The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000051.4(ATM):c.467G>A (p.Trp156Ter)

Version: 1.0

CA382525484

634428 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: 1d59175c-fb11-4dcb-9edd-ffdccb9bd5b0
Approved on: 2025/9/25
Published on: 2025/10/20

HGVS expressions

NM_000051.4(ATM):c.467G>A (p.Trp156Ter)
NM_000051.4:c.467G>A
NC_000011.10:g.108235805G>A
CM000673.2:g.108235805G>A
NC_000011.9:g.108106532G>A
CM000673.1:g.108106532G>A
NC_000011.8:g.107611742G>A
NG_009830.1:g.17974G>A
ENST00000452508.7:c.467G>A
ENST00000713593.1:c.467G>A
ENST00000278616.9:c.467G>A
ENST00000682147.1:n.597G>A
ENST00000682430.1:n.566G>A
ENST00000682516.1:n.601G>A
ENST00000682956.1:n.601G>A
ENST00000683174.1:n.617G>A
ENST00000684029.1:c.467G>A
ENST00000684037.1:c.467G>A
ENST00000684061.1:n.601G>A
ENST00000684179.1:n.465+6482G>A
ENST00000527805.6:c.467G>A
ENST00000675595.1:c.331+6482G>A
ENST00000675843.1:c.467G>A
ENST00000278616.8:c.467G>A
ENST00000452508.6:c.467G>A
ENST00000527805.5:c.467G>A
ENST00000527891.5:c.331+6482G>A
ENST00000530958.5:c.467G>A
NM_000051.3:c.467G>A
NM_001351834.1:c.467G>A
NM_001351834.2:c.467G>A

Pathogenic

Met criteria codes 4

PM3_Strong PM5_Supporting PVS1 PM2_Supporting

Expert Panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

Not Met criteria codes 2

BP4 PP3

Evidence Links 0

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 1.3.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

The c.467G>A (p.Trp156*) variant in ATM gene is a nonsense variant predicted to cause premature stop codon in biologically-relevant-exon 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 (p.Arg3047*), as classified by the HBOP VCEP, and it is expected to be more deleterious. This variant has been detected in at least three unrelated individuals with Ataxia-Telangiectasia (PMIDs: 26896183, 34771661, 24954719). The highest population minor allele frequency in gnomAD v4.1.0 is 0.000001695 in the European (non-Finnish) population, which is lower than the HBOP threshold (≤0.00001) for PM2_Supporting, meeting this criterion. In summary, this variant meets criteria to be classified as pathogenic for autosomal dominant ATM-related cancer predisposition and autosomal recessive Ataxia-Telangiectasia based on the ACMG/AMP criteria applied as specified by the HBOP VCEP. (PVS1, PM5_Supporting, PM3_Strong, PM2_Supporting)

Met criteria codes

PM3_Strong	✔	This Variant has been detected in atleast 3 individuals with Ataxia-Telangiectasia CASE 1-Heterozygous with the pathogenic variant c.790delT -2 points (PMID:26896183)(Jackson et al.,) CASE 2- PMID: 34771661-Second variant unknown—1 point CASE 3- PMID: 24954719- Compound het c.1121_1122delAA(Established pathogenic)- 2 points TOTAL-5 points
PM5_Supporting	✔	The c.467G>A (p.Trp156Ter) variant 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 deleterious.
PVS1	✔	The c.467G>A (p.Trp156Ter) variant in ATM gene is a nonsense variant observed to cause premature truncation of the protein in exon 5/63 and is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism.
PM2_Supporting	✔	Allele count=1

Not Met criteria codes

BP4	✖	The computational splicing predictor SpliceAI gives a score of 0.38 for donor loss, supporting neither a deleterious nor benign impact on splicing. This does not impact PVS1 applied at full strength.
PP3	✖	The computational splicing predictor SpliceAI gives a score of 0.38 for donor loss, supporting neither a deleterious nor benign impact on splicing. This does not impact PVS1 applied at full strength.

Curation History

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