

Variant: *NM_001204.7(BMPR2):c.1202T>C (p.Leu401Ser)*

Version: 1.0

CA350341841 [↗](#)

425892 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: e5c447ba-d798-4f6f-b36c-f8610515e2b5

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HGVS expressions

NM_001204.7:c.1202T>C

NM_001204.7(BMPR2):c.1202T>C (p.Leu401Ser)

NC_000002.12:g.202532658T>C

CM000664.2:g.202532658T>C

NC_000002.11:g.203397381T>C

CM000664.1:g.203397381T>C

NC_000002.10:g.203105626T>C

NG_009363.1:g.161332T>C

ENST00000374580.10:c.1202T>C

ENST00000638587.1:c.1133T>C

ENST00000374574.2:c.1202T>C

ENST00000374580.8:c.1202T>C

NM_001204.6:c.1202T>C

Uncertain Significance

Met criteria codes **2**

PM1

PM2_Supporting

Not Met criteria codes **7**

BA1

BS1

BP4

PS2

PS4

PP3

PM6

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.1202T>C (p.Leu401Ser) variant is a missense variant harboured in exon 9 of the BMPR2 gene, predicted to cause substitution of leucine to serine encoding the functionally relevant catalytic kinase domain but without functional evidence indicating either critical or non-critical amino acid residue (PM1_moderate). This variant is absent from gnomAD v2.1.1 (controls) and v4.1 (PM2_supporting). The REVEL prediction algorithm score is 0.72, below the PH VCEP threshold of ≥ 0.75 for pathogenicity but above the threshold of ≤ 0.25 for benignity (PP3 and BP4 not met). The variant has been identified in a single individual with hereditary PAH, included in two reports (PMID:

32581362 and PMID: 16429395) (PS4 not met). The variant was paternally inherited (PS2 not met). Functional studies have not been conducted for this variant (PS3 not assessed). 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, PP3_not met (VCEP specification version 1.1.0, 1/18/2024)			
Met criteria codes			
PM1			p.Tyr407Ser is located in the catalytic kinase domain.
PM2_Supporting			The variant is absent from gnomAD v2.1.1 controls and v4.1.
Not Met criteria codes			
BA1			The variant is absent from gnomAD v2.1.1 controls and v4.1.
BS1			The variant is absent from gnomAD v2.1.1 controls and v4.1.
BP4			The REVEL score of 0.72 is below the PH VCEP threshold of >=0.75 for pathogenicity and above the threshold of <=0.25 for benignity.
PS2			The variant was paternally inherited.
PS4			The variant was identified in a single individual diagnosed with hereditary PAH.
PP3			The REVEL score of 0.72 is below the PH VCEP threshold of >=0.75 for pathogenicity and above the threshold of <=0.25 for benignity.
PM6			The variant was paternally inherited.

Curation History [↗](#)



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Showing 1 to 1 of 1 rows

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