

Variant: *NM_000059.4(BRCA2):c.7879A>T (p.Ile2627Phe)*

Version: 2.0

CA025321 [↗](#)

52430 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

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HGVS expressions

NM_000059.4:c.7879A>T

NM_000059.4(BRCA2):c.7879A>T (p.Ile2627Phe)

NC_000013.11:g.32362596A>T

CM000675.2:g.32362596A>T

NC_000013.10:g.32936733A>T

CM000675.1:g.32936733A>T

NC_000013.9:g.31834733A>T

NG_012772.3:g.52117A>T

ENST00000470094.2:c.7879A>T

ENST00000528762.2:c.7879A>T

ENST00000530893.7:c.7510A>T

ENST00000665585.2:c.7879A>T

ENST00000666593.2:c.7879A>T

ENST00000700202.2:c.7879A>T

ENST00000700202.1:c.346A>T

ENST00000380152.8:c.7879A>T

ENST00000544455.6:c.7879A>T

ENST00000614259.2:c.7887A>T

ENST00000665585.1:c.444A>T

ENST00000680887.1:c.7879A>T

ENST00000380152.7:c.7879A>T

ENST00000544455.5:c.7879A>T

ENST00000614259.1:n.7887A>T

NM_000059.3:c.7879A>T

Pathogenic

Met criteria codes **3**

PS3 PM2_Supporting PP4_Strong

Not Met criteria codes **3**

PP3 BP4 BP1

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 1.0.0*

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







[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel






ENIGMA BRCA1 and BRCA2 VCEP

The c.7879A>T variant in BRCA2 is a missense variant predicted to cause substitution of Isoleucine by Phenylalanine at amino acid 2627 (p.Ile2627Phe). 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). This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.25 indicating that impact on BRCA2 function via protein change is unclear (score range 0.18-0.30). SpliceAI predictor score of 0.00 suggests that the variant has no impact on splicing (score threshold < 0.10) (no bioinformatic code is applied). Reported by three calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs: 29988080, 33609447, 32444794) (PS3 met). Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 406 (based on Cosegregation LR=1.88; Co-occurrence LR=1.28; Family History LR=168.6), above the threshold for Very strong evidence towards pathogenicity (LR > 350) (PP4_Very strong met; PMID: 17924331, 31853058). In summary, this variant meets the criteria to be classified as a Pathogenic variant for BRCA2-related cancer predisposition based on the ACMG/AMP criteria applied as specified by the ENIGMA BRCA1/2 VCEP (PM2_Supporting, PP4_Very strong, PS3).

Met criteria codes

PS3			Reported by three calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs: 29988080, 33609447, 32444794) (PS3 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).
PP4_Strong			Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 406 (based on Cosegregation LR=1.88; Co-occurrence LR=1.28; Family History LR=168.6), above the threshold for Very strong evidence towards pathogenicity (LR > 350) (PP4_Very strong met; PMID: 17924331).

Not Met criteria codes

PP3			This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.25 indicating that impact on BRCA2 function via protein change is unclear (score range 0.18-0.30). SpliceAI predictor score of 0.00 suggests that the variant has no impact on splicing (score threshold < 0.10) (no bioinformatic code is applied).
BP4			This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.25 indicating that impact on BRCA2 function via protein change is unclear (score range 0.18-0.30). SpliceAI predictor score of 0.00 suggests that the variant has no impact on splicing (score threshold < 0.10) (no bioinformatic code is applied).
BP1			This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.25 indicating that impact on BRCA2 function via protein change is unclear (score range 0.18-0.30). SpliceAI predictor score of 0.00 suggests that the variant has no impact on splicing (score threshold < 0.10) (no bioinformatic code is applied).

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See Report	Preferred Variant Title	Classification <i>i</i>	Condition	Published Date	Version <i>i</i>	Criteria Specification	Gene
View	NM_000059.4(BRCA2):c.7879A>T (p.Ile...	Pathogenic	BRCA2-Related Cancer Predisposition ↗	2024-06-12	2.0	ClinGen ENIGMA BRCA1 and BRCA2 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for BRCA2 Version 1.0.0 ↗	BRCA2 ↗
View	NM_000059.4(BRCA2):c.7879A>T (p.Ile...	Pathogenic	Breast-Ovarian Cancer, Familial, Susceptibility To, 2 ↗	2024-04-23	1.1	ClinGen ENIGMA BRCA1 and BRCA2 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for BRCA2 Version 1.0.0 ↗	BRCA2 ↗
View	NM_000059.4(BRCA2):c.7879A>T (p.Ile...	Pathogenic	Breast-Ovarian Cancer, Familial, Susceptibility To, 2 ↗	2023-10-08	1.0	ClinGen ENIGMA BRCA1 and BRCA2 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for BRCA2 Version 1.0.0 ↗	BRCA2 ↗

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