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# *Variant: NM_004360.4(CDH1):c.1147C>T (p.Gln383Ter)*

Version: 2.0

*CA169687*

*142888 (ClinVar)*

**Gene**: CDH1 (HGNC:999)
**Condition**: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** 85e6ec9e-bbed-4967-a6af-72d3f6999902
**Approved on**: 2023/8/25
**Published on**: 2023/8/25

## *HGVS expressions*

**NM_004360.4(CDH1):c.1147C>T (p.Gln383Ter)**
**NM_004360.4:c.1147C>T**
NC_000016.10:g.68813322C>T
CM000678.2:g.68813322C>T
NC_000016.9:g.68847225C>T
CM000678.1:g.68847225C>T
NC_000016.8:g.67404726C>T
NG_008021.1:g.81031C>T
ENST00000261769.10:c.1147C>T
ENST00000261769.9:c.1147C>T
ENST00000422392.6:c.1137+1059C>T
ENST00000562836.5:n.1218C>T
ENST00000565810.1:n.191C>T
ENST00000566510.5:c.991C>T
ENST00000566612.5:c.1147C>T
ENST00000611625.4:c.1147C>T
ENST00000612417.4:c.1147C>T
ENST00000621016.4:c.1147C>T
NM_004360.3:c.1147C>T
NM_001317184.1:c.1137+1059C>T
NM_001317185.1:c.-469C>T
NM_001317186.1:c.-673C>T
NM_004360.5:c.1147C>T
NM_001317184.2:c.1137+1059C>T
NM_001317185.2:c.-469C>T
NM_001317186.2:c.-673C>T

**Pathogenic**

**Met criteria codes** 4

PVS1 PM2_Supporting PS4_Supporting PM5_Supporting

**Not Met criteria codes** 22

PS1 PS2 PS3 PP1 PP2 PP3 PP4 PM1 PM3 PM4 PM6

## Expert Panel

CDH1 VCEP

## Criteria Specification Information

**Criteria Specification:** *ClinGen CDH1 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 3.1*

BA1 BS1 BS4 BS3 BS2 BP5
BP7 BP4 BP3 BP1 BP2

**Criteria Specification Approval History**
**Criteria Specifications for this VCEP**

Evidence Links 1

Evidence submitted by expert panel

***CDH1 VCEP***

**The c.1147C>T (p.Gln383Ter) variant is predicted to result in a premature stop codon that leads to a truncated or absent protein (PVS1, PM5_Supporting). This variant is absent in the gnomAD cohort (PM2_Supporting; http://gnomad.broadinstitute.org). The variant has been reported in at least one family meeting HDGC clinical criteria (PS4_Supporting; PMID 23709761). In summary, this variant meets criteria to be classified as pathogenic based on the ACMG/AMP criteria applied as specified by the CDH1 Variant Curation Expert Panel (Variant Interpretation Guidelines Version 3.1): PVS1, PM2_Supporting, PS4_Supporting, PM5_Supporting.**

**Met criteria codes**

| | | |
|---|---|---|
| **PVS1** | ✔ | Predicted null variant in exon 9 of 16. Protein is expected to undergo NMD. |
| **PM2_Supporting** | ✔ | Absent in gnomAD |
| **PS4_Supporting** | ✔ | One French family that meets HDGC clinical criteria. Two DGCs in family, one of them < age 50 (PMID: 23709761). One family that does not meet HDGC clinical criteria, with an index case with ductal breast cancer age 36 (DOI: 10.1200/PO.16.00021 JCO Precision Oncology - published online March 29, 2017).<br>French index case with DGC dx age 24 and a family member dx with DGC age 43. PubMed:23709761 |
| **PM5_Supporting** | ✔ | Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD. |

**Not Met criteria codes**

| | | |
|---|---|---|
| **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 |
| **PP1** | ✖ | 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** | ℹ | ✖ | 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 |
| **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 |
| **PM4** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PM6** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BA1** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BS1** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BS4** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BS3** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BS2** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP5** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP7** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP4** | ℹ | ✖ | 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 |

## Curation History

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