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Variant: NM_000018.4(ACADVL):c.1039del (p.Ala347fs)

Version: 1.0

CA1139665145

932848 (ClinVar)

Gene: ACADVL (HGNC:37)
Condition: very long chain acyl-CoA dehydrogenase deficiency (MONDO:0008723)
Inheritance Mode: Autosomal recessive inheritance
UUID: fc2ee444-91dd-4d44-9da2-235a16a4ffb6
Approved on: 2022/9/22
Published on: 2022/9/22

HGVS expressions

NM_000018.4:c.1039del
NM_000018.4(ACADVL):c.1039del (p.Ala347fs)
NC_000017.11:g.7222827del
CM000679.2:g.7222827del
NC_000017.10:g.7126146del
CM000679.1:g.7126146del
NC_000017.9:g.7066870del
NG_007975.1:g.7994del
NG_008391.2:g.2225del
ENST00000356839.10:c.1039del
ENST00000322910.9:c.*994del
ENST00000350303.9:c.973del
ENST00000356839.9:c.1039del
ENST00000543245.6:c.1108del
ENST00000578824.5:n.188del
ENST00000582379.1:n.423del
ENST00000583858.5:c.68del
NM_000018.3:c.1039del
NM_001033859.2:c.973del
NM_001270447.1:c.1108del
NM_001270448.1:c.811del
NM_001033859.3:c.973del
NM_001270447.2:c.1108del
NM_001270448.2:c.811del

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

Not Met criteria codes 2

PM3 PP4

Evidence Links 0

Expert Panel

ACADVL VCEP

Criteria Specification Information

Criteria Specification: *ClinGen ACADVL Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 1*
PDF
Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ACADVL VCEP

The c.1039del (p.Ala347Profs*6) variant in ACADVL is a frameshift 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). This variant has been detected in one individual identified by abnormal newborn screening or presumed positive on newborn screening for very long chain acyl CoA dehydrogenase (VLCAD) deficiency with no reported follow-up plasma acylcarnitine or enzyme activity; a second distinct pathogenic or likely pathogenic variant in ACADVL was not reported in this individual (PMID: 26385305). To our knowledge, functional assays have not been reported for this variant. This variant is absent from gnomAD 2.1.1 (PM2_Supporting). 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: PVS1, PM2_Supporting (ClinGen ACADVL VCEP specifications version#1; 07-03-2022).

Met criteria codes

PVS1	✔	PVS1 is met. The c.1039del (p.Ala347Profs*6) variant in ACADVL is a frameshift 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).
PM2_Supporting	✔	PM2_Supporting is met. This variant is absent from gnomAD 2.1.1 (PM2_Supporting).

Not Met criteria codes

PM3	✖	PM3 is not met at any strength. This variant has been detected in one individual identified by abnormal newborn screening or presumed positive on newborn screening for very long chain acyl CoA dehydrogenase (VLCAD) deficiency with no reported follow-up plasma acylcarnitine or enzyme activity; a second distinct pathogenic or likely pathogenic variant in ACADVL was not reported in this individual (PMID: 26385305).
PP4	✖	PP4 is not met at any strength. This variant has been detected in one individual identified by abnormal newborn screening or presumed positive on newborn screening for very long chain acyl CoA dehydrogenase (VLCAD) deficiency with no reported follow-up plasma acylcarnitine or enzyme activity individual (PMID: 26385305).

Curation History

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