Variant: NM_000020.3(ACVRL1):c.266G>T (p.Cys89Phe)

Version: 1.0

CA16614039

411299 (ClinVar)

Gene: ACVRL1 (HGNC:94)
Condition: telangiectasia, hereditary hemorrhagic, type 2 (MONDO:0010880)
Inheritance Mode: Autosomal dominant inheritance
UUID: e4ccd4ed-4ede-45cb-a924-70d21d029687
Approved on: 2025-12-12
Published on: 2025-12-28

HGVS expressions

NM_000020.3:c.266G>T
NM_000020.3(ACVRL1):c.266G>T (p.Cys89Phe)
NC_000012.12:g.51913303G>T
CM000674.2:g.51913303G>T
NC_000012.11:g.52307087G>T
CM000674.1:g.52307087G>T
NC_000012.10:g.50593354G>T
NG_009549.1:g.10886G>T
ENST00000547400.6:c.308G>T
ENST00000551576.6:c.266G>T
ENST00000552678.2:c.266G>T
ENST00000388922.9:c.266G>T
ENST00000388922.8:c.266G>T
ENST00000419526.6:c.103+768G>T
ENST00000547400.5:c.308G>T
ENST00000550683.5:c.308G>T
ENST00000551576.5:c.266G>T
NM_000020.2:c.266G>T
NM_001077401.1:c.266G>T
NM_001077401.2:c.266G>T

Likely Pathogenic

Met criteria codes 4

PP3 PM2_Supporting PS4_Supporting PM5_Strong

Evidence Links 0

Expert Panel

Hereditary Hemorrhagic Telangiectasia VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Hereditary Hemorrhagic Telangiectasia Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ACVRL1 Version 1.1.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hereditary Hemorrhagic Telangiectasia VCEP

The NM_000020.3: c.266G>T variant in ACVRL1 is a missense variant predicted to cause substitution of cysteine by phenylalanine at amino acid 89 (p.Cys89Phe). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). This variant has been reported in 2 probands with a phenotype consistent with Hereditary Hemorrhagic Telangiectasia (PS4_Supporting, Internal lab contributors). The computational predictor REVEL gives a score of 0.899, which is above the threshold used for predicting a damaging impact on ACVRL1 function (PP3). Other missense variants, c.265T>A (p.Cys89Ser), c.265T>G (p.Cys89Gly), c.265T>C (p.Cys89Arg), and c.267C>G (p.Cys89Trp) in the same codon have been classified as likely pathogenic/pathogenic for Hereditary Hemorrhagic Telangiectasia by the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel rules (PM5_Strong). In summary, this variant meets the criteria to be classified as a variant of uncertain significance for autosomal dominant hereditary hemorrhagic telangiectasia based on the ACMG/AMP criteria applied, as specified by the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Exper Panel. Approved by Expert Panel: 12/12/2025. Evidence used: PM5_Strong, PS4_supporting, PM2_Supporting, and PP3 (specification version 1.1.0; 12/12/2025).

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.899, which is above the threshold used for predicting a damaging impact on ACVRL1 function (PP3).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PS4_Supporting	✔	This variant has been reported in 2 probands with a phenotype consistent with Hereditary Hemorrhagic Telangiectasia (PS4_Supporting, Internal lab contributors).
PM5_Strong	✔	Other missense variants, c.265T>A (p.Cys89Ser), c.265T>G (p.Cys89Gly), c.265T>C (p.Cys89Arg), and c.267C>G (p.Cys89Trp) in the same codon have been classified as likely pathogenic/pathogenic for Hereditary Hemorrhagic Telangiectasia by the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel rules (PM5_Strong).

Curation History

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