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Variant: NM_000059.4(BRCA2):c.7684T>G (p.Phe2562Val)

Version: 1.0

CA025231

182243 (ClinVar)

Gene: BRCA2 (HGNC:675)
Condition: BRCA2-related cancer predisposition (MONDO:0700269)
Inheritance Mode: Autosomal dominant inheritance
UUID: 11729bb9-a157-4483-beee-3d1d9bb5944b
Approved on: 2026/1/5
Published on: 2026/1/5

HGVS expressions

NM_000059.4(BRCA2):c.7684T>G (p.Phe2562Val)
NM_000059.4:c.7684T>G
NC_000013.11:g.32357808T>G
CM000675.2:g.32357808T>G
NC_000013.10:g.32931945T>G
CM000675.1:g.32931945T>G
NC_000013.9:g.31829945T>G
NG_012772.3:g.47329T>G
ENST00000470094.2:c.7684T>G
ENST00000528762.2:c.7684T>G
ENST00000530893.7:c.7315T>G
ENST00000665585.2:c.7684T>G
ENST00000666593.2:c.7684T>G
ENST00000700202.2:c.7684T>G
ENST00000700202.1:c.151T>G
ENST00000380152.8:c.7684T>G
ENST00000544455.6:c.7684T>G
ENST00000614259.2:c.7684T>G
ENST00000665585.1:c.249T>G
ENST00000680887.1:c.7684T>G
ENST00000380152.7:c.7684T>G
ENST00000544455.5:c.7684T>G
ENST00000614259.1:n.7684T>G
NM_000059.3:c.7684T>G

Uncertain Significance

Met criteria codes 2

PM2_Supporting PP3

Not Met criteria codes 2

BS3 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 1.1.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

ENIGMA BRCA1 and BRCA2 VCEP

The c.7684T>G variant in BRCA2 is a missense variant predicted to cause substitution of Phenylalanine by Valine at amino acid 2562 (p.(Phe2562Val)). 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 has a SpliceAI score of 0.27, predicting an impact on splicing (score threshold >0.20) (PP3 met). Missense variant predicted to alter splicing, functional data considered only from assays that measure effect via mRNA and protein. Results from two calibrated studies with cDNA based design not considered for code application (PMID:38417439, 32444794). Reported by two calibrated studies with discordant results. Functional effect similar to pathogenic control variants (PMID:39779857) and similar to benign control variants (PMID:39779848) (PS3 and BS3 not met). In summary, this variant meets the criteria to be classified as a Variant of uncertain significance for BRCA2-related cancer predisposition based on the ACMG/AMP criteria applied as specified by the ENIGMA BRCA1/2 VCEP (PM2_Supporting, PP3).

Met criteria codes

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).
PP3	✔	This BRCA2 missense variant has a SpliceAI score of 0.27, predicting an impact on splicing (score threshold >0.20) (PP3 met).

Not Met criteria codes

BS3	✖	Missense variant predicted to alter splicing, functional data considered only from assays that measure effect via mRNA and protein. Results from two calibrated studies with cDNA based design not considered for code application (PMID:38417439, 32444794). Reported by two calibrated studies with discordant results. Functional effect similar to pathogenic control variants (PMID:39779857) and similar to benign control variants (PMID:39779848) (PS3 and BS3 not met).
PS3	✖	Missense variant predicted to alter splicing, functional data considered only from assays that measure effect via mRNA and protein. Results from two calibrated studies with cDNA based design not considered for code application (PMID:38417439, 32444794). Reported by two calibrated studies with discordant results. Functional effect similar to pathogenic control variants (PMID:39779857) and similar to benign control variants (PMID:39779848) (PS3 and BS3 not met).

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000059.4(BRCA2):c.7684T>G (p.P...	Uncertain Significance	BRCA2-Related Cancer Predisposition	2026-01-05	1.0	ClinGen ENIGMA BRCA1 and BRCA2 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for BRCA2 Version 1.1.0	BRCA2

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