

Variant: *NM_004360.5(CDH1):c.408A>G (p.Gln136=)*

Version: 1.0

CA16614941 [↗](#)

406639 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 79415b55-144f-49d8-8825-e503db2074df

Approved on: 2023/9/25

Published on: 2023/9/27

HGVS expressions

NM_004360.5(CDH1):c.408A>G (p.Gln136=)

NM_004360.5:c.408A>G

NC_000016.10:g.68808444A>G

CM000678.2:g.68808444A>G

NC_000016.9:g.68842347A>G

CM000678.1:g.68842347A>G

NC_000016.8:g.67399848A>G

NG_008021.1:g.76153A>G

ENST00000261769.10:c.408A>G

ENST00000261769.9:c.408A>G

ENST00000422392.6:c.408A>G

ENST00000561751.1:c.175A>G

ENST00000562836.5:n.479A>G

ENST00000564676.5:n.690A>G

ENST00000564745.1:n.403A>G

ENST00000566510.5:c.408A>G

ENST00000566612.5:c.408A>G

ENST00000611625.4:c.408A>G

ENST00000612417.4:c.408A>G

ENST00000621016.4:c.408A>G

NM_004360.3:c.408A>G

NM_001317184.1:c.408A>G

NM_001317185.1:c.-1208A>G

NM_001317186.1:c.-1412A>G

NM_004360.4:c.408A>G

NM_001317184.2:c.408A>G

NM_001317185.2:c.-1208A>G

NM_001317186.2:c.-1412A>G

Likely Benign

Met criteria codes **3**

BS2

BP7

BP4

Not Met criteria codes **4**

BS1

BA1

PP3

PM2

Expert Panel

CDH1 VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

CDH1 VCEP

The c.408A>G (p.Gln136=) variant results in a synonymous change in exon 4 of CDH1. This is a silent variant that occurs at a position that is not highly conserved and for which splicing predictors do not suggest an impact on splicing (BP4, BP7). This variant is absent from the gnomAD population database v3.1.2. This variant was identified in 29 individuals without DGC, LBC, SRC tumours and whose families do not suggest HDGC (BS2; PMID: 30287823, 36436516, and internal laboratory contributors). In summary, this variant is classified as likely benign based on ACMG/AMP criteria applied as likely benign specified by the CDH1 Variant Curation Expert Panel: BS2, BP4, BP7.

Met criteria codes

BS2			This variant was observed in 29 individuals without DGC, LBC, SRC tumours and whose families do not suggest HDGC (internal laboratory data). Please note that this variant has also been observed in one individual with ILC in 40s and an individual with unspecified GC in 40s.
BP7			This is a silent variant for which in silico predictors do not suggest an impact on splicing and that occurs at a position that is not highly conserved.
BP4			No predicted splice impact: SpliceAI - delta 0.02 acceptor loss; MaxEntScan - no difference; varSEAK - class 1, no splicing effect

Not Met criteria codes

BS1			This variant is absent from gnomAD v3.1.2.
BA1			This variant is absent from gnomAD v3.1.2.
PP3			This variant is not predicted to alter splicing by multiple in silico tools.
PM2			This variant is absent from gnomAD v3.1.2. However, this variant has also been identified in more than 10 individuals without DGC, LBC, SRC tumours and whose families do not suggest HDGC (BS2). Therefore, PM2_Supporting is not applied to this variant.

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