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_024675.3(PALB2):c.682C>T (p.Gln228Ter)

Version: 2.0

CA395136420

484222 (ClinVar)

Gene: PALB2 (HGNC:79728)
Condition: PALB2-related cancer predisposition (MONDO:0700272)
Inheritance Mode: Autosomal dominant inheritance
UUID: 4205f611-bd22-45be-b78c-6cd3f98a6621
Approved on: 2023/4/5
Published on: 2025/9/16

HGVS expressions

NM_024675.3(PALB2):c.682C>T (p.Gln228Ter)
NM_024675.3:c.682C>T
NC_000016.10:g.23635864G>A
CM000678.2:g.23635864G>A
NC_000016.9:g.23647185G>A
CM000678.1:g.23647185G>A
NC_000016.8:g.23554686G>A
NG_007406.1:g.10494C>T
ENST00000561514.3:c.688C>T
ENST00000565038.2:c.211+1986C>T
ENST00000566069.6:c.682C>T
ENST00000697377.2:c.688C>T
ENST00000697379.2:c.688C>T
ENST00000561514.2:c.-204C>T
ENST00000697374.1:c.-204C>T
ENST00000697375.1:n.2029C>T
ENST00000697376.1:c.-204C>T
ENST00000697377.1:c.-204C>T
ENST00000697378.1:n.1202C>T
ENST00000697379.1:c.-204C>T
ENST00000697382.1:c.-204C>T
ENST00000697383.1:c.48+5246C>T
ENST00000697384.1:n.836C>T
ENST00000261584.9:c.682C>T
ENST00000261584.8:c.682C>T
ENST00000565038.1:c.86+1986C>T
ENST00000568219.5:c.-204C>T
NM_024675.4:c.682C>T

Pathogenic

Met criteria codes 3

PM2_Supporting PVS1 PM5_Supporting

Not Met criteria codes 2

BA1 BS1

Expert Panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

Criteria Specification Information

Evidence Links 0

Criteria Specification: *ClinGen Hereditary Breast, Ovarian and Pancreatic Cancer Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for PALB2 Version 1.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

The c.682C>T (p.Gln228Ter) variant in PALB2 is a nonsense variant predicted to cause a premature stop codon in biologically-relevant exon 4 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism. This variant is absent in the gnomAD v2.1.1. This alteration results in a termination codon upstream of the most C-terminus pathogenic alteration (PALB2 p.Tyr1183*) as classified by the HBOP VCEP, and is expected to be more deleterious. In summary, this variant meets criteria to be classified as pathogenic for autosomal dominant hereditary breast and pancreatic cancer and autosomal recessive FANCN based on the ACMG/AMP criteria applied as specified by the HBOP VCEP. (PVS1, PM2_Supporting, PM5_Supporting)

Met criteria codes

PM2_Supporting	✔	Variant is absent in the GnomAD v2.1.1 (PM2_Supporting)
PVS1	✔	The c.682C>T (p.Gln228Ter) variant in PALB2 is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-part of exon 4 leading to a premature termination codon impacting a critical domain in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM5_Supporting	✔	This alteration results in a termination codon upstream of the most C-terminus pathogenic alteration (PALB2 p.Tyr1183*) as classified by the ClinGen HBOP Variant Curation Expert Panel, and is expected to be more deleterious (PM5_Supporting)

Not Met criteria codes

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

Curation History

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