*Updated December 2019 (NCCN v1.2020)*

**_ATM_ Mutations**

*Cancer Risks and General Management Recommendations*

| Cancer Type | *ATM* Mutation Carrier Cancer Risks | General Population Lifetime Cancer Risks | Surveillance/Management Recommendations[1] |
|---|---|---|---|
| Female Breast[2-4] | 28%-38% | 12.4% | *Surveillance*<br>• Age 40 years: Annual mammogram with consideration of tomosynthesis; consider breast MRI with contrast<br>  ○ Age to initiate breast surveillance may be modified based on family history (typically 5-10 years earlier than the youngest breast cancer diagnosis in the family, but no later than age 40)<br>*Surgery*<br>• Insufficient evidence for risk-reducing mastectomy (RRM) based on *ATM* mutation status alone; management should be based on personal risk factors and family history<br>*Radiation Exposure*<br>• Individuals with two *ATM* mutations have Ataxia Telangiectasia and are very sensitive to radiation. However, it is not yet clear whether individuals who have one *ATM* mutation are more sensitive to radiation exposure and at what levels.[5-7]<br>• *ATM* mutation should not lead to a recommendation to avoid radiation therapy at this time. |
| Pancreas[8,9] | Increased | <1% | *Surveillance*<br>• Age 50 years: Consider surveillance using annual abdominal MRI/MRCP, EUS, and/or enrollment in research protocols for individuals with pancreatic cancer in ≥1 first- or second-degree relative from the same side of the family as the *ATM* mutation<br>  ○ Age to initiate pancreatic surveillance may be modified based on family history (10 years younger than the earliest diagnosis in the family)<br>  ○ In absence of a close family history of pancreatic cancer, no pancreatic screening is currently recommended |
| Prostate[2,6,8] | Unknown or insufficient evidence | 11.2% | *Surveillance*<br>• No consensus management guidelines<br>• Discuss family history and prostate cancer surveillance options (i.e., PSA, digital rectal exam) with a physician to determine an appropriate surveillance regimen<br>*Treatment*[10]<br>• Olaparib (Lynparza), a PARP inhibitor, is being evaluated for the treatment of metastatic, castration resistant prostate cancer in patients with an *ATM* mutation. However, the use of Olaparib for this indication is considered investigational at this time. Patients should speak with their treating physician for more information regarding Olaparib. |
| Ovary[11] | Potentially increased | 1.3% | • Insufficient evidence to recommend risk-reducing salpingo-oophorectomy (RRSO) based on ATM mutation status alone; |

| | | | |
|---|---|---|---|
| | | | management should be based on personal risk factors and family history. |

Other Cancer Risks: There may be other cancer risks associated with *ATM* mutations for which we do not yet have sufficient evidence to warrant intervention, including melanoma and cancers of the mouth, throat, thyroid, and uterus, as well as leukemias and lymphomas. Further research is needed to make conclusions about these cancer risks.[12,13]

*Implications for Family Members/Reproductive Considerations*

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the familial *ATM* mutation. Second-degree relatives (i.e., nieces/nephews, aunts/uncles, and grandparents) have a 25% chance to have the familial mutation.
- Rarely, individuals inherit two *ATM* mutations (one from each parent), and have Ataxia Telangiectasia (AT).
    - AT significantly effects childhood development, particularly motor control, and greatly increases the risk for multiple types of cancer.
    - *ATM* genetic testing for the partner of an individual with an *ATM* mutation may be appropriate to clarify the risk of having a child with AT.
- For carriers of a known mutation, assisted reproduction (with or without egg or sperm donation), pre-implantation genetic testing, and prenatal diagnosis options exist.
- All family members are encouraged to pursue genetic counseling to clarify their risks. Family members can visit www.FindAGeneticCounselor.com to find genetic services near them.

**References**


1. NCCN Clinical Practice Guidelines in Oncology®: Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Version 1.2020. 2019.
2. Ahmed M, Rahman N. ATM and breast cancer susceptibility. *Oncogene.* 2006;25(43):5906-5911.
3. Angele S, Falconer A, Edwards SM, et al. ATM polymorphisms as risk factors for prostate cancer development. *British journal of cancer.* 2004;91(4):783-787.
4. Bernstein JL, Teraoka S, Southey MC, et al. Population-based estimates of breast cancer risks associated with ATM gene variants c.7271T>G and c.1066-6T>G (IVS10-6T>G) from the Breast Cancer Family Registry. *Human mutation.* 2006;27(11):1122-1128.
5. Bernstein JL, Haile RW, Stovall M, et al. Radiation exposure, the ATM Gene, and contralateral breast cancer in the women's environmental cancer and radiation epidemiology study. *Journal of the National Cancer Institute.* 2010;102(7):475-483.
6. Concannon P, Haile RW, Borresen-Dale AL, et al. Variants in the ATM gene associated with a reduced risk of contralateral breast cancer. *Cancer research.* 2008;68(16):6486-6491.
7. Mao JH, Wu D, DelRosario R, Castellanos A, Balmain A, Perez-Losada J. Atm heterozygosity does not increase tumor susceptibility to ionizing radiation alone or in a p53 heterozygous background. *Oncogene.* 2008;27(51):6596-6600.
8. Roberts NJ, Jiao Y, Yu J, et al. ATM mutations in patients with hereditary pancreatic cancer. *Cancer discovery.* 2012;2(1):41-46.
9. Shindo K, Yu J, Suenaga M, et al. Deleterious Germline Mutations in Patients With Apparently Sporadic Pancreatic Adenocarcinoma. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2017;35(30):3382-3390.
10. Mateo J, Carreira S, Sandhu S, et al. DNA-Repair Defects and Olaparib in Metastatic Prostate Cancer. *The New England journal of medicine.* 2015;373(18):1697-1708.
11. Lilyquist J, LaDuca H, Polley E, et al. Frequency of mutations in a large series of clinically ascertained ovarian cancer cases tested on multi-gene panels compared to reference controls. *Gynecologic oncology.* 2017;147(2):375-380.

12. Dombernowsky SL, Weischer M, Allin KH, Bojesen SE, Tybjaerg-Hansen A, Nordestgaard BG. Risk of cancer by ATM missense mutations in the general population. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2008;26(18):3057-3062.
13. Paglia LL, Lauge A, Weber J, et al. ATM germline mutations in women with familial breast cancer and a relative with haematological malignancy. *Breast cancer research and treatment.* 2010;119(2):443-452.