

Variant: *NM_001204.7:c.1259G>T*

Version: 1.1

CA350341981 [↗](#)

3899317 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: d29a96bb-980a-4925-b8a8-1b094a65267c

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HGVS expressions

NM_001204.7:c.1259G>T

NC_000002.12:g.202532715G>T

CM000664.2:g.202532715G>T

NC_000002.11:g.203397438G>T

CM000664.1:g.203397438G>T

NC_000002.10:g.203105683G>T

NG_009363.1:g.161389G>T

ENST00000374580.10:c.1259G>T

ENST00000638587.1:c.1190G>T

ENST00000374574.2:c.1259G>T

ENST00000374580.8:c.1259G>T

NM_001204.6:c.1259G>T

Likely Pathogenic

Met criteria codes **5**

PM1

PM5

PS4_Supporting

PP3

PM2_Supporting

Not Met criteria codes **2**

BS1

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 2.0.0

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

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

Evidence submitted by expert panel

Pulmonary Hypertension VCEP

BMPR2 c.1259G>T is a missense variant predicted to cause substitution of cysteine to phenylalanine at amino acid position 420 (p.Cys420Phe). The variant is absent from gnomAD v2.1.1 and v4.1 (PM2_supporting). A REVEL score of 0.914 meets PP3_supporting (>0.75). The variant resides in the conserved catalytic kinase domain but does not affect a known critical residue (PM1_moderate). The variant has been reported in two unrelated PAH probands, one heritable (PMID: 27453251) and one idiopathic (PMID: 30578397, 32634488) (PS4_supporting). A different missense variant at the same amino acid residue, p.Cys420Arg (PMID: 11115378, 21801371) was classified by the PH VCEP as pathogenic (PM5_moderate). In summary, this variant meets the criteria to be classified as a likely pathogenic variant for

pulmonary arterial hypertension based on the ACMG/AMP criteria applied, as specified by the ClinGen Pulmonary Hypertension VCEP: PM1_moderate, PM5_moderate, PS4_supporting, PM2_supporting, PP3_supporting (VCEP specification version 2.0, 1/30/2026).			
Met criteria codes			
PM1			Resides in conserved catalytic kinase domain.
PM5			p.Cys420Arg (PMID: 11115378, 21801371) was previously classified by the PH VCEP as pathogenic.
PS4_Supporting			1 HPAH proband (PMID: 27453251), 1 IPAH proband (PMID: 3264488 and 30578397). Two probands meets the PS4_supporting threshold of >1 proband.
PP3			REVEL = 0.914, above the threshold of >+0.75.
PM2_Supporting			Absent from gnomad and v2.1.1 and v4.1.0.
Not Met criteria codes			
BS1			Absent in gnomad v2.1.1 and v4.1.0.
BA1			Absent in gnomad v2.1.1 and v4.1.0.

Curation History



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