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# *Variant: NM_004360.5(CDH1):c.1443del (p.Asn481fs)*

Version: 3.0

*CA658683954*

*491497 (ClinVar)*

**Gene**: CDH1 (HGNC:999)
**Condition**: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** 12091b2d-cd93-4041-be48-e1f93b317490
**Approved on**: 2023/8/4
**Published on**: 2023/8/4

## *HGVS expressions*

**NM_004360.5:c.1443del**
**NM_004360.5(CDH1):c.1443del (p.Asn481fs)**
NC_000016.10:g.68815637del
CM000678.2:g.68815637del
NC_000016.9:g.68849540del
CM000678.1:g.68849540del
NC_000016.8:g.67407041del
NG_008021.1:g.83346del
ENST00000261769.10:c.1443del
ENST00000261769.9:c.1443del
ENST00000422392.6:c.1260del
ENST00000562836.5:n.1514del
ENST00000566510.5:c.*109del
ENST00000566612.5:c.1443del
ENST00000611625.4:c.1506del
ENST00000612417.4:c.1443del
ENST00000621016.4:c.1443del
NM_004360.3:c.1443del
NM_001317184.1:c.1260del
NM_001317185.1:c.-106del
NM_001317186.1:c.-377del
NM_004360.4:c.1443del
NM_001317184.2:c.1260del
NM_001317185.2:c.-106del
NM_001317186.2:c.-377del

**Pathogenic**

**Met criteria codes** 3

PVS1 PM2_Supporting PM5_Supporting

**Not Met criteria codes** 23

BS1 BS4 BS3 BS2 BP5 BP7 BP4 BP3 BP1 BP2 PS1 PS2 PS3 PS4 PM1 PM3 PM4

## 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**

BA1 PM6 PP1 PP2 PP3 PP4

Evidence Links 0

Criteria Specifications for this VCEP

Evidence submitted by expert panel

***CDH1 VCEP***

**The c.1443del (p.Asn481fs) variant is predicted to result in a premature stop codon that leads to nonsense mediate decay (PVS1 and PM5_supporting). The variant is absent in the gnomAD cohort (PM2_supporting; http://gnomad.broadinstitute.org). Therefore, 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 (CDH1 VCEP specifications version 3.1): PVS1, PM2_supporting, PM5_supporting.**

**Met criteria codes**

| | | |
|---|---|---|
| **PVS1** | ✔ | Frameshift variant predicted to result in NMD and stop codon at aa 521 |
| **PM2_Supporting** | ✔ | Variant is not present in gnomAD |
| **PM5_Supporting** | ✔ | Frameshift variant predicted to result in NMD and stop codon at aa 521 |

**Not Met criteria codes**

| | | |
|---|---|---|
| **BS1** | ✖ | Variant is not present in gnomAD |
| **BS4** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BS3** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BS2** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP5** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP7** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BP4** | ✖ | 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** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PS1** | | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PS2** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PS3** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PS4** | ℹ | ✖ | Proband with unknown primary and family history of gastric cancer in mother and grandmother diagnosed at 40s and 70s, respectively (Not Met; no pathology available; SCV000689453.2) |
| **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 |
| **BA1** | ℹ | ✖ | Variant is not present in gnomAD |
| **PM6** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PP1** | ℹ | ✖ | 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 |

## Curation History

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