

Clinician Management Resource for individuals with a germline predisposition to myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML)

This overview of clinical management guidelines is based on this patient’s positive test result. Unless otherwise stated, medical management guidelines used here are limited to those published in the Nordic Guidelines for Germline Predisposition to Myeloid Neoplasms in Adults¹ since U.S. consensus practice guidelines have not been developed. Please consult the referenced guideline for complete details and further information.

Clinical correlation with the patient’s past medical history, treatments, surgeries, and family history may lead to changes in clinical management decisions; therefore, other management recommendations may be considered. Genetic testing results and published guidelines help inform medical management decisions but do not constitute formal recommendations. Discussions of medical management decisions and individualized treatment plans should be made in consultation between each patient and his or her healthcare provider and may change.

SCREENING/SURGICAL CONSIDERATIONS ¹	AGE TO START	FREQUENCY
Myelodysplastic syndrome (MDS) and Acute Myeloid Leukemia (AML)*		
Complete blood count (CBC) with manual differential	Baseline	Every 6 months
Bone marrow aspirate/biopsy with cytogenetic analysis	Baseline	Repeat only if CBC changes
Testing for somatic gene mutations using a next generation sequencing myeloid gene panel with high coverage and reading depth	Baseline (bone marrow)	Annually (blood)
Management and surveillance of other organ dysfunction		
Referral to a hereditary cancer clinic or to relevant medical specialists to ensure screening for solid tumors and organ dysfunction	Individualized, depending on the underlying condition	Individualized, depending on the underlying condition
Other		
Referral to genetic counseling when family planning is relevant, preferably before pregnancy	Individualized	Individualized
Consideration of allogeneic hematopoietic stem cell transplant (allo-HSCT)**	Individualized	Individualized

* Very little evidence-based data exist on the efficacy and benefit of surveillance in individuals with germline predisposition to MDS and AML, and published recommendations for surveillance are based on expert opinion.¹

** All patients of a suitable age who have developed myeloid neoplasms on the basis of a genetic predisposition, except those diagnosed with AML associated with germline variants in *CEBPA*, are potential candidates for allo-HSCT. Each case should be referred for discussion with an expert transplantation panel that may include international specialists in the field.

1. Baliakas P, Tesi B, Wartiovaara-Kautto U, Stray-Pedersen A, FriisL S, Dybedal I, Hovland R, Jahnukainen K, Raaschou-Jensen K, Ljungman P, Rustad CF, Lautrup CK, Kilpivaara O, Kittang AO, Grønbaek K, Cammenga J, Hellström-Lindberg E, Andersen MK. Nordic guidelines for germline predisposition to myeloidneoplasms in adults: Recommendations for genetic diagnosis, clinical management and follow-up. *HemaSphere*,2019;3:6. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6924562/>

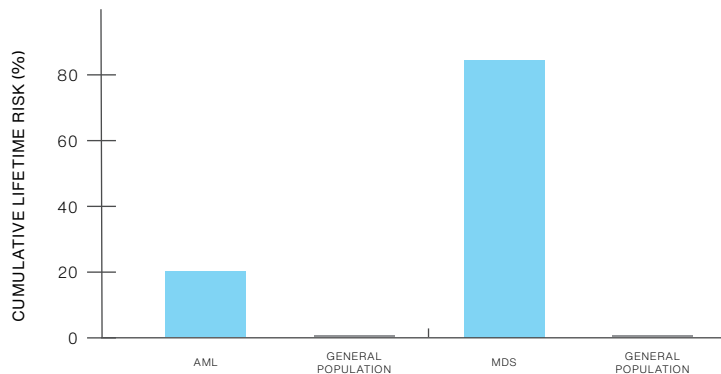
Understanding Your Positive *GATA2* Genetic Test Result

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

5 Things To Know

1	<i>GATA2</i> mutation	Your testing shows that you have a pathogenic mutation or a variant that is likely pathogenic in the <i>GATA2</i> gene. A <i>GATA2</i> mutation may be in a person's body from birth (germline mutation), or the mutation may have occurred at some point during a person's lifetime (somatic mutation).
2	<i>GATA2</i> deficiency	People with germline pathogenic or likely pathogenic <i>GATA2</i> mutations have <i>GATA2</i> deficiency.
3	Cancer risks and other medical concerns	<i>GATA2</i> deficiency causes problems with the immune system, making you more susceptible to infections. Other common features of <i>GATA2</i> deficiency include a type of lung disease called pulmonary alveolar proteinosis, excessive swelling (lymphedema), and a reduction in the number of blood cells. The reduction in blood cells can result in a condition called myelodysplastic syndrome (MDS), which can progress to acute myeloid leukemia (AML). However, <i>GATA2</i> deficiency can present with a wide variety of symptoms in many different parts of the body. Somatic <i>GATA2</i> mutations do not run in families and cannot be passed on to children; however, they may occur because of an active blood disorder such as leukemia. It is important to discuss your result in detail with your healthcare provider.
4	What you can do	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.
5	Family	Family members may also be at risk – they can be tested for the <i>GATA2</i> 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.

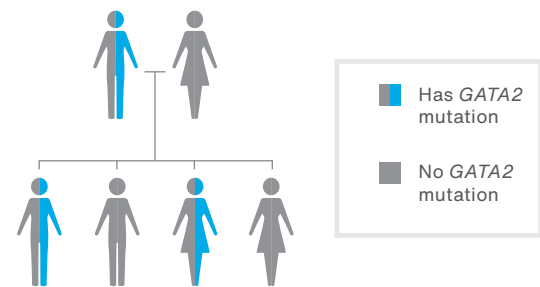
GATA2 Germline Mutation Lifetime Cancer Risks*



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

Germline *GATA2* Mutations in the Family

There is a 50/50 random chance to pass on a germline *GATA2* mutation to each of your children. The image below shows that everyone can carry and pass on these mutations, regardless of their sex at birth.



RESOURCES

- American Cancer Society [cancer.org](https://www.cancer.org)
- Genetic Alliance [geneticalliance.org](https://www.geneticalliance.org)
- National Organization for Rare Diseases (NORD) [rarediseases.org](https://www.rarediseases.org)
- National Society of Genetic Counselors [nsgc.org](https://www.nsgc.org)
- Canadian Society of Genetic Counsellors [cagc-accg.ca](https://www.cagc-accg.ca)

Please discuss this information with your healthcare provider. The cancer genetics field is continuously evolving, so updates related to your *GATA2* 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.