

Variant: *NM_000152.5(GAA):c.643G>T (p.Glu215Ter)*

Version: 1.0

CA401362407 [↗](#)

935900 (ClinVar) [↗](#)

Gene: GAA ([HGNC:2548](#))

Condition: glycogen storage disease II ([MONDO:0009290](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 53392e14-6e75-40d5-9261-362e0ad21850

Approved on: 2025/12/16

Published on: 2026/1/26

HGVS expressions

NM_000152.5:c.643G>T

NM_000152.5(GAA):c.643G>T (p.Glu215Ter)

NC_000017.11:g.80105845G>T

CM000679.2:g.80105845G>T

NC_000017.10:g.78079644G>T

CM000679.1:g.78079644G>T

NC_000017.9:g.75694239G>T

NG_009822.1:g.9290G>T

ENST00000570803.6:c.643G>T

ENST00000572080.2:c.643G>T

ENST00000577106.6:c.643G>T

ENST00000302262.8:c.643G>T

ENST00000302262.7:c.643G>T

ENST00000390015.7:c.643G>T

ENST00000570803.5:c.643G>T

NM_000152.3:c.643G>T

NM_001079803.1:c.643G>T

NM_001079804.1:c.643G>T

NM_000152.4:c.643G>T

NM_001079803.2:c.643G>T

NM_001079804.2:c.643G>T

NM_001079803.3:c.643G>T

NM_001079804.3:c.643G>T

Pathogenic

Met criteria codes **3**

PVS1

PM3_Supporting

PM2_Supporting

Not Met criteria codes **1**

PP4

Evidence Links **0**

Expert Panel

[Lysosomal Diseases VCEP](#) [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** *ClinGen Lysosomal Storage Disorders Variant Curation Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2*

[↗](#) **PDF**

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

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

Lysosomal Diseases VCEP

The NM_000152.5(GAA):c.643G>T (p.Glu215Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 3/20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). One patient with this variant has been reported with late onset Pompe disease, however, GAA enzyme activity levels were not provided. This patient is compound heterozygous for the c.643G>T (p.Glu215Ter) variant and a variant in GAA that has been classified as pathogenic by the ClinGen Lysosomal Diseases VCEP, c.-32-13T>G. The phase of the variants is unknown (PM3_Supporting). While this patient was diagnosed with late onset Pompe disease, GAA enzyme activity values were not provided. As a result, PP4 was not applied (PMID: 19588081). The variant is absent from gnomAD v4.1.0. There is a ClinVar entry for this variant (Variation ID: 935900; 1 star review status) with one submitter classifying the variant as pathogenic. In summary, the variant meets the criteria to be classified as pathogenic for Pompe disease by the ClinGen Lysosomal Diseases Variant Curation Expert Panel. GAA-specific ACMG/AMP criteria applied (Specifications version 2.0.0): PVS1, PM2_Supporting, PM3_Supporting. (Classification approved by the ClinGen Lysosomal Diseases Variant Curation Expert Panel on December 16, 2025).

Met criteria codes

PVS1			The NM_000152.5:c.643G>T (p.Glu215Ter) variant in GAA is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 3/20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM3_Supporting			This variant has been detected in at least one individual with Pompe disease. This patient was compound heterozygous for the variant and a variant classified as pathogenic by the ClinGen Lysosomal Diseases VCEP (c.-32-13T>G). Phase of the variants was not confirmed. 0.5 Points. PM3_Supporting.
PM2_Supporting			This variant is absent in gnomAD v4.1.0. (PM2_Supporting).

Not Met criteria codes

PP4			At least one patient with this variant was diagnosed with Pompe disease. Diagnosis was based on neurological examination, muscular biopsy findings from biceps brachialis, autopsy findings, paraffin-embedded cardiac biopsy and dry-blood spot analysis. GAA enzyme activity results were not provided. PP4 was not applied.
-----	---	---	--

▼

▼

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.