

Variant: *NM_000059.4(BRCA2):c.7759C>T (p.Leu2587Phe)*

Version: 1.0

CA025261 [↗](#)

141335 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: f5cdac22-eb4f-453b-9e3f-a1d351529c9d

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HGVS expressions

NM_000059.4(BRCA2):c.7759C>T (p.Leu2587Phe)

NM_000059.4:c.7759C>T

NC_000013.11:g.32357883C>T

CM000675.2:g.32357883C>T

NC_000013.10:g.32932020C>T

CM000675.1:g.32932020C>T

NC_000013.9:g.31830020C>T

NG_012772.3:g.47404C>T

ENST00000470094.2:c.7759C>T

ENST00000528762.2:c.7759C>T

ENST00000530893.7:c.7390C>T

ENST00000665585.2:c.7759C>T

ENST00000666593.2:c.7759C>T

ENST00000700202.2:c.7759C>T

ENST00000700202.1:c.226C>T

ENST00000380152.8:c.7759C>T

ENST00000544455.6:c.7759C>T

ENST00000614259.2:c.7759C>T

ENST00000665585.1:c.324C>T

ENST00000680887.1:c.7759C>T

ENST00000380152.7:c.7759C>T

ENST00000544455.5:c.7759C>T

ENST00000614259.1:n.7759C>T

NM_000059.3:c.7759C>T

Benign

Met criteria codes **4**

[BS1_Supporting](#) [BS3](#) [BP5_Stand](#)
[Alone](#) [BP4](#)

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.7759C>T variant in BRCA2 is a missense variant predicted to cause substitution of leucine by phenylalanine at amino acid 2587 (p.Leu2587Phe). The highest non-cancer, non-founder population filter allele frequency in gnomAD v2.1 (exomes only, non-cancer subset, read depth ≥20) or gnomAD v3.1 (non-cancer subset, read depth ≥20) is 0.00004512 in the European (non-Finnish) population which is within the ENIGMA BRCA1/2 VCEP threshold (>0.00002 to ≤ 0.0001) for BS1_Supporting (BS1_Supporting met). This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.15, which is below the recommended threshold of 0.18 for predicting no impact on BRCA2 via protein change. A SpliceAI score of 0.04 predicts no impact on splicing (score threshold <0.10) (BP4 met). Reported by four calibrated studies to exhibit protein function similar to benign control variants (PMIDs:38417439, 33293522, 39779857, 39779848) (BS3 met). Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.0022 (based on Cosegregation LR=0.092; Pathology LR=0.675; Family History LR=0.0345), below the thresholds for Very strong benign evidence (LR <0.00285) (BP5_Very strong met; PMID 34597585, 31853058). In summary, this variant meets the criteria to be classified as a Benign variant for BRCA2-related cancer predisposition based on the ACMG/AMP criteria applied as specified by the ENIGMA BRCA1/2 VCEP (BS1_Supporting, BP4, BS3, BP5_Very strong).

Met criteria codes

BS1_Supporting			The highest non-cancer, non-founder population filter allele frequency in gnomAD v2.1 (exomes only, non-cancer subset, read depth ≥20) or gnomAD v3.1 (non-cancer subset, read depth ≥20) is 0.00004512 in the European (non-Finnish) population which is within the ENIGMA BRCA1/2 VCEP threshold (>0.00002 to ≤ 0.0001) for BS1_Supporting (BS1_Supporting met).
BS3			Reported by four calibrated studies to exhibit protein function similar to benign control variants (PMIDs:38417439, 33293522, 39779857, 39779848) (BS3 met).
BP5_Stand Alone			Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.0022 (based on Cosegregation LR=0.092; Pathology LR=0.675; Family History LR=0.0345), below the thresholds for Very strong benign evidence (LR <0.00285) (BP5_Very strong met; PMID 34597585, 31853058).
BP4			This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.15, which is below the recommended threshold of 0.18 for predicting no impact on BRCA2 via protein change. A SpliceAI score of 0.04 predicts no impact on splicing (score threshold <0.10) (BP4 met).

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