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_000018.4(ACADVL):c.1153C>T (p.Arg385Trp)

Version: 1.1

CA239438

193786 (ClinVar)

Gene: ACADVL (HGNC:37)
Condition: very long chain acyl-CoA dehydrogenase deficiency (MONDO:0008723)
Inheritance Mode: Autosomal recessive inheritance
UUID: c0051ae4-c173-42f5-9416-90f68e29222d
Approved on: 2026/1/21
Published on: 2026/1/21

HGVS expressions

NM_000018.4(ACADVL):c.1153C>T (p.Arg385Trp)
NM_000018.4:c.1153C>T
NC_000017.11:g.7223208C>T
CM000679.2:g.7223208C>T
NC_000017.10:g.7126527C>T
CM000679.1:g.7126527C>T
NC_000017.9:g.7067251C>T
NG_007975.1:g.8375C>T
NG_008391.2:g.1843G>A
ENST00000356839.10:c.1153C>T
ENST00000322910.9:c.*1108C>T
ENST00000350303.9:c.1087C>T
ENST00000356839.9:c.1153C>T
ENST00000542255.6:c.11C>T
ENST00000543245.6:c.1222C>T
ENST00000578579.2:n.102C>T
ENST00000578824.5:n.569C>T
ENST00000579425.5:n.177C>T
ENST00000582379.1:n.804C>T
ENST00000583858.5:c.182C>T
ENST00000585203.6:n.361C>T
NM_000018.3:c.1153C>T
NM_001033859.2:c.1087C>T
NM_001270447.1:c.1222C>T
NM_001270448.1:c.925C>T
NM_001033859.3:c.1087C>T
NM_001270447.2:c.1222C>T
NM_001270448.2:c.925C>T

Likely Pathogenic

Met criteria codes 4

PM3 PM2_Supporting PP3 PP4_Moderate

Evidence Links 0

Expert Panel

ACADVL VCEP

Criteria Specification Information

Criteria Specification: *ClinGen ACADVL Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ACADVL Version 2.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ACADVL VCEP

The c.1153C>T (NM_000018.4) variant in ACADVL is a missense variant predicted to cause substitution of arginine by tryptophan at amino acid (p.385). The highest population minor allele frequency in gnomAD v4.1 is 0.00015 in the Admixed American population, which is lower than the ClinGen ACADVL Variant Curation Expert Panel threshold (<0.001) for PM2_Supporting, meeting this criterion (PM2_Supporting). The computational predictor REVEL gives a score of 0.91, which is above the threshold of 0.75, evidence that correlates with impact to ACADVL function (PP3). This variant has been detected in at least 6 individuals with very long chain acyl CoA dehydrogenase (VLCAD) deficiency. Of those individuals, 2 were compound heterozygous for the variant and distinct pathogenic or likely pathogenic variant and 1 of those were confirmed in trans by parental/family testing, other methods. No individuals were homozygous for the variant (PM3 points: 1.25) (PMID: 33150772, 28755359, 32655480, 15210884, 25655073, 16488171) (PM3). Four patients compound heterozygous for the variant and distinct pathogenic or likely pathogenic variant displayed increased C14:1 Levels (PMID: 25655073), or reduced enzyme levels to 0.69 C16/C8 (PMID: 15210884), below detection rate (PMID: 28755359), and 19.3% (PMID: 33150772) respectively, which is highly specific for VLCAD deficiency (PP4_Moderate). In summary, this variant meets the criteria to be classified as likely pathogenic for autosomal recessive very long chain acyl-CoA dehydrogenase (VLCAD) deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen ACADVL Variant Curation Expert Panel: PM3 _Moderate, PP4_Moderate, PM2_Supporting, PP3. (ACADVL VCEP Specifications Version 1; Approved November 8, 2021)

Met criteria codes

PM3	✔	This variant has been detected in at least 6 individuals with very long chain acyl CoA dehydrogenase (VLCAD) deficiency. Of those individuals, 2 were compound heterozygous for the variant and distinct pathogenic or likely pathogenic variant and 1 of those were confirmed in trans by parental/family testing, other methods. No individuals were homozygous for the variant (PM3 points: 1.25) (PMID: 33150772, 28755359, 32655480, 15210884, 25655073, 16488171) (PM3)
PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v4.1 is 0.00015 in the Admixed American population, which is lower than the ClinGen ACADVL Variant Curation Expert Panel threshold (<0.001) for PM2_Supporting, meeting this criterion (PM2_Supporting).
PP3	✔	The computational predictor REVEL gives a score of 0.91, which is above the threshold of 0.75, evidence that correlates with impact to ACADVL function (PP3).
PP4_Moderate	✔	Four patients compound heterozygous for the variant and distinct pathogenic or likely pathogenic variant displayed increased C14:1 Levels (PMID: 25655073), or reduced enzyme levels to 0.69 C16/C8 (PMID: 15210884), below detection rate (PMID: 28755359), and 19.3% (PMID: 33150772) respectively, which is highly specific for VLCAD deficiency (PP4_Moderate)

Curation History

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