

Variant: *NM_001204.7(BMPR2):c.1175T>C (p.Val392Ala)*

Version: 1.0

CA350341779 [↗](#)

425889 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 8ce94f69-5d6f-4c30-bee8-b5174220c1f0

Approved on: 2024/11/6

Published on: 2024/11/6

HGVS expressions

NM_001204.7:c.1175T>C

NM_001204.7(BMPR2):c.1175T>C (p.Val392Ala)

NC_000002.12:g.202532631T>C

CM000664.2:g.202532631T>C

NC_000002.11:g.203397354T>C

CM000664.1:g.203397354T>C

NC_000002.10:g.203105599T>C

NG_009363.1:g.161305T>C

ENST00000374580.10:c.1175T>C

ENST00000638587.1:c.1106T>C

ENST00000374574.2:c.1175T>C

ENST00000374580.8:c.1175T>C

NM_001204.6:c.1175T>C

Uncertain Significance

Met criteria codes **3**

PM2_Supporting PP3 PM1

Not Met criteria codes **5**

BA1 BP4 BS1 BS2 PS4

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 NM_001204.7(BMPR2) c.1175T>C (p.Val392Ala) variant is located in exon 9 of the BMPR2 gene and is absent from gnomAD v2.1.1 (controls) and v4.1.0 (PM2_supporting). The variant is located in the functionally relevant catalytic kinase domain (PM1_met) but is not a critical or non-critical residue. The variant has been reported in only one individual with IPAH (PMID: 21737554 and 20002458) (PS4 not met). The REVEL score for the variant is 0.954, which is greater than the PH VCEP threshold of ≥ 0.75 , and the AlphaMissense score is 0.9795, indicating pathogenicity (PP3_met). No segregation or parental data were found (PP1 and PS2 not evaluated). No other amino acid

change at the same position has been reported for PAH (PS1 and PM5 not evaluated). No functional evidence was found (PS3 not evaluated). 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: PM2_supporting, PM1, PP3 (VCEP specification version 1.1.0, 1/18/2024).

Met criteria codes

PM2_Supporting			Variant absent in GnomAD v 4.1.0
PP3			REVEL score is 0.954 which is ≥ 0.75 cutoff and alpha missense score of 0.9795, predicted to be likely pathogenic
PM1			Variant located within the kinase domain (aa203-504)

Not Met criteria codes

BA1			Variant absent in GnomAD v 4.1.0
BP4			REVEL score is 0.954 which is greater than 0.25
BS1			Variant absent in GnomAD v 4.1.0
BS2			Variant absent in Gnomad v.4.1.0
PS4			PMID: 21737554 and 20002458 refer to the variant in the same IPAH Chinese patient.

Curation History



 ▾

 ▾

Showing 1 to 1 of 1 rows

--

