

Variant: *NM_000059.4(BRCA2):c.68-7del*

Version: 2.0

[CA024535](#)

[52188 \(ClinVar\)](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UID: ae883dc2-3266-494c-88fd-5231ac12a103

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HGVS expressions

NM_000059.4:c.68-7del

- NM_000059.4(BRCA2):c.68-7del
- NC_000013.11:g.32319070del
- CM000675.2:g.32319070del
- NC_000013.10:g.32893207del
- CM000675.1:g.32893207del
- NC_000013.9:g.31791207del
- NG_012772.3:g.8591del
- NG_017006.2:g.1303del
- ENST00000470094.2:c.68-7del
- ENST00000528762.2:c.68-7del
- ENST00000530893.7:c.-302-7del
- ENST00000665585.2:c.68-7del
- ENST00000666593.2:c.68-7del
- ENST00000700202.2:c.68-7del
- ENST00000700200.1:n.191+2543del
- ENST00000700201.1:c.68-7del
- ENST00000380152.8:c.68-7del
- ENST00000544455.6:c.68-7del
- ENST00000614259.2:c.68-7del
- ENST00000680887.1:c.68-7del
- ENST00000380152.7:c.68-7del
- ENST00000530893.6:n.266-7del
- ENST00000544455.5:c.68-7del
- ENST00000614259.1:n.68-7del
- NM_000059.3:c.68-7del

Benign

Met criteria codes **5**

- BP4
- BP5
- BP7_Strong
- BS1_Supporting
- BS3

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*

Evidence submitted by expert panel

ENIGMA BRCA1 and BRCA2 VCEP

The c.68-7del variant is an intronic variant occurring in intron 2 of the BRCA2 gene. 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 0.00002293 in the Latino/Admixed American population which is within the ENIGMA BRCA1/2 VCEP threshold (>0.00002 to ≤ 0.0001) for BS1_Supporting (BS1_Supporting met). This BRCA2 intronic variant is outside of the native donor and acceptor 1,2 splice sites, and SpliceAI predictor score of 0.04 suggests that the variant has no impact on splicing (score threshold <0.10) (BP4 met). This is an intronic variant, and mRNA experimental analysis indicates no impact on splicing (PMIDs: 10534775, 21673748, 22505045), considered strong evidence against pathogenicity (BP7_Strong (RNA)). Reported by one calibrated study to exhibit protein function similar to benign control variants (PMID: 35979650) (BS3 met). Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.32 (based on Pathology LR=0.32), within the thresholds for Supporting benign evidence (LR 0.23-0.48) (BP5 met; PMID: 35979650). 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, BP7_Strong (RNA), BS3, BP5).

Met criteria codes

BP4			This BRCA2 intronic variant is outside of the native donor and acceptor 1,2 splice sites, and SpliceAI predictor score of 0.04 suggests that the variant has no impact on splicing (score threshold <0.10) (BP4 met).
BP5			Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.32 (based on Pathology LR=0.32), within the thresholds for Supporting benign evidence (LR 0.23-0.48) (BP5 met; PMID: 35979650).
BP7_Strong			This is an intronic variant, and mRNA experimental analysis indicates no impact on splicing (PMIDs: 10534775, 21673748, 22505045), considered strong evidence against pathogenicity (BP7_Strong (RNA)).
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 0.00002293 in the Latino/Admixed American population which is within the ENIGMA BRCA1/2 VCEP threshold (>0.00002 to ≤ 0.0001) for BS1_Supporting (BS1_Supporting met).
BS3			Reported by one calibrated study to exhibit protein function similar to benign control variants (PMID: 35979650) (BS3 met).

Curation History [↗](#)

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