Positive test results identify a change, or “misspelling,” of DNA that is known or predicted to cause an increased risk for cancer. DNA is the blueprint of life—it carries all of the genetic information needed for our bodies to function. A section of DNA with a specific job is called a gene. A pathogenic variant is a change in a gene that is known to cause increased risk for cancer. A likely pathogenic variant is a change in a gene that is very likely to cause increased risk for cancer.

After a positive test result, there can be many questions about what to do next. This guide is a supplement to Riscover® Hereditary Cancer test results, helping patients and healthcare providers understand the results and together determine the best path forward.

Navigate Your Results

Learn | page 2
Review the test results along with this guide, and discuss the meaning of these results with your healthcare provider.

Plan | page 3
Develop a healthcare plan for early detection and prevention of specific cancers.

Share | page 4
Understand the risks for other family members, and consider how to inform relatives of their risks.

Connect | page 5
Reach out to medical experts and find local and national groups that can provide more information and support.

Glossary of Terms

Gene: A section of DNA with a specific job.

MRI: An abbreviation for magnetic resonance imaging, a test that provides detailed pictures of a specific part of the body.

Pathogenic: Causing or capable of causing disease.

Risk: The chance, or possibility, of developing a disease.

Salpingo-oophorectomy: Surgical removal of the ovaries and fallopian tubes.

Variant: A change, or “misspelling,” in the DNA sequence. Variants can be benign (not associated with disease), pathogenic (associated with disease), or of uncertain significance.
Your Diagnosis
Pathogenic/likely pathogenic variants in the RAD51C gene are associated with an increased risk of ovarian cancer and possibly breast cancer in women. Increased cancer risk related to the RAD51C gene is a relatively new discovery, and the frequency of individuals with pathogenic/likely pathogenic variants is unknown, but research is ongoing.

The cancer risks described below are for individuals with one pathogenic/likely pathogenic variant in the RAD51C gene. People who have two pathogenic/likely pathogenic variants (one inherited from each parent) are affected with a condition called Fanconi anemia.

Your Risk
Not all people with positive test results will develop cancer, but the chance for cancer is higher than the general population risk. The graphs below show how much the risk for cancer increases when a pathogenic variant is found. The cancer risks are presented in ranges based on multiple studies of families who have a pathogenic variant. There is not enough evidence available to give a specific risk to a person or family.

<table>
<thead>
<tr>
<th>LIFETIME CANCER RISKS</th>
<th>General population</th>
<th>People with RAD51C positive results</th>
</tr>
</thead>
<tbody>
<tr>
<td>OVARIAN Females</td>
<td>1.3%</td>
<td>Up to 13%</td>
</tr>
<tr>
<td>BREAST Females</td>
<td>12%</td>
<td>Possible increased risk</td>
</tr>
</tbody>
</table>
## Your Screening and Management Options

Listed below are the intervention options that are recommended by medical experts for individuals who carry this cancer gene variant. Your healthcare provider can explain these options in more detail, and together you can make a plan for cancer prevention and/or early detection.

### OVARIAN CANCER (FEMALES)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk-reducing salpingo-oophorectomy (RRSO)</td>
<td>Consider removal of the ovaries and fallopian tubes, typically performed between 45 – 50 years of age, or earlier based on family history.</td>
</tr>
</tbody>
</table>

### BREAST CANCER (FEMALES)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast self-exams</td>
<td>Periodic, consistent breast self-exams at the end of your period may be considered.</td>
</tr>
<tr>
<td>Clinical breast exam</td>
<td>Regular clinical breast exams performed by your healthcare provider are recommended.</td>
</tr>
<tr>
<td>Breast MRI</td>
<td>Your healthcare provider may consider a breast MRI based on your personal and family history.</td>
</tr>
<tr>
<td>Mammogram</td>
<td>Your healthcare provider can recommend mammography options based on your personal and family history.</td>
</tr>
</tbody>
</table>
Your Family Matters

Cancer gene variants are inherited in an autosomal dominant manner. This means that when a parent tests positive, each child has a 1 in 2 chance to inherit the variant. Some people who inherit the variant will develop cancer, and some will not, but the risks are significantly increased compared to the average person. People in the same family may develop different types of cancers at varying ages, and the pattern of cancer and age of onset can differ from family to family.

Gene variants can be passed through families for many generations. When a gene variant is identified in one person in the family, relatives can be tested for just that variant. Sharing information about test results with family members is important, because it allows them to make informed choices about their healthcare and to decide whether they want genetic testing.

Some people who have pathogenic and likely pathogenic variants are interested in learning how to avoid passing these variants on to their children. If you are planning to have a child, you may wish to consult with a reproductive medicine specialist to discuss all of your reproductive options, including use of an egg or sperm donor, preimplantation genetic diagnosis, and prenatal genetic testing.

The likelihood for family members to carry the same gene variant depends on how closely related they are to the person with a known gene variant.
Your Expert Team

As you take your next steps, it can help to have a team of experts on your side. This team may include your primary care provider and a number of specialists who will help along the way.

If you haven’t already done so, you may wish to speak with a genetic counselor. Genetic counselors are healthcare professionals with specialized training in medical genetics and counseling. They can help you understand your test results, discuss your healthcare plan, and connect to other resources in your area. Your healthcare provider may be able to provide a referral to a local genetic counselor. You can also find a genetic counselor through the National Society of Genetic Counselors at www.nsgc.org.

For questions about your test results, our genetic counseling team is available to help. To reach a genetic counselor, call +1 855-293-2639 and select option 3.

Helpful Resources

National Comprehensive Cancer Network (NCCN)
nccn.org
Expert guidelines for cancer screening and treatment. Versions available for both providers and patients.

Facing Our Risk of Cancer Empowered (FORCE)
facingourrisk.org
A patient advocacy group whose mission is to improve the lives of individuals and families affected by hereditary breast, ovarian, and related cancers.

REFERENCES


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