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Variant: NM_000051.4(ATM):c.1396C>T (p.Gln466Ter)

Version: 1.0

CA10579008

233553 (ClinVar)

Gene: ATM (HGNC:472)
Condition: ATM-related cancer predisposition (MONDO:0700270)
Inheritance Mode: Autosomal dominant inheritance
UUID: 88756329-6368-459a-b1e3-a90dc4a0673c
Approved on: 2024-11-26
Published on: 2025-01-13

HGVS expressions

NM_000051.4:c.1396C>T
NM_000051.4(ATM):c.1396C>T (p.Gln466Ter)
NC_000011.10:g.108250861C>T
CM000673.2:g.108250861C>T
NC_000011.9:g.108121588C>T
CM000673.1:g.108121588C>T
NC_000011.8:g.107626798C>T
NG_009830.1:g.33030C>T
ENST00000452508.7:c.1396C>T
ENST00000713593.1:c.*867C>T
ENST00000278616.9:c.1396C>T
ENST00000682516.1:n.1530C>T
ENST00000682956.1:n.1530C>T
ENST00000683174.1:n.1546C>T
ENST00000683605.1:n.891C>T
ENST00000684037.1:c.*331C>T
ENST00000684061.1:n.1530C>T
ENST00000684179.1:n.1365C>T
ENST00000527805.6:c.1396C>T
ENST00000675595.1:c.1231C>T
ENST00000675843.1:c.1396C>T
ENST00000278616.8:c.1396C>T
ENST00000452508.6:c.1396C>T
ENST00000527805.5:c.1396C>T
NM_000051.3:c.1396C>T
NM_001351834.1:c.1396C>T
NM_001351834.2:c.1396C>T

Pathogenic

Met criteria codes 4

PM2_Supporting PM5_Supporting PM3_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 1.3.0

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

The c.1396C>T (p.Gln466*) variant in ATM is a nonsense 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 was observed in at least 1 individual with Ataxia-Telangiectasia (PMID: 26896183). This variant is absent from gnomAD v2.1.1. 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 Variant Curation Expert Panel. (PVS1, PM5_Supporting, PM3_Supporting, PM2_Supporting)

Met criteria codes

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 (p.Arg3047*)
PM3_Supporting	✔	This variant was also observed in the compound heterozygous state in an individual with ataxia-telangiectasia.
PVS1	✔	This variant in ATM is a nonsense variant 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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