCE (VUS) IDENTIFIED

Details About Non-Clinically Significant Variants: All individuals carry DNA changes (i.e., variants), and most variants do not increase an individual's risk of cancer or other diseases. When identified, variants of uncertain significance (VUS) are reported. Likely benign variants (Favor Polymorphisms) and benign variants (Polymorphisms) are not reported and available data indicate that these variants most likely do not cause increased cancer risk. Present evidence does not suggest that non-clinically significant variant findings be used to modify patient medical management beyond what is indicated by the personal and family history and any other clinically significant findings.

Variant Classification: Myriad's myVision[™] Variant Classification Program performs ongoing evaluations of variant classifications. In certain cases, healthcare providers may be contacted for more clinical information or to arrange family testing to aid in variant classification. When new evidence about a variant is identified and determined to result in clinical significance and management change, that information will automatically be made available to the healthcare provider through an amended report.



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ADDITIONAL INFORMATION

Genes Analyzed: Sequencing (seq) and large rearrangement analyses were performed for all coding exons in the following genes, unless otherwise indicated:

APC, ATM, AXIN2, BAP1, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, CTNNA1, FH, FLCN, HOXB13 (seq only), MEN1, MET, MLH1, MSH2, MSH3 (excluding repetitive portions of exon 1), MSH6, MUTYH, NTHL1, PALB2, PMS2, PTEN, RAD51C, RAD51D, SDHA, SDHB, SDHC, SDHD, SMAD4, STK11, TP53, TSC1, TSC2, VHL.

Limited promoter regions may also be analyzed for large rearrangements.

Sequencing (seq) and/or large rearrangement (LR) analyses were performed only for the gene portions indicated in parenthesis for the following genes:

EGFR (exons 18-21, seq and LR), EPCAM (exons 8-9, LR only), GREM1 (exon 1 and upstream regulatory regions, LR only), MITF (c.952, seq only), POLE (exonuclease domain, seq only), POLD1 (exonuclease domain, seq only), RET (exons 5, 8, 10, 11, 13-16 seq and LR), TERT (promoter region 71 bases upstream of the translation start, c.-71_-1, seq only).

** Other genes not analyzed with this test may also be associated with cancer.

Indication for Testing: It is our understanding that this individual was identified for testing due to a personal or family history suggestive of a hereditary predisposition for cancer.

Patient Information: Sex assigned at birth is a label given to an individual at birth, typically "male" or "female". In this report, the terms "male", "female", "he", "she", "woman", and "man" refer to sex assigned at birth.

Associated Cancer Risks and Clinical Management: The "MyRisk Management Tool" associated with this report provides a summary of cancer risk and professional society medical management guidelines that may be useful in developing a plan for this patient based on any clinically significant test results and/or reported personal/family history. In some cases, a MyRisk Management Tool cannot be provided, such as when the result has a special interpretation or includes a mutation with unusual characteristics.

Analysis Description: The Technical Specifications summary (myriad.com/technical-specifications) describes the analysis, method, performance, nomenclature, and interpretive criteria of this test. Current testing technologies are unable to definitively determine whether a variant is germline or somatic in origin, which may significantly impact risk estimates and medical management; therefore, these results should be correlated with this patient's personal and family history. The interpretation of this test may also be impacted if the patient has a hematologic malignancy or an allogeneic bone marrow transplant.

CLASSIFICATION DISCLAIMER

THE CLASSIFICATION AND INTERPRETATION OF ALL VARIANTS IDENTIFIED IN THIS ASSAY REFLECTS THE CURRENT STATE OF MYRIAD'S SCIENTIFIC UNDERSTANDING AT THE TIME THIS REPORT WAS ISSUED. VARIANT CLASSIFICATION AND INTERPRETATION MAY CHANGE FOR A VARIETY OF REASONS, INCLUDING BUT NOT LIMITED TO, IMPROVEMENTS TO CLASSIFICATION TECHNIQUES, AVAILABILITY OF ADDITIONAL SCIENTIFIC INFORMATION, AND OBSERVATION OF A VARIANT IN MORE PATIENTS.





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Breast Cancer RiskScore®



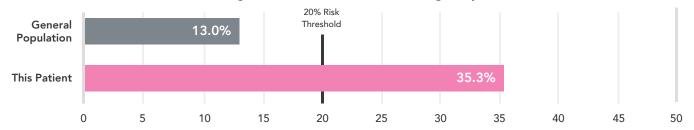
Breast Cancer RiskScore®:

35.3%

RESULT: 35.3% Remaining Lifetime Breast Cancer Risk

1.7% 5-Year Breast Cancer Risk

Remaining Lifetime Breast Cancer Risk (Age-Adjusted)



BREAST CANCER RISKSCORE® INTERPRETATION

The breast cancer RiskScore provides an estimate of the remaining lifetime risk for breast cancer. A risk estimate at or above 20% is associated with specific modified medical recommendations, including consideration of more aggressive breast cancer screening and additional risk reduction measures. If applicable, details of these recommendations are provided in the accompanying MyRisk Medical Management Tool or other supplemental material. Individuals with a risk estimate below 20% may still be appropriate for consideration of modified medical management based on other clinical factors or estimates from other breast cancer risk models, such as Tyrer-Cuzick, Claus, and Gail.

TYRER-CUZICK BREAST CANCER RISK CALCULATION

REMAINING LIFETIME BREAST CANCER RISK: 18.5%

5-YEAR BREAST CANCER RISK: 0.8%

The National Comprehensive Cancer Network (NCCN) provides medical management recommendations for individuals with an estimated remaining lifetime breast cancer risk of 20% or greater based on Tyrer-Cuzick. These recommendations are summarized on the MyRisk Management Tool (MMT). If an MMT is not included with this report, current management recommendations from the NCCN Breast Cancer Screening and Diagnosis panel can be accessed at www.nccn.org. Version 8.0 of the Tyrer-Cuzick model was used for this risk estimate. Tyrer-Cuzick model is available for download at the EMS-Trials website, http://www.ems-trials.org/riskevaluator.





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BREAST CANCER RISKSCORE® ANALYSIS DESCRIPTION

The breast cancer RiskScore provides 5-year and remaining lifetime breast cancer risks, based on an analysis of genetic markers combined with patient clinical and family history data. The Technical Specifications summary (http://myriad.com/technical-specifications) describes the RiskScore eligibility criteria, analysis, method, performance and interpretive criteria of this test. Data from 149 biomarkers are analyzed during next generation sequencing (NGS). The allele status of these markers has been weighted to generate a polygenic odds ratio of 2.1 for this patient, which is combined with clinical and family history information to generate the final RiskScore. This odds ratio is adjusted for overlap between the risk captured by the biomarkers and the clinical factors and has not been validated for use with other risk models. The Clinical and Cancer Family History Information section of this report displays the data used for this analysis and explains important limitations on the accuracy of RiskScore (including significant over- or under-estimates of breast cancer risk) that can be caused by errors and/or omissions in the reported clinical and family history data.

Please contact Myriad Medical Services at 1-800-469-7423 X 3850 to discuss any questions regarding this result.

These test results should only be used in conjunction with the patient's clinical history and any previous analysis of appropriate family members. The patient's clinical history and test results should not be disclosed to a third party, unless related to treatment or payment for treatment, without the patient's express written authorization. It is strongly recommended that these results be communicated to the patient in a setting that includes appropriate genetic consultation. This test was developed and its performance characteristics determined by Myriad Genetic Laboratories. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that clearance or approval for laboratory-developed tests is not required.

This **Authorized Signature** pertains to this laboratory report:

Benjamin B. Roa, PhD Diplomate ABMGG Laboratory Director Genetic testing was completed by CLIA and CAP accredited laboratories in the United States located at: 320 Wakara Way Salt Lake City, UT 84108 CLIA IDs: 46D0880690 The following personnel codes and laboratory director signature may reflect remote review of digital data: 2987, 4476





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Clinical & Cancer Family History Information



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Report Date:

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PATIENT
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Pt First Name
Date of Birth: Apr 22, 1985

Patient ID: Patient id

Sex at Birth: F

Accession #: 07283343-BLD Requisition #: 47624609

PERSONAL / FAMILY CANCER HISTORY SUMMARY					
FAMILY MEMBER	CANCER / CLINICAL DIAGNOSIS	AGE AT DIAGNOSIS			
Patient	None				
Aunt Paternal	Breast, Invasive	62			

PATIENT CLINICAL HISTORY SUMMARY					
Patient's age	39	Hormone Replacement Therapy (HRT)	No		
Ancestry	White/Non-Hispanic	- HRT: Treatment Type	N/A		
Height	5 ft 7 in	- HRT: Current user	N/A		
Weight	175 lbs	- Number of years ago started	N/A		
Age of menarche	13	- Additional years of intended use	N/A		
Patient's menopausal status	Pre-menopausal	- HRT: Past user	N/A		
- Age of onset	N/A	- Number of years ago ended	N/A		
Age of first live birth	27	Breast biopsy	Not Specified		
NUMBER OF PATIENT'S FEMALE RELATIVES		MAMMOGRAPHIC DENSITY			
Daughters	1	Breast Density Assessed	Not Specified		
Sisters	2	Volpara [®] Volumetric Density	Not Specified		
Maternal Aunts	2	Vas Percentage Density	Not Specified		
Paternal Aunts	2	BI-RADS [®] ATLAS Density	Not Specified		





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Clinical & Cancer Family History Information

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The clinical information displayed here was provided by a qualified healthcare provider on the Test Request Form and other documents, and was not verified by Myriad. Female relatives refers to sex assigned at birth, which is a label given to an individual at birth, typically "male" or "female". Family members listed as "other" are not included in a Tyrer-Cuzick breast cancer risk estimate or other personal/family history assessments. For more information see the Specifications for Personal/Family History Analysis at http://myriad.com/technical-specifications.

The accuracy and completeness of the information provided in the Clinical and Cancer Family History Information section of the report (e.g. height and weight, age of menarche) may significantly affect the accuracy of breast cancer risk estimates provided based on either Tyrer-Cuzick or RiskScore.

RiskScore is not valid, and may significantly over- or under-estimate breast cancer risk for individuals who do not meet the eligibility criteria in effect when the testing was performed. The current criteria are: 1) sex assigned at birth is female 2) age is 18 to 84 years, 3) no personal history of breast cancer, LCIS, hyperplasia (with or without atypia), or a breast biopsy with unknown results, 4) there is no mutation detected in a breast cancer risk gene (other than a monoallelic *CHEK2* mutation in a White/Non-Hispanic or Ashkenazi Jewish individual), 5) the individual's relatives have not been found to have a mutation in a high-penetrance breast cancer risk gene and 6) the sample was submitted with a current Test Request Form and the ordering healthcare provider has not determined that RiskScore is inappropriate for the patient. If this is an amended report for a patient tested in the past, please refer to the MyRisk Technical Specifications at http://myriad.com/technical-specifications for the eligibility criteria in effect at the time of the original testing.



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Hereditary Cancer Test

Pt First Name

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GENETIC RESULT: NEGATIVE - NO CLINICALLY SIGNIFICANT MUTATION IDENTIFIED

Note: "CLINICALLY SIGNIFICANT," as defined in this report, is a genetic change that is associated with the potential to alter medical intervention.





BREAST CANCER RISKSCORE®: REMAINING LIFETIME RISK 35.3%

This level of risk is at or above 20% threshold for consideration of modified medical management. See RiskScore Interpretation Section for more information.



CLINICAL HISTORY ANALYSIS: NO ADDITIONAL MANAGEMENT GUIDELINES IDENTIFIED **BASED ON THE CLINICAL HISTORY PROVIDED**

Other clinical factors may influence individualized management. This analysis may be incomplete if details about cancer diagnoses, ages, family relationships or other factors were omitted or ambiguous. If this patient also has a clinically significant mutation, the recommendations based on the clinical history analysis should be considered in light of the possibility that this mutation explains all or some of the cancer history in the family.

BREAST CANCER RISKSCORE®

THIS BREAST CANCER RISKSCORE® IS ASSOCIATED WITH THE FOLLOWING CANCER RISKS:

At or above 20%

ELEVATED RISK: Female Breast

No clinically significant mutations were identified in this patient. However, based on personal/family history, the patient's cancer risks may still be increased over the general population. See information below.

Please see the Genetic Test Result for more details on any variant(s) detected in this patient, including variant classification information.

The terms "male", "female", "he", "she", "women", and "men" refer to sex assigned at birth.

ADDITIONAL FINDINGS: NO VARIANT(S) OF UNCERTAIN SIGNIFICANCE (VUS) IDENTIFIED

TYRER-CUZICK BREAST CANCER RISK CALCULATION

REMAINING LIFETIME BREAST CANCER RISK: 18.5%

5-YEAR BREAST CANCER RISK: 0.8%

The Tyrer-Cuzick breast cancer risk estimate is only calculated for individuals who meet the following criteria: 1) sex assigned at birth is female 2) age is younger than 85 years, 3) no known mutation or inconclusive result has been found in the individual or any of their relatives, and 4) the sample was submitted with a current Test Request Form that includes all of the fields required to collect the information used in the calculation, and the provider has not indicated on the Test Request Form that the Tyrer-Cuzick calculation is not appropriate for the patient. Version 8.0 of the Tyrer-Cuzick model was used for this risk estimate. Tyrer-Cuzick model is available for download at the EMS-Trials website, http://www.ems-trials.org/riskevaluator.

CLINICAL OVERVIEW OF GENETIC FINDINGS

Remaining Lifetime Breast Cancer Risk Estimated to be 20% or Higher



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- This woman has an estimated remaining lifetime risk for breast cancer at or above the 20% threshold based on RiskScore. This is the estimated risk of developing breast cancer from this woman's current age to age 85.
- RiskScore is partially based on the analysis of selected genetic markers known to have an impact on breast cancer risk. Although the level
 of risk associated with each individual marker is small, results from the combined analysis of multiple markers can have a significant impact
 on breast cancer risk estimates.
- The RiskScore estimate is also based on information about the woman's personal medical history and any history of breast and ovarian cancer in her relatives, as reported by the healthcare provider. RiskScore will be less accurate if any of the information that was provided is incomplete or incorrect. The RiskScore estimate is not valid, and may significantly over- or under-estimate risk, if the woman is ineligible for RiskScore based on the criteria described on the RiskScore Clinical & Family History page of the report.
- Currently there are no guidelines for the medical management of breast cancer risk in women based on RiskScore. However, it may be
 appropriate to consider options based on guidelines for other situations where the estimated remaining lifetime breast cancer risk is at or
 above the 20% threshold.

WHAT ARE THE PATIENT'S CANCER RISKS?

These risk tables show the clinically significant cancer risks identified as part of this patient's testing. Testing for some patients does not include some of the analyses listed:

- · GENETIC RESULT: Mutations detected in any of the hereditary cancer genes included on the MyRisk panel.
- BREAST CANCER RISKSCORE: RiskScore estimate of remaining lifetime breast cancer risk if 20% or greater
- CLINICAL HISTORY ANALYSIS for breast cancer risk: Tyrer-Cuzick model estimate of remaining lifetime breast cancer risk of 20% or greater
- CLINICAL HISTORY ANALYSIS for breast, colorectal, pancreatic, prostate and melanoma cancer: Analysis of the patient's personal and family history.

The risks for each of these results are provided separately. If the risk for any individual cancer is affected by more than one of these results, the risk associated with each finding is listed in a separate table. At this time, there is not enough information to estimate risks for cancers affected by more than one gene mutation, or risks based on both gene mutations and personal/family history.

Breast cancer risk estimate at or above the 20% threshold based on RiskScore® and/or the Tyrer-Cuzick model

CANCER TYPE	CANCER RISK	RISK FOR GENERAL POPULATION	RELATED TO
FEMALE BREAST			
Remaining lifetime risk (age at time of testing to age 85)	35.3%	13.0%	RiskScore at or above the 20% threshold

WHAT MANAGEMENT FOR CANCER RISKS SHOULD BE CONSIDERED?

This overview of clinical management guidelines is based on the patient's genetic test results and the Clinical History Analysis. Medical management guidelines are summarized from established medical societies, primarily the National Comprehensive Cancer Network (NCCN). If there are overlapping management guidelines for any individual cancer due to more than one of these results, the guidelines associated with each finding are listed in separate tables, even if they are the same. At this time, there are no medical society guidelines for how to adjust management when there are multiple sources of risk, such as from more than one gene mutation, or a mutation and a personal/family history of cancer. In these cases, it may be appropriate to use the most aggressive of the management options provided.

The overview provided below should not be used as the sole source of information to determine medical management. The references cited should always be consulted for more details and updates to the recommendations.



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MyRisk Management Tool

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No information is provided related to treatment of a previous or existing cancer or polyps. The recommendation summaries below may require modification due to the patient's personal medical history, past surgeries and other treatments. Patients with a past history of cancer, benign tumors, or pre-cancerous findings may be candidates for long term surveillance and risk-reduction strategies beyond what is necessary for the treatment of their initial diagnosis. Any discussion of medical management options is for general information purposes only and does not constitute a recommendation. While genetic testing and medical society recommendations provide important and useful information, medical management decisions should be made in consultation between each patient and his or her healthcare provider.

Management Options for a breast cancer risk estimate at or above the 20% threshold based on RiskScore® and/or the Tyrer-Cuzick model

PROCEDURE	AGE TO BEGIN	FREQUENCY Unless otherwise indicated by findings	RELATED TO
FEMALE BREAST			
Currently there are no specific medical management guidelines for breast cancer risk based on RiskScore. However, the estimated remaining lifetime risk at or above the 20% threshold warrants consideration of risk-reduction strategies similar to those listed below, which are recommended for women with an estimated lifetime risk of 20% or greater based on other risk prediction methods. ^{1,2}	At age identified as being at increased risk	NA	RiskScore at or above the 20% threshold
Breast awareness - Women should be familiar with their breasts and promptly report changes to their healthcare provider. Periodic, consistent breast self-examination (BSE) may facilitate breast awareness. ¹	Individualized	NA	RiskScore at or above the 20% threshold
Clinical encounter, including clinical breast exam, ongoing risk assessment and risk-reduction counseling $^{\rm 1}$	At age identified as being at increased risk, but not before age 21	Every 6 to 12 months	RiskScore at or above the 20% threshold
Mammography, with tomosynthesis if available ¹	10 years younger than the earliest diagnosis in the family, but to begin no younger than age 30 but no later than age 40	Annually	RiskScore at or above the 20% threshold
Breast MRI with contrast ¹	10 years younger than the earliest diagnosis in the family, but no later than age 40	Annually	RiskScore at or above the 20% threshold
Consider additional risk-reduction strategies. ¹	Individualized	NA	RiskScore at or above the 20% threshold

^{1.} Bevers TB, et al. NCCN Clinical Practice Guidelines in Oncology[®]: Breast Cancer Screening and Diagnosis. V 1.2022. Jun 2. Available at https://www.nccn.org.

Notes for Personalized Management:



^{2.} Daly M et al. NCCN Clinical Practice Guidelines in Oncology[®]: Genetic/Familial High-Risk Assessment: Breast, Ovarian and Pancreatic. V 3.2023. Feb 13. Available at https://www.nccn.org.



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INFORMATION ON HOW CANCER RISKS AND MANAGEMENT ARE DETERMINED

The MyRisk Management Tool provides cancer risk levels based on analysis of genetic test results (see MyRisk Genetic Result) and a summary of medical society management recommendations based on both the genetic test results and a limited analysis of the patient's clinical history related to the risk for breast, colorectal, prostate, melanoma and pancreatic cancers. Here are some important points to understand as you interpret this test report and decide on the best plan for management:

- Comprehensive patient management. The management recommendations presented in this report are a summary of management options recommended by the National Comprehensive Cancer Network (NCCN) and other established medical societies and are general in nature. The patient's actual management should be modified based on personal medical history, surgeries and other treatments. A comprehensive risk assessment and management plan may take into account this report and other aspects of the patient's personal/family medical history (e.g., all known clinical diagnoses), as well as lifestyle, environmental and other factors.
- Risk estimates based on provider-supplied information. Some of the risk estimates and management recommendation summaries
 provided in this report are based on our interpretation of information supplied by the ordering health care provider on the test request
 form (see Specifications for Personal/Family History analysis at myriad.com/technical-specifications). The patient's actual risks and
 appropriate management may be significantly different if details provided for cancer diagnoses, ages, family relationships or other factors
 were incorrect, omitted, ambiguous or have since changed. Please review the clinical history listed on the Clinical & Family History
 Information page of this report to make sure that the information used was provided and interpreted correctly.
- Variability in Tyrer-Cuzick risk estimates. Tyrer-Cuzick estimates of breast cancer risk can vary significantly based on the way in which the
 model is used, and the estimate provided here may be higher or lower than what would be calculated by other users. For complete
 details of how Myriad calculates Tyrer-Cuzick risk estimates, including how Myriad handles information provided in a format not
 compatible with the model, please see the Specifications for Personal/Family History analysis at myriad.com/technical-specifications.
 These Specifications also include information for recalculating the Tyrer-Cuzick breast cancer risk estimate if desired.
- What is meant by "High Risk" and "Elevated Risk"? In the Genetic Test Result Summary, a gene-associated cancer risk is described as "High Risk" for a cancer type if all of the following conditions are met: the absolute risk of cancer is approximately 5% or higher, the increase in risk over the general population is approximately 2 to 3-fold or higher, and there is significant data from multiple studies supporting the cancer risk estimate. A gene is described as "Elevated Risk" for a cancer type if there is sufficient data to support an increase in cancer risk over the general population risk, but not all criteria for "High Risk" are met.

INFORMATION FOR FAMILY MEMBERS

Family members should talk to their healthcare providers about hereditary cancer testing to help define their own risk and assist in the interpretation of this patient's genetic test result.

Additional Information for Remaining Lifetime Breast Cancer Risk Estimated to be 20% or Higher

• This patient has an estimated remaining lifetime risk of breast cancer at or above the 20% threshold based on the breast cancer RiskScore estimate, which includes both genetic and non-genetic factors that may be shared within the family. Female relatives of this patient may also be at a significantly increased risk for breast cancer and should consult with a healthcare provider to discuss their own risk.

Please contact Myriad Medical Services at 1-800-469-7423 X 3850 to discuss any questions regarding this result.

END OF MANAGEMENT TOOL

