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_000314.6(PTEN):c.195C>G (p.Tyr65Ter)

Version: 1.0

CA10582757

237643 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: 994ade45-e2c0-40c5-9bb6-a646666f386c
Approved on: 2019/3/5
Published on: 2019/7/23

HGVS expressions

NM_000314.6:c.195C>G
NM_000314.6(PTEN):c.195C>G (p.Tyr65Ter)
NC_000010.11:g.87925543C>G
CM000672.2:g.87925543C>G
NC_000010.10:g.89685300C>G
CM000672.1:g.89685300C>G
NC_000010.9:g.89675280C>G
NG_007466.2:g.67105C>G
ENST00000700029.2:c.195C>G
ENST00000710265.1:c.195C>G
ENST00000472832.3:c.195C>G
ENST00000688158.2:n.930C>G
ENST00000688922.2:c.195C>G
ENST00000700021.1:c.165-5503C>G
ENST00000700022.1:c.195C>G
ENST00000700029.1:c.29C>G
ENST00000706954.1:c.195C>G
ENST00000706955.1:c.*230C>G
ENST00000686459.1:c.195C>G
ENST00000688158.1:c.*306C>G
ENST00000688308.1:c.195C>G
ENST00000688922.1:c.64C>G
ENST00000693560.1:c.714C>G
ENST00000371953.8:c.195C>G
ENST00000371953.7:c.195C>G
ENST00000498703.1:n.21C>G
ENST00000610634.1:c.93C>G
NM_000314.5:c.195C>G
NM_001304717.2:c.714C>G
NM_001304718.1:c.-541-5503C>G
NM_000314.7:c.195C>G
NM_001304717.5:c.714C>G
NM_001304718.2:c.-541-5503C>G
NM_000314.8:c.195C>G

Pathogenic

Met criteria codes 3

PM2 PS4_Supporting PVS1

Not Met criteria codes 21

PM6 PM1 PM3 PM5 PM4
BA1 BS1 BS4 BS3 BS2 BP5
BP7 BP4 BP3 BP1 BP2 PS1
PS2 PP1 PP2 PP3

Evidence Links 5

Expert Panel

PTEN VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

PTEN VCEP

PTEN c.195C>G (p.Y65X) meets criteria to be classified as 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). PVS1: Null variant predicted to result in nonsense-mediated decay or causing truncation/frameshift at or 5' to c.1121 (NM_000314.4). PM2: Absent in large sequenced populations (PMID 27535533). PS4_P: Proband(s) with phenotype specificity score of 1-1.5. (PMID 23335809)

Met criteria codes

PM2	✔	KS: Absent in gnomAD. MP agrees.
PS4_Supporting	✔	Bubien 2013 Per K. Sesock: Patient 4 with CS. Present: mucocutaneous lesions, facial papules, oral mucosal papillomatosis, acral keratoses, speckled penis, GI polyps, benign thyroid. OFC = not done. CC score = about 17. Per J. Mester: per personal correspondence from Dr. Longy (corresponding author), pt was adult with goiter at age 20, left hemicolectomy at 33 y for polyposis coli with hamartomatous polyps, mild mental retardation, oral papillomatosis, cutaneous fibroma, acral keratosis, genital lentigines, meningioma. Recalculated CC score = 34 based on updated polyp information, PS4_P applies. PubMed:23335809 Variant listed in Table S2 as identified in a proband who is age 31.1. Authors report that probands met relaxed International Cowden Consortium operational criteria for CS. PubMed:21194675 Case 190 with BRRS, autism, macrocephaly, and hyperactivity. Child CC score = 4. PubMed:28454995
PVS1	✔	KS: Premature termination codon (nonsense) subject to NMD. MP agrees.

Not Met criteria codes

PM6	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4	✖	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

BS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3		✖	PubMed:29785012 PubMed:29706350
BS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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