

Variant: *NM_001204.7(BMPR2):c.1126G>A (p.Glu376Lys)*

Version: 1.0

CA350341606 [↗](#)

977222 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 1bf87321-26f3-4002-89f6-676c672578d4

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HGVS expressions

NM_001204.7:c.1126G>A

NM_001204.7(BMPR2):c.1126G>A (p.Glu376Lys)

NC_000002.12:g.202530952G>A

CM000664.2:g.202530952G>A

NC_000002.11:g.203395675G>A

CM000664.1:g.203395675G>A

NC_000002.10:g.203103920G>A

NG_009363.1:g.159626G>A

ENST00000374580.10:c.1126G>A

ENST00000638587.1:c.1057G>A

ENST00000374574.2:c.1126G>A

ENST00000374580.8:c.1126G>A

NM_001204.6:c.1126G>A

Uncertain Significance

Met criteria codes **2**

PM1

PM2

Not Met criteria codes **4**

BP4

PS4

PP3

PM6

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.1126G>A (p.Glu376Lys) variant is an exonic variant located 3 base pairs before the end of exon 8. The variant is absent from gnomAD v2.1.1 (controls) and v4.1 (PM2_Supporting). The variant has not been reported in pulmonary arterial hypertension patients to date. The variant has been identified in a patient with progressive myositis ossificans and a patient with unknown phenotype (ClinVar ID 977222) (PS4_not met). The variant is located in the well-established kinase domain (PM1_met). However, protein and splice-site prediction algorithms do not predict pathogenicity ((REVEL score 0.47 (>0,25-<0.75); Splice AI score 0 (benign)) (PP3_not met, BP4_not met). PP1

was not evaluated due to absence of co-segregation data. No other missense variants at the same amino acid have been reported for PAH (PS1, PM5 not assessed). In summary, this variant meets the criteria to be classified as VUS for pulmonary arterial hypertension based on the ACMG/AMP criteria applied, as specified by the ClinGen Pulmonary Hypertension VCEP: PM1, PM2_supporting (VCEP specification version 1.1.0, 1/18/2024).

Met criteria codes

PM1			Variant is located in the well-established kinase domain. PM1_met
PM2			Variant is absent from gnomAD (controls) v2.1.1 and v4.1

Not Met criteria codes

BP4			Protein and splice-site prediction algorithms do not predict benign character (REVEL score 0.47 (>0.25); Splice AI score 0 (benign)). BP4_not met.
PS4			The variant has not been reported in PAH patients to date. The variant has been identified in a patient with progressive myositis ossificans and in a patient with unknown phenotype (ClinVar ID 977222) (PS4_not met).
PP3			Protein and splice-site prediction algorithms do not predict pathogenic character (REVEL score 0.47 (<0.75); Splice AI score 0 (benign)). PP3_not met
PM6			No variants have been reported for pulmonary arterial hypertension.

Curation History



 

 

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