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.220C>T (p.Arg74Ter)

Version: 2.0

CA10583404

239891 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: 8e4651fc-c286-49aa-95c4-13401d26f84a
Approved on: 2023/8/29
Published on: 2023/8/29

HGVS expressions

NM_004360.4:c.220C>T
NM_004360.4(CDH1):c.220C>T (p.Arg74Ter)
NC_000016.10:g.68801726C>T
CM000678.2:g.68801726C>T
NC_000016.9:g.68835629C>T
CM000678.1:g.68835629C>T
NC_000016.8:g.67393130C>T
NG_008021.1:g.69435C>T
ENST00000261769.10:c.220C>T
ENST00000261769.9:c.220C>T
ENST00000422392.6:c.220C>T
ENST00000562836.5:n.291C>T
ENST00000564676.5:n.502C>T
ENST00000564745.1:n.215C>T
ENST00000566510.5:c.220C>T
ENST00000566612.5:c.220C>T
ENST00000611625.4:c.220C>T
ENST00000612417.4:c.220C>T
ENST00000621016.4:c.220C>T
NM_004360.3:c.220C>T
NM_001317184.1:c.220C>T
NM_001317185.1:c.-1396C>T
NM_001317186.1:c.-1600C>T
NM_004360.5:c.220C>T
NM_001317184.2:c.220C>T
NM_001317185.2:c.-1396C>T
NM_001317186.2:c.-1600C>T

Pathogenic

Met criteria codes 4

PVS1 PM5_Supporting PM2_Supporting PS4_Supporting

Not Met criteria codes 22

PM1 PM3 PM4 PM6 BA1 BS2 BS1 BS4 BS3 BP5 BP7

Expert Panel

CDH1 VCEP

Criteria Specification Information

Criteria Specification: *ClinGen CDH1 Expert Panel Specifications to the ACMG/AMP Variant Interpretation*

BP4 BP3 BP1 BP2 PS1 PS2
PS3 PP1 PP2 PP3 PP4

Evidence Links 1

Guidelines Version 3.1

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

CDH1 VCEP

The c.220C>T p.(Arg74Ter) variant is predicted to result in a premature stop codon that leads to a truncated or absent protein (PVS1, PM5_Supporting). The 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; SCV000288456.3). 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

PVS1	✔	Predicted NMD.
PM5_Supporting	✔	Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.
PM2_Supporting	✔	Not observed in population database.
PS4_Supporting	✔	Found in one individual (76 yo) with gastric adenocarcinoma with suspected family history of gastric cancer (mother, brother), but NOT germline. SCV000288456.3 - one proband meet IGCLC HDGC criteria. - one proband does not meet IGCLC HDGC criteria. SCV000661607.2 - 3 cases do not meet HDGC criteria with unknown pathology. Found in one individual (76 yo) with gastric adenocarcinoma with suspected family history of gastric cancer (mother, brother), but NOT germline. PubMed:25123297

Not Met criteria codes

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	✖	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

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		✖	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
BP7		✖	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
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
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		✖	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

Curation History

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