The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000314.8(PTEN):c.91A>G (p.Asn31Asp)

Version: 1.0

CA377784410

943637 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: 7af2f998-2e92-4fe3-a10d-a16cc797dd3e
Approved on: 2023/8/4
Published on: 2023/10/19

HGVS expressions

NM_000314.8:c.91A>G
NM_000314.8(PTEN):c.91A>G (p.Asn31Asp)
NC_000010.11:g.87894036A>G
CM000672.2:g.87894036A>G
NC_000010.10:g.89653793A>G
CM000672.1:g.89653793A>G
NC_000010.9:g.89643773A>G
NG_007466.2:g.35598A>G
ENST00000700029.2:c.91A>G
ENST00000710265.1:c.91A>G
ENST00000472832.3:c.91A>G
ENST00000688158.2:n.899+13598A>G
ENST00000688922.2:c.91A>G
ENST00000700021.1:c.91A>G
ENST00000700022.1:c.91A>G
ENST00000706954.1:c.91A>G
ENST00000706955.1:c.*126A>G
ENST00000686459.1:c.91A>G
ENST00000688158.1:c.*275+13598A>G
ENST00000688308.1:c.91A>G
ENST00000693560.1:c.610A>G
ENST00000371953.8:c.91A>G
ENST00000371953.7:c.91A>G
ENST00000462694.1:n.93A>G
ENST00000610634.1:c.-12A>G
NM_000314.5:c.91A>G
NM_000314.6:c.91A>G
NM_001304717.2:c.610A>G
NM_001304718.1:c.-615A>G
NM_000314.7:c.91A>G
NM_001304717.5:c.610A>G
NM_001304718.2:c.-615A>G

Likely Pathogenic

Met criteria codes 6

BS3_Supporting PS2 PP2 PP3 PM2_Supporting PS4_Supporting

Not Met criteria codes 1

PP1

Evidence Links 0

Expert Panel

PTEN VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen PTEN Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for PTEN Version 3.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

PTEN VCEP

NM_000314.8(PTEN):c.91A>G (p.Asn31Asp) meets criteria to be classified as likely pathogenic for PTEN Hamartoma Tumor syndrome in an autosomal dominant manner using modified ACMG criteria (ACMG Classification Rules Specified for PTEN Variant Curation version 3.0.0). Please see a summary of the rules and criteria codes in the "PTEN ACMG Specifications Summary" document (assertion method column). PS2: De novo (both maternity and paternity confirmed) observation in a patient with the disease and no family history. [internal laboratory contributor(s)] PS4_P: Proband(s) with phenotype specificity score of 1-1.5. [internal laboratory contributor(s)] PM2_P: Absent in large sequenced populations OR present at extremely low (<0.00001, 0.001%) allele frequency in the gnomAD cohort. (PMID 27535533). PP2: PTEN is defined by the PTEN Expert Panel as a gene that has a low rate of benign missense variation and where missense variants are a common mechanism of disease. PP3: in silico REVEL score of 0.966 (>0.7) BS3_P: Well-established functional studies show no deleterious effect: Phosphatase activity >0 (score = 0.549559228) per Mighell et al. 2018 (PMID: 29706350). Using the Bayesian point system (PMID: 29300386) for this variant with conflicting evidence: 1 pathogenic strong, 4 pathogenic supporting and 1 benign supporting codes get (4*1) + (1*4)+ (- 1*1) points = total is 7 (Likely Pathogenic).

Met criteria codes

BS3_Supporting	✔	Mighell PMID: 29706350 (0.225696942) WT_like, BS3_supp
PS2	✔	De novo (both maternity and paternity confirmed) observation in a patient with the disease and no family history. (GeneDx)
PP2	✔	PTEN is defined by the PTEN Expert Panel as a gene that has a low rate of benign missense variation and where missense variants are a common mechanism of disease.
PP3	✔	REVEL score: 0.919 (>0.7)
PM2_Supporting	✔	Absent in large sequenced populations OR present at extremely low (<0.00001, 0.001%) allele frequency in the gnomAD cohort. (PMID 27535533).
PS4_Supporting	✔	GeneDx case: de novo via exome trio in child with extreme macrocephaly, hydrocephalus, GI polyps, motor delay, brain venous anomaly. Gets PS2 and 1 point towards PS4_P

Not Met criteria codes

PP1	✖	GeneDx case: child with delays, hypotonia, macrocephaly NOS. Variant inherited from mother with macrocephaly. No PS4_P points but counts as one meiosis towards PP1.

Curation History

Showing 1 to 1 of 1 rows

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