riscover®
HEREDITARY CANCER

Result Navigator

⊕ Positive Test Result: *TP53*

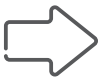
Positive test results identify a change, or "misspelling," of DNA that is known or predicted to cause an increased risk for cancer. DNA is the blueprint of life—it carries all of the genetic information needed for our bodies to function. A section of DNA with a specific job is called a gene. A pathogenic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

Breast tomosynthesis: Advanced three-dimensional (3-D) breast imaging.

Colonoscopy: Visual exam of the inside of the colon with a flexible, lighted tube inserted through the rectum.

Gene: A section of DNA with a specific job.

Mastectomy: Surgical removal of the breast tissue.

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.

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: Li-Fraumeni Syndrome

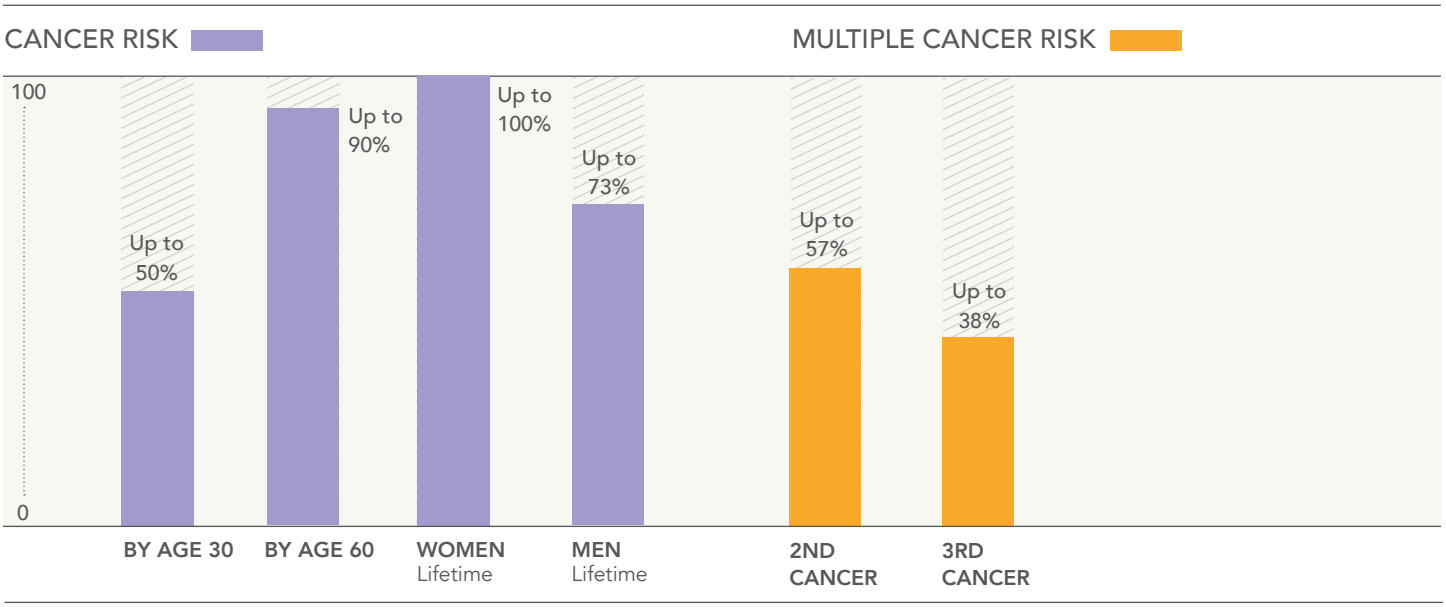
Pathogenic/likely pathogenic variants in the *TP53* gene are associated with an inherited cancer disorder called Li-Fraumeni syndrome (LFS). People with LFS most commonly develop sarcomas in the bone or soft tissue, breast cancer, and cancers of the brain and adrenal system, including adrenocortical carcinomas, astrocytomas, glioblastomas, medulloblastomas, and choroid plexus carcinomas.

There is also an increased lifetime risk for gastrointestinal cancer, genitourinary cancer, leukemia, lymphoma, lung cancer, neuroblastoma, skin cancer, thyroid cancer, and other types. Cancer can have onset as early as childhood and multiple cancer diagnoses happen in over half of people with LFS.

Somewhere between 1 in 5,000 and 1 in 20,000 people in the general population have LFS. Most people with LFS have a family history consistent with the disorder, but up to 1 in 5 people diagnosed with LFS are the first in their family to be affected.

Your Risk

With Li-Fraumeni syndrome, the risk to develop cancer is significant. The graphs below show the risk for cancer to develop over time, and also highlight the chance that a second or third cancer develops. There is not enough evidence available to give a specific risk to a person or family.



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.

ALL CANCER RISK	
Physical examination	A comprehensive physical exam, including a neurological exam, every 6 – 12 months by your healthcare provider for any evidence of cancer.
Education	Beginning at diagnosis, it is important that you learn about signs and symptoms of a variety of cancers to understand what changes should prompt clinical evaluation with your healthcare provider.
Avoid radiation therapy	Radiation therapy should be avoided when possible.

BREAST CANCER (FEMALES)	
Breast self-exams	Periodic, consistent breast self-exams at the end of your period may be considered.
Clinical breast exam	A clinical breast exam performed by your healthcare provider is recommended every 6-12 months, starting at age 20, or at the age of the earliest diagnosed breast cancer in the family, if below age 20.
Breast MRI	An annual breast MRI is recommended starting at age 25, or earlier if you have a family history of breast cancer diagnosed before age 30. These are usually performed until age 75, and can be considered on an individual basis after that.
Mammogram	Annual mammograms with consideration for breast tomosynthesis are recommended starting at age 30 or earlier based on your family history. These are usually performed until age 75, and can be considered on an individual basis after that.
Risk-reducing mastectomy	Risk-reducing mastectomy can be considered on an individual basis.

ADRENOCORTICAL CARCINOMA	
Abdominal ultrasound	An abdominal ultrasound is recommended every 3 – 4 months beginning in childhood or at time of diagnosis.
Lab Tests	Lab tests including complete urinalysis, ESR, LDH, ß-hCG, alpha-fetoprotein, 17-hydroxyprogesterone, testosterone, DHEAS, androstenedione are recommended every 3 – 4 months beginning in childhood or at time of diagnosis until age 40.

BRAIN CANCER	
Brain MRI	An annual brain MRI recommended beginning at diagnosis, children included.

SOFT TISSUE AND BONE SARCOMA	
Whole body MRI	An annual whole body MRI recommended beginning at diagnosis, children included.
Abdominal ultrasound	An abdominal ultrasound every 3-4 months is recommended starting at age 18.

GASTROINTESTINAL CANCER	
Colonoscopy	A colonoscopy and an upper endoscopy every 2 – 5 years is recommended beginning at age 25 or 5 years before the earliest known colorectal cancer in the family.

MELANOMA	
Dermatology exam	Annual skin examination by your healthcare provider, beginning at age 18.

LEUKEMIA/LYMPHOMA	
Lab tests (CBC profile/LDH/ESR)	Lab tests including CBC profile/LDH/ESR are recommended every 3 – 4 months beginning at diagnosis, children included.

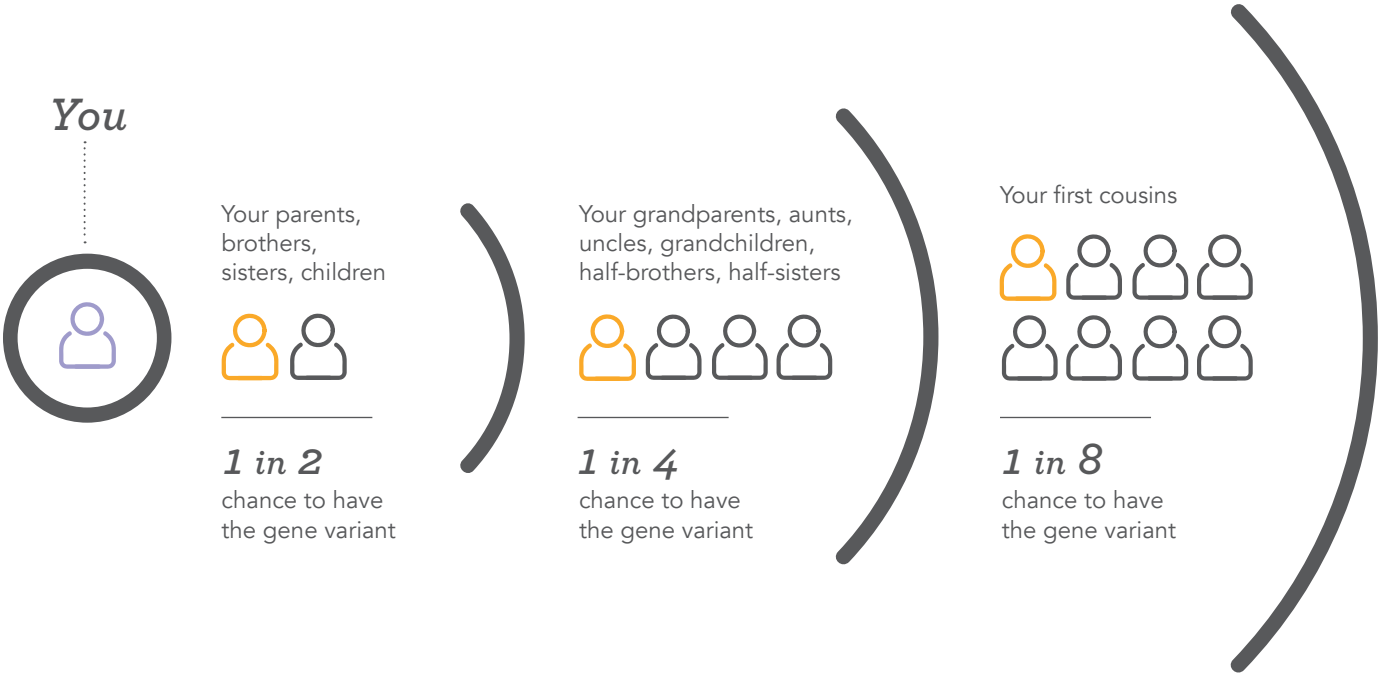
Your Family Matters

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

GeneReviews
ncbi.nlm.nih.gov/books/NBK1311
A detailed clinical summary of Li-Fraumeni syndrome written for healthcare providers.

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

Li-Fraumeni Syndrome Association
lfsassociation.org
A patient advocacy group whose mission is to provide a wide range of information, advocacy, and support services for individuals and families with Li-Fraumeni Syndrome.

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