riscover®
HEREDITARY CANCER

Result Navigator

⊕ Positive Test Result: *PTEN*

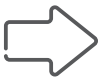
Positive test results identify a change, or "misspelling," of DNA that is known or predicted to cause an increased risk for cancer. DNA is the blueprint of life—it carries all of the genetic information needed for our bodies to function. A section of DNA with a specific job is called a gene. A pathogenic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

Endometrial biopsy: A procedure that takes a small sample of tissue from inside the uterus (womb) for laboratory testing.

Hysterectomy: Surgical removal of the uterus.

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.

Transvaginal ultrasound: An imaging test performed by inserting an ultrasound probe into the vagina to take detailed images 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: *PTEN* Hamartoma Tumor Syndrome

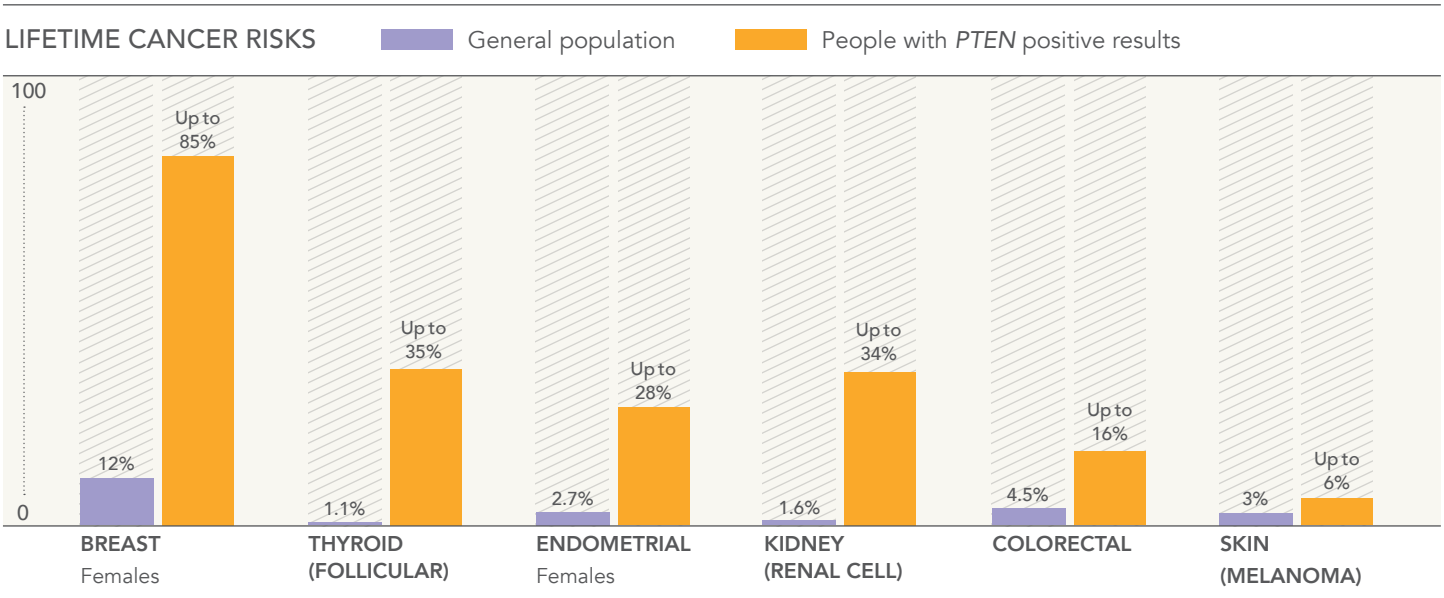
Pathogenic/likely pathogenic variants in the *PTEN* gene are associated with an inherited cancer disorder called *PTEN* hamartoma tumor syndrome (PHTS). People with PHTS are at risk for breast cancer, endometrial cancer, thyroid cancer (usually follicular), kidney cancer, colon cancer, and melanoma.

Some people with *PTEN* mutations have other clinical signs and symptoms unrelated to cancer. These include a large head size (macrocephaly), pigmentation changes on the skin of the penis, hamartomas or ganglioneuromas in the gastrointestinal system, other skin lesions (trichilemmoma, facial papules, papillomatosis around the mouth, keratosis on the hands and feet, lipomas), intellectual disability, and autism. Depending on the combination of signs and symptoms a person has, this condition is sometimes given other names, including Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome, *PTEN*-Related Proteus syndrome, and Proteus-Like syndrome.

PHTS is rare: about 1 in 200,000 people in the general population have this syndrome. Some people with PHTS have a family history consistent with the disorder, while other people diagnosed with PHTS 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.



The overall lifetime risk to develop cancer for females is 87%.
The overall lifetime risk to develop cancer for males is 56%.

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.

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 25, or 5 – 10 years before the earliest known breast cancer in the family.
Breast MRI	An annual breast MRI is recommended starting at age 30 – 35, or 5 – 10 years before the earliest known breast cancer in the family.
Mammogram	Annual mammograms with consideration for breast tomosynthesis are recommended starting at age 30 – 35, or 5 – 10 years before the earliest known breast cancer in the family.
Risk-reducing mastectomy	Risk-reducing mastectomy can be considered on an individual basis.

ENDOMETRIAL CANCER (FEMALES)

Dysfunctional uterine bleeding warrants evaluation	Seek evaluation with your healthcare provider when present.
Endometrial biopsies and/or transvaginal ultrasound	Screening via endometrial biopsy every 1 – 2 years can be considered. Transvaginal ultrasound may be considered in postmenopausal women at your clinician's discretion.
Hysterectomy	Hysterectomy can be considered after a woman has had her last child.

THYROID CANCER

Thyroid ultrasound	Annual thyroid ultrasounds are recommended starting at diagnosis, including in childhood.
Physical examination	An annual physical exam performed by your healthcare provider with particular attention to the thyroid is recommended starting at age 18, or 5 years before the earliest diagnosis of a Cowden syndrome-related cancer in the family.

RENAL (KIDNEY) CANCER

Renal ultrasound	Consider a renal ultrasound every 1 – 2 years, starting at age 40.

COLORECTAL CANCER

Colonoscopy	A colonoscopy is recommended every 5 years starting at age 35, or 5 – 10 years before the earliest known colorectal cancer in the family. May be recommended more frequently if additional symptoms or polyps are present.

MELANOMA

No specific guidelines	Your healthcare provider can recommend screening options based on your personal and family history of melanoma/dermatologic findings.

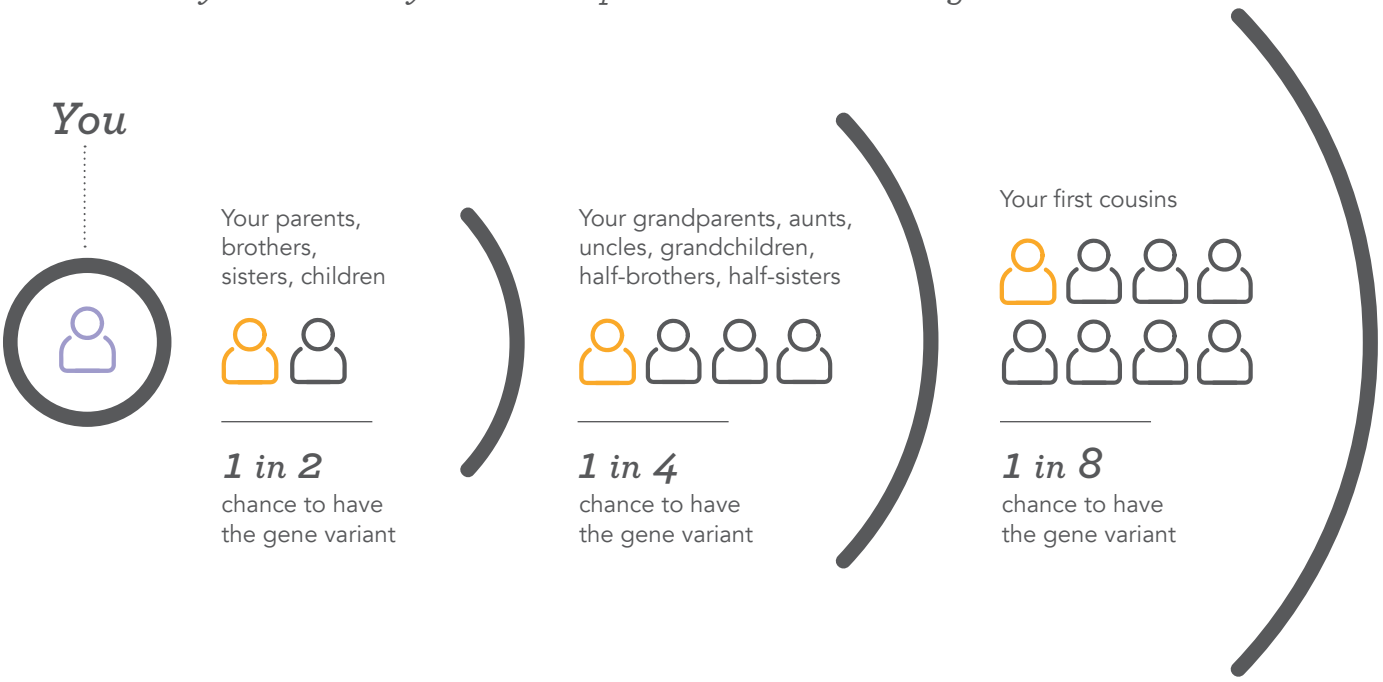
Your Family Matters

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/NBK1488
A detailed clinical summary of *PTEN* hamartoma 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.

***PTEN* Hamartoma Tumor Syndrome Foundation**
ptenfoundation.org
A patient advocacy group whose mission is to educate about *PTEN* syndromes, provide financial support to patients, support research, and to promote awareness.

REFERENCES

Eng C. PTEN Hamartoma Tumor Syndrome. 2001 Nov 29 [Updated 2016 Jun 2]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1488/

National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast and Ovarian (Version 2.2019). Available from: http://www.nccn.org/.