

Variant: *NM_004360.4(CDH1):c.187C>T (p.Arg63Ter)*

156496 (ClinVar) [↗](#)

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

Condition: CDH1-related diffuse gastric and lobular breast cancer ([MONDO:0007648](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: be4384f2-4317-4809-956c-12533c2847e1

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HGVS expressions

NM_004360.4(CDH1):c.187C>T (p.Arg63Ter)

NM_004360.4:c.187C>T

NM_004360.5(CDH1):c.187C>T (p.Arg63Ter)

Pathogenic

Met criteria codes **4**

PM2_Supporting

PS4_Supporting

PM5_Supporting

PVS1

Not Met criteria codes **22**

BA1

BP3

BP1

BP4

BP2

BP7

BP5

BS2

BS4

BS3

BS1

PP2

PP3

PP1

PP4

PS1

PS2

PS3

PM6

PM4

PM3

PM1

Evidence Links **1**

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**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

CDH1 VCEP

The c.187C>T (p.Arg63*) variant is predicted to result in a premature stop codon that leads to a truncated or absent protein (PVS1, PM5_Supporting). This variant is absent in the gnomAD cohort (PM2_Supporting; <http://gnomad.broadinstitute.org>). The variant has been reported in at least one family meeting HDGC clinical criteria (PS4_Supporting; PMID: 9751616). In summary, 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 (Variant Interpretation Guidelines Version 3.1): PVS1, PM2_Supporting, PS4_Supporting, PM5_Supporting.

Met criteria codes

PM2_Supporting



Absent from gnomAD

PS4_Supporting			Observed in an individual with bilateral LBC at 39yo. Father DGC at 47 (not known if carrier), brother DGC at 39yo (not known if carrier), sister DGC at 44yo (not known if carrier), Paternal Aunt breast in 60s. From excel document. Used PMID: 9751616 only for PS4_Supporting code.
			Variant identified in father and son with gastric cancer. PubMed:9751616 
PM5_Supporting			Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.
PVS1			Truncating variant in Exon 3 of 16.

Not Met criteria codes

BA1			Absent from gnomAD
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
BP4			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
BP7			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			Absent from gnomAD

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
PP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4		✖	Observed in an individual with bilateral LBC at 39yo. Father DGC at 47 (not known if carrier), brother DGC at 39yo (not known if carrier), sister DGC at 44yo (not known if carrier), Paternal Aunt breast in 60s. Excel document.
PS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3		✖	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
PM4		✖	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
PM1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 



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