

Variant: NM_001317186.2:c.-403G>A

Version: 1.0

CA288037 [↗](#)

127914 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 83921f5d-95da-4bbf-9dbe-4afe1c1ec6e6

Approved on: 2023/8/3

Published on: 2023/8/3

HGVS expressions

NM_001317186.2:c.-403G>A

NC_000016.10:g.68815611G>A

CM000678.2:g.68815611G>A

NC_000016.9:g.68849514G>A

CM000678.1:g.68849514G>A

NC_000016.8:g.67407015G>A

NG_008021.1:g.83320G>A

ENST00000261769.10:c.1417G>A

ENST00000261769.9:c.1417G>A

ENST00000422392.6:c.1234G>A

ENST00000562836.5:n.1488G>A

ENST00000566510.5:c.*83G>A

ENST00000566612.5:c.1417G>A

ENST00000611625.4:c.1480G>A

ENST00000612417.4:c.1417G>A

ENST00000621016.4:c.1417G>A

NM_004360.3:c.1417G>A

NM_001317184.1:c.1234G>A

NM_001317185.1:c.-132G>A

NM_001317186.1:c.-403G>A

NM_004360.4:c.1417G>A

NM_004360.5:c.1417G>A

NM_001317184.2:c.1234G>A

NM_001317185.2:c.-132G>A

Likely Benign

Met criteria codes **1**

BS2

Not Met criteria codes **13**

BA1

BS1

BS4

BS3

BP5

BP2

PS2

PS3

PS4

PP1

PP3

PM6

PM2

Evidence Links **0**

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**

CDH1 VCEP

The c.1417G>A (p.Val473Ile) variant results in a conservative missense change in the Cadherin 3 domain of CDH1. This variant was observed in 5 of 152,172 alleles in the gnomAD v3.1.2 population database. However, this variants has also been observed in more than 10 individuals without GC, DGC, gastric SRC tumours or LBC and whose families do not suggest HDGC (BS2). In summary, this variant meets criteria to be classified as Likely Benign based on the ACMG/AMP criteria applied as specified by the CDH1 Variant Curation Expert Panel: BS2. (CDH1 VCEP specifications version 3.1; 05/22/2023)

Met criteria codes

BS2			This variant has been observed in ~383 families without HDGC. This variant was also identified in two families with a history of unspecified gastric and gastrointestinal cancer and two probands with ILC in 60s.
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Not Met criteria codes

BA1			This variant occurs at a frequency of 3.3x10-5 (5 in 152,172 alleles) in gnomAD.
BS1			This variant occurs at a frequency of 3.3x10-5 (5 in 152,172 alleles) in gnomAD.
BS4			To our knowledge, this variant has not been reported in a family meeting IGCLC criteria for HDGC.
BS3			To our knowledge, splicing studies have not been reported for this variant.
BP5			To our knowledge, this variant has not been reported in a case with an alternate molecular basis for disease.
BP2			To our knowledge, this variant has not been reported in a family meeting IGCLC criteria for HDGC.
PS2			To our knowledge, this variant has not been reported in a proband with HDGC.
PS3			To our knowledge, splicing studies have not been reported for this variant.
PS4			This variant has been observed in ~383 families without HDGC. This variant was also identified in two families with a history of unspecified gastric and gastrointestinal cancer and two probands with ILC in 60s.
PP1			To our knowledge, this variant has not been reported in a family meeting IGCLC criteria for HDGC.
PP3			This variant is not predicted to result in abnormal splicing.
PM6			To our knowledge, this variant has not been reported in a proband with HDGC.

PM2



This variant occurs at a frequency of 3.3x10-5 (5 in 152,172 alleles) in gnomAD.

Curation History [↗](#)

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