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:c.152ATG[1]

Version: 1.0

CA645559021

640550 (ClinVar)

Gene: PTEN
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: 72ac9fd5-2f91-490d-a1de-f561657d95e4
Approved on: 2023/12/1
Published on: 2023/12/14

HGVS expressions

NM_000314.8:c.152ATG[1]
NC_000010.11:g.87894100_87894102del
CM000672.2:g.87894100_87894102del
NC_000010.10:g.89653857_89653859del
CM000672.1:g.89653857_89653859del
NC_000010.9:g.89643837_89643839del
NG_007466.2:g.35662_35664del
ENST00000700029.2:c.155_157del
ENST00000710265.1:c.155_157del
ENST00000472832.3:c.155_157del
ENST00000688158.2:n.899+13662_899+13664del
ENST00000688922.2:c.155_157del
ENST00000700021.1:c.155_157del
ENST00000700022.1:c.155_157del
ENST00000706954.1:c.155_157del
ENST00000706955.1:c.*190_*192del
ENST00000686459.1:c.155_157del
ENST00000688158.1:c.*275+13662_*275+13664del
ENST00000688308.1:c.155_157del
ENST00000688922.1:c.24_26del
ENST00000693560.1:c.674_676del
ENST00000371953.8:c.155_157del
ENST00000371953.7:c.155_157del
ENST00000462694.1:n.157_159del
ENST00000610634.1:c.53_55del
NM_000314.5:c.155_157del
NM_000314.6:c.155_157del
NM_001304717.2:c.674_676del
NM_001304718.1:c.-551_-549del
NM_000314.7:c.155_157del
NM_001304717.5:c.674_676del
NM_001304718.2:c.-551_-549del
NM_000314.8:c.155_157del

Met criteria codes 4

Expert Panel

Likely Pathogenic

PS3_Moderate PS4_Moderate PM2_Supporting PS2

Not Met criteria codes 1

PM4

Evidence Links 0

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

PTEN c.892C>G (p.Gln298Glu) meets criteria to be classified as likely pathogenic for PTEN Hamartoma Tumor syndrome in an autosomal dominant manner using modified ACMG criteria (PMID 30311380). 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) SCV001905678.1). PS4_M: Probands with phenotype specificity score of 2-3.5. (PMID: 21194675, Internal laboratory contributor(s) SCV001905678.1). PS3_M: Massively parallel functional assay interrogating phosphatase activity demonstrating a statistically significant difference from wild type (PMID: 29706350). PM2_P: Absent in large sequenced populations (PMID: 27535533).

Met criteria codes

PS3_Moderate	✔	Mighell et al (2018): high confidence variant, score = -3.437
PS4_Moderate	✔	Identified in 4 individuals: Father (43 yo) and son (16.9 yo), both with macrocephaly, lipomas and speckled penis' [Tan et al 2011, PMID 21194675]; A 2 yo index patient with macrocephaly, DD and rectal polyps [University Hospital Tübingen - ClinVar: SCV001905678.1]; and a 19 yo M with macrocephaly (64.2 cm), lipoma, penile macules, >6 cutaneous signs (acral keratoses, palmar & plantar keratoses, facial papules), mucosal neuroma, tongue lesion [Lachlan et al 2007, PMID 17526800].
PM2_Supporting	✔	Absent in gnomAD
PS2	✔	Confirmed de novo in a 2 yo patient with macrocephaly, DD and rectal polyps (ClinVar: SCV001905678.1).

Not Met criteria codes

PM4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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