

Variant: *NM_000059.4(BRCA2):c.8378G>T (p.Gly2793Val)*

Version: 1.0

CA025615 [↗](#)

38158 (ClinVar) [↗](#)

Gene: BRCA2 ([HGNC:675](#))

Condition: BRCA2-related cancer predisposition ([MONDO:0700269](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: b1baf39c-b1a3-4367-b6a6-c47152a2510b

Approved on: 2026/7/15

Published on: 2026/7/15

HGVS expressions

NM_000059.4:c.8378G>T

NM_000059.4(BRCA2):c.8378G>T (p.Gly2793Val)

NC_000013.11:g.32370448G>T

CM000675.2:g.32370448G>T

NC_000013.10:g.32944585G>T

CM000675.1:g.32944585G>T

NC_000013.9:g.31842585G>T

NG_012772.3:g.59969G>T

ENST00000470094.2:c.8378G>T

ENST00000528762.2:c.8378G>T

ENST00000530893.7:c.8009G>T

ENST00000665585.2:c.8378G>T

ENST00000666593.2:c.8378G>T

ENST00000700202.2:c.8378G>T

ENST00000700202.1:c.845G>T

ENST00000380152.8:c.8378G>T

ENST00000544455.6:c.8378G>T

ENST00000614259.2:c.8386G>T

ENST00000665585.1:c.943G>T

ENST00000680887.1:c.8378G>T

ENST00000380152.7:c.8378G>T

ENST00000544455.5:c.8378G>T

NM_000059.3:c.8378G>T

Likely Pathogenic

Met criteria codes **3**

PM2_Supporting PS3 PP3

Not Met criteria codes **5**

BS3 PVS1 BP5 BP7 PP4

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**

ENIGMA BRCA1 and BRCA2 VCEP

The c.8378G>T variant in BRCA2 is a missense variant predicted to cause substitution of Glycine by Valine at amino acid 2793 (p. (Gly2793Val)). This variant is absent from gnomAD v4.1 (read depth $\geq 25\times$ in >90% samples, PM2_Supporting met). This BRCA2 missense variant is within a key functional domain and a SpliceAI score of 0.36 predicts an impact on splicing (score threshold >0.20). The computational predictor BayesDel (noAF) gives a score of 0.59, above the recommended threshold of 0.3 for prediction of impact on BRCA2 function via protein change (PP3 met). Missense variant predicted to alter splicing, functional data considered only from assays that measure effect via mRNA and protein. Reported by two calibrated studies incorporating mRNA splicing effect to exhibit function similar to pathogenic control variants (PMIDs: 39779857, 39779848). Additionally, this variant is reported to exhibit function similar to pathogenic control variants in two assays with cDNA based design (PMIDs: 38417439, 32444794) (PS3 met). This variant is reported to result in aberrant mRNA splicing. RT-PCR and agarose gel electrophoresis demonstrated that the variant impacts splicing by exon 19 skipping (PMID: 32123317). The percent full-length and aberrant transcripts produced from the variant allele was not stated (PVS1 (RNA) and BP7_Strong (RNA) not met). Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.87 (based on Family History LR=0.87), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; PMID: 31853058). 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, PP3, PS3).

Met criteria codes

PM2_Supporting			This variant is absent from gnomAD v4.1 (read depth $\geq 25\times$ in >90% samples, PM2_Supporting met).
PS3			Missense variant predicted to alter splicing, functional data considered only from assays that measure effect via mRNA and protein. Reported by two calibrated studies incorporating mRNA splicing effect to exhibit function similar to pathogenic control variants (PMIDs: 39779857, 39779848). Additionally, this variant is reported to exhibit function similar to pathogenic control variants in two assays with cDNA based design (PMIDs: 38417439, 32444794) (PS3 met).
PP3			This BRCA2 missense variant is within a key functional domain and a SpliceAI score of 0.36 predicts an impact on splicing (score threshold >0.20). The computational predictor BayesDel (noAF) gives a score of 0.59, above the recommended threshold of 0.3 for prediction of impact on BRCA2 function via protein change (PP3 met).

Not Met criteria codes

BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1			This variant is reported to result in aberrant mRNA splicing. RT-PCR and agarose gel electrophoresis demonstrated that the variant impacts splicing by exon 19 skipping (PMID: 32123317). The percent full-length and aberrant transcripts produced from the variant allele was not stated (PVS1 (RNA) and BP7_Strong (RNA) not met).
BP5			Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.87 (based on Family History LR=0.87), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; PMID: 31853058).

BP7	 	This variant is reported to result in aberrant mRNA splicing. RT-PCR and agarose gel electrophoresis demonstrated that the variant impacts splicing by exon 19 skipping (PMID: 32123317). The percent full-length and aberrant transcripts produced from the variant allele was not stated (PVS1 (RNA) and BP7_Strong (RNA) not met).
PP4	 	Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.87 (based on Family History LR=0.87), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; PMID: 31853058).

Curation History 

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.