

Variant: *NM_001317186.2:c.-460G>A*

Version: 1.0

CA288034 [↗](#)

127912 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: b815fbd2-a123-4504-8023-98f8e3c79c7e

Approved on: 2023/8/3

Published on: 2023/8/3

HGVS expressions

NM_001317186.2:c.-460G>A

NC_000016.10:g.68815554G>A

CM000678.2:g.68815554G>A

NC_000016.9:g.68849457G>A

CM000678.1:g.68849457G>A

NC_000016.8:g.67406958G>A

NG_008021.1:g.83263G>A

ENST00000261769.10:c.1360G>A

ENST00000261769.9:c.1360G>A

ENST00000422392.6:c.1177G>A

ENST00000562836.5:n.1431G>A

ENST00000566510.5:c.*26G>A

ENST00000566612.5:c.1360G>A

ENST00000611625.4:c.1423G>A

ENST00000612417.4:c.1360G>A

ENST00000621016.4:c.1360G>A

NM_004360.3:c.1360G>A

NM_001317184.1:c.1177G>A

NM_001317185.1:c.-189G>A

NM_001317186.1:c.-460G>A

NM_004360.4:c.1360G>A

NM_004360.5:c.1360G>A

NM_001317184.2:c.1177G>A

NM_001317185.2:c.-189G>A

Likely Benign

Met criteria codes **1**

BS2

Not Met criteria codes **14**

BA1

BP2

BP5

BS1

BS4

BS3

PP1

PP3

PS2

PS3

PS4

PM6

PM2

PM5

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.1360G>A (p.Val454Ile) variant results in a conservative missense change in the Cadherin 3 domain of CDH1. This variant was observed in 4 in 152,164 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 155 families hot meeting IGCLC criteria for HDGC. This variant was also identified in one family with a history of unspecified gastric cancer and a proband with ILC in their 40s.
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Not Met criteria codes

BA1			This variant occurs at a frequency of 2.6x10-5 (4 in 152,164 alleles) in gnomAD.
BP2			To our knowledge, this variant has not been observed in a family meeting IGCLC criteria for HDGC.
BP5			To our knowledge, this variant has not been reported in a case with an alternate molecular basis for disease.
BS1			This variant occurs at a frequency of 2.6x10-5 (4 in 152,164 alleles) in gnomAD.
BS4			To our knowledge, this variant has not been observed in an HDGC family.
BS3			To our knowledge, splicing studies for this variant have not been reported.
PP1			To our knowledge, this variant has not been observed in an HDGC family.
PP3			This variant is not predicted to alter splicing.
PS2			To our knowledge, this variant has not been observed in a proband meeting IGCLC criteria for HDGC.
PS3			To our knowledge, splicing studies for this variant have not been reported.
PS4			This variant has been observed in 155 families hot meeting IGCLC criteria for HDGC. This variant was also identified in one family with a history of unspecified gastric cancer and a proband with ILC in their 40s.
PM6			To our knowledge, this variant has not been observed in a proband meeting IGCLC criteria for HDGC.

PM2	✖	This variant occurs at a frequency of 2.6x10-5 (4 in 152,164 alleles) in gnomAD.
PM5	✖	PM5 is not applicable for missense variants in CDH1.

Curation History ↗	
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