

Variant: *NM_001204.7(BMPR2):c.140G>A (p.Gly47Asp)*

Version: 1.0

CA350399236 [↗](#)

425707 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: a93496fb-2127-40d1-b171-77028c2dd33c

Approved on: 2025/1/22

Published on: 2025/1/22

HGVS expressions

NM_001204.7(BMPR2):c.140G>A (p.Gly47Asp)

NM_001204.7:c.140G>A

NC_000002.12:g.202464872G>A

CM000664.2:g.202464872G>A

NC_000002.11:g.203329595G>A

CM000664.1:g.203329595G>A

NC_000002.10:g.203037840G>A

NG_009363.1:g.93546G>A

ENST00000374580.10:c.140G>A

ENST00000638587.1:c.65G>A

ENST00000374574.2:c.140G>A

ENST00000374580.8:c.140G>A

ENST00000479069.1:n.47G>A

NM_001204.6:c.140G>A

Uncertain Significance

Met criteria codes **2**

PM1

PM2

Not Met criteria codes **7**

PS1

PS4

BA1

PP3

PM5

BS1

BP4

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 1.1.0*

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

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

Evidence submitted by expert panel

Pulmonary Hypertension VCEP

The NM_001204.7(BMPR2):c.140G>A (p.Gly47Asp) variant is a missense variant located within exon 2 of BMPR2, predicted to cause substitution of glycine to an aspartic acid. This variant is located within the conserved extracellular domain of the protein but does not affect a known critical residue (PM1_moderate). The variant is absent from gnomAD v2.1.1 (controls) and v4.1 (PM2_supporting). The REVEL prediction algorithm score is 0.55, which is below our threshold of ≥ 0.75 for pathogenicity (PP3_not met) and above our threshold

for benignity (BP4 not met). The variant has been reported in an individual with PAH associated with congenital heart disease (PMID: 15358693) but not in patients with hereditary or idiopathic PAH (PS4 not met). Alternative alleles at the same nucleotide or amino acid have not been reported (PS1 and PM5 not met). Functional studies have not been reported (PS3, not evaluated). Neither segregation or maternity/paternity studies have not been reported (PS2, PP1, BS4 not evaluated). In summary, this variant meets the criteria to be classified as a variant of unknown significance for pulmonary arterial hypertension based on the ACMG/AMP criteria applied, as specified by the ClinGen Pulmonary Hypertension VCEP: PM1_moderate, PM2_supporting (VCEP specification version 1.1.0, 1/18/2024).

Met criteria codes			
PM1			Located within the conserved extracellular domain of the protein but does not affect a known critical residue.
PM2			The variant is absent from gnomAD v2.1.1 (controls) and v4.1.
Not Met criteria codes			
PS1			Alternative alleles at the same nucleotide or amino acid have not been reported.
PS4			The variant has been reported in an individual with PAH associated with congenital heart disease (PMID: 15358693) but not in patients with hereditary or idiopathic PAH.
BA1			The variant is absent from gnomAD v2.1.1 (controls) and v4.1.
PP3			The REVEL prediction algorithm score is 0.55, which is below our threshold of >=0.75 for pathogenicity and above our threshold for benignity.
PM5			Alternative alleles at the same nucleotide or amino acid have not been reported.
BS1			The variant is absent from gnomAD v2.1.1 (controls) and v4.1.
BP4			The REVEL prediction algorithm score is 0.55, which is below our threshold of >=0.75 for pathogenicity and above our threshold for benignity.

Curation History 

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