

Variant: *NM_001204.7(BMPR2):c.247+2del*

Version: 1.1

CA645294002 [↗](#)

425732 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: d38b386c-73a2-4970-b3e4-063f9fa11106

Approved on: 2026/5/7

Published on: 2026/5/7

HGVS expressions

NM_001204.7:c.247+2del

NM_001204.7(BMPR2):c.247+2del

NC_000002.12:g.202464981del

CM000664.2:g.202464981del

NC_000002.11:g.203329704del

CM000664.1:g.203329704del

NC_000002.10:g.203037949del

NG_009363.1:g.93655del

ENST00000374580.10:c.247+2del

ENST00000638587.1:c.174del

ENST00000374574.2:c.247+2del

ENST00000374580.8:c.247+2del

ENST00000479069.1:n.154+2del

NM_001204.6:c.247+2del

Likely Pathogenic

Met criteria codes **3**

PS1_Supporting

PM2_Supporting

PVS1_Strong

Not Met criteria codes **1**

PS4

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. 247+2del variant is in the canonical donor site of intron 2, leading to in frame exon skipping. The variant is absent from gnomAD v4.1.0 and v2.1.1 (controls) (PM2_supporting). This variant has been reported in one heritable PAH proband (PMID:26387786) (PS4 not met). The in frame deletion removes 5.5% of the protein, including part of the critical ligand binding domain (PVS1_strong). RNA data showed two transcripts, one deleting amino acids 47-82 and one deleting aa63-82, both removing critical cysteine residues (Cys60

and Cys66) (PMID:26387786). SpliceAI (0.95) is consistent with a detrimental effect on splicing. Another variant in the same splice region, c.247+1, was classified as likely pathogenic by the PH VCEP (PS1_supporting). PP1, PS2, and PM6 were not assessed due to absence of co-segregation data. In summary, this variant meets the criteria to be classified as likely pathogenic for pulmonary arterial hypertension based on the ACMG/AMP criteria applied, as specified by the ClinGen Pulmonary Hypertension VCEP: PVS1_strong(RNA), PS1_supporting, PM2_supporting (VCEP specification version 2.0, 1/30/2026)

Met criteria codes

PS1_Supporting			Another variant in the same splice region, c.247+1, was classified as likely pathogenic by the PH VCEP.
PM2_Supporting			The variant is absent from gnomAD v2.1.1 controls and v4.1.
PVS1_Strong			Exon skipping preserves the reading frame but removes 5.5% of the protein, including part of the extracellular ligand binding domain (PVS1_strong). RNA data show two transcripts, one deleting amino acids 47-82 and one deleting aa63-82, both removing critical cysteine residues (Cys60 and Cys66). SpliceAI (0.95) is consistent with a detrimental effect on splicing.

Not Met criteria codes

PS4			The variant has been reported in one heritable PAH proband (PMID:26387786).
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Curation History



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