riscover®
HEREDITARY CANCER

Result Navigator

Positive Test Result: *MEN1*

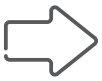
Positive test results identify a change, or "misspelling," of DNA that is known or predicted to cause an increased risk for cancer. DNA is the blueprint of life—it carries all of the genetic information needed for our bodies to function. A section of DNA with a specific job is called a gene. A pathogenic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

Central nervous system: System in the body that includes the brain and spinal cord.

CT (CAT Scan): Computerized tomography; combines a series of X-ray pictures taken from different angles.

Endocrine: A system of glands in the body that produce and release hormones to help with bodily functions.

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.

Scintigraphy: A test that creates a 2-D image of an internal body part by administering medication to emit radiation to capture the image.

Sella: The compartment in the skull that houses the pituitary gland.

Serum: A component of blood.

Sestamibi with SPECT scan: A test used to help determine the location of parathyroid tumor/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.

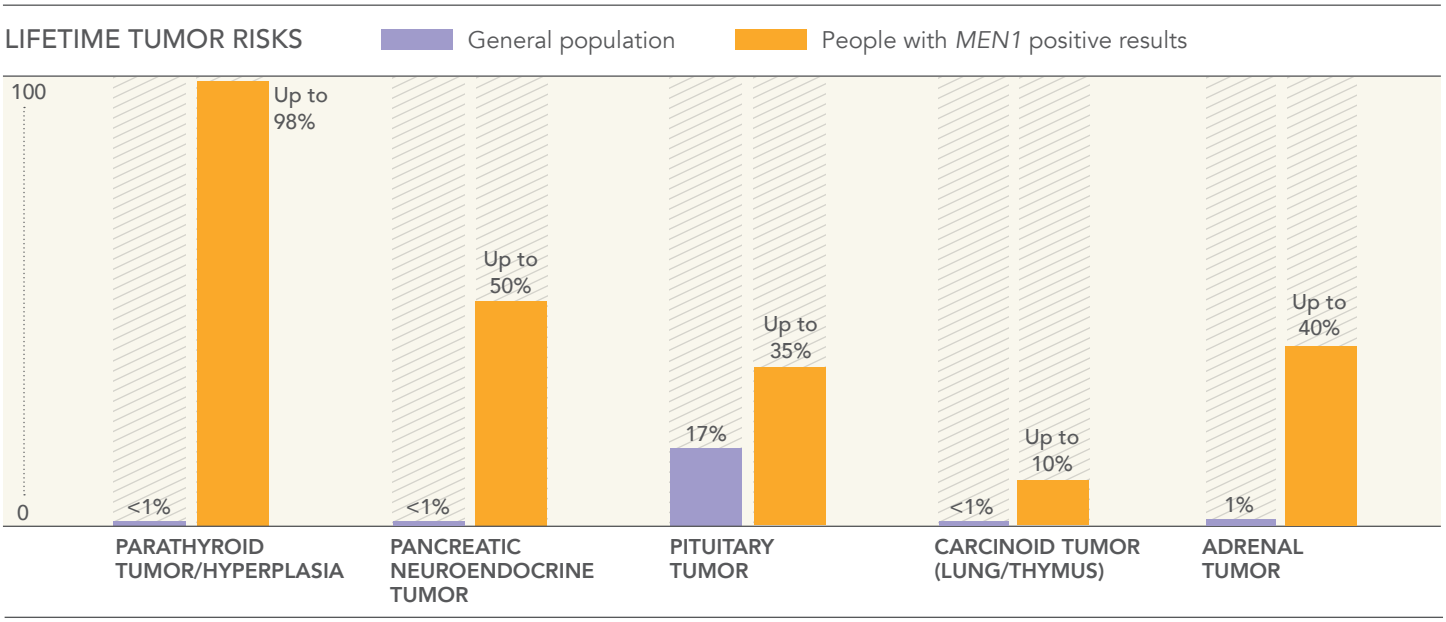
Your Diagnosis: Multiple Endocrine Neoplasia Type 1

Multiple Endocrine Neoplasia Type 1 (MEN1) is an inherited disorder caused by a pathogenic/likely pathogenic variant in the *MEN1* gene. MEN1 is associated with an increased lifetime risk of developing endocrine and non-endocrine tumors. The endocrine tumors occur in the parathyroid glands, pancreas, pituitary gland, adrenal gland, and lung/thymus (carcinoid tumors). Some of the non-endocrine tumors include uterine fibroids, skin tumors (facial angiofibromas, collagenomas, and lipomas), and central nervous system tumors (meningiomas and ependymomas).

A clinical diagnosis of MEN1 includes the presence of any two of the following tumors: parathyroid, pituitary, and/or pancreatic neuroendocrine. About 1 in 30,000 people carry a pathogenic variant in the *MEN1* gene. Many people with pathogenic variants in the *MEN1* gene have a family history consistent with the disorder, while about 1 in 10 are the first in the family to be affected.

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.



Note that the risks in this table are for the development of tumors. Not all tumors will be cancerous, but may need still need to be screened for and treated when appropriate.

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.

SPECIALIST MANAGEMENT

Referral to endocrinology	A regular follow-up with an endocrinologist is recommended. Endocrinologists specialize in diseases like MEN1, and can coordinate screening and management decisions described here.
Biochemical evaluation	A regular biochemical evaluation is recommended.

PARATHYROID TUMOR

Serum calcium and parathyroid hormone (PTH)	Annual evaluation of calcium and PTH is recommended.
Neck ultrasound or parathyroid sestamibi with SPECT scan or 4-D CT	Consider one of these tests to follow up on elevated calcium levels or as clinically indicated.
Neck CT or MRI with contrast	Consider one of these tests, if clinically indicated.
Parathyroidectomy	A parathyroidectomy is frequently recommended for people with MEN1. Surgical options and timing should be discussed by your healthcare provider when appropriate.

PANCREATIC NEUROENDOCRINE TUMOR

Abdominal/pelvic CT or MRI	Abdominal/pelvic CT or MRI should be considered every 1 – 3 years.
Endoscopic ultrasound (EUS) and/or Somatostatin receptor-based imaging	Serial endoscopic ultrasound (EUS) and/or somatostatin receptor-based imaging can be considered.

PITUITARY TUMOR

Pituitary or Sella MRI	An MRI with contrast of the pituitary is recommended every 3 – 5 years.
Pituitary hormones	Testing of prolactin, IGF-1, and other previously abnormal pituitary hormones is recommended every 3 – 5 years or as symptoms indicate.

LUNG/THYMUS CARCINOID TUMOR

Chest CT or MRI	A chest CT or MRI with contrast is recommended every 1 – 3 years

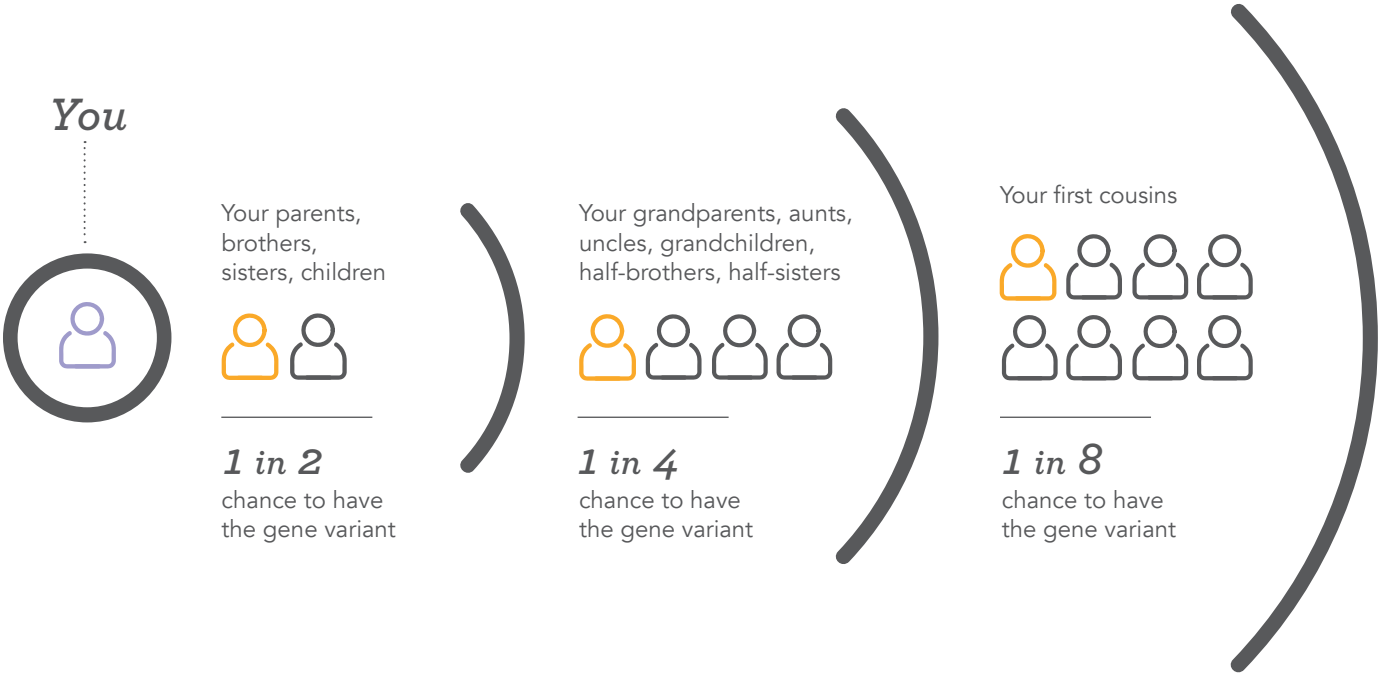
Your Family Matters

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/NBK1538
A detailed clinical summary of Multiple Endocrine Neoplasia Type 1 written for healthcare providers.

American Multiple Endocrine Neoplasia Support
amensupport.org
An organization dedicated to research, education, and support to improve awareness, diagnosis, treatment, and quality of life for those affected by MEN1.

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

REFERENCES

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