

Variant: *NM_000173.7:c.1039G>T*

Version: 1.0

CA397319701 [↗](#)

Gene: GP1BA ([HGNC:2811](#))

Condition: Bernard-Soulier syndrome ([MONDO:0009276](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: a93d0f40-ca46-471c-b340-f0c9f3ce5eff

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HGVS expressions

NM_000173.7:c.1039G>T

NC_000017.11:g.4933643G>T

CM000679.2:g.4933643G>T

NC_000017.10:g.4836938G>T

CM000679.1:g.4836938G>T

NC_000017.9:g.4777718G>T

NG_008767.2:g.6349G>T

ENST00000329125.6:c.1039G>T

ENST00000649830.1:c.-888+699C>A

ENST00000329125.5:c.1039G>T

ENST00000611961.1:c.1039G>T

NM_000173.6:c.1039G>T

Likely Pathogenic

Met criteria codes **3**

PVS1_Strong

PP4

PM2_Supporting

Not Met criteria codes **1**

PM3

Evidence Links **0**

Expert Panel

[Platelet Disorders VCEP](#) [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** *ClinGen Platelet Disorders Expert*

Panel Specifications to the ACMG/AMP Variant

Interpretation Guidelines for GP1BA Version 1.0.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Platelet Disorders VCEP

The NM_000173.7(GP1BA):c.1039G>T (p.Glu347Ter) variant is a nonsense variant in exon 2 of 2, that may cause loss of function of the protein; it is predicted to escape nonsense mediated decay and truncate 47% of the protein (PVS1_Strong). One patient has been reported with this variant (Case I, of PMID: 23414566) and had no aggregation response to ristocetin and decreased thrombin-induced aggregation but normal aggregation with ADP and collagen, additionally GPIb α expression was completely absent on patient platelets, which is highly specific to Bernard-Soulier syndrome (PP4). Additionally, the patient had excessive mucocutaneous bleeding and macrothrombocytopenia which are consistent with BSS. This variant is absent from gnomAD v4.1 (PM2_Supporting). In summary, this variant meets the criteria to

be classified as Likely Pathogenic for autosomal recessive Bernard-Soulier syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen PD VCEP: PVS1_strong, PP4, PM2_supporting.

Met criteria codes

PVS1_Strong			The NM_000173.7(GP1BA):c.1039G>T (p.Glu347Ter) variant is a nonsense variant in exon 2 of 2, that may cause loss of function of the protein; it is predicted to escape nonsense mediated decay and truncate 47% of the protein (PVS1_Strong). The expected truncation product was observed in case 1 of PMID: 23414566.
PP4			Case I, of PMID: 23414566, had no aggregation response to ristocetin and decreased thrombin-induced aggregation but normal aggregation with ADP and collagen, additionally GPIbα expression was completely absent on patient platelets, which is highly specific to Bernard-Soulier syndrome. Additionally, the patient had excessive mucocutaneous bleeding and macrothrombocytopenia which are consistent with BSS.
PM2_Supporting			This variant is absent from gnomAD v4.1 (PM2_Supporting).

Not Met criteria codes

PM3			Case I is compound heterozygous for the paternal Glu347Ter (reported as Glu331Ter) and maternal c.1480del (reported as c.1444del, classified Pathogenic by the PD VCEP) variants. Not considered here to avoid circularity.
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Curation History

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