

Variant: *NM_001204.7(BMPR2):c.1424C>A (p.Ser475Ter)*

Version: 1.0

CA350344424 [↗](#)

425943 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: e689411a-9ea5-436f-ad52-c1b1bd9b8ae1

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HGVS expressions

NM_001204.7(BMPR2):c.1424C>A (p.Ser475Ter)

NM_001204.7:c.1424C>A

NC_000002.12:g.202552726C>A

CM000664.2:g.202552726C>A

NC_000002.11:g.203417449C>A

CM000664.1:g.203417449C>A

NC_000002.10:g.203125694C>A

NG_009363.1:g.181400C>A

ENST00000374580.10:c.1424C>A

ENST00000638587.1:c.1355C>A

ENST00000374574.2:c.1424C>A

ENST00000374580.8:c.1424C>A

NM_001204.6:c.1424C>A

Pathogenic

Met criteria codes **3**

PVS1

PS4_Supporting

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 1.1.0

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

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

Evidence submitted by expert panel

Pulmonary Hypertension VCEP

The BMPR2 c.1424C>A variant is a nonsense mutation in the kinase domain (exon 11 of 13). It is predicted to result in nonsense mediated mRNA decay, and therefore meets the criteria for PVS1. It is absent from gnomAD v2.1.1 (all samples), meeting PM2_supporting. There are three reports of this variant in the literature (PMIDs 16429395, 20534176 and 32581362). However, since PMID 16429395 summarized data from multiple countries, including the UK and French populations that were the subject of the later papers, it is not possible to determine if all three probands are independent. Thus conservatively, only counted 2 probands were counted (PS4_supporting). In summary, the

variant meets the criteria to be classified as pathogenic for pulmonary arterial hypertension based on ACMG/AMP criteria applied, as specified by the ClinGen Pulmonary Hypertension VCEP: PVS1, PM2_supporting, PS4_supporting (VCEP specification version 1.1, 1/18/2024).

Met criteria codes

PVS1			Truncating variant in the kinase domain, predicted to undergo NMD.
PS4_Supporting			Present in >1 probands.
PM2_Supporting			Absent in gnomAD v2.1.1.

Not Met criteria codes

BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History



 

 

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