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Variant: NM_000059.4(BRCA2):c.566A>G (p.Asp189Gly)

Version: 1.0

CA022922

37986 (ClinVar)

Gene: BRCA2 (HGNC:675)
Condition: BRCA2-related cancer predisposition (MONDO:0700269)
Inheritance Mode: Autosomal dominant inheritance
UUID: 349e363d-bab4-4401-844c-efef434e6f57
Approved on: 2026/7/15
Published on: 2026/7/15

HGVS expressions

NM_000059.4(BRCA2):c.566A>G (p.Asp189Gly)
NM_000059.4:c.566A>G
NC_000013.11:g.32326548A>G
CM000675.2:g.32326548A>G
NC_000013.10:g.32900685A>G
CM000675.1:g.32900685A>G
NC_000013.9:g.31798685A>G
NG_012772.3:g.16069A>G
ENST00000470094.2:c.566A>G
ENST00000528762.2:c.566A>G
ENST00000530893.7:c.197A>G
ENST00000665585.2:c.566A>G
ENST00000666593.2:c.566A>G
ENST00000700202.2:c.566A>G
ENST00000700200.1:n.437A>G
ENST00000700201.1:c.*345A>G
ENST00000380152.8:c.566A>G
ENST00000544455.6:c.566A>G
ENST00000614259.2:c.566A>G
ENST00000680887.1:c.566A>G
ENST00000380152.7:c.566A>G
ENST00000530893.6:n.764A>G
ENST00000544455.5:c.566A>G
ENST00000614259.1:n.566A>G
NM_000059.3:c.566A>G

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

Not Met criteria codes 1

PP3

Evidence Links 0

Expert Panel

ENIGMA BRCA1 and BRCA2 VCEP

Criteria Specification Information

Criteria Specification: *ClinGen ENIGMA BRCA1 and BRCA2 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for BRCA2 Version 1.1.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ENIGMA BRCA1 and BRCA2 VCEP

The c.566A>G variant in BRCA2 is a missense variant predicted to cause substitution of aspartic acid by glycine at amino acid 189 (p.(Asp189Gly)). This variant is absent from gnomAD v4.1 (read depth ≥25x in >90% samples, PM2_Supporting met). This BRCA2 missense variant has a SpliceAI score of 0.7, predicting an impact on splicing (score threshold ≥0.2) (PP3 not applied because a PVS1 code is met). This variant is reported to result in aberrant mRNA splicing. Minigene, RT-PCR, and RNAseq demonstrated that the variant causes deletion of part of the exon (r.562_631del), resulting in an out-of-frame transcript. The percent aberrant transcript produced from the variant allele using allele specific assessment with sequence analysis was determined to be >90% (ENIGMA unpublished data, Ambry internal data, Internal lab contributor). Final code strength determined by the rubric: PVS1 (RNA). In summary, this variant meets the criteria to be classified as a Likely pathogenic variant for BRCA2-related cancer predisposition based on the ACMG/AMP criteria applied as specified by the ENIGMA BRCA1/2 VCEP (PM2_Supporting, PVS1 (RNA)).

Met criteria codes

PVS1	✔	This variant is reported to result in aberrant mRNA splicing. Minigene, RT-PCR, and RNAseq demonstrated that the variant causes deletion of part of the exon (r.562_631del), resulting in an out-of-frame transcript. The percent aberrant transcript produced from the variant allele using allele specific assessment with sequence analysis was determined to be >90% (ENIGMA unpublished data, Ambry internal data, Internal lab contributor). Final code strength determined by the rubric: PVS1 (RNA).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1 (read depth ≥25x in >90% samples, PM2_Supporting met).

Not Met criteria codes

PP3	✖	This BRCA2 missense variant has a SpliceAI score of 0.7, predicting an impact on splicing (score threshold ≥0.2) (PP3 not applied because a PVS1 code is met).

Curation History

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