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_004360.4(CDH1):c.59G>A (p.Trp20Ter)

Version: 2.0

CA280996

12239 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: 7421ee61-7174-481d-b6bd-1800d58e9755
Approved on: 2023/8/29
Published on: 2023/8/29

HGVS expressions

NM_004360.4:c.59G>A
NM_004360.4(CDH1):c.59G>A (p.Trp20Ter)
NC_000016.10:g.68738307G>A
CM000678.2:g.68738307G>A
NC_000016.9:g.68772210G>A
CM000678.1:g.68772210G>A
NC_000016.8:g.67329711G>A
NG_008021.1:g.6016G>A
ENST00000261769.10:c.59G>A
ENST00000261769.9:c.59G>A
ENST00000422392.6:c.59G>A
ENST00000566510.5:c.59G>A
ENST00000566612.5:c.59G>A
ENST00000611625.4:c.59G>A
ENST00000612417.4:c.59G>A
ENST00000621016.4:c.59G>A
NM_004360.3:c.59G>A
NM_001317184.1:c.59G>A
NM_001317185.1:c.-1557G>A
NM_001317186.1:c.-1761G>A
NM_004360.5:c.59G>A
NM_001317184.2:c.59G>A
NM_001317185.2:c.-1557G>A
NM_001317186.2:c.-1761G>A

Pathogenic

Met criteria codes 4

PS4_Moderate PVS1 PM2_Supporting PM5_Supporting

Not Met criteria codes 22

PS1 PS2 PS3 PP1 PP2 PP3 PP4 PM1 PM3 PM4 PM6 BA1 BS1 BS4 BS3 BS2 BP5 BP7 BP4 BP3 BP1 BP2

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

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Evidence submitted by expert panel

CDH1 VCEP

The c.59G>A (p.Trp20*) variant is predicted to result in a premature stop codon in exon 2 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). This variant has been reported in at least two families meeting HDGC clinical criteria (PS4_Moderate; PMID: 10072428, 26182300). 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_Moderate, PM5_Supporting.

Met criteria codes

PS4_Moderate	✔	This variant was identified in two families meeting IGCLC criteria for HDGC (PMID: 10072428, 26182300). This variant was reported as a somatic event in an individual with lobular breast cancer. This variant is also reported as a somatic mutation in two breast tumours (COSMIC ID: COSM19502). PubMed:10094558 This variant was identified in an individual with a personal and family history of diffuse gastric cancer. PubMed:10072428 This variant was identified in one family meeting IGCLC criteria for HDGC. PubMed:26182300
PVS1	✔	This variant is predicted to result in a premature stop codon in exon 2.
PM2_Supporting	✔	Allele is absent from populations in gnomAD, ExAC, 1000 Genomes and ESP.
PM5_Supporting	✔	Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.

Not Met criteria codes

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
PP1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2	✖	Not applicable.

PP3	ℹ	✖	Not applicable.
PP4		✖	Not applicable.
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	✖	Not applicable.
PM6	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	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
BP5	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7	ℹ	✖	Not applicable.
BP4	ℹ	✖	Not applicable.
BP3		✖	Not applicable.
BP1		✖	Not applicable.
BP2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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