Ambry Genetics®

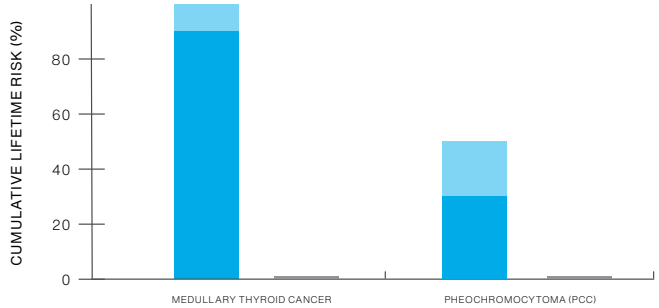
Understanding Your Positive *RET* Genetic Test Result

INFORMATION FOR PATIENTS WITH A PATHOGENIC MUTATION OR VARIANT, LIKELY PATHOGENIC

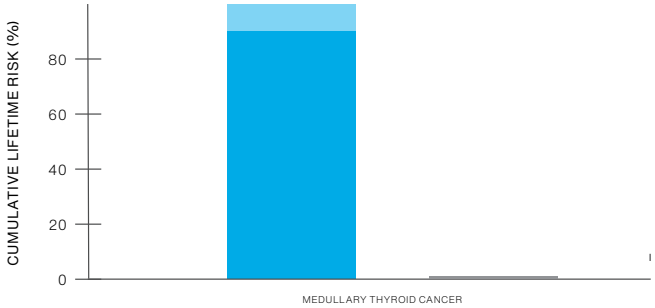
6 Things to Know

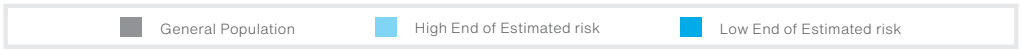
1	*RET* mutation	Your testing shows that you have a pathogenic mutation or a variant that is likely pathogenic in the *RET* gene.
2	*RET*-related conditions	People with *RET* mutations have multiple endocrine neoplasia type 2 (MEN2) or a variant of MEN2 called familial medullary thyroid carcinoma (FMTC). MEN2 is divided into 2 subtypes, MEN2A and MEN2B. Each of these conditions is determined by the specific *RET* mutation and causes slightly different medical concerns.
3	Cancer Risks	Your cancer risks will differ depending on the specific *RET* mutation you have: • MEN2A and MEN2B: increased risk for medullary thyroid cancer and pheochromocytoma (PCC). Thyroid cancer is often diagnosed in childhood or young adulthood. • FMTC: increased risk for medullary thyroid cancer only. People with FMTC are usually diagnosed with thyroid cancer later in life (after age 40) compared to people with MEN2.
4	Non-cancerous tumors and other medical concerns	Subtypes of MEN2 can involve non-cancerous medical concerns: • MEN2A: increased risk for parathyroid overgrowth that can cause hyperparathyroidism and a skin condition known as cutaneous amyloidoses lichen • MEN2B: increased risk for non-cancerous tumors in the mouth (neuromas), non-cancerous tumors known as ganglioneuromas, and skeletal abnormalities • A small number of people with MEN2 or FMTC may also have a condition known as Hirschsprung disease (HD). HD is usually present from birth and can cause blockage in a baby's large intestine.
5	What you can do	The specific *RET* gene mutation you have may determine which subtype you have, and may provide you more information about your specific tumor/cancer risks. Talk to your healthcare provider about which tumors and cancers you are at risk for. Risk management decisions are very personal. There are options to detect cancer early or lower the risk to develop cancer. It is important to discuss these options with your healthcare provider and decide on a plan that works for you.
6	Family	Family members may also be at risk – they can be tested for the *RET* mutation that was found in you. It is recommended that you share this information with your family members so they can learn more and discuss with their healthcare providers.

MEN2A and MEN2B: Lifetime cancer risks*



Familial Medullary Thyroid Carcinoma (FMTC): Lifetime Cancer risks*

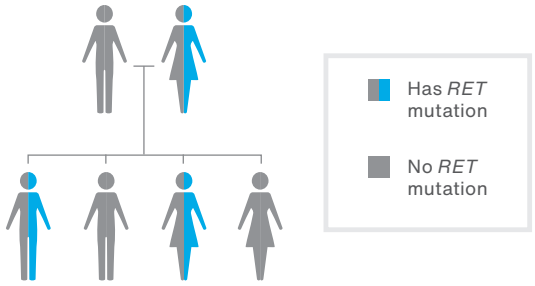




* Because risk estimates vary in different studies, only approximate risks are given. Cancer risks will differ based on individual and family history.

RET Mutations in the Family

There is a 50/50 random chance to pass on a *RET* mutation to your sons and daughters. The image to the right shows that both men and women can carry and pass on these mutations.



Reach Out	RESOURCES	• Association for Multiple Endocrine Neoplasia Disorders (AMEND) amend.org.uk • Thyca: Thyroid Cancer Survivors' Association thyca.org • Genetic Information Nondiscrimination Act (GINA) ginahelp.org • National Society of Genetic Counselors nsgc.org • Canadian Society of Genetic Counsellors cagc-accg.ca • American Multiple Endocrine Neoplasia Support amensuport.org

Please discuss this information with your healthcare provider. The cancer genetics field is continuously evolving, so updates related to your *RET* result, medical recommendations, and/or potential treatments may be available over time. This information is not meant to replace a discussion with a healthcare provider, and should not be considered or interpreted as medical advice.

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