

Variant: *NM\_004360.5(CDH1):c.1636del (p.Ala546fs)*

Version: 2.0

CA658658492 [↗](#)

481028 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Autosomal dominant inheritance

**UUID:** e09eb7dc-fe49-4010-a553-8d846a5b2e71

**Approved on:** 2023/8/4

**Published on:** 2023/8/4

## HGVS expressions

**NM\_004360.5(CDH1):c.1636del (p.Ala546fs)**

**NM\_004360.5:c.1636del**

NC\_000016.10:g.68819350del

CM000678.2:g.68819350del

NC\_000016.9:g.68853253del

CM000678.1:g.68853253del

NC\_000016.8:g.67410754del

NG\_008021.1:g.87059del

ENST00000261769.10:c.1636del

ENST00000261769.9:c.1636del

ENST00000422392.6:c.1453del

ENST00000562836.5:n.1707del

ENST00000566510.5:c.\*302del

ENST00000566612.5:c.1566-2651del

ENST00000611625.4:c.1699del

ENST00000612417.4:c.1636del

ENST00000621016.4:c.1636del

NM\_004360.3:c.1636del

NM\_001317184.1:c.1453del

NM\_001317185.1:c.88del

NM\_001317186.1:c.-254-2651del

NM\_004360.4:c.1636del

NM\_001317184.2:c.1453del

NM\_001317185.2:c.88del

NM\_001317186.2:c.-254-2651del

**Pathogenic**

**Met criteria codes** 3

PVS1 PM5\_Supporting

PM2\_Supporting

**Not Met criteria codes** 23

BA1 BS1 BS4 BS3 BS2 BP5  
BP7 BP4 BP3 BP1 BP2 PS1  
PS2 PS3 PS4 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

[↗](#) **Criteria Specification Approval History**

Evidence submitted by expert panel

*CDH1 VCEP*

The c.1636del p.(Ala546fs) 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           |  |  | Exon 11 of 16. Predicted NMD.   |
| PM5_Supporting |  |  | Exon 11 of 16. Predicted NMD.   |
| PM2_Supporting |  |  | Absent in population databases. |

Not Met criteria codes

|     |                                                                                     |                                                                                     |                                                                                                                            |
|-----|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| BA1 |  |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| BS1 |  |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| 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 |                                                                                     |   |                                                                                                                            |
| <b>BP3</b>                                                                                                                 |                                                                                     | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>BP1</b>                                                                                                                 |                                                                                     | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>BP2</b>                                                                                                                 |    | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PS1</b>                                                                                                                 |                                                                                     | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PS2</b>                                                                                                                 |    | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PS3</b>                                                                                                                 |    | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PS4</b>                                                                                                                 |   | ✖ | SCV000665113.2 (Ambry) - proband ILC in 40s, but family history does not meet criteria. Not in published studies.          |
| <b>PP1</b>                                                                                                                 |  | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PP2</b>                                                                                                                 |                                                                                     | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PP3</b>                                                                                                                 |  | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PP4</b>                                                                                                                 |                                                                                     | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PM1</b>                                                                                                                 |                                                                                     | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PM3</b>                                                                                                                 |                                                                                     | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PM4</b>                                                                                                                 |  | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| <b>PM6</b>                                                                                                                 |  | ✖ |                                                                                                                            |

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History [↗](#)

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