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.12G>A (p.Trp4Ter)

Version: 3.0

CA396451249

548782 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: a5d1c624-204f-4283-a6ba-356be9baf780
Approved on: 2023/8/4
Published on: 2023/8/4

HGVS expressions

NM_004360.5:c.12G>A
NM_004360.5(CDH1):c.12G>A (p.Trp4Ter)
NC_000016.10:g.68737427G>A
CM000678.2:g.68737427G>A
NC_000016.9:g.68771330G>A
CM000678.1:g.68771330G>A
NC_000016.8:g.67328831G>A
NG_008021.1:g.5136G>A
ENST00000261769.10:c.12G>A
ENST00000261769.9:c.12G>A
ENST00000422392.6:c.12G>A
ENST00000566510.5:c.12G>A
ENST00000566612.5:c.12G>A
ENST00000611625.4:c.12G>A
ENST00000612417.4:c.12G>A
ENST00000621016.4:c.12G>A
NM_004360.3:c.12G>A
NM_001317184.1:c.12G>A
NM_001317185.1:c.-1604G>A
NM_001317186.1:c.-1808G>A
NM_004360.4:c.12G>A
NM_001317184.2:c.12G>A
NM_001317185.2:c.-1604G>A
NM_001317186.2:c.-1808G>A

Pathogenic

Met criteria codes 3

PVS1 PM5_Supporting PM2_Supporting

Not Met criteria codes 23

PM1 PM3 PM4 PM6 BA1 BS2 BS1 BS4 BS3 BP4 BP3 BP1 BP2 BP5 BP7 PS1 PS2 PS3 PS4 PP1 PP2 PP3 PP4

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 Links 2

Evidence submitted by expert panel

CDH1 VCEP

The c.12G>A (p.Trp4Ter) 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

PVS1	✔	This variant produces a nonsense codon in exon 1.
PM5_Supporting	✔	This variant produces a nonsense codon in exon 1.
PM2_Supporting	✔	This allele is absent from populations in gnomAD, ExAC, 1000 Genomes and ESP.

Not Met criteria codes

PM1	✖	Not applicable.
PM3	✖	Not applicable.
PM4	✖	Not applicable.
PM6	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	✖	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
BS1	✖	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	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
BP5	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7	ℹ	✖	Not applicable.
PS1		✖	Not applicable.
PS2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3	ℹ	✖	Not applicable.
PS4	ℹ	✖	This variant was identified in an individual meeting clinical testing criteria for hereditary breast and ovarian cancer (PMID: 26022348). However, detailed family gastric cancer history for this case was not reported. This variant has been additionally identified in tumour tissue from an individual with plasmacytoid carcinoma of the bladder (PMID: 26901067). The patient in ClinVar (SCV000785509.2) also lack detailed information. Somatic variant identified in an individual with plasmacytoid carcinoma of the bladder. PubMed:26901067 Variant identified in one individual meeting clinical testing criteria for hereditary breast and ovarian cancer. PubMed:26022348
PP1	ℹ	✖	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.

Curation History

Showing 1 to 3 of 3 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.