

Variant: *NM_001204.7(BMPR2):c.1019T>C (p.Leu340Pro)*

Version: 2.0

CA350341382 [↗](#)

425864 (ClinVar) [↗](#)

Gene: BMPR2 ([HGNC:659](#))

Condition: pulmonary arterial hypertension ([MONDO:0015924](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 2e2cb93e-28ce-44fe-bca0-ce623262cce9

Approved on: 2026/4/9

Published on: 2026/4/9

HGVS expressions

NM_001204.7(BMPR2):c.1019T>C (p.Leu340Pro)

NM_001204.7:c.1019T>C

NC_000002.12:g.202530845T>C

CM000664.2:g.202530845T>C

NC_000002.11:g.203395568T>C

CM000664.1:g.203395568T>C

NC_000002.10:g.203103813T>C

NG_009363.1:g.159519T>C

ENST00000374580.10:c.1019T>C

ENST00000638587.1:c.950T>C

ENST00000374574.2:c.1019T>C

ENST00000374580.8:c.1019T>C

NM_001204.6:c.1019T>C

Likely Pathogenic

Met criteria codes 5

PP2 PP3 PM1 PM2_Supporting

PS4_Supporting

Not Met criteria codes 3

PS1 PM5 PVS1

Evidence Links 0

Expert Panel

Pulmonary Hypertension VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen Pulmonary Hypertension Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for BMPR2 Version 2.0.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Pulmonary Hypertension VCEP

The BMPR2 c.1019T>C (p.Leu340Pro) variant is an exonic variant which is located in exon 8. This variant is absent from gnomAD v2.1.1 controls and v4.1 (PM2_supporting met). The variant is located in a well-established protein kinase domain (PM1_met) and has been identified in 3 apparently unrelated individuals with PAH to date (PMIDs 18356561, 19555857, 32581362; PS4_supporting met). BMPR2 has a low rate of benign missense variation and missense variants are a common mechanism of disease (PP2). In silico prediction is consistent with a pathogenic effect ((REVEL score 0.980 (>0.75; PP3 met)). PP1 was not assessed due to absence of co-segregation data. No other

missense variants at the same amino acid have been reported for pulmonary arterial hypertension (PS1, PM5 not assessed). In summary, this variant meets the criteria to be classified as a likely pathogenic for pulmonary arterial hypertension based on the ACMG/AMP criteria applied, as specified by the ClinGen Pulmonary Hypertension VCEP: PM1, PM2_supporting, PP2, PP3, PS4_supporting (VCEP specification version 2.0, 1/30/2026).

Met criteria codes

PP2			In gnomAD v4.1, BMPR2 has a z-score of 3.28 for missense variants which is above the threshold of 3.09 (PMID: 404967) for constraint.
PP3			REVEL score: 0.980. SpliceAI score: 0.01 (benign)
PM1			Variant present in established Kinase domain
PM2_Supporting			Variant absent from gnomAD
PS4_Supporting			PS4_supp: met (+1). Three independent patients. PMID 18356561 (Sztrymf et al., 2008; French PH network): 1 patient (IPAH/HPAH) PMID 19555857 (Machado et al., 2009): 1 HPAH patient PMID 32581362 (Turro et al, 2020) WGS study (1 PAH patient E010683, supplemental data). No segregation or functional data present to date (11-09-2024)

Not Met criteria codes

PS1			No reported pathogenic variants for p.Leu340
PM5			No reported pathogenic variants for p.Leu340
PVS1			Missense variant with no apparent effect on splicing (SpliceAi score 0.01)

Curation History



 

 

Showing 1 to 2 of 2 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

[ClinGen Terms of Use.](#)

[✕ Powered by BCM's Genboree.](#)