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Variant: NM_000020.3(ACVRL1):c.293A>G (p.Asn98Ser)

Version: 1.0

CA384898102

426011 (ClinVar)

Gene: ACVRL1 (HGNC:94)
Condition: telangiectasia, hereditary hemorrhagic, type 2 (MONDO:0010880)
Inheritance Mode: Autosomal dominant inheritance
UUID: ccc50676-c1fa-40ab-a808-bc0676b7e7de
Approved on: 2025/12/12
Published on: 2025/12/28

HGVS expressions

NM_000020.3:c.293A>G
NM_000020.3(ACVRL1):c.293A>G (p.Asn98Ser)
NC_000012.12:g.51913330A>G
CM000674.2:g.51913330A>G
NC_000012.11:g.52307114A>G
CM000674.1:g.52307114A>G
NC_000012.10:g.50593381A>G
NG_009549.1:g.10913A>G
ENST00000547400.6:c.335A>G
ENST00000551576.6:c.293A>G
ENST00000552678.2:c.293A>G
ENST00000388922.9:c.293A>G
ENST00000388922.8:c.293A>G
ENST00000419526.6:c.103+795A>G
ENST00000547400.5:c.335A>G
ENST00000550683.5:c.335A>G
NM_000020.2:c.293A>G
NM_001077401.1:c.293A>G
NM_001077401.2:c.293A>G

Likely Pathogenic

Met criteria codes 3

PS4 PM2_Supporting PS3_Supporting

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.293A>G variant in ACVRL1 is a missense variant predicted to cause substitution of asparagine by serine at amino acid 98 (p.Asn98Ser). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). The computational predictor REVEL gives a score of 0.508, which is neither above nor below the thresholds predicting a damaging or benign impact on ACVRL1 function. Functional assays showed the variant protein to be non-functional (PS3_Supporting; Internal lab contributors). This variant has been reported in 5 probands with a phenotype consistent with HHT (PS4_Strong; PMIDs: 16690726, 18498373, Internal lab contributors). In summary, this variant meets the criteria to be classified as Likely Pathogenic for autosomal dominant hereditary hemorrhagic telangiectasia based on the ACMG/AMP criteria applied, as specified by the ClinGen Hereditary Hemorrhagic Telangiectasia Variant Curation Expert Panel. Approved by Expert Panel:12/12/2025. Evidence used: PS4_Strong, PM2_Supporting, PS3_Supporting (specification version 1.1.0; 12/12/2025).

Met criteria codes

PS4	✔	This variant has been reported in 5 probands with a phenotype consistent with HHT (PS4_Strong; PMIDs: 16690726, 18498373, Internal lab contributors).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PS3_Supporting	✔	Functional assays showed the variant protein to be non-functional (PS3_Supporting; Internal lab contributors).

Curation History

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