MYRIAD myRisk®

Hereditary Cancer

myriad®

Understanding Your Result

The Power of Knowing

Q. What does a positive result mean?

A. Testing positive on the Myriad myRisk® Hereditary Cancer test means that one of the genes that has been passed down to you through your family is altered, or carries a gene mutation, that increases your risk for hereditary cancer.

This result provides a better understanding of your cancer risks based on your gene mutation.

The report tells you the specific gene mutation as well as the associated cancers. With this information, you and your healthcare provider may better understand your risk and develop a medical management plan that is right for you.

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Integrated BRAC*Analysis*® with Myriad myRisk™ Hereditary Cancer

myRisk Management Tool

MYRIAD myRisk™ Hereditary Cancer | Powered by myVision

RECEIVING HEALTHCARE PROVIDER	SPECIMEN		PATIENT	
Physician Name, MD	Specimen Type:	**Buccal**	Name:	**Patient Name**
Myriad Healthcare Partners	Draw Date:	**Jun 8, 2014**	Date of Birth:	**Jan 12, 1970**
320 Wakara Way	Accession Date:	**Jun 9, 2014**	Patient ID:	**1144**
Salt Lake City, UT 84108	Report Date:	**Jun 30, 2014**	Gender:	**Female**
			Accession #:	**00001144-BLD**
ORDERING PHYSICIAN: **Physician Name, MD**			Requisition #:	**000000**

GENETIC TEST RESULTS SUMMARY INFORMATION

RESULT: POSITIVE—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.

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

GENE	MUTATION	THIS GENETIC TEST RESULT IS ASSOCIATED WITH THE FOLLOWING CANCER RISKS:
BRCA1	c.68_69del (p.Glu23Valfs*17)	**HIGH RISK:** Female Breast, Ovarian
		ELEVATED RISK: Pancreatic

PERSONAL / FAMILY HISTORY SUMMARY AND MANAGEMENT INFORMATION

FAMILY MEMBER	CANCER / CLINICAL DIAGNOSIS	AGE AT DIAGNOSIS
Patient	None	
Mother	Breast	45
Maternal Aunt	Breast	55

MODIFIED MEDICAL MANAGEMENT MAY BE APPROPRIATE

This information was provided by a qualified healthcare provider on the test request form and was not verified by Myriad.

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- Positive result with SINGLE SITE testing:
  —When a member of your family has tested positive for a mutation, your provider may order testing for only that mutation to see if you carry it. This is known as single site testing. If you get a positive single site test result, you DO carry the mutation that is in your family and need follow-up in management associated with the identified mutation. Because single site testing does not look for other mutations or family history, there are limitations to the information. Positive results on single site tests will include a myRisk Management Tool that is specific ONLY to your gene mutation.

- SPECIAL INTERPRETATION results:
  —Occasionally there may be genetic changes that are difficult to interpret, or simply cannot be classified as either positive or negative. When possible, Myriad will perform additional lab work and have the case extensively reviewed by laboratory directors to make sure everything is done to understand the result. Please refer to the customized genetic test report for details.

Q. What kind of cancer am I at risk for?

A. The overview section of the Myriad myRisk® Test Report explains the hereditary cancers associated with your gene mutation. This summary will help you understand your risks and help you talk to your family as well. All of the management recommendations in the report are based on statements made by leading medical societies.

Q. So what are my risks?

A. Your risk for the cancer or cancers associated with your gene mutation is higher than the risk for those individuals without the mutation, sometimes far higher. Your test report shows your risk and also the risk compared to the general population.

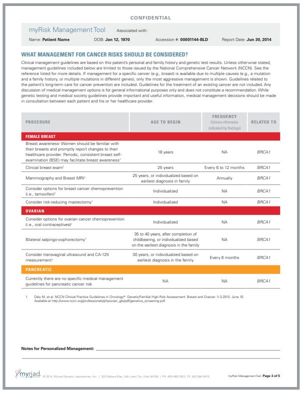
Q. What is "modified medical management?"

A. In addition to your genetic test result, your personal and family cancer history plays an important role in your medical management. The * symbol on the report means that the way you will be checked for cancer may change. Your test report may highlight management options you and your healthcare provider may consider. Other clinical factors may also influence individualized management. You and your provider will work together to determine the best management plan for you.

Q. How will this information change what I do?

A. Your test report provides information about each of the cancers associated with gene mutations like yours.

In general, the changes to your cancer risk management can take four possible directions. First, you may be screened more often and perhaps with different or additional tests than you have had previously. Second, it might also be recommended that you take medication (known as chemoprevention) to reduce your risk. Third, there may be surgical steps to discuss. Finally, you may discuss lifestyle changes with your provider.



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myRisk Management Tool Associated with:

Name: **Patient Name** DOB: **Jan 12, 1970** Accession #: **00001144-BLD** Report Date: **Jun 30, 2014**

WHAT MANAGEMENT FOR CANCER RISKS SHOULD BE CONSIDERED?

Clinical management guidelines are based on this patient's personal and family history and genetic test results. Unless otherwise stated, management guidelines included below are limited to those issued by the National Comprehensive Cancer Network (NCCN). See the reference listed for more details. If management for a specific cancer (e.g., breast) is available due to multiple causes (e.g., a mutation and a family history, or multiple mutations in different genes), only the most aggressive management is shown. Guidelines related to the patient's long-term care for cancer prevention are included. Guidelines for the treatment of an existing cancer are not included. Any discussion of medical management options is for general informational purposes only and does not constitute a recommendation. While genetic testing and medical society guidelines provide important and useful information, medical management decisions should be made in consultation between each patient and his or her healthcare provider.

PROCEDURE	AGE TO BEGIN	FREQUENCY (Unless otherwise indicated by findings)	RELATED TO
FEMALE BREAST			
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]	18 years	NA	*BRCA1*
Clinical breast exam[1]	25 years	Every 6 to 12 months	*BRCA1*
Mammography and Breast MRI[1]	25 years, or individualized based on earliest diagnosis in family	Annually	*BRCA1*
Consider options for breast cancer chemoprevention (i.e., tamoxifen)[1]	Individualized	NA	*BRCA1*
Consider risk-reducing mastectomy[1]	Individualized	NA	*BRCA1*
OVARIAN			
Consider options for ovarian cancer chemoprevention (i.e., oral contraceptives)[1]	Individualized	NA	*BRCA1*
Bilateral salpingo-oophorectomy[1]	35 to 40 years, after completion of childbearing, or individualized based on the earliest diagnosis in the family	NA	*BRCA1*
Consider transvaginal ultrasound and CA-125 measurement[1]	30 years, or individualized based on earliest diagnosis in the family	Every 6 months	*BRCA1*
PANCREATIC			
Currently there are no specific medical management guidelines for pancreatic cancer risk	NA	NA	*BRCA1*

1. Daly M, et al. NCCN Clinical Practice Guidelines in Oncology®: Genetic/Familial High-Risk Assessment: Breast and Ovarian. V 3.2013. June 10. Available at http://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf.

Notes for Personalized Management: ______

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The personal management plan that you and your provider develop together will take all of these factors into account.

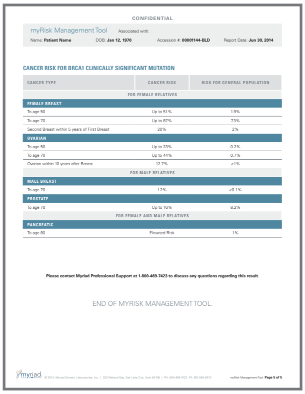
Q. Why is my family history important?

A. Because your personal and family history influences your management plan, it is important to share accurate and up-to-date information with your healthcare provider. As things change, make sure you update your history.

The family history you provided appears on the myRisk® Management tool.

Q. What does my family need to do?

A. It is important to share information about your test results with your family. They may want to talk with a healthcare provider about how this affects them and the possibility of genetic testing. Your report shows risk levels associated with your gene mutation for family members.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myRisk Management Tool Associated with:

Name: **Patient Name** DOB: **Jan 12, 1970** Accession #: **00001144-BLD** Report Date: **Jun 30, 2014**

CANCER RISK FOR BRCA1 CLINICALLY SIGNIFICANT MUTATION

CANCER TYPE	CANCER RISK	RISK FOR GENERAL POPULATION
FOR FEMALE RELATIVES		
FEMALE BREAST		
To age 50	Up to 51%	1.9%
To age 70	Up to 87%	7.3%
Second Breast within 5 years of First Breast	20%	2%
OVARIAN		
To age 50	Up to 23%	0.2%
To age 70	Up to 44%	0.7%
Ovarian within 10 years after Breast	12.7%	<1%
FOR MALE RELATIVES		
MALE BREAST		
To age 70	1.2%	<0.1%
PROSTATE		
To age 70	Up to 16%	8.2%
FOR FEMALE AND MALE RELATIVES		
PANCREATIC		
To age 80	Elevated Risk	1%

Please contact Myriad Professional Support at 1-800-469-7423 to discuss any questions regarding this result.

END OF MYRISK MANAGEMENT TOOL.

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Q. What are "variants not requiring clinical action?"

A. A variant is a genetic change that is detected on the test. Most non-clinically significant variants are harmless and do not require any changes in your medical management.

- Your testing may have found one or more "Variants of Uncertain Significance (VUS)." A VUS is not currently known to be associated with an increased cancer risk. Myriad has made a major commitment to understanding the nature of these variants. If new evidence about a variant is identified, that information will be made available to your healthcare provider. Medical interventions should not be based on the VUS result alone.


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myRisk Genetic Result

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RECEIVING HEALTHCARE PROVIDER	SPECIMEN	PATIENT
Physician Name, MD Myriad Healthcare Partners 320 Wakara Way Salt Lake City, UT 84108	Specimen Type: **Buccal** Draw Date: **Jun 8, 2014** Accession Date: **Jun 9, 2014** Report Date: **Jun 30, 2014**	Name: **Patient Name** Date of Birth: **Jan 12, 1970** Patient ID: **1144** Gender: **Female** Accession #: **00001144-BLD** Requisition #: **000000**

ORDERING PHYSICIAN: **Physician Name, MD**

RESULT: POSITIVE—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.

GENE	MUTATION	INTERPRETATION
BRCA1	**c.68_69del (p.Glu23Valfs*17)** Heterozygous	**HIGH CANCER RISK** This patient has Hereditary Breast and Ovarian Cancer (HBOC) syndrome.

DETAILS ABOUT: **BRCA1 c.68_69del (p.Glu23Valfs*17): NM_007294.3; AKA: 187delAG**

Functional Significance: Deleterious – Abnormal Protein Production and/or Function
The heterozygous germline *BRCA1* mutation c.68_69del is predicted to result in the premature truncation of the *BRCA1* protein at amino acid position 39 (p.Glu23Valfs*17).

Clinical Significance: High Cancer Risk
This mutation is associated with increased cancer risk and should be regarded as clinically significant.

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 significant clinical findings.

Variant Classification: Myriad's myVision™ Variant Reclassification Program continuously 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, that information will automatically be made available to the healthcare provider through an amended report.

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Resources

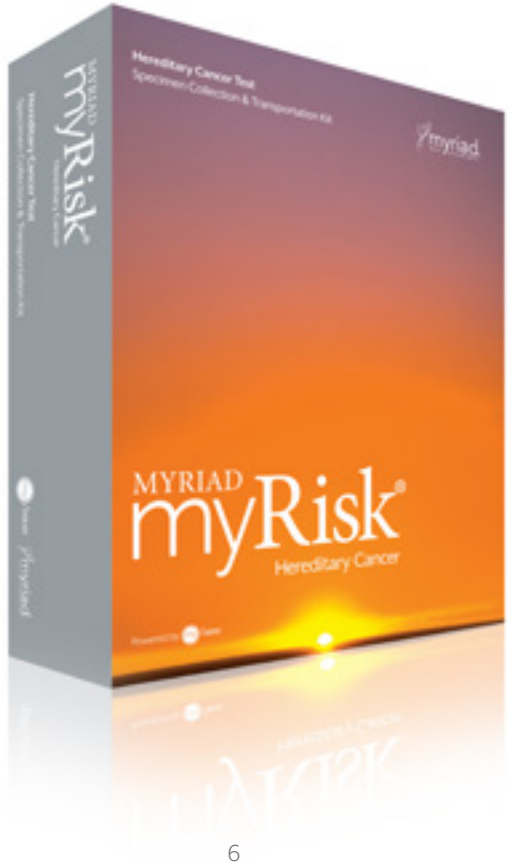
Your healthcare provider is always your number one resource. You are also invited to visit mySupport360.com, the Myriad program offering information and support for patients. You will find valuable information that will help you better understand your test result, and you can join a community of people who are on the same hereditary cancer testing journey as you. You may also contact Myriad's Medical Services team at 1-800-469-7423 x3850 to speak to a genetic counselor.

Next Steps

Working with your healthcare provider, the two of you will determine the appropriate next steps for you. Here are some possible actions to consider:

- Obtain a copy of your test result
- Schedule consultations with appropriate healthcare providers
- Create a plan for medical management. Possible options include:
  - Increased surveillance
  - Chemoprevention
  - Preventive surgery
  - Lifestyle changes
- Share your genetic test result with your relatives (identify your specific mutation)
- Recontact your healthcare provider on a regular basis to update your family cancer history and discuss any new medical management plans related to hereditary cancer

Notes


Hereditary Cancer Test
Specimen Collection & Transportation Kit
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