RET gene

Associated Syndrome Name: Multiple endocrine neoplasia type 2A (MEN2A), familial medullary thyroid cancer (FMTC), or multiple endocrine neoplasia type 2B (MEN2B)

RET Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Endocrine	High Risk
Other	High Risk

RET gene Overview

Multiple endocrine neoplasia type 2A (MEN2A), familial medullary thyroid cancer (FMTC), or multiple endocrine neoplasia type 2B (MEN2B) [1, 2]

- Individuals with *RET* gene mutations have one of three conditions, each of which has different cancer risks and medical management recommendations. These conditions are multiple endocrine neoplasia type 2A (MEN2A), familial medullary thyroid cancer (FMTC), and multiple endocrine neoplasia type 2B (MEN2B). In most cases, it is possible to predict whether the individual has MEN2A, FMTC, or MEN2B based on which *RET* mutation was found. **If this patient's *RET* mutation is known to be associated with one of these conditions, that information is provided in the DETAILS ABOUT: *RET* section of the Genetic Result.**
- Almost everyone with one of these conditions will develop medullary thyroid cancer. Medullary thyroid cancer can be aggressive, and it is therefore important to remove the thyroid before the cancer has a chance to spread to other parts of the body.
- MORE ABOUT MEN2A: Medullary thyroid cancer usually develops in late childhood or adulthood in patients with MEN2A. Patients with MEN2A also have a high risk for adrenal gland tumors (pheochromocytomas) and a high risk for enlarged parathyroid glands (parathyroid hyperplasia) and parathyroid adenomas. These conditions lead to excessive production of parathyroid hormone and high levels of calcium in the blood (hypercalcemia). High calcium levels can cause serious health issues affecting mental health (depression and confusion), the heart, the digestive system, the kidneys and bones. Some individuals with MEN2A will have Hirschsprung disease. This is a condition where the large intestine does not function properly from birth, leading to constipation, diarrhea and vomiting. Some individuals with MEN2A also have a non-cancerous skin condition known as lichen amyloidosis.
- MORE ABOUT FMTC: Medullary thyroid cancer usually develops in adults with FMTC. Patients with FMTC only have a high risk for medullary thyroid cancer. Their risk for pheochromocytomas and parathyroid problems is low.
- MORE ABOUT MEN2B: Medullary thyroid cancer usually develops in infants or young children with MEN2B. They also have a high risk for adrenal gland tumors (pheochromocytomas). Almost everyone with MEN2B will develop painless nodules on the lips and tongues (mucosal neuromas). Other signs of MEN2B are a tall and thin body type, dry eyes with a lack of tears, and constipation due to nerve cell tumors in the digestive system (intestinal ganglioneuromas). There is a small chance for ganglioneuromas to become malignant (cancer). Patients with MEN2B have a low risk for parathyroid problems.
- While individuals with MEN2A, FMTC, and MEN2B have a high risk for cancers and other serious health concerns, these risks can be greatly reduced with appropriate medical management. The exact recommendations depend on the specific *RET* mutation identified, since this usually predicts whether the patient has MEN2A, FMTC, or MEN2B, the risks for the different health problems, and the age at which medullary thyroid cancer is likely to develop. A limited summary of detailed guidelines from the National Comprehensive Cancer Network (NCCN) and the American Association of Cancer Research (AACR) is provided below. Since MEN2A, FMTC, and MEN2B are complicated conditions affecting a wide variety of organs, it is recommended that individuals with *RET* gene mutations be managed by a multidisciplinary team with expertise in endocrinology, medical genetics and the care of patients with this condition.

RET gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Medullary Thyroid	Lifetime risk[1, 2, 3, 4]	Up to 100%	<0.1%
Pheochromocytoma	To age 80[1, 2, 3, 4]	Up to 50%	<0.1%

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Other MEN2A, FMTC and MEN2B-associated tumors and cancers	To age 80[1, 2, 3]	Depends on gene mutation	NA

RET Cancer Risk Management Table

The overview of medical management options provided is a summary of professional society guidelines. The most recent version of each guideline should be consulted for more detailed and up-to-date information before developing a treatment plan for a particular patient.

This overview is provided for informational purposes only and does not constitute a recommendation. While the medical society guidelines summarized herein provide important and useful information, medical management decisions for any particular patient should be made in consultation between that patient and his or her healthcare provider and may differ from society guidelines based on a complete understanding of the patient's personal medical history, surgeries and other treatments.

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Medullary Thyroid	Thyroidectomy[2, 5]	Individualized, based on risk associated with specific RET mutations (infancy, early childhood, or after screening detects signs of thyroid cancer)	NA
	Screening with biochemical testing, physical exam and thyroid ultrasound for patients with lower risk mutations[2, 3]	Age 6 months to 5 years	Every 6 months to annually
Pheochromocytoma	Biochemical screening of blood and urine[2, 3]	Individualized, based on risk associated with specific RET mutations (age 8 to 16)	Annually or prior to any surgery or anesthesia
	Abdominal/pelvic MRI (preferred) or CT[2, 3]	If biochemical screening is abnormal	Individualized
Other MEN2A, FMTC and MEN2B-associated tumors and cancers	Biochemical screening for hypercalcemia for individuals with *RET* mutations associated with hyperparathyroidism[2]	Age 11 to 16	Annually
	Additional clinical monitoring for clinical features of MEN2A and MEN2B based on mutation identified[2]	Individualized	Individualized
For Patients With A Cancer Diagnosis	For patients with a gene mutation and a diagnosis of cancer, targeted therapies may be available as a treatment option for certain tumor types (e.g., RET kinase inhibitors).[5]	NA	NA

Information for Family Members

The following information for Family Members will appear as part of the MMT for a patient found to have a mutation in the RET gene.

This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.

Family members should talk to a healthcare provider about genetic testing. Close relatives such as parents, children, brothers and sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance of carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention.

Genetic testing should be considered in childhood or infancy for children of a parent known to have MEN2A, FMTC, or MEN2B, since thyroidectomy and/or various screenings may be a consideration at that age.[2]

Approximately 9% of individuals with MEN2A, and 50% of individuals with MEN2B, have not inherited the *RET* mutation from a parent. In these cases the mutation has developed spontaneously in that individual (a de novo mutation). Once this occurs, the children of that individual are each at 50% risk of inheriting the mutation.[2]

References

1. Eng C. Multiple Endocrine Neoplasia Type 2. 2023 Aug 10. In: Adam MP, et al., editors. GeneReviews® [Internet]. PMID: 20301434.
2. Wasserman JD, et al. Multiple Endocrine Neoplasia and Hyperparathyroid-Jaw Tumor Syndromes: Clinical Features, Genetics, and Surveillance Recommendations in Childhood. Clin Cancer Res. 2017 23:e123-e132. PMID: 28674121.
3. Bergsland E, et al. NCCN Clinical Practice Guidelines in Oncology®: Neuroendocrine and Adrenal Tumors. V 1.2025. Mar 27. Available at https://www.nccn.org.
4. SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. [Cited 2025 Apr 1]. Available from https://seer.cancer.gov/explorer/.
5. Haddad RI et al. NCCN Clinical Practice Guidelines in Oncology®: Thyroid Carcinoma. V 1.2025. Mar 27. Available at https://www.nccn.org.

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