NF1 Mutations (Neurofibromatosis Type 1 (NF1))

What you should know about *NF1* mutations/Neurofibromatosis Type 1 (NF1)

Individuals with NF1 have an increased for several types of tumors. These tumors can be cancerous or benign. The main features of NF1 include skin findings (café au lait spots, freckling, and neurofibromas) and lisch nodules (benign tumors of the iris). Individuals with NF1 also have an increased risk for breast cancer, brain tumors, stomach tumors (called GISTs), and other cancers. The signs of NF1 vary from person to person, even within the same family.

Cancer risks associated with a *NF1* mutation

Individuals with NF1 usually develop numerous benign neurofibromas of the skin. Approximately 50% of people with NF1 will also develop plexiform neurofibromas (typically internal) and approximately 16% will develop a malignant peripheral nerve sheath tumor (MPNST). Males and females with NF1 have a 5-25% chance to develop an optic glioma, a 4% chance to develop a brainstem tumor, and up to a 15% chance to develop a pheochromocytoma. Both males and females with NF1 also have an increased chance to develop leukemia or gastrointestinal stromal tumors (GISTs). Females with NF1 have up to a 62% (5-fold) lifetime chance for breast cancer, depending on their age.

Risks to family members

Mutations in the *NF1* gene are inherited in an autosomal dominant manner. This means that children, brothers, sisters, and parents of individuals with a *NF1* mutation have a 1 in 2 (50%) chance of having the mutation as well and should be evaluated. Both males and females can inherit a familial *NF1* mutation and can pass it on to their children. Approximately 50% of individuals with NF1 have inherited the mutation from their parents, while the other 50% have a new (or "de novo") mutation that was not inherited from either parent. This new mutation can still be passed down to children.

Managing cancer risks

The following surveillance is recommended by the National Comprehensive Cancer Network (v2.2020) and the American Associated for Cancer Research (AACR, 2017).

- Males and Females:
    - Annual physical exam (including skin, neurologic, musculoskeletal and blood pressure exams)
    - Ophthalmic examination every 6-12 months for children under the age of 8, and every 1-2 years from age 8 to 20 for detection of glioma
- Females:
    - Annual mammography with consideration of tomosynthesis starting at age 30 and consideration of breast MRI with contrast from ages 30-50

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