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Variant: NM_000059.4(BRCA2):c.7868A>T (p.His2623Leu)

Version: 1.0

CA387747085

922959 (ClinVar)

Gene: BRCA2 (HGNC:675)
Condition: BRCA2-related cancer predisposition (MONDO:0700269)
Inheritance Mode: Autosomal dominant inheritance
UUID: 23509fa2-5ef6-4507-a1e5-5b1a314fe53d
Approved on: 2026/7/15
Published on: 2026/7/15

HGVS expressions

NM_000059.4(BRCA2):c.7868A>T (p.His2623Leu)
NM_000059.4:c.7868A>T
NC_000013.11:g.32362585A>T
CM000675.2:g.32362585A>T
NC_000013.10:g.32936722A>T
CM000675.1:g.32936722A>T
NC_000013.9:g.31834722A>T
NG_012772.3:g.52106A>T
ENST00000470094.2:c.7868A>T
ENST00000528762.2:c.7868A>T
ENST00000530893.7:c.7499A>T
ENST00000665585.2:c.7868A>T
ENST00000666593.2:c.7868A>T
ENST00000700202.2:c.7868A>T
ENST00000700202.1:c.335A>T
ENST00000380152.8:c.7868A>T
ENST00000544455.6:c.7868A>T
ENST00000614259.2:c.7876A>T
ENST00000665585.1:c.433A>T
ENST00000680887.1:c.7868A>T
ENST00000380152.7:c.7868A>T
ENST00000544455.5:c.7868A>T
ENST00000614259.1:n.7876A>T
NM_000059.3:c.7868A>T

Likely Pathogenic

Met criteria codes 3

PM2_Supporting PP3 PS3

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.7868A>T variant in BRCA2 is a missense variant predicted to cause substitution of Histidine by Leucine at amino acid 2623 (p.(His2623Leu)). 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 0.27, predicting an impact on splicing (score threshold ≥0.2). The computational predictor BayesDel (noAF) gives a score of 0.45, above the recommended threshold of 0.30 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 2 calibrated studies incorporating mRNA splicing effects to exhibit function similar to pathogenic control variants (PMIDs: 39779857, 39779848) (PS3 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 (v1.2) (PM2_Supporting, PP3, PS3).

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v4.1 (read depth ≥25x in >90% samples, PM2_Supporting met).
PP3	✔	This BRCA2 missense variant has a SpliceAI score of 0.27, predicting an impact on splicing (score threshold ≥0.2). The computational predictor BayesDel (noAF) gives a score of 0.45, above the recommended threshold of 0.30 for prediction of impact on BRCA2 function via protein change (PP3 met).
PS3	✔	Missense variant predicted to alter splicing, functional data considered only from assays that measure effect via mRNA and protein. Reported by 2 calibrated studies incorporating mRNA splicing effects to exhibit function similar to pathogenic control variants (PMIDs: 39779857, 39779848) (PS3 met).

Curation History

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