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_004360.5(CDH1):c.1746dup (p.Leu583fs)

Version: 2.0

CA645369677

428629 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: d32a3080-b708-4479-87cd-50fd1bc4f1e9
Approved on: 2023/8/4
Published on: 2023/8/4

HGVS expressions

NM_004360.5:c.1746dup
NM_004360.5(CDH1):c.1746dup (p.Leu583fs)
NC_000016.10:g.68822035dup
CM000678.2:g.68822035dup
NC_000016.9:g.68855938dup
CM000678.1:g.68855938dup
NC_000016.8:g.67413439dup
NG_008021.1:g.89744dup
ENST00000261769.10:c.1746dup
ENST00000261769.9:c.1746dup
ENST00000422392.6:c.1563dup
ENST00000562836.5:n.1817dup
ENST00000566510.5:c.*412dup
ENST00000566612.5:c.1600dup
ENST00000611625.4:c.1809dup
ENST00000612417.4:c.1746dup
ENST00000621016.4:c.1746dup
NM_004360.3:c.1746dup
NM_001317184.1:c.1563dup
NM_001317185.1:c.198dup
NM_001317186.1:c.-220dup
NM_004360.4:c.1746dup
NM_001317184.2:c.1563dup
NM_001317185.2:c.198dup
NM_001317186.2:c.-220dup

Pathogenic

Met criteria codes 3

PM2_Supporting PVS1 PM5_Supporting

Not Met criteria codes 23

BA1 PP1 PP2 PP3 PP4 PM6 PM1 PM3 PM4 BS1 BS4 BS3 BS2 PS1 PS2 PS3

Expert Panel

CDH1 VCEP

Criteria Specification Information

Criteria Specification: *ClinGen CDH1 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 3.1*
Criteria Specification Approval History

PS4 BP5 BP7 BP4 BP3 BP1 BP2

Criteria Specifications for this VCEP

Evidence Links 0

Evidence submitted by expert panel

CDH1 VCEP

The c.1746dup p.(Leu583fs) variant is predicted to result in a premature stop codon that leads to nonsense mediate decay (PVS1 and PM5_supporting). The variant is absent in the gnomAD cohort (PM2_supporting; http://gnomad.broadinstitute.org). Therefore, this variant meets criteria to be classified as pathogenic based on the ACMG/AMP criteria applied as specified by the CDH1 Variant Curation Expert Panel (CDH1 VCEP specifications version 3.1): PVS1, PM2_supporting, PM5_supporting.

Met criteria codes

PM2_Supporting	✔	Absent in population databases.
PVS1	✔	Exon 12 of 16, predicted NMD.
PM5_Supporting	✔	Exon 12 of 16, predicted NMD.

Not Met criteria codes

BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PM3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4	ℹ	✖	SCV000778897.2 (GeneDx) - 2 cases gastric cancer but no pathology. SCV000580707.3 (Ambry) - does not meet clinical criteria. PMID: 28152038 (Ambry internal data, Aliso Viejo, CA)
BP5	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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