

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

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HGVS expressions

NM_004360.4(CDH1):c.220C>T (p.Arg74Ter)

NM_004360.4:c.220C>T

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

PM2_Supporting

PVS1

PM5_Supporting

PS4_Supporting

Not Met criteria codes 22

PS1

PS2

PS3

BA1

PP1

PP2

PP3

PP4

PM1

PM3

PM4

Expert Panel

CDH1 VCEP [↗](#)

Criteria Specification Information

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

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

PM2_Supporting			Not observed in population database.
PVS1			Predicted NMD.
PM5_Supporting			Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.
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

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
BA1			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
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
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
BS2			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

Curation History 	
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