

Variant: *NM_004360.5(CDH1):c.1137+2T>C*

Version: 2.1

CA194301 [↗](#)

186267 (ClinVar) [↗](#)

Gene: CDH1 ([HGNC:999](#))

Condition: CDH1-related diffuse gastric and lobular breast cancer ([MONDO:0100488](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: b74cbc6f-6e60-4c2e-a118-4341cfa4777f

Approved on: 2023-10-23

Published on: 2023-11-10

HGVS expressions

NM_004360.5:c.1137+2T>C

NM_004360.5(CDH1):c.1137+2T>C

NC_000016.10:g.68812265T>C

CM000678.2:g.68812265T>C

NC_000016.9:g.68846168T>C

CM000678.1:g.68846168T>C

NC_000016.8:g.67403669T>C

NG_008021.1:g.79974T>C

ENST00000261769.10:c.1137+2T>C

ENST00000261769.9:c.1137+2T>C

ENST00000422392.6:c.1137+2T>C

ENST00000562836.5:n.1208+2T>C

ENST00000565810.1:n.181+2T>C

ENST00000566510.5:c.981+2T>C

ENST00000566612.5:c.1137+2T>C

ENST00000611625.4:c.1137+2T>C

ENST00000612417.4:c.1137+2T>C

ENST00000621016.4:c.1137+2T>C

NM_004360.3:c.1137+2T>C

NM_001317184.1:c.1137+2T>C

NM_001317185.1:c.-479+2T>C

NM_001317186.1:c.-683+2T>C

NM_004360.4:c.1137+2T>C

NM_001317184.2:c.1137+2T>C

NM_001317185.2:c.-479+2T>C

NM_001317186.2:c.-683+2T>C

Likely Pathogenic

Met criteria codes 4

PS4_Supporting PM5_Supporting

PVS1_Strong PM2_Supporting

Not Met criteria codes 22

PS1 PS2 PS3 BA1 PP1 PP2

PP3 PP4 PM6 PM1 PM3

Expert Panel

Criteria Specification Information

[↗](#) **Criteria Specification:** *ClinGen CDH1 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 3.1*

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

[PM4](#) [BS1](#) [BS4](#) [BS3](#) [BS2](#)
[BP5](#) [BP7](#) [BP4](#) [BP3](#) [BP1](#) [BP2](#)

[Criteria Specifications for this VCEP](#)









Evidence Links 2

Evidence submitted by expert panel
















CDH1 VCEP

This c.1137+2T>C variant occurs at the canonical donor splice site of exon 8 (PVS1_strong, PM5_Supporting). This variant is absent from populations in gnomAD (PM2_Supporting; <http://gnomad.broadinstitute.org>) and has been observed in at least one individual meeting IGCLC criteria for HDGC (PS4_supporting; internal laboratory data). In summary, this variant meets criteria to be classified as likely pathogenic based on ACMG/AMP criteria applied as specified by the CDH1 Variant Curation Expert Panel: PVS1_strong, PM2_Supporting, PS4_supporting, PM5_Supporting (Variant Interpretation Guidelines Version 3.1).

Met criteria codes

PS4_Supporting			This variant was observed in an individual with DGC in 30s (Invitae). This variant has also been reported in an individual with IDC at 43 years and first-degree relative with gastric cancer of unknown histology, but whose family does not meet IGCLC criteria for HDGC (SCV000216580.4; PMID: 31296550).
PM5_Supporting			Apply PM5_Supporting to the variant with the alteration at canonical splicing site.
PVS1_Strong			This variant occurs at the canonical splice donor site of exon 8.
PM2_Supporting			This variant is absent from gnomAD.

Not Met criteria codes

PS1			PS1 does not apply to this variant.
PS2			To our knowledge, this variant has not been reported as de novo.
PS3			To our knowledge, this variant has not been assessed for splicing defects in vitro. Abnormal splicing has been observed associated with the CDH1 c.1137G>A allele. PubMed:15831593 Abnormal splicing has been observed associated with the CDH1 c.1137+1delG allele. PubMed:31642931
BA1			This variant is absent from gnomAD.
PP1			To our knowledge, segregation of this variant has not been reported.
PP2			PP2 does not apply to CDH1.
PP3			PP3 does not apply to this variant.
PP4			PP4 does not apply to CDH1.
PM6			To our knowledge, this variant has not been reported as de novo.

PM1			PM1 does not apply to CDH1.
PM3			PM3 does not apply to CDH1.
PM4			PM4 does not apply to this variant.
BS1			This variant is absent from gnomAD.
BS4			To our knowledge, segregation of this variant has not been reported.
BS3			To our knowledge, this variant has not been assessed for splicing defects in vitro. <hr/> Abnormal splicing has been observed associated with the CDH1 c.1137G>A allele. PubMed:15831593 Abnormal splicing has been observed associated with the CDH1 c.1137+1delG allele. PubMed:31642931
BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5			To our knowledge, this variant has not been found in a case with an alternate molecular basis for disease.
BP7			BP7 does not apply to this variant.
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3			BP3 does not apply to CDH1.
BP1			BP1 does not apply to CDH1.
BP2			To our knowledge, this variant has not been observed in cis or trans with a pathogenic variant.

Curation History [↗](#)

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