

Variant: *NM_001204.7(BMPR2):c.1220A>C (p.Tyr407Ser)*

Version: 1.0

CA350341886 [↗](#)

425895 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 06fc6939-a4d4-4983-a3d1-9e886ac9e5ea

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HGVS expressions

NM_001204.7:c.1220A>C

NM_001204.7(BMPR2):c.1220A>C (p.Tyr407Ser)

NC_000002.12:g.202532676A>C

CM000664.2:g.202532676A>C

NC_000002.11:g.203397399A>C

CM000664.1:g.203397399A>C

NC_000002.10:g.203105644A>C

NG_009363.1:g.161350A>C

ENST00000374580.10:c.1220A>C

ENST00000638587.1:c.1151A>C

ENST00000374574.2:c.1220A>C

ENST00000374580.8:c.1220A>C

NM_001204.6:c.1220A>C

Uncertain Significance

Met criteria codes **3**

PM2_Supporting

PP3

PM1

Not Met criteria codes **5**

BS2

BS1

BP4

PS4

BA1

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 c.1220A>C (p. Tyr407Ser) variant is a missense variant located in exon 9 of the BMPR2 gene, predicted to cause substitution of tyrosine to serine at amino acid position 407. The variant is present in the conserved catalytic kinase domain but without functional evidence indicating a critical or non-critical amino acid residue (PM1_moderate). The variant is absent from gnomAD v2.1.1 controls and v4.1 (PM2_supporting). The REVEL prediction algorithm score is 0.981 and AlphaMissense is 0.9904 indicating pathogenicity (PP3_met). The variant has been reported in only one individual with PAH (PMID: 26387786) (PS4 not met). PS2 was not assessed due to lack of

paternity data. No functional studies have been conducted for this variant (PS3 not assessed). In summary, this variant meets the criteria to be classified as a variant of uncertain significance for pulmonary arterial hypertension based on the ACMG/AMP criteria applied, as specified by the ClinGen Pulmonary Hypertension VCEP: PM1_moderate, PM2_supporting, PP3_supporting (VCEP specification version 1.1.0, 1/18/2024).

Met criteria codes

PM2_Supporting			Variant is absent from gnomAD v2.1.1 controls and v4.1.
PP3			The REVEL score is 0.981 which is above the pathogenicity threshold of ≥ 0.75 , and the alpha missense score of 0.9904 predicted to be likely pathogenic.
PM1			Variant changes an amino acid in the kinase domain but without functional evidence indicating critical or non-critical.

Not Met criteria codes

BS2			Variant absent in gnomAD v2.1.1, v4.1
BS1			Variant is absent from gnomAD v2.1.1 controls and v4.1.
BP4			The REVEL score is 0.981 which is above the pathogenicity threshold of ≥ 0.75 , and the alpha missense score of 0.9904 predicted to be likely pathogenic.
PS4			The variant has been reported in a single PAH patient (PMID: 26387786).
BA1			Variant is absent from gnomAD v2.1.1 controls and v4.1.

Curation History



 

 

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