

Variant: *NM_000407.5(GP1BB):c.423C>A (p.Cys141Ter)*

Version: 1.0

CA410677482 [↗](#)

1324499 (ClinVar) [↗](#)

Gene: GP1BB ([HGNC:2812](#))

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 994e5aca-0757-46ba-a777-2db182610bfc

Approved on: 2026/1/20

Published on: 2026/1/23

HGVS expressions

NM_000407.5:c.423C>A

NM_000407.5(GP1BB):c.423C>A (p.Cys141Ter)

NC_000022.11:g.19724266C>A

CM000684.2:g.19724266C>A

NC_000022.10:g.19711789C>A

CM000684.1:g.19711789C>A

NC_000022.9:g.18091789C>A

NG_007974.1:g.5724C>A

ENST00000366425.4:c.423C>A

ENST00000366425.3:c.423C>A

ENST00000431044.5:c.*1508C>A

NM_000407.4:c.423C>A

NR_037611.1:n.4163C>A

NR_037612.1:n.2667C>A

Pathogenic

Met criteria codes **5**

PVS1_Strong

PP1_Moderate

PM3

PM2_Supporting

PP4

Not Met criteria codes **1**

PS4

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 GP1BB Version 1.1.0

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

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

Evidence submitted by expert panel

Platelet Disorders VCEP

The c.423C>A (p.Cys141Ter) variant in GP1BB is a nonsense variant that may cause loss of function of the protein, however it is predicted to escape nonsense mediated decay and remove >10% of the protein (PVS1_Strong). At least one patient (Patient ID.1 in PMID: 33657022) with this variant had multiplate aggregation data showing virtually absent ristocetin agglutination in the proband and their affected sibling, which is disproportional to aggregation with other agonists. Platelet function studies in this manuscript were performed by

multiplate aggregation and not light transmission aggregometry which is the gold standard. The very low platelet counts, characteristic of BSS, explain why aggregation with other agonists are decreased and not normal as specified in the rule specifications for PP4. Additionally, the patient had excessive mucocutaneous bleeding. This pattern of results unequivocally supports a diagnosis of Bernard-Soulier Syndrome. This variant has been detected in at least 2 probands with Bernard-Soulier syndrome (Patient ID.1 in PMID: 33657022, Patient 1 in PMID: 22343686). Both individuals were homozygous for the variant (1 PM3 point, PM3). The variant has been reported to segregate in the proband plus two additional homozygous BSS affected family members (PMID:33657022), 2 PP1 points, PP1_Moderate). The MAF allele frequency in gnomAD v4.1.0 is 0.00002178 (based on 1/45916 alleles) in the Remaining population, which is lower than the ClinGen PD VCEP threshold (<0.00006517; PM2_Supporting). In summary, this variant meets the criteria to be classified as Pathogenic for autosomal recessive Bernard-Soulier syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen PD VCEP: PVS1_Strong, PP1_Moderate, PP4, PM2_Supporting and PM3 (VCEP specifications version 1.1).

Met criteria codes

PVS1_Strong			The c.423C>A (p.Cys141Ter) variant in GP1BB is a nonsense variant that may cause loss of function of the protein, however it is predicted to escape nonsense mediated decay and remove >10% of the protein (PVS1_Strong).
PP1_Moderate			The variant has been reported to segregate in the proband plus two additional homozygous BSS affected family members (PMID:33657022), 2 PP1 points, PP1_Moderate).
PM3			This variant has been detected in at least 2 probands with Bernard-Soulier syndrome (Patient ID.1 in PMID: 33657022, Patient 1 in PMID: 22343686). Both individuals were homozygous for the variant (1 PM3 point, PM3).
PM2_Supporting			The MAF allele frequency in gnomAD v4.1.0 is 0.00002178 (based on 1/45916 alleles) in the Remaining population, which is lower than the ClinGen PD VCEP threshold (<0.00006517; PM2_Supporting).
PP4			At least one patient (Patient ID.1 in PMID: 33657022) with this variant had multiplate aggregation data showing virtually absent ristocetin agglutination in the proband and their affected sibling, which is disproportional to aggregation with other agonists. Platelet function studies in this manuscript were performed by multiplate aggregation and not light transmission aggregometry which is the gold standard. The very low platelet counts, characteristic of BSS, explain why aggregation with other agonists are decreased and not normal as specified in the rule specifications for PP4. Additionally, the patient had excessive mucocutaneous bleeding. This pattern of results unequivocally supports a diagnosis of Bernard-Soulier Syndrome.

Not Met criteria codes

PS4			One individual is heterozygous for the variant and is considered informative due to presenting with macrothrombocytopenia. (PMID 36173017; 0.25 PS4 points).
-----	--	---	--

Curation History 

Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.