

Variant: NM_004360.5(CDH1):c.1A>G (p.Met1Val)

Version: 2.0

CA396451176 [↗](#)

532457 (ClinVar) [↗](#)

Gene: CDH1 ([HGNC:999](#))

Condition: CDH1-related diffuse gastric and lobular breast cancer ([MONDO:0100488](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 6d19d5b0-c34b-4794-89e5-d0173e561a83

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HGVS expressions

NM_004360.5:c.1A>G

NM_004360.5(CDH1):c.1A>G (p.Met1Val)

NC_000016.10:g.68737416A>G

CM000678.2:g.68737416A>G

NC_000016.9:g.68771319A>G

CM000678.1:g.68771319A>G

NC_000016.8:g.67328820A>G

NG_008021.1:g.5125A>G

ENST00000261769.10:c.1A>G

ENST00000261769.9:c.1A>G

ENST00000422392.6:c.1A>G

ENST00000566510.5:c.1A>G

ENST00000566612.5:c.1A>G

ENST00000611625.4:c.1A>G

ENST00000612417.4:c.1A>G

ENST00000621016.4:c.1A>G

NM_004360.3:c.1A>G

NM_001317184.1:c.1A>G

NM_001317185.1:c.-1615A>G

NM_001317186.1:c.-1819A>G

NM_004360.4:c.1A>G

NM_001317184.2:c.1A>G

NM_001317185.2:c.-1615A>G

NM_001317186.2:c.-1819A>G

Pathogenic

Met criteria codes 4

PM2_Supporting PP1

PS4_Supporting PVS1

Not Met criteria codes 22

BA1 BP4 BP3 BP1 BP2 BP5
BP7 BS2 BS1 BS4 BS3 PP2
PP3 PP4 PS1 PS2 PS3 PM6
PM1 PM3 PM5 PM4

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 submitted by expert panel

CDH1 VCEP

The c.1A>G (p.Met1Val) variant alters the start codon of the CDH1 coding sequence and is predicted to lead to an absent protein (PVS1). This variant is absent in the gnomAD cohort (PM2_supporting; <http://gnomad.broadinstitute.org>). This variant has been reported in at least one proband meeting HDGC clinical criteria (PS4_supporting; SCV000760810.2). This variant was also found to co-segregate with disease in multiple affected family members (PP1; SCV000760810.2). In summary, this variant meets criteria to be classified as pathogenic based on the ACMG/AMP Variant Interpretation Guidelines Version 3.1 as specified by the CDH1 Variant Curation Expert Panel: PVS1, PS4_supporting, PM2_supporting, PP1.

Met criteria codes

PM2_Supporting			Absent from all population databases
PP1			This variant has been observed to segregate with gastric cancer in a family (SCV000760810.2).
PS4_Supporting			One proband meet HDGC phenotype criteria (SCV000760810.2).
PVS1			PVS1 applies to initiation codon variants

Not Met criteria codes

BA1			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
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
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
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
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
PM6			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			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

Curation History [↗](#)

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