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Variant: NM_000059.4(BRCA2):c.7787G>A (p.Gly2596Glu)

Version: 1.0

CA16619771

421439 (ClinVar)

Gene: BRCA2 (HGNC:675)
Condition: BRCA2-related cancer predisposition (MONDO:0700269)
Inheritance Mode: Autosomal dominant inheritance
UUID: 15ebd6ed-65a2-4f92-8fdb-cd0021488264
Approved on: 2025/8/18
Published on: 2025/8/18

HGVS expressions

NM_000059.4(BRCA2):c.7787G>A (p.Gly2596Glu)
NM_000059.4:c.7787G>A
NC_000013.11:g.32357911G>A
CM000675.2:g.32357911G>A
NC_000013.10:g.32932048G>A
CM000675.1:g.32932048G>A
NC_000013.9:g.31830048G>A
NG_012772.3:g.47432G>A
ENST00000470094.2:c.7787G>A
ENST00000528762.2:c.7787G>A
ENST00000530893.7:c.7418G>A
ENST00000665585.2:c.7787G>A
ENST00000666593.2:c.7787G>A
ENST00000700202.2:c.7787G>A
ENST00000700202.1:c.254G>A
ENST00000380152.8:c.7787G>A
ENST00000544455.6:c.7787G>A
ENST00000614259.2:c.7787G>A
ENST00000665585.1:c.352G>A
ENST00000680887.1:c.7787G>A
ENST00000380152.7:c.7787G>A
ENST00000544455.5:c.7787G>A
ENST00000614259.1:n.7787G>A
NM_000059.3:c.7787G>A

Likely Pathogenic

Met criteria codes 3

PS3 PP3 PM2_Supporting

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 1.2.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

ENIGMA BRCA1 and BRCA2 VCEP

The c.7787G>A variant in BRCA2 is a missense variant predicted to cause substitution of Glycine by Glutamic Acid at amino acid 2596 (p.(Gly2596Glu)). This variant is absent from gnomAD v2.1 (exomes only, non-cancer subset, read depth ≥25) and gnomAD v3.1 (non-cancer subset, read depth ≥25) (PM2_Supporting met). Reported by four calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs:38417439, 39779848, 39779857, 33293522) (PS3 met). This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.46, above the recommended threshold of 0.30 for prediction of impact on BRCA2 function via protein change. A SpliceAI score of 0.02 predicts no impact on splicing (score threshold <0.10) (PP3 met). 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, PS3, PP3).

Met criteria codes

PS3	✔	Reported by four calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs:38417439, 39779848, 39779857, 33293522) (PS3 met).
PP3	✔	This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.46, above the recommended threshold of 0.30 for prediction of impact on BRCA2 function via protein change. A SpliceAI score of 0.02 predicts no impact on splicing (score threshold <0.10) (PP3 met).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1 (exomes only, non-cancer subset, read depth ≥25) and gnomAD v3.1 (non-cancer subset, read depth ≥25) (PM2_Supporting met).

Curation History

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