

Variant: *NM_001204.7(BMPR2):c.2526G>T (p.Arg842Ser)*

Version: 1.0

CA2061546 [↗](#)

1398400 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: d12c3caa-4bb0-4292-acb4-ae0e8ae64e24

Approved on: 2024/9/10

Published on: 2024/9/10

HGVS expressions

NM_001204.7(BMPR2):c.2526G>T (p.Arg842Ser)

NM_001204.7:c.2526G>T

NC_000002.12:g.202556191G>T

CM000664.2:g.202556191G>T

NC_000002.11:g.203420914G>T

CM000664.1:g.203420914G>T

NC_000002.10:g.203129159G>T

NG_009363.1:g.184865G>T

ENST00000374580.10:c.2526G>T

ENST00000638587.1:c.2457G>T

ENST00000374574.2:c.1586+3303G>T

ENST00000374580.8:c.2526G>T

NM_001204.6:c.2526G>T

Uncertain Significance

Met criteria codes **1**

PM2_Supporting

Not Met criteria codes **6**

BS1

BP4

PS1

PP3

PM1

PM5

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 BMPR2 c.1882A>G variant is a missense variant predicted to result in an arginine to serine substitution at amino acid position 842 (p.Arg842Ser). The highest population minor allele frequency in gnomAD v.2.1.1 controls is 0.000070 in the European (non-Finnish) population thus meeting the threshold for PM2_supporting, resultantly neither BS1 nor BA1 were met. Computational evidence for pathogenicity as evaluated by REVEL generated a score of 0.468 indicating that neither BP4 nor PP3 were met. Additionally, the SpliceAI algorithm predicts no deleterious impact on putative acceptor or donor splice sites. The BMPR2 C-terminus is of unclear functional and/or

structural relevance, hence PM1 is not met. Due to no evidence of familial segregation PP1, PM6 and PS2 were not assessed. BS3 and PS3 were not evaluated as functional data is unavailable for this variant. In summary, the variant meets the criteria to be classified as a variant of uncertain significance (VUS) for pulmonary arterial hypertension based on the ACMG/AMP criteria applied, as specified by the ClinGen Pulmonary Hypertension VCEP: PM2_supporting (VCEP specification version 1.1, 1/18/2024).

Met criteria codes

PM2_Supporting			Allele frequency in European (non-Finnish) population (gnomAD v2.1.1 controls) is less than 0.01% (MAF: 3/42744 = 0.000070)
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Not Met criteria codes

BS1			Allele frequency is less than 0.01% in gnomAD v2.1.1 controls.
BP4			REVEL score is 0.468 hence does not meet the threshold to be classified as benign (REVEL<0.25)
PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3			REVEL score is 0.468 hence does not meet the threshold to be classified as deleterious (REVEL>0.75)
PM1			Variant is located in the C-terminus, of unclear functional and/or structural relevance.
PM5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History



 

 

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