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.2446A>T (p.Lys816Ter)

Version: 2.3

CA396471960

496818 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: 1c8a70db-00a5-46ce-b1a3-4a18a909c3cf
Approved on: 2024/3/25
Published on: 2024/3/27

HGVS expressions

NM_004360.5(CDH1):c.2446A>T (p.Lys816Ter)
NM_004360.5:c.2446A>T
NC_000016.10:g.68833296A>T
CM000678.2:g.68833296A>T
NC_000016.9:g.68867199A>T
CM000678.1:g.68867199A>T
NC_000016.8:g.67424700A>T
NG_008021.1:g.101005A>T
ENST00000261769.10:c.2446A>T
ENST00000261769.9:c.2446A>T
ENST00000422392.6:c.2263A>T
ENST00000562118.1:n.664A>T
ENST00000562836.5:n.2517A>T
ENST00000566510.5:c.*1112A>T
ENST00000566612.5:c.*686A>T
ENST00000611625.4:c.2509A>T
ENST00000612417.4:c.1854-895A>T
ENST00000621016.4:c.1866-907A>T
NM_004360.3:c.2446A>T
NM_001317184.1:c.2263A>T
NM_001317185.1:c.898A>T
NM_001317186.1:c.481A>T
NM_004360.4:c.2446A>T
NM_001317184.2:c.2263A>T
NM_001317185.2:c.898A>T
NM_001317186.2:c.481A>T

Likely Pathogenic

Met criteria codes 3

PVS1_Strong PM2_Supporting PS4_Supporting

Not Met criteria codes 23

PS1 PS2 PS3 PP1 PP2 PP3 PP4 PM1 PM3 PM5 PM4 PM6 BA1 BS1 BS4 BS3

Expert Panel

CDH1 VCEP

Criteria Specification Information

Criteria Specification: *ClinGen CDH1 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 3.1*

BS2 BP5 BP7 BP4 BP3 BP1 BP2

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence Links 0

Evidence submitted by expert panel

CDH1 VCEP

The c.2446A>T (p.Lys816Ter) variant is predicted to result in a premature stop codon that leads to a truncated or absent protein within the NMD-resistant zone and located upstream the most 3’ well-characterized pathogenic variant c.2506G>T (p.Glu836Ter) (PVS1_Strong). The variant is absent in the gnomAD cohort (PM2_Supporting; http://https://gnomad.broadinstitute.org/). The variant has been reported in one family meeting clinical criteria for HDGC (PS4_Supporting; PMID: 29798843). In summary, this variant meets criteria to be classified as Likely Pathogenic based on the ACMG/AMP criteria applied as specified by the CDH1 Variant Curation Expert Panel(Variant Interpretation Guidelines Version 3.1): PVS1_Strong, PM2_Supporting, PS4_Supporting.

Met criteria codes

PVS1_Strong	✔	truncation in NMD-resistant zone located upstream the most 3' well-characterized pathogenic variant c.2506G>T (p.Glu836Ter)
PM2_Supporting	✔	variant not present in gnomAD database
PS4_Supporting	✔	1 family meeting HDGC criteria

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	✖	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
PM5		✖	Not predicted/proved to undergo NMD.
PM4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4	ℹ	✖	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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