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Variant: NM_000051.4:c.4389del

Version: 2.0

CA2695202151

3028907 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: 405e96c4-7187-482f-a56d-ec56ddb8e774
Approved on: 2024/2/26
Published on: 2025/9/15

HGVS expressions

NM_000051.4:c.4389del
NC_000011.10:g.108289754del
CM000673.2:g.108289754del
NC_000011.9:g.108160481del
CM000673.1:g.108160481del
NC_000011.8:g.107665691del
NG_009830.1:g.71923del
ENST00000452508.7:c.4389del
ENST00000713593.1:c.*3860del
ENST00000278616.9:c.4389del
ENST00000533733.6:n.1652del
ENST00000683174.1:n.4539del
ENST00000527805.6:c.4389del
ENST00000675595.1:c.4224del
ENST00000675843.1:c.4389del
ENST00000278616.8:c.4389del
ENST00000452508.6:c.4389del
ENST00000524792.5:n.604del
ENST00000531525.2:c.396del
ENST00000533733.5:n.818del
NM_000051.3:c.4389del
NM_001351834.1:c.4389del
NM_001351834.2:c.4389del

Pathogenic

Met criteria codes 4

PM3_Strong PM2_Supporting PM5_Supporting PVS1

Evidence Links 0

Expert Panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Hereditary Breast, Ovarian and Pancreatic Cancer Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ATM Version 1.2.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

The c.4389del p. Phe1463Leufs*10 variant in ATM is a frameshift variant in a biologically-relevant-exon predicted to cause a premature stop codon leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism. This alteration results in a termination codon upstream of the most C-terminus pathogenic alteration (ATM p.Arg3047*), as classified by the HBOP VCEP, and is expected to be more deleterious. This variant is absent from gnomAD v2.1.1. This variant has been detected in at least 1 individual with Ataxia-Telangiectasia (PMID: 26896183, 9463314). In summary, this variant meets criteria to be classified as pathogenic for autosomal dominant hereditary breast cancer and autosomal recessive Ataxia-Telangiectasia based on the ACMG/AMP criteria applied, as specified by the HBOP VCEP (PVS1, PM2_Supporting, PM3_Strong, PM5_supporting).

Met criteria codes

PM3_Strong	✔	4pts for confirmed in trans with a pathogenic variant, phenotype confident for one patient. This variant has been detected in at least 1 individual with Ataxia-Telangiectasia (PMID: 26896183, 9463314).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1.
PM5_Supporting	✔	This alteration results in a termination codon upstream of the most C-terminus pathogenic alteration (ATM p.Arg3047*), as classified by the HBOP VCEP, and is expected to be more deleterious.
PVS1	✔	The c.4389del p. Phe1463Leufs*10 variant in ATM is a frameshift variant in a biologically-relevant-exon predicted to cause a premature stop codon leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism.

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000051.4:c.4389del	Pathogenic	ATM-Related Cancer Predisposition	2025-09-15	2.0	ClinGen Hereditary Breast, Ovarian and Pancreatic Cancer Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ATM Version 1.2.0	ATM
View	NM_000051.4:c.4389del	Pathogenic	Hereditary Breast Cancer	2024-03-08	1.0	ClinGen Hereditary Breast, Ovarian and Pancreatic Cancer Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ATM Version 1.2.0	ATM

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