

Variant: NM_004360.3(CDH1):c.4G>A (p.Gly2Ser)

Version: 3.0

CA187442 [↗](#)

183998 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: a870dd72-f029-4e34-b558-341fb7b9051c

Approved on: 2023/8/17

Published on: 2023/8/17

HGVS expressions

NM_004360.3(CDH1):c.4G>A (p.Gly2Ser)

NM_004360.3:c.4G>A

NC_000016.10:g.68737419G>A

CM000678.2:g.68737419G>A

NC_000016.9:g.68771322G>A

CM000678.1:g.68771322G>A

NC_000016.8:g.67328823G>A

NG_008021.1:g.5128G>A

ENST00000261769.10:c.4G>A

ENST00000261769.9:c.4G>A

ENST00000422392.6:c.4G>A

ENST00000566510.5:c.4G>A

ENST00000566612.5:c.4G>A

ENST00000611625.4:c.4G>A

ENST00000612417.4:c.4G>A

ENST00000621016.4:c.4G>A

NM_001317184.1:c.4G>A

NM_001317185.1:c.-1612G>A

NM_001317186.1:c.-1816G>A

NM_004360.4:c.4G>A

NM_004360.5:c.4G>A

NM_001317184.2:c.4G>A

NM_001317185.2:c.-1612G>A

NM_001317186.2:c.-1816G>A

Likely Benign

Met criteria codes **1**

BS2

Not Met criteria codes **25**

BA1	BS1	BS4	BS3	BP5	BP7
BP4	BP3	BP1	BP2	PVS1	
PS1	PS2	PS3	PS4	PP1	PP2
PP3	PP4	PM1	PM3	PM5	
PM4	PM6	PM2			

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 CDH1 c.4G>A (p.Gly2Ser) missense variant has a frequency of 0.00002 (2 of 128,626) in gnomAD, with a maximum allele frequency of 0.00008 (2 of 24,378) in the Latino subpopulation (<http://gnomad.broadinstitute.org>). This variant has been observed in ≥10 individuals without DGC, SRC tumours or LBC and whose families do not suggest HDGC (BS2; unpublished). In summary, the clinical significance of this variant is classified as likely benign based on BS2 alone. ACMG/AMP criteria applied, as specified by the CDH1 Variant Curation Expert Panel (Variant Interpretation Guidelines Version 3.1): BS2.

Met criteria codes

BS2			This variant has been observed in at least 20 individuals without DGC, SRC tumours or LBC and whose families do not suggest HDGC (SCV000213609.4, SCV000545414.5, SCV000566808.5). Therefore, this variant meets criteria for BS2, which specifies that the variant is seen in ≥10 individuals without DGC, SRC tumors, or LBC and whose families do not suggest HDGC.
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Not Met criteria codes

BA1			This allele is observed at a frequency of 0.00002 (2 of 128,626) in gnomAD, with a maximum allele frequency of 0.00008 (2 of 24,378) in the Latino subpopulation. Therefore, this variant does not meet the minimum criteria for BA1, which requires an allele frequency of greater than 0.002.
BS1			This allele is observed at a frequency of 0.00002 (2 of 128,626) in gnomAD, with a maximum allele frequency of 0.00008 (2 of 24,378) in the Latino subpopulation. Therefore, this variant does not meet the minimum criteria for BS1, which requires an allele frequency of greater than 0.001.
BS4			This information is not available.
BS3			BS3 does not apply to missense variants.
BP5			This variant was identified in an individual with other personal and family cancer history not suggestive of HDGC and with a pathogenic germline variant in BRCA2. Given a lack of cancer history consistent with HDGC and a confirmed variant in a gene associated with other inherited cancer syndromes, BP5 cannot be applied in this case.
BP7			BP7 does not apply to missense variants.
BP4			BP4 does not apply to missense variants in CDH1.
BP3			BP3 does not apply to CDH1.

BP1		✖	BP1 does not apply to CDH1.
BP2		✖	This information is not available.
PVS1		✖	PVS1 does not apply to missense variants.
PS1		✖	To our knowledge, there are no known pathogenic variants in codon 2 of CDH1.
PS2		✖	This information is not available.
PS3		✖	PS3 does not apply to missense variants.
PS4		✖	To our knowledge, this variant has not been observed in a family meeting HDGC criteria.
PP1		✖	This information is not available.
PP2		✖	PP2 does not apply to CDH1.
PP3		✖	PP3 does not apply to missense variants in CDH1.
PP4		✖	PP4 does not apply to CDH1.
PM1		✖	PM1 does not apply to CDH1.
PM3		✖	PM3 does not apply to CDH1.
PM5		✖	PM5 does not apply to CDH1.
PM4		✖	PM4 does not apply to missense variants.
PM6		✖	This information is not available.
PM2		✖	This allele is observed at a frequency of 0.00002 (2 of 128,626) in gnomAD, with a maximum allele frequency of 0.00008 (2 of 24,378) in the Latino subpopulation. Therefore, this variant does not meet the minimum criteria for PM2, which requires a frequency of less than 1 in 100,000 alleles (0.00001) or less than 1 in 50,000 (0.00002) in a given subpopulation.

