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COLARISAP® with Myriad myRisk® Hereditary Cancer

myRisk Genetic Result

MYRIAD myRisk® Hereditary Cancer | Powered by myVision®

RECEIVING HEALTHCARE PROVIDER		SPECIMEN		PATIENT	
Test Ordering HCP, MD		Specimen Type:	**Blood**	Name:	**Pt Last Name, Pt First Name**
Test Medical Center		Draw Date:	**Feb 12, 2019**	Date of Birth:	**Feb 12, 1980**
123 Main St		Accession Date:	**Feb 12, 2019**	Patient ID:	**Patient id**
Testville, TX 55555		Report Date:	**Feb 12, 2019**	Gender:	**Female**
				Accession #:	**07566478-BLD**
				Requisition #:	**90679209**

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 31.2%

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.

ADDITIONAL FINDINGS: VARIANT(S) OF UNCERTAIN SIGNIFICANCE (VUS) IDENTIFIED

GENE	VARIANT(S) OF UNCERTAIN SIGNIFICANCE	INTERPRETATION
ATM	c.8057T>G (p.Phe2686Cys)	**UNCERTAIN CLINICAL SIGNIFICANCE** There are currently insufficient data to determine if these variants cause increased cancer risk.

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.

myRisk Genetic Result

Name: **Pt Last Name, Pt First Name** DOB: **Feb 12, 1980** Accession #: **07566478-BLD** Report Date: **Feb 12, 2019**

ADDITIONAL INFORMATION

Genes Analyzed: Unless otherwise noted sequencing and large rearrangement analyses were performed on the following genes:

APC, *ATM*, *AXIN2*, *BARD1*, *BMPR1A*, *BRCA1*, *BRCA2*, *BRIP1*, *CDH1*, *CDK4*, *CDKN2A*, *CHEK2*, *EPCAM* (large rearrangement only), *HOXB13* (sequencing only), *GALNT12*, *MLH1*, *MSH2*, *MSH3* (excluding repetitive portions of exon 1), *MSH6*, *MUTYH*, *NBN*, *NTHL1*, *PALB2*, *PMS2*, *PTEN*, *RAD51C*, *RAD51D*, *RNF43*, *RPS20*, *SMAD4*, *STK11*, *TP53*. Sequencing was performed for select regions of *POLE* and *POLD1*, and large rearrangement analysis was performed for select regions of *GREM1* (see technical specifications).

** 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.

Associated Cancer Risks and Clinical Management: Please see the "myRisk Management Tool" associated with this report for a summary of cancer risk and professional society medical management guidelines that may be useful in developing a plan for this patient based on test results and reported personal/family history, if applicable. Testing of other family members may assist in the interpretation of this patient's test result.

Analysis Description: The Technical Specifications summary (https://www.myriadpro.com/documents-and-forms/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.

myRisk Genetic Result

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Breast Cancer riskScore™

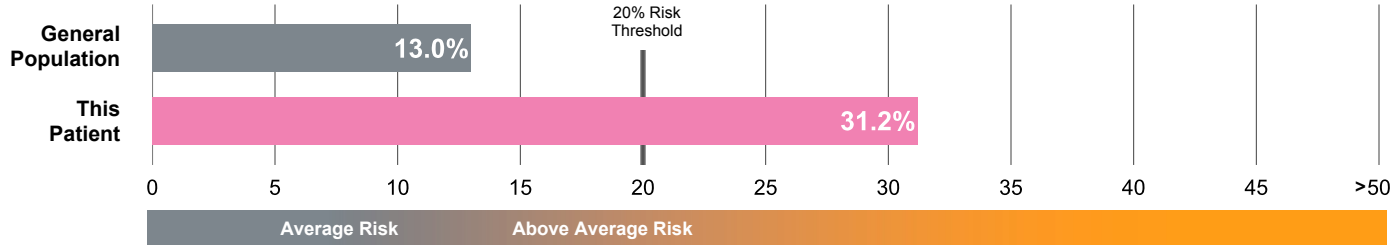
MYRIAD myRisk® Hereditary Cancer | riskScore™ BREAST CANCER

Breast Cancer riskScore™:

31.2%

RESULT: 31.2% Remaining Lifetime Risk for Breast Cancer
1.5% 5-Year Risk for Breast Cancer

Breast Cancer riskScore™ - **Remaining Lifetime Risk**



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. Women 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.

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 (https://www.myriadpro.com/documents-and-forms/technical-specifications/) describes the riskScore™ eligibility criteria, analysis, method, performance and interpretive criteria of this test. Data from 86 biomarkers are analyzed during next generation sequencing (NGS). The allele status of these markers is weighted and combined with patient clinical and family history data in the riskScore™ calculation. 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.

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 women with an estimated remaining lifetime breast cancer risk greater than 20% 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 7.02 of the Tyrer-Cuzick model was used for this risk estimate. Tyrer-Cuzick model Versions 7.02 and 8.0 are available for download at the EMS-Trials website, http://www.ems-trials.org/riskevaluator.

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

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

Benjamin B. Roa, PhD
Diplomate ABMG
Laboratory Director

Johnathan M. Lancaster, MD, PhD
Diplomate ABOG, FACOG, FACS
Chief Medical Officer

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.

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COLARISAP® with Myriad myRisk® Hereditary Cancer

Clinical & Cancer Family History Information

MYRIAD myRisk® Hereditary Cancer | Powered by myVision®

RECEIVING HEALTHCARE PROVIDER

Test Ordering HCP, MD
Test Medical Center
123 Main St
Testville, TX 55555

SPECIMEN

Specimen Type:	**Blood**
Draw Date:	**Feb 12, 2019**
Accession Date:	**Feb 12, 2019**
Report Date:	**Feb 12, 2019**

PATIENT

Name:	**Pt Last Name, Pt First Name**
Date of Birth:	**Feb 12, 1980**
Patient ID:	**Patient id**
Gender:	**Female**
Accession #:	**07566478-BLD**
Requisition #:	**90679209**

PATIENT CLINICAL HISTORY SUMMARY

Woman'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

PERSONAL / FAMILY CANCER HISTORY SUMMARY

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

NUMBER OF PATIENT'S FEMALE RELATIVES

Daughters	1	Sisters	2	Maternal Aunts	2	Paternal Aunts	2

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. 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 https://www.myriadpro.com/documents-and-forms/technical-specifications/. The accuracy of the information provided in the Clinical and Cancer Family History Information section of the report may significantly affect the accuracy of breast cancer risk estimates provided based on either Tyrer-Cuzick or riskScore™.

riskScore™ is only calculated for women who meet the eligibility criteria listed below. riskScore™ is not valid, and may significantly over- or under-estimate breast cancer risk for a woman who does not meet these criteria: 1) ancestry is exclusively White/Non-Hispanic (includes Ashkenazi Jewish), 2) age is 85 or younger, 3) no personal history of breast cancer, LCIS, hyperplasia (with or without atypia), or a breast biopsy with unknown results, 4) no known mutation in a breast cancer risk gene has been found in the woman or any of her relatives, and 5) 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.

myriad WHEN DECISIONS MATTER

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COLARISAP® with Myriad myRisk® Hereditary Cancer

myRisk Management Tool

MYRIAD myRisk® Hereditary Cancer | Powered by myVision®

RECEIVING HEALTHCARE PROVIDER	SPECIMEN		PATIENT	
Test Ordering HCP, MD	Specimen Type:	**Blood**	Name:	**Pt Last Name, Pt First Name**
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			Accession #:	**07566478-BLD**
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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 31.2%

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.

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.

ADDITIONAL FINDINGS: 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 not calculated if one or more of the following conditions apply: the woman is known to carry a mutation in a gene associated with breast cancer risk, age is 85 or older, if the sample was submitted with a version of the Test Request Form that does not include all of the fields required to collect the clinical information used in the calculation, or if the provider indicates on the Test Request Form that the Tyrer-Cuzick calculation is not appropriate for the patient. Version 7.02 of the Tyrer-Cuzick model was used for this risk estimate. Tyrer-Cuzick model Versions 7.02 and 8.0 are available for download at the EMS-Trials website, http://www.ems-trials.org/riskevaluator.

myRisk Management Tool

Name: **Pt Last Name, Pt First Name** DOB: **Feb 12, 1980** Accession #: **07566478-BLD** Report Date: **Feb 12, 2019**

OVERVIEW

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

- 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 not of solely White/Non-Hispanic ancestry, or was otherwise 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 GENE-RELATED CANCER RISKS?

If more than one gene mutation increases a specific cancer risk (e.g., breast), only the highest cancer risk is shown. If this patient has more than one gene mutation, risks may be different, as this analysis does not account for possible interactions between gene mutations.

CANCER TYPE	CANCER RISK	RISK FOR GENERAL POPULATION	RELATED TO
FEMALE BREAST			
Current age to age 85	31.2%	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 personal and family history and genetic test results. Medical management guidelines are summarized from established medical societies, primarily the National Comprehensive Cancer Network (NCCN). The reference cited should always be consulted for more details. If management for a specific cancer (e.g. breast) is available due to multiple causes (e.g. a mutation and a Tyrer-Cuzick risk estimate >20%, or multiple mutations in different genes), only the most aggressive management is shown. Only guidelines for the patient's long-term care related to cancer prevention are included.

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.

myRisk Management Tool

Name: **Pt Last Name, Pt First Name** DOB: **Feb 12, 1980** Accession #: **07566478-BLD** Report Date: **Feb 12, 2019**

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 greater than 20% 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.[2]	Individualized	NA	*riskScore™ at or above the 20% threshold*
Clinical encounter, including clinical breast exam, ongoing risk assessment and risk-reduction counseling[2]	At age identified as being at increased risk	Every 6 to 12 months	*riskScore™ at or above the 20% threshold*
Mammography, with consideration of tomosynthesis[2]	10 years younger than the earliest diagnosis in the family, but not younger than 30	Annually	*riskScore™ at or above the 20% threshold*
Breast MRI with contrast[2]	10 years younger than the earliest diagnosis in the family, but not younger than 25	Annually	*riskScore™ at or above the 20% threshold*
Consider additional risk-reduction strategies.[2]	Individualized	NA	*riskScore™ at or above the 20% threshold*

1. Daly M et al. NCCN Clinical Practice Guidelines in Oncology®: Genetic/Familial High-Risk Assessment: Breast and Ovarian. V 2.2019. July 30. Available at http://www.nccn.org.
2. Bevers TB, et al. NCCN Clinical Practice Guidelines in Oncology®: Breast Cancer Screening and Diagnosis. V 2.2018. May 18. Available at http://www.nccn.org.

Notes for Personalized Management: _____

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 a combined analysis of the genetic test results and, when possible, personal clinical factors and personal/family cancer history. 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 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 https://myriadpro.com/documents-and-forms/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 https://myriadpro.com/documents-and-forms/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 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.

- 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 MYRISK MANAGEMENT TOOL