

Variant: *NM_001114753.3(ENG):c.1319T>G (p.Val440Gly)*

Version: 1.0

CA374977914 [↗](#)

528065 (ClinVar) [↗](#)

Gene: ENG ([HGNC:2022](#))

Condition: telangiectasia, hereditary hemorrhagic, type 1
([MONDO:0008535](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: c8cc47f6-4fbb-491f-94e4-4ea9bffa1b71

Approved on: 2024/11/12

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HGVS expressions

NM_001114753.3:c.1319T>G

NM_001114753.3(ENG):c.1319T>G (p.Val440Gly)

NC_000009.12:g.127818825A>C

CM000671.2:g.127818825A>C

NC_000009.11:g.130581104A>C

CM000671.1:g.130581104A>C

NC_000009.10:g.129620925A>C

NG_009551.1:g.40944T>G

ENST00000480266.6:c.773T>G

ENST00000373203.9:c.1319T>G

ENST00000344849.4:c.1319T>G

ENST00000373203.8:c.1319T>G

ENST00000480266.5:c.773T>G

NM_000118.3:c.1319T>G

NM_001114753.2:c.1319T>G

NM_001278138.1:c.773T>G

NR_136302.1:n.1568+114A>C

NM_001278138.2:c.773T>G

Likely Pathogenic

Met criteria codes **4**

PP1_Strong

PP4_Moderate

PS4_Moderate

PM2_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 ENG Version 1.1.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Hereditary Hemorrhagic Telangiectasia VCEP

The NM_001114753.3: c.1319T>G variant in ENG is a missense variant predicted to cause substitution of valine by glycine at amino acid 440 (p.Val440Gly). This variant has been reported in more than 2 probands with a phenotype consistent with HHT (PS4_Moderate; Internal lab contributors). At least one patient's phenotype meets Curacao Criteria for HHT, and sequencing and large deletion/duplication analysis was performed for ENG and ACVRL1, which is highly specific for HHT (PP4_Moderate; Internal lab contributors). The variant has been reported to segregate with Hereditary Hemorrhagic Telangiectasia in 5 affected meioses from 1 family (PP1_Strong; Internal lab contributors). This variant is absent from gnomAD v.2.1.1 (PM2_Supporting). The computational predictor REVEL gives a score of 0.385, which is neither above nor below the thresholds predicting a damaging or benign impact on ENG function. 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: PP1_Strong, PS4_Moderate, PP4_Moderate, PM2_Supporting (specifications version 1.1.0; 11/12/2024).

Met criteria codes

PP1_Strong			The variant has been reported to segregate with Hereditary Hemorrhagic Telangiectasia in 5 affected meioses from 1 family (PP1_Strong;Internal lab contributors).
PP4_Moderate			At least one patient's phenotype meets Curacao Criteria for HHT, and sequencing and large deletion/duplication analysis was performed for ENG and ACVRL1, which is highly specific for HHT (PP4_Moderate; Internal lab contributors).
PS4_Moderate			This variant has been reported in more than 2 probands with a phenotype consistent with HHT (PS4_Moderate; Internal lab contributors).
PM2_Supporting			This variant is absent from gnomAD v.2.1.1 (PM2_Supporting).

Curation History

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