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Variant: NM_000018.4(ACADVL):c.956C>A (p.Ser319Ter)

Version: 1.0

CA8337912

557676 (ClinVar)

Gene: ACADVL (HGNC:37)
Condition: very long chain acyl-CoA dehydrogenase deficiency (MONDO:0008723)
Inheritance Mode: Autosomal recessive inheritance
UUID: 9ddd44b9-b03b-41f5-89a3-9356428a1807
Approved on: 2024/5/14
Published on: 2024/5/16

HGVS expressions

NM_000018.4:c.956C>A
NM_000018.4(ACADVL):c.956C>A (p.Ser319Ter)
NC_000017.11:g.7222744C>A
CM000679.2:g.7222744C>A
NC_000017.10:g.7126063C>A
CM000679.1:g.7126063C>A
NC_000017.9:g.7066787C>A
NG_007975.1:g.7911C>A
NG_008391.2:g.2307G>T
ENST00000356839.10:c.956C>A
ENST00000322910.9:c.*911C>A
ENST00000350303.9:c.890C>A
ENST00000356839.9:c.956C>A
ENST00000543245.6:c.1025C>A
ENST00000578824.5:n.105C>A
ENST00000581378.5:c.674C>A
ENST00000582379.1:n.340C>A
NM_000018.3:c.956C>A
NM_001033859.2:c.890C>A
NM_001270447.1:c.1025C>A
NM_001270448.1:c.728C>A
NM_001033859.3:c.890C>A
NM_001270447.2:c.1025C>A
NM_001270448.2:c.728C>A

Pathogenic

Met criteria codes 3

PVS1 PM2_Supporting PP4

Evidence Links 0

Expert Panel

ACADVL VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ACADVL VCEP

The c.956C>A (p.Ser319Ter)(NM_000018.3) variant in ACADVL is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 10/20 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1; PMIDs 9973285, 11590124). At least one patient with this variant displayed NBS and follow-up data, which is highly specific for VLCAD deficiency (PP4_supporting, PMID: 27209629). The highest population minor allele frequency in gnomAD v2.1.1 is 0.00006 in the African population, which is lower than the ClinGen ACADVL Variant Curation Expert Panel threshold (<0.001) for PM2_Supporting, meeting this criterion (PM2_Supporting). In summary, this variant meets the criteria to be classified as 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: PVS1, PP4_supporting, PM2_supporting (ACADVL VCEP specifications version 1; approved November 9, 2021).

Met criteria codes

PVS1	✔	Premature stop codon exon 10 of 20.
PM2_Supporting	✔	gnomAD v2.1.1 is 0.00006 in the African population
PP4	✔	NBS C14:1 Levels from >0.8 µM

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000018.4(ACADVL):c.956C>A (p.S...	Pathogenic	Very Long Chain Acyl-CoA Dehydrogenase Deficiency	2024-05-16	1.0	-	ACADVL

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