NF1 gene

Associated Syndrome Name: Neurofibromatosis 1

NF1 Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Breast	High Risk
Endocrine	High Risk
Other	High Risk

NF1 gene Overview

Neurofibromatosis 1 [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14]

- Individuals with *NF1* mutations have Neurofibromatosis 1 (NF1).
- Individuals with NF1 are at an increased risk of developing breast cancer. This risk is especially pronounced under the age of 50 and those diagnosed tend to have a worse prognosis than those with sporadic (non-hereditary) breast cancers.
- Individuals with NF1 also have an increased risk for cancers of the nervous system, including malignant peripheral nerve sheath tumors (MPNSTs) and tumors of the adrenal gland (pheochromocytomas). These cancers are extremely rare in the general population but should be considered in individuals with NF1 who are symptomatic or have other high risk factors. It is important for children and adults with NF1 to be followed and monitored regularly by specialists with expertise in the condition.
- Some studies have described a possible increased risk for a wide range of other cancers in individuals with *NF1* mutations, including male breast cancer, childhood leukemia, and sarcomas. However, these studies are not conclusive and there are currently no medical management guidelines to address these possible risks.
- Individuals with NF1 often have a wide variety of other, non-cancerous features associated with this condition, many of which require medical attention. Benign tumors can occur throughout the body (i.e., neurofibromas, gliomas), including in the skin, brain, eyes, or nervous system. Other common issues in individuals with NF1 include hypertension; skeletal problems such as dysplasia, scoliosis, or osteoporosis; and neuropsychiatric conditions such as learning difficulties or behavioral disorders.
- Although there are increased risks for cancer and a high risk for other medical problems in individuals with NF1, these risks can be managed with appropriate medical care. Guidelines from the National Comprehensive Cancer Network (NCCN), American Association for Cancer Research (AACR), and the American College of Medical Genetics and Genomics (ACMG) are listed below. Since NF1 is a complex condition, individuals with *NF1* mutations and a diagnosis of NF1 should be managed by a multidisciplinary team with expertise in medical genetics and the prevention and treatment of the complications associated with this condition.

NF1 gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Overall Cancer Risk	To age 50[7, 8, 9]	20%-39%	4.7%
	To age 70[7, 8, 9, 15]	36%-60%	19.8%
Female Breast	To age 50[3, 15]	10%	2.2%
	To age 70[3, 15]	24%	7.6%
Malignant Peripheral Nerve Sheath Tumors (MPNST)	Lifetime risk[4]	8%-13%	<0.1%
Pheochromocytoma	Lifetime risk[5, 6]	Up to 15%	<0.1%
Other - Non-malignant features of NF1	All ages[10, 11, 12]	NF1 is associated with non-malignant clinical features, some of which may require medical intervention as early as infancy (see Overview).	NA

NF1 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)
Female Breast	Mammogram[12, 13]	30 years	Annually
	Consider breast MRI with and without contrast.[12, 13]	30 years	Annually until age 50
	Consider additional risk-reduction strategies.[13]	Individualized	NA
Malignant Peripheral Nerve Sheath Tumors (MPNST)	Patient education about the signs and symptoms of MPNST[12]	Individualized	NA
	Whole-body MRI[14, 16]	Baseline between 16 to 20 years	NA
Pheochromocytoma	There are currently no specific medical management recommendations for pheochromocytoma risk in asymptomatic mutation carriers.	NA	NA
Other - Non-malignant features of NF1	Multiple screenings recommended, which may include comprehensive physical exam, skin exam, eye exam, neurological exam, blood pressure monitoring, and evaluations for neuropsychiatric disorders.[11, 12, 16]	At time of diagnosis of NF1	Varies

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 NF1 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.

It is appropriate to offer genetic counseling to individuals with NF1 who are of reproductive age to discuss reproductive risks and options. There are additional considerations before and during pregnancy for individuals with NF1.[10, 12]

Approximately half of individuals with NF1 have not inherited the *NF1* 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.[10]

Since *NF1* mutations carry a risk for complications in children, consideration should be given to mutation testing in childhood.[10, 11]

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