

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:** 2026-01-05

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## HGVS expressions

**NM\_000059.4:c.7684T>G**

**NM\_000059.4(BRCA2):c.7684T>G (p.Phe2562Val)**

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**

**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**

|                       |                                                                                   |                                                                                   |                                                                                                                                                                    |
|-----------------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>PM2_Supporting</b> |  |  | 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). |
| <b>PP3</b>            |  |  | 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**

|            |                                                                                     |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>BS3</b> |  |  | 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). |
| <b>PS3</b> |  |  | 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). |

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