

Variant: *NM_001204.7(BMPR2):c.1512T>G (p.Leu504=)*

Version: 1.0

CA2061382 [↗](#)

898481 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 31b37b7a-c652-4665-b6e0-a563c20d152d

Approved on: 2024/5/2

Published on: 2024/5/2

HGVS expressions

NM_001204.7:c.1512T>G

NM_001204.7(BMPR2):c.1512T>G (p.Leu504=)

NC_000002.12:g.202552814T>G

CM000664.2:g.202552814T>G

NC_000002.11:g.203417537T>G

CM000664.1:g.203417537T>G

NC_000002.10:g.203125782T>G

NG_009363.1:g.181488T>G

ENST00000374580.10:c.1512T>G

ENST00000638587.1:c.1443T>G

ENST00000374574.2:c.1512T>G

ENST00000374580.8:c.1512T>G

NM_001204.6:c.1512T>G

Likely Benign

Met criteria codes **2**

BP7 BP4

Not Met criteria codes **3**

BS1 BA1 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.1512T>G;p.(leu504=) variant is a synonymous (silent) variant that is not predicted by SpliceAI to impact splicing. The highest population minor allele frequency in gnomAD v2.1.1 controls is 0.0138% (2/14452 alleles) in the North-Western European population, which is lower than the ClinGen Pulmonary Hypertension VCEP threshold of >0.1% for BS1 and >1% for BA1, but higher than the threshold of <0.01% for PM2 (BS1, BA1 and PM2 are not met). BS2 was not met as the variant was not observed as a homozygous allele in gnomAD v2.1.1 controls. BP4 is met based on the computational predictor, CADD, giving a score of 8.3 which is below the threshold of ≤10.0 for

BP4. Due to the absence of segregation data, **PP1**, **PM6** and **PS2** could not be evaluated. Due to absence of functional data, **BS3** and **PS3** could not be evaluated. In summary, the variant meets the criteria to be classified as a likely benign variant for pulmonary arterial hypertension based on the ACMG/AMP criteria applied, as specified by the ClinGen Pulmonary Hypertension VCEP: BP4, BP7 (VCEP specification version 1.1, 1/18/2024).

Met criteria codes

BP7			SpliceAI: 0.00 (no loss or gain of splice sites) Vertebrate PhyloP: -0.023 (nucleotide not conserved)
BP4			CADD score is <10 with 8.3 (GRCh37-v.1.7); REVEL not applicable

Not Met criteria codes

BS1			GnomAD v.2.1.1 controls: 0.014% (2/14452 alleles) in North West Europeans with >1000 allele counts, which is smaller than 0.1%
BA1			GnomAD v.2.1.1 controls: 0.014% (2/14452 alleles) in North West Europeans with >1000 allele counts, which is not greater than 1%
PM2			GnomAD v.2.1.1 controls: 0.014% (2/14452 alleles) in North West Europeans with >1000 allele counts, which is higher than the cut-off value for PM2 of 0.01%

Curation History



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