ONCOLOGY

A PATIENT'S GUIDE

MYRIAD myRisk® Hereditary Cancer

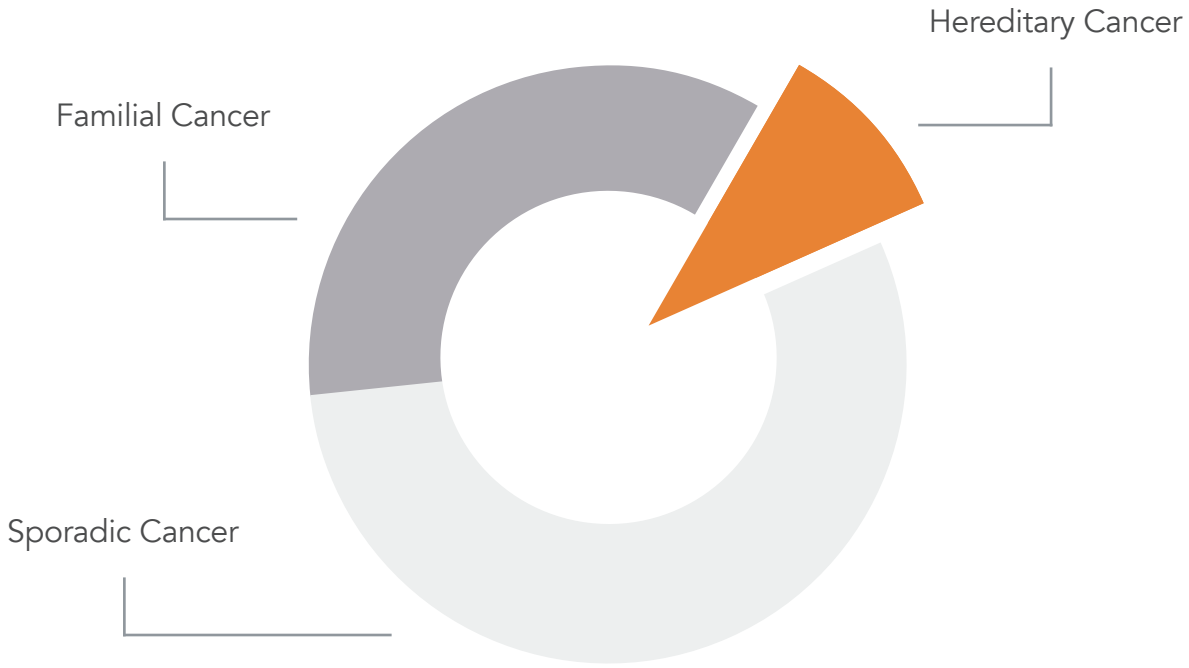
A patient's guide to Hereditary Cancer.

Is hereditary cancer testing right for you?

myriad® WHEN DECISIONS MATTER | ONCOLOGY

What is Hereditary Cancer?

Most cancers occur in people who do not have a strong family history of that cancer. This is often called "sporadic cancer". In some families, we see more of the same kind, or related kinds, of cancer than we would expect to see when compared to the general population. This pattern of related cancers can be categorized as either "familial cancer" or "hereditary cancer". In those families with hereditary cancer, that cancer risk is passed down through generations by inheriting altered genes (in other words, genes with mutations) which increase the risk to develop cancer. Determining which of these families have cancer related to an inherited gene mutation is important, as the cancer risks in hereditary cancer families are much higher than the general population.



Hereditary Cancer:

Occurs when an altered gene (gene with a mutation) is passed down in the family from parent to child. People with hereditary cancer are more likely to have relatives with the same type or related type of cancer. They may develop more than one cancer and their cancer often occurs at an earlier than average age.

Familial Cancer:

Likely caused by a combination of genetic and environmental factors. People with familial cancer may have one or more relatives with the same type of cancer; however, there does not appear to be a specific pattern of inheritance (e.g., the cancer risk is not clearly passed from parent to child).

Sporadic Cancer:

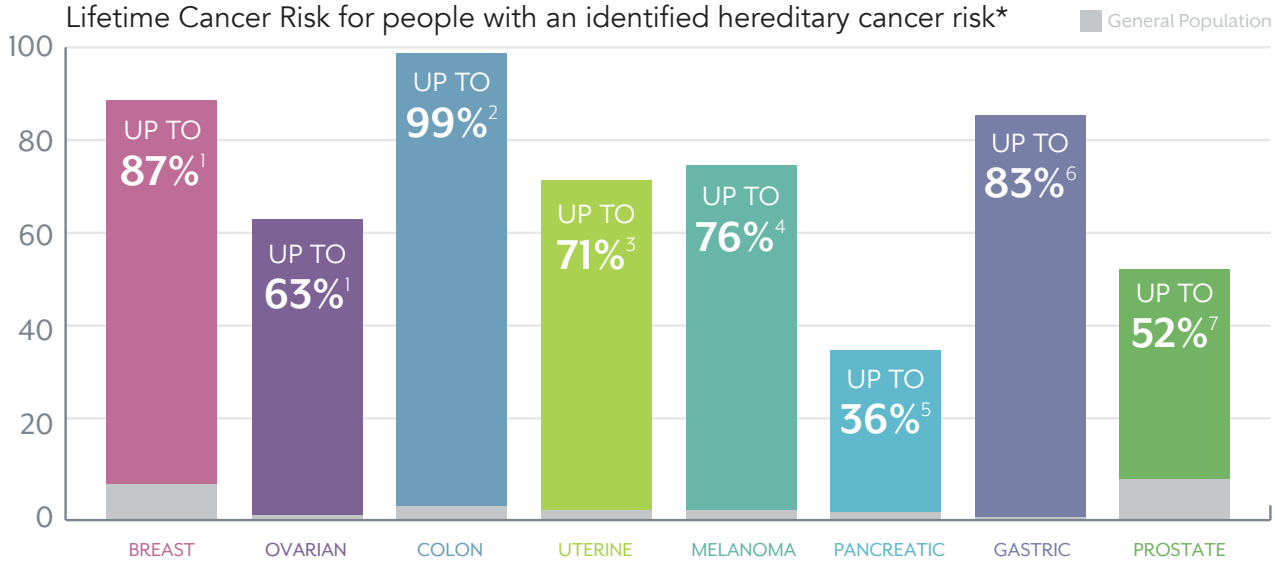
Occurs by chance. People with sporadic cancer typically do not have relatives with the same type of cancer.

Personal and/or Family History Risk Factors

PERSONAL HISTORY OF	• Breast cancer at any age • Ovarian cancer at any age • Metastatic prostate cancer at any age • Pancreatic cancer at any age • Colon, rectal or uterine cancer at age 64 or younger • Male breast cancer at any age
FAMILY HISTORY OF	• Breast cancer at 49 or younger • Two breast cancers in one relative at any age • Three or more breast cancers in relatives on the same side of the family at any age • Ovarian, metastatic prostate, pancreatic cancer, or male breast cancer at any age • Colon, rectal, uterine cancer at age 49 or younger (1st degree relative) • A gene mutation found in a family member • Ashkenazi Jewish ancestry with breast cancer in one relative at any age

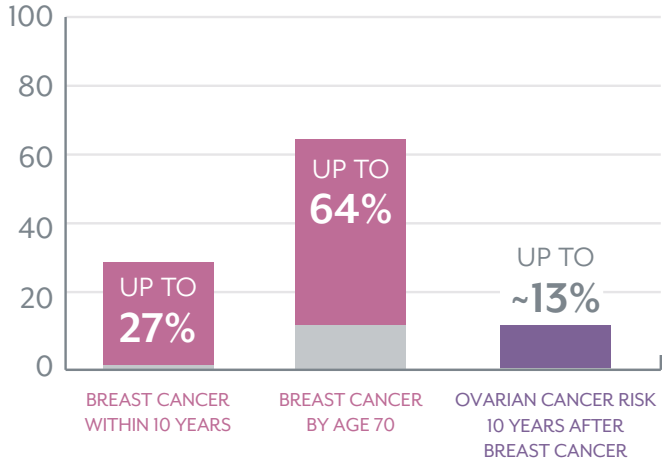
Certain ancestries may have greater risk for hereditary cancer syndromes (e.g., Ashkenazi Jewish ancestry).
Family members include first-, second-, and third-degree blood relatives on both your mother and father's side.

Lifetime Cancer Risk for people with an identified hereditary cancer risk*

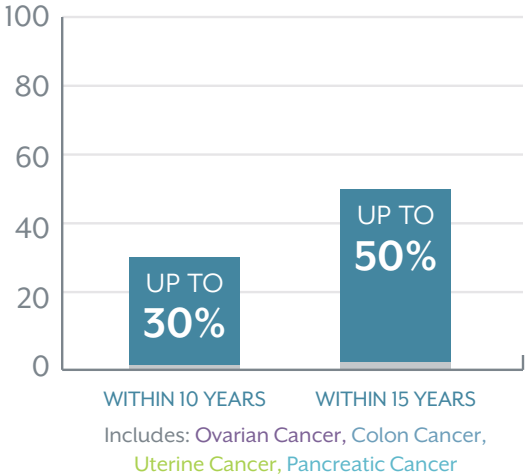


If you have a genetic mutation found in a hereditary cancer syndrome, your risk of developing a second cancer are significantly increased. Below are examples of the HBOC and Lynch genes.

GENETIC MUTATIONS IN THE HBOC GENES



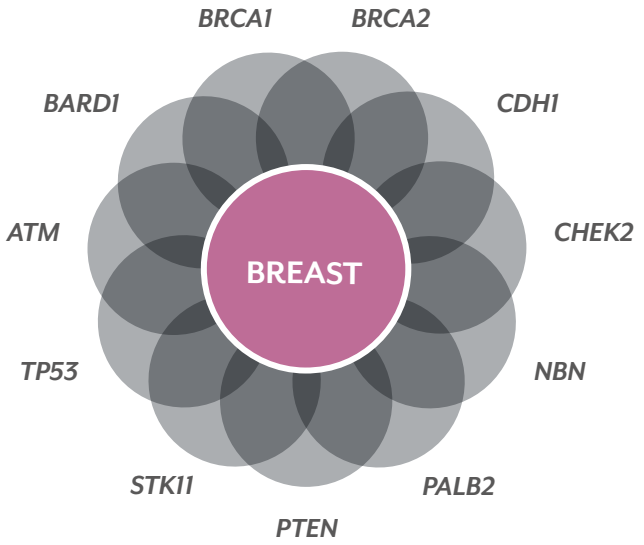
GENETIC MUTATIONS IN THE LYNCH GENES



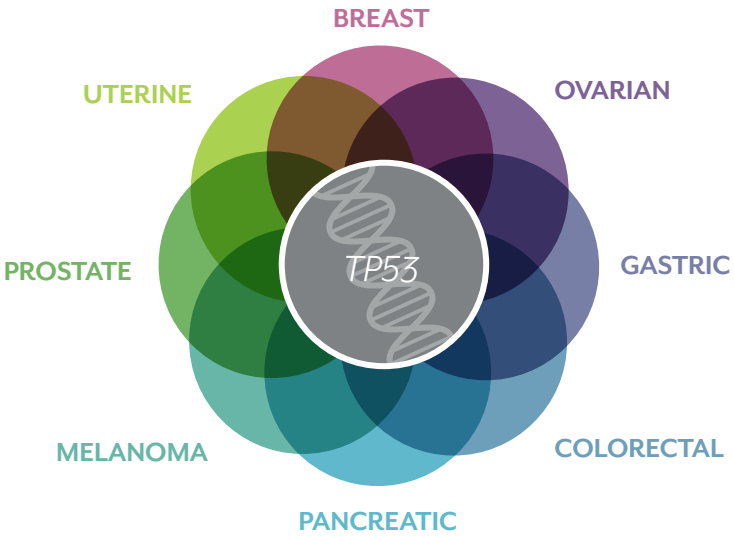
Includes: Ovarian Cancer, Colon Cancer, Uterine Cancer, Pancreatic Cancer

*For the most up-to-date general population and gene-associated cancer risks, refer to the Gene Tables located at http://myriadmyrisk.com/products/myriad-myrisk/myrisk-gene-table

Multiple genes can be associated with a single cancer



Multiple cancers can be associated with a single gene



Multiple Genes Across 8 Important Cancer Types

Gene	Breast	Ovarian	Colorectal	Endometrial	Melanoma	Pancreatic	Gastric	Prostate	Other Cancers
BRCA1	●	●				●		●	
BRCA2	●	●			●	●		●	
MLH1		●	●	●		●	●	●	●
MSH2		●	●	●		●	●	●	●
MSH6		●	●	●		●	●	●	●
PMS2		●	●	●		●	●	●	●
EPCAM		●	●	●		●	●	●	●
APC			●			●	●		●
MUTYH (2 copies)			●						●
MUTYH (1 copy)			●						
NTHL1	●		●						
CDKN2A (p16INK4a)					●	●			
CDKN2A (p14ARF)					●	●			
CDK4					●	●			
TP53	●	●	●	●	●	●	●	●	●
PTEN	●		●	●	●				●
STK11	●	●	●	●		●	●		●
CDH1	●		●				●		
BMPR1A			●			●	●		●
SMAD4			●			●	●		●
PALB2	●	●				●			
CHEK2	●		●						
ATM	●					●			
NBN	●							●	
BARD1	●								
BRIP1, RAD51C, RAD51D		●							
HOXB13								●	
POLD1, POLE, GREM1, AXIN2, GALNT12, MSH3, RPS20, RNF43			●						

Possible Myriad myRisk® Test Results

Positive Result A mutation has been identified	• A genetic mutation was found in one or more of the genes tested • You are at increased risk for cancer • A summary of medical management guidelines will be provided specific to your gene mutation(s)
Elevated Result	• No genetic mutation was found in the genes tested • You are at elevated risk for cancer based on an analysis of additional genetic markers, personal clinical risk factors, and/or your family's history of cancer • A summary of medical management guidelines will be provided based on your elevated risk
Negative Result	• No genetic mutation was found in the genes tested • The common causes of hereditary cancer have been ruled out, but depending on family history of cancer, increased risks could still remain • Depending on your family history, medical management is usually based on general population screening guidelines; however, you should talk with your healthcare provider to determine if there are any changes in medical management that are right for you
Variant of Uncertain Significance	• A change in a gene has been identified • It is not yet known if the change is associated with increased cancer risk • Medical management based on personal and family history of cancer until more is understood about this specific change

If you are a woman*, you may also receive a riskScore® result and/or a Tyrer-Cuzick breast cancer risk estimate.

riskScore® is a breast cancer risk prediction result that provides women, who are unaffected by breast cancer, with a personalized calculation of their future breast cancer risk. riskScore result uses a combination of genetic markers and clinical factors in its calculation.

Tyrer-Cuzick is a breast cancer risk model used to predict a woman's risk of developing breast cancer. The Tyrer-Cuzick model takes into consideration family history of cancer and other personal clinical risk factors.

If your remaining lifetime breast cancer risk is calculated to be 20% or greater with Tyrer-Cuzick or riskScore, a summary of medical management guidelines will be provided.

*Based on research at time of product launch, riskScore® is only calculated for women of solely European ancestry under the age of 85 and without a personal history of breast cancer, LCIS, hyperplasia, atypical hyperplasia, or a breast biopsy of unknown results. riskScore® is not calculated if a woman or a blood relative is known to carry a mutation in a breast cancer risk gene.

MANAGING HEREDITARY RISK

Increased Surveillance

Close and continuous observation and testing

For Example:

- Breast MRI in addition to mammogram
- Annual colonoscopy

Risk Reducing Medication

The use of drugs to prevent the development of cancer.

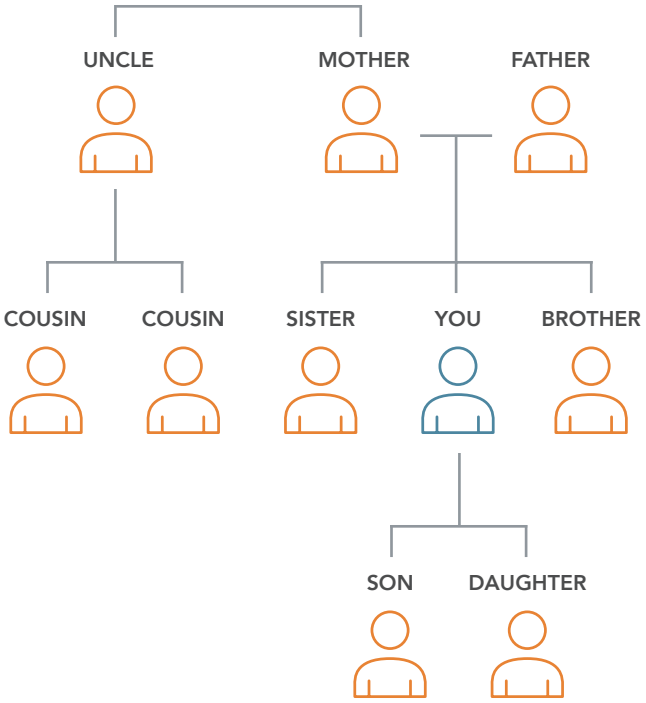
Risk Reducing Surgery

Based on individual considerations, the following surgical considerations may be recommended:

- Removal of the breasts
- Removal of the uterus
- Removal of the ovaries and fallopian tubes
- Removal of the colon

It's a Family Affair

- If you have a gene mutation, your parent, your children and your brothers and sisters could have a 50% chance of having the same genetic mutation.
- Other relatives (aunts, uncles and cousins) on the same side of the family are at risk of carrying the same genetic mutation.
- Testing is the only way to identify gene mutations which could impact your medical management.
- Remember, you can inherit a gene mutation from either your mother or your father, so it is important to look at both sides of your family.



Myriad Promise™

Because patients and their families use test results to make life saving medical decisions, Myriad promises to provide affordable access to testing, a lifetime commitment to accurate results, and comprehensive support for ALL appropriate patients and their families.

If you encounter ANY financial hardship associated with your genetic test, Myriad will work with your toward your complete satisfaction. Myriad provides payment plans without interest, where you can pay as little as $15/month if you have a bill.

For more information visit **myriadpromise.com**

Privacy

The Health Insurance Portability and Accountability Act (HIPAA) of 1996 created federal privacy protections that apply to all health information created or maintained by healthcare providers, health plans, and healthcare clearinghouses. Myriad Genetic Laboratories complies with HIPAA practices.

For more information on specific privacy practices, please visit: myriad.com/patients-families/the-myriad-difference/your-privacy.

References:

1. Ford D, et al. Risks of cancer in BRCA1-mutation carriers. Breast Cancer Linkage Consortium. Lancet. 1994 343:692-5.
2. Brand R, et al. MUTYH-Associated Polyposis. 2012 Oct 04. In: Pagon RA, et al., editors. GeneReviews® [Internet]. Available from http://www.ncbi.nlm.nih.gov/books/NBK107219/
3. Baglietto L, et al. Risks of Lynch syndrome cancers for MSH6 mutation carriers. J Natl Cancer Inst. 2010 102:193-201.
4. Begg CB, et al. Genes Environment and Melanoma Study Group. Lifetime risk of melanoma in CDKN2A mutation carriers in a population-based sample. J Natl Cancer Inst. 2005 97:1507-15.
5. Provenzale D, et al. NCCN Clinical Practice Guidelines in Oncology® Genetic/Familial High-Risk Assessment: Colorectal. V 2.2014. May 19. Available at http://www.nccn.org.
6. Pharoah PD, et al. International Stomach Cancer Linkage Consortium. Incidence of stomach cancer and breast cancer in CDH1 (E-cadherin) mutation carriers from hereditary diffuse stomach cancer families. Gastroenterology. 2001 121:1348-53.
7. Beebe-Dimmer, et al: Cancer Epidemiol Biomarkers Prev. 2015 Sep;24(9):1366-72.

Notice and Statement Concerning Nondiscrimination and Accessibility

Discrimination is Against the Law

Myriad Genetic Laboratories, Inc. (Myriad) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Myriad does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex.

Aids and Services

Myriad provides free aids and services to people with disabilities to communicate effectively with us, such as TTY/TDD calls or written information in suitable formats. Myriad will also provide free language services to people whose primary language is not English through qualified interpreters..

If you need these services, contact:
Don Martin
Compliance Director
320 Wakara Way
Salt Lake City, UT 84108
Telephone: (801) 584-3600
Fax: (801) 883-3472
Email: compliance@myriad.com

Grievances

If you believe that Myriad has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex. You can file a grievance by mail, telephone, fax, or email. If you need help filing a grievance, Mr. Martin is available to help you (see contact information above).

Grievance Procedure

1. Any person who believes someone has been subjected to discrimination by Myriad on the basis of race, color, national origin, sex, age or disability may file a grievance with Myriad. It is against the law for Myriad to retaliate against anyone who opposes discrimination, files a grievance, or participates in the investigation of a grievance.

2. Grievances must be submitted within 60 days of the date the person filing the grievance becomes aware of the alleged discriminatory action.

3. The complaint must be in writing, containing the name and address of the person filing it. The complaint must state the problem or action alleged to be discriminatory and the remedy or relief sought.

4. Myriad will conduct an investigation of the complaint. This investigation may be informal, but it will be thorough, affording all interested persons an opportunity to submit evidence relevant to the complaint. Myriad will maintain the files and records relating to such grievances. To the extent possible, and in accordance with applicable law, Myriad will take appropriate steps to preserve the confidentiality of files and records relating to grievances and will share them only with those who have a need to know.

5. Myriad will issue a written decision on the grievance, based on a preponderance of the evidence, no later than 30 days after its filing, including a notice to the complainant of their right to pursue further administrative or legal remedies.

6. The person filing the grievance may appeal Myriad's decision in writing to the President of Myriad Genetic Laboratories, Inc. within 15 days of receiving Myriad's initial decision. The President will issue a written decision in response to the appeal no later than 30 days after its filing.

7. Individuals seeking access to Section 1557 and its implementing regulations may be facilitated by contacting Mr. Martin (see contact information above).

8. The availability and use of this grievance procedure does not prevent a person from pursuing other legal or administrative remedies, including filing a complaint of discrimination on the basis of race, color, national origin, sex, age or disability in court or with the U.S. Department of Health and Human Services, Office for Civil Rights. A person can file a complaint of discrimination electronically through the Office for Civil Rights Complaint Portal, which is available at:

https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201

9. Complaint forms are available at: http://www.hhs.gov/ocr/office/file/index.html. Such complaints must be filed within 180 days of the date of the alleged discrimination. Myriad will make appropriate arrangements to ensure that individuals with disabilities and individuals with limited English proficiency are provided auxiliary aids and services or language assistance services, respectively, if needed to participate in this grievance process. Mr. Martin will be responsible for such arrangements.

Español (Spanish)
Myriad Genetic Laboratories, Inc. cumple con las leyes federales de derechos civiles aplicables y no discrimina por motivos de raza, color, nacionalidad, edad, discapacidad o sexo. ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1-801-584-3600.

繁體中文 (Chinese)
Myriad Genetic Laboratories, Inc. 遵守適用的聯邦民權法律規定，不因種族、膚色、民族血統、年齡、殘障或性別而歧視任何人。注意：如果┌使用繁體中文，┌可以免費獲得語言援助服務。請致電1−801−584−3600.

Tiếng Việt (Vietnamese)
Myriad Genetic Laboratories, Inc. tuân thủ luật dân quyền hiện hành của Liên bang và không phân biệt đối xử dựa trên chủng tộc, màu da, nguồn gốc quốc gia, độ tuổi, khuyết tật, hoặc giới tính. Updated December 2019 CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-801-584-3600.

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Myriad Genetic Laboratories, Inc.은(는) 관련 연방 공민권법을 준수하며 인종, 피부색, 출신 국가, 연령, 장애 또는 성별을 이유로 차별하지 않습니다.
주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 1-801-584-3600. 번으로 전화해 주십시오..

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Sumusunod ang Myriad Genetic Laboratories, Inc. sa mga naaangkop na Pederal na batas sa karapatang sibil at hindi nandidiskrimina batay sa lahi, kulay, bansang pinagmulan, edad, kapansanan o kasarian. PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 1-801-584- 3600.

Русский (Russian)
Myriad Genetic Laboratories, Inc. соблюдает применимое федеральное законодательство в области гражданских прав и не допускает дискриминации по признакам расы, цвета кожи, национальной принадлежности, возраста, инвалидности или пола. ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1-801-584-3600.

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ملحوظة: إذا كنت تتحدث اذكر اللغة، فإن خدمات المساعدة اللغوية تتوافر لك بالمجان. اتصل برقم1-801-584-3600

Kreyòl Ayisyen (French Creole)
Myriad Genetic Laboratories, Inc. konfòm ak lwa sou dwa sivil Federal ki aplikab yo e li pa fè diskriminasyon sou baz ras, koulè, peyi orijin, laj, enfimite oswa sèks. ATANSYON: Si w pale Kreyòl Ayisyen, gen sèvis èd pou lang ki disponib gratis pou ou.
Rele 1-801-584-3600.

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Myriad Genetic Laboratories, Inc. respecte les lois fédérales en vigueur relatives aux droits civiques et ne pratique aucune discrimination basée sur la race, la couleur de peau, l'origine nationale, l'âge, le sexe ou un handicap. ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement.
Appelez le 1-801-584-3600.

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Myriad Genetic Laboratories, Inc. cumpre as leis de direitos civis federais aplicáveis e não exerce discriminação com base na raça, cor, nacionalidade, idade, deficiência ou sexo. ATENÇÃO: Se fala português, encontram-se disponíveis serviços linguísticos, grátis. Ligue para 1-801-584-3600.

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Myriad Genetic Laboratories, Inc. è conforme a tutte le leggi federali vigenti in materia di diritti civili e non pone in essere discriminazioni sulla base di razza, colore, origine nazionale, età, disabilità o sesso. ATTENZIONE: In caso la lingua parlata sia l'italiano, sono disponibili servizi di assistenza linguistica gratuiti.
Chiamare il numero 1-801-584-3600.

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توجه: اگر به زبان فارسی گفتگو می کنید، تسهیلات زبانی بصورت رایگان برای شما فراهم می باشد. با 1-801-584-3600 تماس بگیرید.

Next Steps:

☐ Pursue Testing by giving blood or saliva sample

☐ Decline Testing-
Medical management based on personal and family history of cancer

☐ Undecided / Talk to Family

Who to Contact with questions: _____

Provider Testing Options to be discussed with your physician or genetic counselor.

☐ Integrated BRAC*Analysis*® with Myriad myRisk® Hereditary Cancer Update Test

- ☐ Multisite 3 BRAC*Analysis*
  - ☐ **REFLEX** to Integrated BRAC*Analysis* with Myriad myRisk Hereditary Cancer Update Test if the Multisite 3 is negative.
  - ☐ **Check here** if a family member has tested positive for one of the 3 Ashkenazi Jewish founder mutations.

☐ COLARIS® PLUS with Myriad myRisk Hereditary Cancer Update Test

☐ COLARIS *AP*® PLUS with Myriad myRisk Hereditary Cancer Update Test

☐ Single Site Testing (for family of known mutation carriers) **Specify Gene:** _____ **and Mutation:** _____

Relationship: My patient is the _____ (e.g. maternal aunt) of the known mutation carrier. **Required:** Include a copy of the known mutation carrier's report.

☐ Myriad myRisk Update Test

☐ Other: _____

Resources:

Your healthcare provider is always your number one resource. You are also invited to visit www.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 will 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 ext. 3850.

MYSUPPORT360

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