

Result Navigator

Positive Test Result: *RET*

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. Another name for these types of variants is mutation.

After a positive test result, there can be many questions about what to do next.

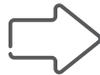
This guide is a supplement to RiscoverTM Hereditary Cancer test results, helping patients and healthcare providers understand the results and together determine the best path forward.

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

Adenoma: A type of benign tumor.

Calcitonin: A hormone that participates in the regulation of calcium levels by inhibiting loss of calcium from bone to the blood.

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

Endocrine gland: A gland that produces hormones.

Gene: A section of DNA with a specific job.

Mutation: A change in a gene that causes or is capable of causing disease. Another word for pathogenic/likely pathogenic variants.

Neuroma: A tumor formed of nerve tissue.

Pathogenic: Causing or capable of causing disease.

Pheochromocytoma: A usually-benign tumor of the adrenal gland or the sympathetic nervous system in which the affected cells secrete increased amounts of epinephrine or norepinephrine.

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

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

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

Thyroidectomy: Removal of all or a part of the thyroid gland.

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 2

Multiple Endocrine Neoplasia, type 2 (MEN2) is caused by pathogenic variants in the *RET* gene, which has a role in regulating cell growth. MEN2 leads to increased risk for the development of tumors in the body's endocrine glands. These tumors can be noncancerous or cancerous. MEN2 is divided into three subtypes: type 2A, type 2B, and familial medullary thyroid carcinoma (FMTC). These subtypes are distinguished by clinical signs and symptoms in addition to the specific pathogenic variant detected in a family.

All subtypes involve an increased risk for medullary thyroid cancer. MEN2A and MEN2B have an increased risk for pheochromocytoma (PCC); MEN2A has an increased risk for parathyroid adenoma or hyperplasia. MEN2B has an increased risk for mucosal neuromas of the lips and tongue and affected people may have characteristic physical features.

MEN2 is a rare syndrome with an incidence of 1 in 35,000 live births. Some people with pathogenic variants in the *RET* gene have a family history consistent with the disorder, while others are the first in their family to be affected.

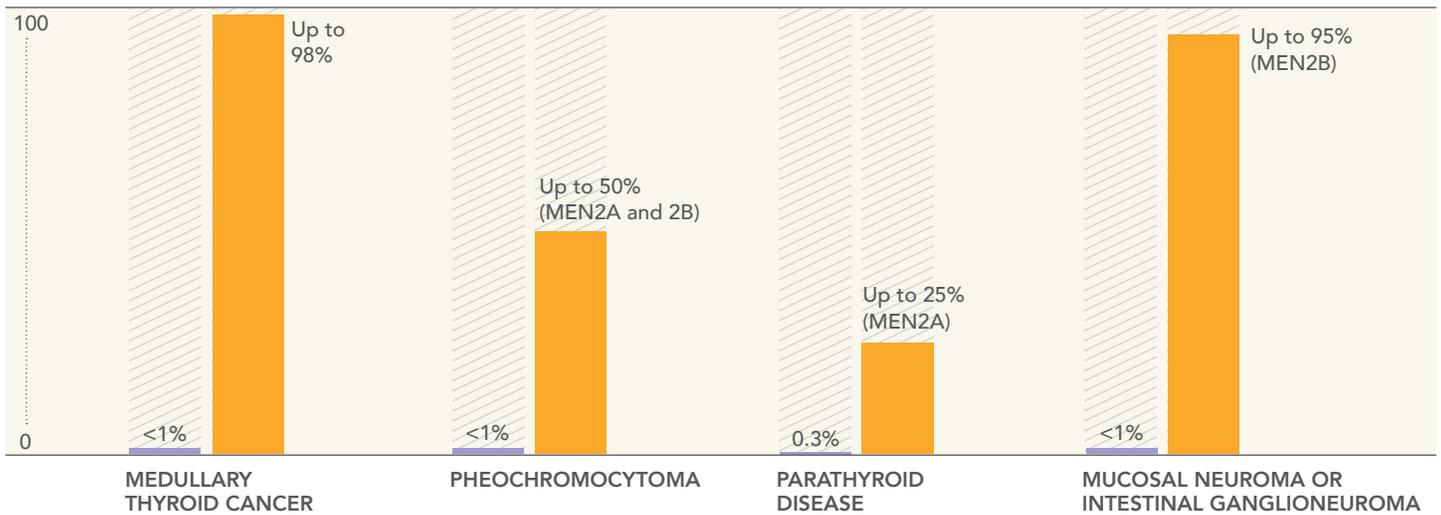
Your Risk

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.

LIFETIME TUMOR RISKS

General population

People with *RET* positive results



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 MEN2, and can coordinate screening and management decisions described here.
Biochemical evaluation	Routine biochemical evaluation is recommended beginning at diagnosis.

THYROID CANCER

Central and lateral neck compartment ultrasound	A central and lateral neck compartment ultrasound is recommended on a routine basis by your healthcare provider beginning at diagnosis.
Thyroidectomy	Removal of the thyroid is typically recommended for prevention of thyroid cancer. The timing of surgery may depend on your personal and family history of thyroid cancer.

PHEOCHROMOCYTOMA

MRI or multiphasic CT of abdomen	MRI or multiphasic CT of the abdomen is recommended on a routine basis by your healthcare provider, beginning at diagnosis.
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PARATHYROID DISEASE

Neck ultrasound or parathyroid sestamibi scan	Neck ultrasound or parathyroid sestamibi scan is recommended by your healthcare provider.
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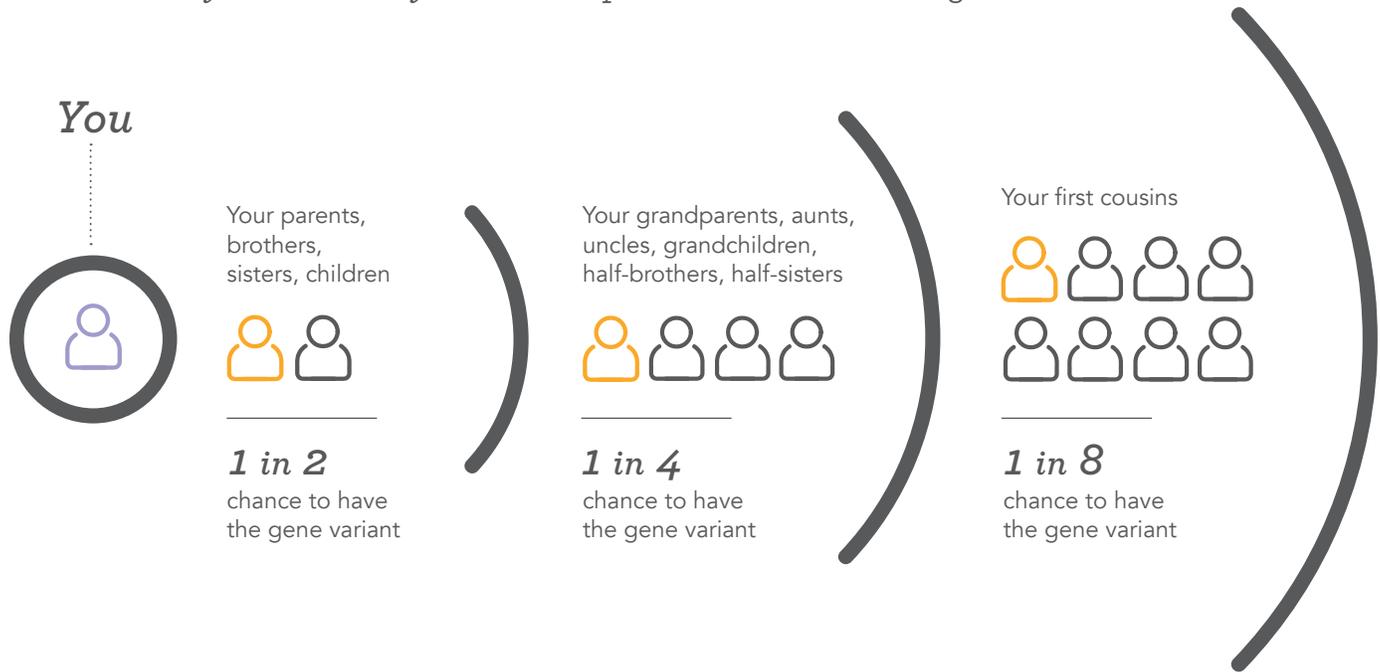
Your Family Matters

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, Progenity's 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/NBK1257

A detailed clinical summary of hereditary breast and ovarian cancer written for healthcare providers.

National Comprehensive Cancer Network (NCCN)

nccn.org

Expert guidelines for cancer screening and treatment. Versions available for both providers and patients.

American Multiple Endocrine Neoplasia Support

amensupport.org/wp/

An organization dedicated to research, education, and support to improve awareness, diagnosis, treatment, and quality of life for those affected by MEN.

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