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_024675.4(PALB2):c.839del (p.Asn280fs)

Version: 2.0

CA494462159

480243 (ClinVar)

Gene: PALB2 (HGNC:79728)
Condition: PALB2-related cancer predisposition (MONDO:0700272)
Inheritance Mode: Autosomal dominant inheritance
UUID: 00a3410e-0fb0-4098-8488-6a237f88c850
Approved on: 2023/4/5
Published on: 2025/9/16

HGVS expressions

NM_024675.4:c.839del
NM_024675.4(PALB2):c.839del (p.Asn280fs)
NC_000016.10:g.23635712del
CM000678.2:g.23635712del
NC_000016.9:g.23647033del
CM000678.1:g.23647033del
NC_000016.8:g.23554534del
NG_007406.1:g.10651del
ENST00000561514.3:c.845del
ENST00000565038.2:c.211+2143del
ENST00000566069.6:c.839del
ENST00000697377.2:c.845del
ENST00000697379.2:c.845del
ENST00000561514.2:c.-47del
ENST00000697374.1:c.-47del
ENST00000697375.1:n.2186del
ENST00000697376.1:c.-47del
ENST00000697377.1:c.-47del
ENST00000697378.1:n.1359del
ENST00000697379.1:c.-47del
ENST00000697382.1:c.-47del
ENST00000697383.1:c.48+5403del
ENST00000697384.1:n.993del
ENST00000261584.9:c.839del
ENST00000261584.8:c.839del
ENST00000565038.1:c.86+2143del
ENST00000568219.5:c.-47del
NM_024675.3:c.839del

Pathogenic

Met criteria codes 3

PVS1 PM2_Supporting PM5_Supporting

Evidence Links 0

Expert Panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

Criteria Specification Information

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.839del (p.Asn280fs) variant in PALB2 is a frameshift 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 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. This variant is absent from gnomAD v2.1.1. 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, PM5_Supporting, PM2_Supporting).

Met criteria codes

PVS1	✔	The p.Asn280Thrfs*8 variant is predicted to result in a premature stop codon that leads to truncated or absent protein (PVS1)
PM2_Supporting	✔	Variant is absent in the GnomAD cohort (PM2_Supporting)
PM5_Supporting	✔	This alteration results in a termination codon upstream of the most C-terminus pathogenic alteration (PALB2 c.3549C>A (p.Tyr1183Ter)), as classified by the ClinGen Hereditary Breast, Ovarian, and Pancreatic Cancer VCEP, and is expected to be more deleterious (PM5_Supporting

Curation History

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