Genetic Insights: quick reference guide for healthcare providers

This guide is intended to facilitate a discussion between a provider and their patient.

Genetic Insights test results: ***ATM*-associated hereditary cancer**

Key results

A DNA variant associated with an increased risk of female breast cancer, pancreatic cancer, and possibly certain other cancers, was found in the *ATM* gene.[1-6]

Next steps

Clinical recommendations	Resources
Genetic Insights is a screening test and not intended for diagnosis. A follow-up genetic test should be performed in a clinical setting before any other action is taken.	**Ready to order?** Check with your institution and/or patient's insurance about the preferred testing laboratory. Blueprint Genetics® offers hereditary cancer testing. To confirm this test result, **targeted variant testing** for the variant identified is available. You can order a confirmation test here: Blueprint Genetics/TVT **Have questions?** Call **1.866.GENE.INFO** (1.866.436.3463) to speak to a specialized Quest genetic counselor or geneticist available to healthcare providers to discuss test selection and results.
Refer your patient to a genetic counselor specializing in hereditary cancer. *Genetic counselors can provide counseling on the implications of this test result and next steps for your patient.*	Your patient can schedule a 1-on-1 remote genetic counseling session through their online Genetic Insights Cancer Risk Report at no additional cost. To find a genetic counselor with expertise in hereditary cancer practicing in your patient's area for an in-person session, please visit FindAGeneticCounselor.NSGC.org

Patient conversation starters:

Patient conversation starters summarize the preceding information in plain language to support meaningful conversations between you and your patient.

FindAGeneticCounselor.NSGC.org

Your Genetic Insights test is a screening test. The next step is to have your result confirmed with a second genetic test.

It's also important that you talk with a genetic counselor. Genetic counselors are experts in genetics and can help you understand this result and potential next steps.

You can access a genetic counselor through your online Genetic Insights dashboard at no additional cost to you, and we can discuss a referral to a local genetic counselor.

Visit QuestDiagnostics.com/Genetic-Health-Screening for more information about this test.

What is *ATM*-associated hereditary cancer?

DNA variants in the *ATM* gene are associated with a higher lifetime risk of certain cancers, especially breast cancer in females and pancreatic cancer, often with an earlier age of onset than the general population.[7]

Emerging evidence suggests there may also be an increased risk for other cancer types such as colon, gastric, ovarian, and prostate cancers.[1]

However, cancer risks may vary based on family history, the specific DNA variant identified, and other factors.[7]

People with a confirmed *ATM* DNA variant are recommended to undergo more frequent cancer screening, typically starting at earlier ages than in the general population.[7]

See the Management options section for more detail.

Patient conversation starters:

People with a DNA variant in the *ATM* gene have a higher chance of developing certain cancers. For example, females with a DNA variant in this gene have a higher than typical chance of developing breast cancer. People may also have a higher chance of developing pancreatic cancer.

However not all people with a DNA variant in this gene will develop cancer.

People with this DNA variant should have cancer screenings earlier in life and more often than typical. This increases the chance that if cancer develops, it's detected as early as possible.

What this result means for family members

Family members may have the same DNA variant. The DNA variant was most likely inherited from a parent. Full siblings and children have a 50% chance of having this variant.

In people with a confirmed DNA variant in the *ATM* gene, cascade genetic testing for other family members 18 years and older may help inform their risks and screening protocols.[5-7] A genetic counselor can help determine the most appropriate testing options.

It is also important to note that if 2 people, each with 1 *ATM* variant, have children together, each child has a 1 in 4 chance of having a serious condition called ataxia-telengiectasia.[1]

Therefore, it is strongly recommended that people share their results with their biological relatives and reproductive partners.

Patient conversation starters:

DNA variants in the *ATM* gene can be inherited or passed down from parents to their children.

Your close relatives, like your parents, full siblings, and children, have a 50% (or 1 in 2) chance of having the same DNA variant. Other relatives might also have the same DNA variant.

Also, if 2 people who both have an *ATM* DNA variant have children together, then each of their children would have an increased chance (1 in 4) of having a serious but rare condition that affects the muscles and immune system.

Sharing these results with your family members and reproductive partners is important so they can decide if they want to have genetic testing.

Cancer risk

Select cancer risks in people with a confirmed *ATM* DNA variant are listed in this chart. However, research is ongoing to better understand the cancer types linked to variants in the *ATM* gene and the associated risks. Therefore, this risk information may change over time.

Cancer type	Approximate lifetime risk with a DNA variant in the *ATM* gene	Approximate lifetime risk in the general population
Assigned female at birth:		
Breast	Up to 40%[3,4]	13%[5]
Males and females:		
Pancreas	6%[2]	1.7%[6]

Management options

There are options for cancer risk management for people with a DNA variant in the *ATM* gene. Clinical guidelines from the National Comprehensive Cancer Network® (NCCN®) for people with a confirmed *ATM* DNA variant and no personal history of an associated cancer include[7]:

Cancer Type	Guidelines for people with 1 *ATM* DNA variant
Breast (assigned female at birth)	Annual mammogram starting at 40 years (or earlier based on family history) Consideration of breast MRI with contrast starting at age 30-35 years (or earlier based on family history) Discuss risk-reducing options based on family history
Ovarian	Discuss options based on family history
Pancreatic	Consider pancreatic cancer screening based on family history
Prostate	Unknown or insufficient evidence for screening or management beyond standard guidelines

Patient conversation starters:

It's recommended that people with a DNA variant in the ATM gene have cancer screenings earlier and more often than typical. This way, cancer is more likely to be caught in the early stages when it's most treatable.

If your test result is confirmed, it's important to work with the right specialists—like a medical oncologist and a geneticist—to find cancer screening and risk-reducing options that are right for you.

See NCCN for complete recommendations. Guidelines and recommendations may change over time.
If the test result is confirmed, local centers for excellence in hereditary cancer should be consulted for further clinical management.

Additional resources

The following advocacy groups have additional information and resources about *ATM*-associated hereditary cancer:

Facing Our Risk of Cancer Empowered (FORCE): FacingOurRisk.org
Foundation for Women's cancer: FoundationForWomensCancer.org
Susan B. Komen Foundation: Komen.org

References

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3. Lee AJ, Cunningham AP, Tischkowitz M, et al. Incorporating truncating variants in PALB2, CHEK2, and ATM into the BOADICEA breast cancer risk model. *Genet Med*. 2016;18(12):1190-1198. doi:10.1038/gim.2016.31
4. Marabelli M, Cheng SC, Parmigiani G. Penetrance of ATM gene mutations in breast cancer: a meta-analysis of different measures of risk. *Genet Epidemiol*. 2016;40(5):425- 431. doi:10.1002/gepi.21971
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6. National Cancer Institute. Cancer Stat Facts: Pancreatic Cancer. Accessed December 15, 2022. https://seer.cancer.gov/statfacts/html/pancreas.html
7. Network®. NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic (Version 3.2023). Accessed February 20, 2023. www.nccn.org