

Variant: *NM_001204.7(BMPR2):c.1481C>T (p.Ala494Val)*

Version: 1.0

CA2061380 [↗](#)

333645 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 7cf9ea5c-6013-409f-9df8-4e4b68cbf8fb

Approved on: 2024/5/3

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HGVS expressions

NM_001204.7:c.1481C>T

NM_001204.7(BMPR2):c.1481C>T (p.Ala494Val)

NC_000002.12:g.202552783C>T

CM000664.2:g.202552783C>T

NC_000002.11:g.203417506C>T

CM000664.1:g.203417506C>T

NC_000002.10:g.203125751C>T

NG_009363.1:g.181457C>T

ENST00000374580.10:c.1481C>T

ENST00000638587.1:c.1412C>T

ENST00000374574.2:c.1481C>T

ENST00000374580.8:c.1481C>T

NM_001204.6:c.1481C>T

Uncertain Significance

Met criteria codes **3**

PP3 PM1 BS1

Not Met criteria codes **5**

PS1 PS3 PS4 PM5 PM2

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.1481C>T variant is a missense variant predicted to result in an alanine to valine substitution at amino acid 494 (p.Ala494Val). The minor allele frequency in gnomAD v2.1.1 controls "Other East Asian" is 0.0016% (11/7044 alleles), which exceeds the PH VCEP threshold of >0.1% for BS1. The variant is located in the kinase domain of BMPR2 (amino acids 203-504) but there is no functional evidence for or against this residue being critical, thus meeting PM1 without modification. The REVEL score is 0.872, exceeding the threshold of 0.75 (PP3). In summary, the variant meets the criteria to be classified as uncertain significance for pulmonary arterial

hypertension based on the ACMG/AMP criteria applied, as specified by the ClinGen Pulmonary Hypertension VCEP: BS1, PM1, PP3 (VCEP specification version 1.1, 1/18/2024).

Met criteria codes

PP3			REVEL score is 0.872, exceeding the threshold of 0.75.
PM1			Variant changes an amino acid in the kinase domain (aa 203-504) but without functional evidence indicating if it is critical or non-critical.
BS1			The frequency in gnomAD v2.1.1 "Other East Asian" controls is 0.0016, exceeding the VCEP specification threshold of 0.1%.

Not Met criteria codes

PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3			No functional studies were identified for this variant.
PS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5			No other missense change has been reported at this residue.
PM2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History



 

 

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