

Variant: NM_007294.4(BRCA1):c.4159T>C (p.Ser1387Pro)

Version: 1.0

CA10575944 [↗](#)
224433 (ClinVar) [↗](#)

Gene: BRCA1 ([HGNC:672](#))
Condition: BRCA1-related cancer predisposition ([MONDO:0700268](#))
Inheritance Mode: Autosomal dominant inheritance
UUID: 9c48d2a8-1cec-4a03-88ae-2d943288ce71
Approved on: 2025/5/23
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HGVS expressions

- NM_007294.4:c.4159T>C**
NM_007294.4(BRCA1):c.4159T>C (p.Ser1387Pro)
NC_000017.11:g.43090970A>G
CM000679.2:g.43090970A>G
NC_000017.10:g.41242987A>G
CM000679.1:g.41242987A>G
NC_000017.9:g.38496513A>G
NG_005905.2:g.127014T>C
ENST00000461574.2:c.4159T>C
ENST00000470026.6:c.4159T>C
ENST00000473961.6:c.4033T>C
ENST00000476777.6:c.4156T>C
ENST00000477152.6:c.4081T>C
ENST00000478531.6:c.847T>C
ENST00000489037.2:c.4081T>C
ENST00000493919.6:c.709T>C
ENST00000494123.6:c.4159T>C
ENST00000497488.2:c.3271T>C
ENST00000618469.2:c.4159T>C
ENST00000634433.2:c.4036T>C
ENST00000644379.2:c.4159T>C
ENST00000644555.2:c.709T>C
ENST00000652672.2:c.4018T>C
ENST00000484087.6:c.727T>C
ENST00000700182.1:c.769T>C
ENST00000357654.9:c.4159T>C
ENST00000471181.7:c.4159T>C
ENST00000644379.1:c.480T>C
ENST00000352993.7:c.733T>C
ENST00000357654.7:c.4159T>C
ENST00000461221.5:c.*3942T>C
ENST00000461574.1:c.453T>C
ENST00000468300.5:c.850T>C
ENST00000471181.6:c.4159T>C
ENST00000478531.5:c.847T>C
ENST00000484087.5:c.472T>C
ENST00000487825.5:c.475T>C

	ENST00000491747.6:c.850T>C
	ENST00000493795.5:c.4018T>C
	ENST00000493919.5:c.709T>C
	ENST00000586385.5:c.5-27019T>C
	ENST00000591534.5:c.-43-16449T>C
	ENST00000591849.5:c.-99+34301T>C
	NM_007294.3:c.4159T>C
	NM_007297.3:c.4018T>C
	NM_007298.3:c.850T>C
	NM_007299.3:c.850T>C
	NM_007300.3:c.4159T>C
	NR_027676.1:n.4295T>C
	NM_007297.4:c.4018T>C
	NM_007299.4:c.850T>C
	NM_007300.4:c.4159T>C
	NR_027676.2:n.4336T>C

Likely Benign

Met criteria codes 2

BP5BP1_Strong

Not Met criteria codes 4

PS3PM2BS1BS3

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 BRCA1 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.4159T>C variant in BRCA1 is a missense variant predicted to cause substitution of serine by proline at amino acid 1387 (p.Ser1387Pro). This variant is present in gnomAD v2.1 (exomes only, non-cancer subset) or gnomAD v3.1 (non-cancer subset) but is below the ENIGMA BRCA1/2 VCEP threshold >0.00002 for BS1_Supporting (PM2_Supporting, BS1, and BA1 are not met). This missense variant is located outside of a key functional domain and was not predicted to alter mRNA splicing using SpliceAI (score 0.00, score threshold ≤0.1) (BP1_Strong met). Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.364 (based on Family History LR=0.364), within the thresholds for supporting benign evidence (LR >0.23 & ≤0.48) (BP5 met; PMID 31853058). In summary, this variant meets the criteria to be classified as a likely benign variant for BRCA1-related cancer predisposition based on the ACMG/AMP criteria applied as specified by the ENIGMA BRCA1/2 VCEP (BP1_Strong, BP5).			
Met criteria codes			
BP5			Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.364 (based on Family History LR=0.364), within the thresholds for supporting benign evidence (LR >0.23 & ≤0.48) (BP5 met; PMID 31853058).
BP1_Strong			

This missense variant is located outside of a key functional domain and was not predicted to alter mRNA splicing using SpliceAI (score 0.00, score threshold ≤ 0.1) (BP1_Strong met).

Not Met criteria codes

PS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			This variant is present in gnomAD v2.1 (exomes only, non-cancer subset) or gnomAD v3.1 (non-cancer subset) but is below the ENIGMA BRCA1/2 VCEP threshold >0.00002 for BS1_Supporting (PM2_Supporting, BS1, and BA1 are not met).
BS3			No calibrated studies were performed for this variant.

Curation History



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