POST-ORLANDO 2025
Novità dal Meeting della Società Americana di Ematologia

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Torino
Centro Congressi Lingotto
19-21 febbraio 2026

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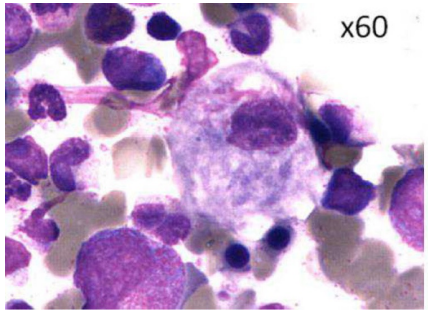
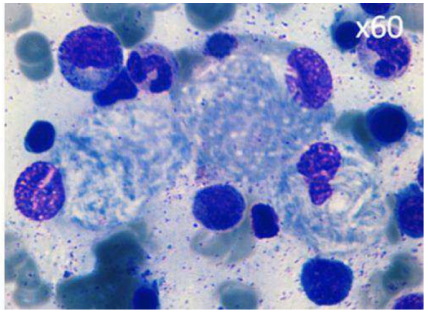
BMS						X	
Vertex						X	x
Pfizer			X				

Gaucher Disease

- Rare lysosomal storage disease
- Autosomal recessive
- 1:40.000-100.000
- **Gene *GBA*** *(over 300 mutations) (1q21)*
- Deficient beta-glucocerebrosidase activity


Philippe Gaucher (1854-1918)

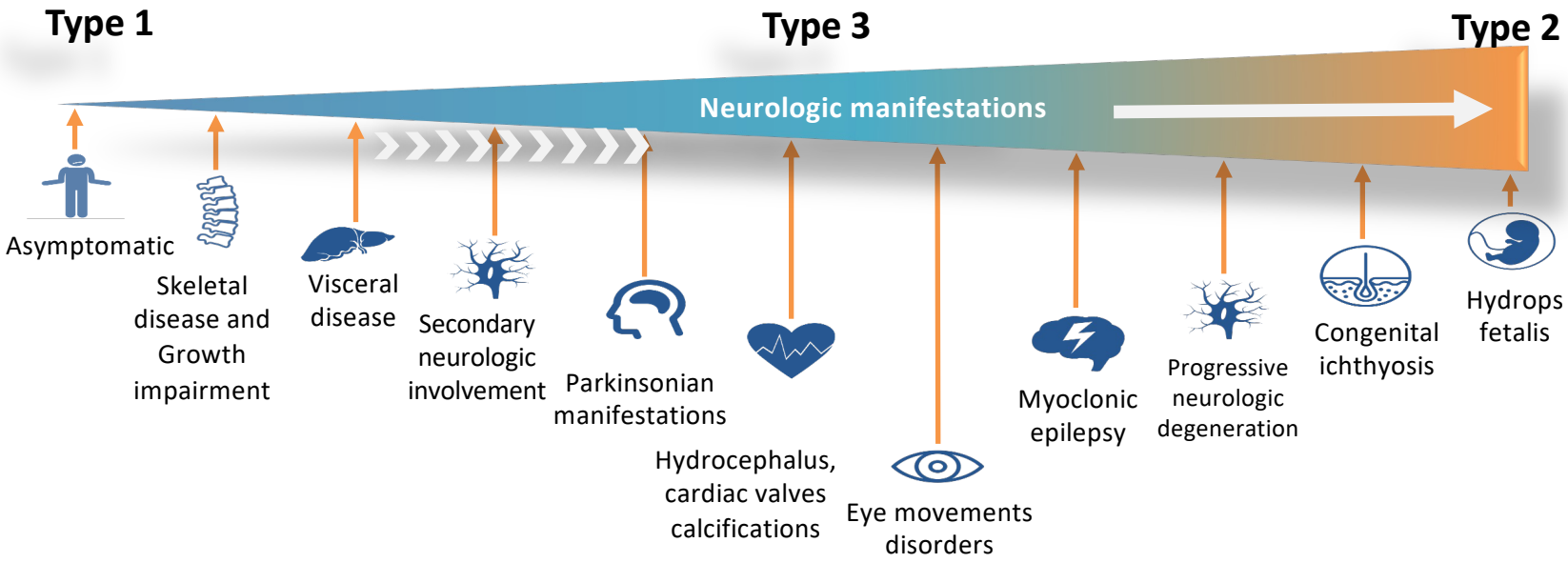




ERT: Enzyme Replecement Therapy

SRT: Substrate Reduction Therapy

Clinical Manifestations



In each patient can be present a wide spectrum of symptoms

Grabowski GA, Am J Hematol 2015
Linari S, Clin Cases Miner Bone Metab 2015
Goker-Alpan O, J Pediatr 2003

Clinical Manifestations

- Fatigue
- Risk of bleeding
- Hyperferritinemia (>80%)
- MGUS

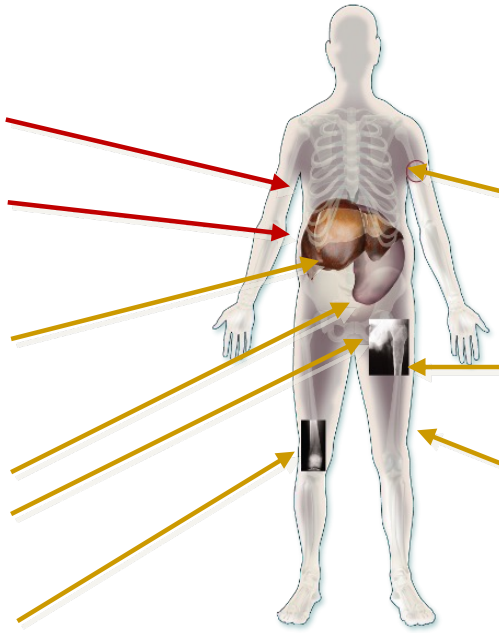
Bone pain (63%)
Bone crisis(33%)

Cholelitiasis (32%)

Hepatomegaly (79%)
Splenomegaly (87%)

Anemia (64%)
Thrombocytopenia (56%)

Erlenmeyer flask deformity (46%)



Pathological fractures (15%)

Osteonecrosis (25%)
Osteopenia (42%)

Bone Marrow Infiltration (40%)

Charrow J, Arch Intern Med 2000

ERT

Characteristics	Imiglucerasi	Alfa-Velaglucerasi	Alfa-Taliglucerasi
Immunogenicity	Low	Very low	Low-medium
Infusional reactions	Rare	Very rare	More frequent
Use	First ERT	More recent	Alternative
Indications	Adult	Adult / Pediatric patients	Adult
Costs	Good	Good	Very good

- **Recombinat Glucerobrosidase in Gaucher's Disease Type 1. No efficacy on CNS**
- Doses: 30-60 U/Kg iv every 2 weeks if mild-moderate o moderate-severe disease respectively
- In children: 60 U/Kg
- Dose min efficacy: 15 U/Kg
- Dose reduction, if good response, after 12-24 months of disease stability : 60 → 45 → 30 U/Kg

SRT

Characteristics	Eliglustat	Miglustat
Type	SRT selective	SRT non selective
Age	Adult	Adult
Genotype required	Yes (CYP2D6)	no
Efficacy	High	Moderate
Tollerability	Good	Limitate
Activity	Good alternative ERT	Last choice

- **SRT reduces the production of the substrate (glucosylceramide) that accumulates due to β-glucocerebrosidase deficiency, instead of replacing the enzyme** (as ERT does)
- The CYP2D6 phenotype describes how effectively a person **metabolizes drugs that depend on the CYP2D6 enzyme** (such as Eliglustat)
- It is essential before starting Eliglustat SRT

ERT vs SRT

Characteristics	ERT	SRT
Route	Intravenous	Oral
Dosage	Every 2 weeks	Daily
Drugs	**Imiglucerasi** **Alfa-Velaglucerasi** **Alfa-Taliglucerasi**	**Eliglustat** **Miglustat**
Dose	30-60 U/Kg every 2 weeks	Eliglustat 84 mg x 1 cp/die if PM Eliglustat 84 mg 1 cp x 2/die if EM / IM Miglustat 100 mg x 3/die
First choice	Yes Standard of care	No Alternative
CNS	No active	No active
Pediatric	Yes	No

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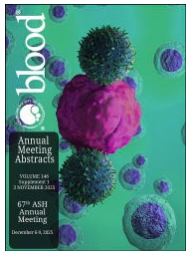

509. BONE MARROW FAILURE AND CANCER PREDISPOSITION SYNDROMES: CONGENITAL

When growth hormone deficiency isn't the answer: A case of gaucher disease

Noha Alaqsam[1], *Aws Aldajani*[1], *Amani Alrajabi*[1], *Ranya Bajuo*[1], *Abrar Batwie*[1], *Somaya Salama*[1], *Ohoud Kashari*[1]

[1] Alazizyah Children Hospital, Hematology Department, Jeddah, Saudi Arabia

GD may present with growth impairment—a nonspecific feature that can mimic growth hormone deficiency (GHD), and lead to diagnostic confusion. Early recognition and initiation of enzyme replacement therapy (ERT) are crucial to prevent irreversible complications and support normal development.

Clinical case

- 9 year-old female
- **Diagnosis: growth hormone deficiency (GHD),** because of short stature (< 3rd percentile) and low growth velocity (1.9 cm over 3 months). Bone age 7 y 10 m compared to a chronological age of 8 y 8 m. **She was started on recombinant GH**

Clinical case

- She was hospitalized for gastroenteritis, dehydration, and splenomegaly
- Cytopenia, with average values: WBC 3.2 x10^9/L, Hgb 9.3 g/dL, PLT 93x10^9/L, MCV 73 fL, MCH 23.3 pg and ferritin 233 ng/mL. Abdomen US revealed splenomegaly (cm 15)
- Bone marrow aspiration showed infiltration by large abnormal macrophages with a honeycomb appearance
- **Family history: two paternal cousins diagnosed with GD**

- **Genetic testing**: homozygous c.152G>T (p.Ser51Ile) mutation in GBA, not common
- **Plasma Lyso-Gb1**, a specific and sensitive GD biomarker, was **747.3 ng/mL** (normal values <14)

- Therapy: ERT with Imiglucerase (50 mg/kg biweekly → 60 mg/kg); GH therapy was discontinued
- **Lyso-Gb1: 407.3 ng/mL → 199.0 ng/mL after six months**

- Splenic size reduced to 11.5 cm
- Height reached (5th–10th percentile)

Discussion

- This case highlights the diagnostic challenge of distinguishing GD from GHD in children presenting with isolated short stature
- Chronic systemic illnesses can suppress the GH–IGF-1 axis, mimicking GHD, **but early signs such as cytopenias or organomegaly should prompt investigated for underlying metabolic diseases**
- A pedigree analysis of **23 family members** revealed multiple affected individuals, including a sibling previously diagnosed with GHD, raising suspicion of undiagnosed GD
- The p.Ser51Ile mutation identifed in this family is rare globally but may represent a regionally relevant variant
- Despite a positive family history, cultural stigma and paternal resistance initially delayed the screening of at-risk relatives

Conclusions

GD can present as isolated growth failure, mimicking GHD**. In cases of unexplained short stature or cytopenias should be considered systemic or metabolic causes. Early diagnosis, targeted screening, and prompt initiation of ERT**

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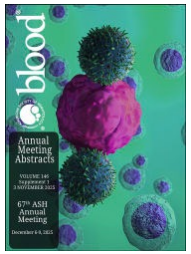

201. GRANULOCYTES, MONOCYTES, AND MACROPHAGES

Evaluation of clinical significance of circulating growth differentiation factor-15 levels in patients with gaucher disease

Veroniki Komninaka [1], Aimilia Mantzou [2], Nikolaos Tsagarakis [1], Ioulia Chaliori [1], Dimitrios Liakopoulos [1], Stefanos Papadhimitriou [1], Sofia Chaniotaki [1], Theodoros Marinakis [3], Christos Poziopoulos [4], Eleni Pergantou [5], Ioannis Papassotiriou [2]

significant multifactorial role of GDF-15 cytokine in patients with GD, as its levels correlated significantly with clinical and laboratory features of the disease. These findings support the emerging role of GDF-15 in GD

Background

- Growth Differentiation Factor 15 (GDF-15) is a member of the TGF-superfamily
- **GDF-15 controls hematopoietic growth, energy homeostasis, adipose tissue metabolism, body growth, bone remodeling, and response to stress signals**
- **Elevated circulating levels of GDF-15** have been reported **in patients with inborn errors of metabolism such as mitochondrial diseases, while in non-mitochondrial diseases such as GD** the reports are limited

Aim

- To investigate the clinical significance of circulating GDF-15 levels in patients with GD, and to explore possible correlations with disease activity, spleen and liver volume, bone deformities as well as genotype

Results and Discussion

- **Thirty adult GD patients under ERT and 20 healthy controls matched for sex and age**

	GD Patients	Controls	p-values
GDF-15 (ng/ml)	3,147±1,316 (390-18,381)	665.0±50.9 (269.6-1,129)	<0.001

- **GDF-15 levels significantly correlated with chitotriosidase* activity r=0.606, p<0.001**
- **Chitotriosidase: enzyme produced by macrophages, marker of immune system activation**

- **GDF-15 levels:**
  -- independent of patients' **age** (p> 0.106)
  -- **Hb** (r=-0.534, p=0.02); **RDW** r=0.805, p<0.001; **PLT** r=-0.602, p=0.008
  -- **Iron** r=-0.744, p<0.001; **Ferritin** r=0.617, p=0.006
  -- **Spleen volume** r=0.633, p=0.009
  -- **Bone Mineral Density** L1-L4 vertebrae r= -0.581, p<0.01

- **Higher GDF-15 were associated with lower total and HDL-cholesterol p<0.01**
- **GDF-15 levels decreased** slowly with **ERT** r=-0.461, p=0.053, slope -0.060
- GDF-15 levels decreased faster with **chitotriosidase** activity r=-0.649, p=0.004, slope -2.3 and **ferritin** levels r=-0.730, p<0.001, slope -1.8

Conclusions

Significant multifactorial role of GDF-15 cytokine in patients with GD, as its levels correlated significantly with clinical and laboratory features of the disease

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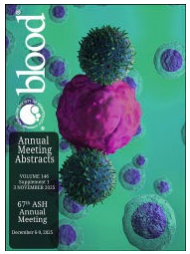

652. MGUS, AMYLOIDOSIS, AND OTHER NON-MYELOMA PLASMA CELL DYSCRASIAS: CLINICAL AND EPIDEMIOLOGICAL

Monoclonal gammopathy in patients with type I gaucher disease: Data from the Russian gaucher registry

Rodion Ponomarev[1], Elena Sysoeva[2], Valentina Dvirnyk[3], Yulia Chabaeva[3], Sergei Kulikov[3], Elena Lukina[2]

Chronic antigenic stimulation and sphingolipid-driven macrophage dysfunction underlie B-cell dysregulation in GD, explaining its high frequency of monoclonal gammopathies and associated multiple myeloma risk.

Background

GD is associated with polyclonal and monoclonal gammopathies. This results from chronic B-lymphocyte stimulation by macrophage-derived cytokines and chemokines (IL-6, IL-10, CCL18)

Go RS, Blood 2018
Weinreb NJ, Blood 208
Giuffrida Eur J Haem 2023

Materials

- Data from the Russian Gaucher Disease Registry: **336 GD patients** (93% of participants) at the National Medical Research Center of Hematology

Methods

- **Analyzed 1,171 serum protein immunochemical, pre- and during disease-specific therapy (ERT/SRT)**
- Patients with monoclonal gammopathy were monitored for 24–228 months (median 54)

Results

- **Monoclonal gammopathy in 24 patients (7**%), with IgG:IgA:IgM paraprotein ratios of 15:7:2
- One patient had symptomatic Multiple Myeloma at GD diagnosis
- Median age at gammopathy detection was 47 years (range: 30–71), male 54% and 17% splenectomized
- **Gammopathy first appeared: pre-treatment (46%), during ERT (37%), or SRT (17%).** Paraprotein concentrations increased progressively (mean rate: 0.5 g/L/year)
- The 15-year probability of developing monoclonal gammopathy was 18%, significantly higher in patients >40 years (20%; p=0.001) and with splenomegaly >200 mm (36%; p=0.0007)

Conclusions

Chronic CD1d-presented glycosphingolipid antigen stimulation and sphingolipid-driven **macrophage dysfunction underlie B-cell dysregulation in GD**, explaining its high frequency of monoclonal gammopathies and associated multiple myeloma risk

blood
How I Treat
Check for updates

How I manage monoclonal gammopathy of undetermined significance

Ronald S. Go and S. Vincent Rajkumar 2018

TO THE EDITOR:

MGUS, lymphoplasmacytic malignancies, and Gaucher disease: the significance of the clinical association

Neal J. Weinreb,[1,2] Pramod K. Mistry,[3] Barry E. Rosenbloom,[4,5] and Madhav V. Dhodapkar[6] 2018

Therefore, when reading the recent highly informative article "How I manage monoclonal gammopathy of undetermined significance,"[6] in *Blood*, we noticed with some chagrin that GD was not even mentioned in a fairly long list of concurrent conditions with which monoclonal gammopathy of undetermined significance (MGUS) has been associated. In fact, MGUS in association with GD was described as long ago as 1968,[7] and it is now well recognized that the risk for myeloma in affected individuals may be 25- to 50-fold greater than expected in the general US and European populations.[8] Furthermore, we now know that the monoclonal antibodies found in GD patients with MGUS and myeloma are specifically directed at macrophage CD1d-presented glycosphingolipid antigens.[9] This observation strongly supports the hypothesis that attributes GD-associated gammopathy to somatic mutations driven by chronic immune stimulation abetted by inflam-matory cytokines.[10,11]

Received: 19 June 2023 | Revised: 8 September 2023 | Accepted: 11 September 2023
DOI: 10.1111/ejh.14105

ORIGINAL ARTICLE

European Journal of Haematology
WILEY

Gaucher disease prevalence in 600 patients affected by monoclonal gammopathy of undetermined significance

Gaetano Giuffrida[1] | Uros Markovic[1] | Annalisa Condorelli[1,2] | Andrea Duminuco[1,2] | Valeria Calafiore[1] | Concetta Conticello[1] | Alessandra Romano[1,3] | Stephanie Grasso[1] | Carla Riccobene[1] | Marco Tindaro Valentino Ragusa[1] | Benedetta Esposito[1,2] | Daniela Nicolosi[1] | Marianna Calagna[1,2] | Antonella Nardo[1,2] | Ugo Consoli[4] | Giuseppina Uccello[4] | Valeria Di Giacomo[5] | Santo Neri[5] | Maria Rocca Cingari[6] | Filippo Rodà[7] | Vanessa Innao[4] | Agata Fiumara[8] | Giovanni Duro[9] | Carmela Zizzo[9] | Francesco Di Raimondo[1,2]

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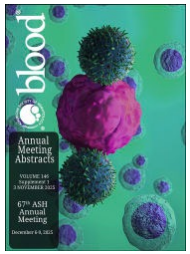

905. OUTCOMES RESEARCH: NON-MALIGNANT CONDITIONS EXCLUDING HEMOGLOBINOPATHIES

Phenotypic spectrum and treatment outcomes in Russian gaucher disease patients: Real-world experience with biosimilar imiglucerase

Rodion Ponomarev[1], *Elena Sysoeva*[1], *Rolanda Chavynchak*[1], *Margarita Galimova*[1], *Elena Lukina*[1]

The Russian GD cohort demonstrates significant splenectomy-associated skeletal morbidity. National access programs enable high treatment coverage (84%), with the remaining 16% having mild type 1 GD not meeting current criteria for initiation of therapy. Biosimilar imiglucerase constitutes 69% of ERT use.

Background

Russian National access programs enable high treatment coverage (84%) of GD patients, with the remaining 16% having mild type 1 GD not meeting current criteria for initiation of therapy

This study characterizes the Russian GD cohort and evaluates outcomes under national therapy protocols, including predominant use of biosimilar imiglucerase

Materials and Methods

- Single-center, observational study; data from Russian GD Registry; n=383 patients, age >18 years, followed 12-months

Results and Discussion

- 383 patients (M 43% F 57%), median age 42 years (range: 18–93). Splenectomy: 35% (median age at procedure: 12.5 yrs)
- Anemia 65%, thrombocytopenia 74% (100% in non-splenectomized), leukopenia 43%
- **Osteonecrosis (femoral diaphyses) in 72% splenectomized vs. 59% non-splenectomized patients (p=0.128); avascular necrosis affected 41% vs. 10% (p<0.001)**
- Therapy: 321 patients
  - **ERT: 92% (imiglucerase-biosimilar 69%,** velaglucerase 30%, taliglucerase 1%)
  - SRT: 8% (eliglustat)

Outcomes: after 7 years of ERT, anemia persisted in 6% and severe thrombocytopenia (platelets <60000/µL) in 4.5%
Maintenance ERT (15–20 U/kg monthly) administered to 137 patients (46%) achieving therapeutic goals

Conclusions

The Russian GD cohort demonstrates significant splenectomy-associated skeletal morbidity. Biosimilar imiglucerase is 69% of ERT use. Maintenance dosing in nearly half of treated patients underscores its role in sustainable disease control. **Real-world outcomes confirm efficacy of this approach, with >93% achieving hematologic stability on long-term therapy**

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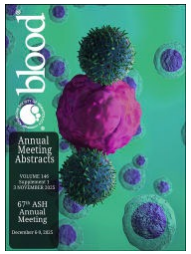

905. OUTCOMES RESEARCH: NON-MALIGNANT CONDITIONS EXCLUDING HEMOGLOBINOPATHIES

Real-world outcomes with eliglustat for gaucher disease type 1 in China: A multicenter retrospective study

Yongxin Zhou[1], *Zijian Hao*[1], *Zhuang Qilin*[1], *Miao Chen*[1], *Junling Zhuang*[1], *Bing Han*[1]

[1]Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Department of Hematology, Beijing, China

Eliglustat showed significant real-world effectiveness and a favorable safety profile in Chinese GD1 patients, suggesting its potential as a first-line treatment in resource-limited settings where ERT access is challenging.

Background

- Enzyme replacement therapy (ERT) has long been the standard treatment; however, its biweekly intravenous infusions pose logistical challenges, especially in resource-limited regions like China
- **Eliglustat, an oral substrate reduction therapy (SRT), offers a more convenient and cost-effective alternative**
- Global trials have demonstrated Eliglustat's efficacy and safety, real-world evidence specific to Chinese GD1 patients remains scarce. **This study provides the first multicenter, real-world evaluation of Eliglustat in this population, focusing on its effectiveness, safety, and potential as a first-line therapy in resource-limited settings**

Methods

- **Retrospective, Multicenter Study on adult GD1 patients from 15 hospitals in China treated with Eliglustat for 6 months**
- Eliglustat was administered at a fixed dose of 84 mg twice daily
- Key clinical outcomes: glucosylsphingosine (Lyso-GL1), Hb, PLTs count, liver and spleen volume, at baseline and follow-up
- Safety was evaluated based on adverse events (AEs) graded per CTCAE v5.0

Results

- **19 patients** (M:F 9:10); median age: 36 years [range: 18–55]; **median follow-up duration of 7 months (range: 6–9)**
- **Lyso-GL1 levels decreased** significantly from 468 ng/mL to 210 ng/mL (p <0.0001)
- **PLTs increased** from 109 x 10^9/L to 132 x 10^9/L (p = 0.019), 58.3% (7/12) thrombocytopenic patients improving
- **Hb increased** from 125 g/L to 134 g/L (p=0.275), 83.3% (5/6) anemic patients improving, 33.3% (2/6) normalizing
- **Liver and spleen volumes decreased** (liver: 2128 mL to 1501 mL, p=0.031; spleen: 961 mL to 786 mL, p=0.032)
- Subgroup analysis: greater Lyso-GL1 reductions in naïve patients vs transitioning from ERT (55.1% vs. 43.1%, p = 0.049)
- Grade I/II AEs were reported in 31.6% of patients, with no grade III or higher AEs, treatment discontinuations, or deaths.

Conclusions

Eliglustat showed significant real-world effectiveness and a favorable safety profile in Chinese GD1 patients, suggesting its potential as a first-line treatment in resource-limited settings where ERT access is challenging

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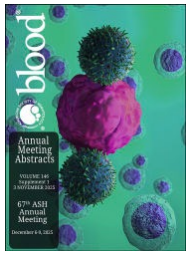

801. GENE THERAPIES

Trial in progress: Galileo-3, a Phase 3 safety and efficacy trial of FLT201 gene therapy in patients with gaucher disease type 1

Shoshana Revel-Vilk[1,2], Ozlem Goker-Alpan[3], Ida Schwartz[4], Reena Sharma[5], Pilar Giraldo[6], Pamela Foulds[7], Philip Yin[7], Daniel Wolf[7], Simon Flynn[7], Derralynn Hughes[8,9]

GALILEO-3 is a pivotal phase 3 switch study that is designed to evaluate the safety and efficacy of FLT201 in adult GD1 participants on stable ERT/SRT therapy. This study is intended to support the registration of FLT201 in the adult GD1 population.

Background

FLT201 is a clinical-stage, liver-directed gene therapy candidate designed to overcome the limitations of ERT with a single infusion. It leverages a rationally designed **liver-selective adeno-associated virus capsid (AAVS3) to deliver a transgene encoding GCase85, a novel, engineered GCase variant with enhanced stability.** This approach enables continuous systemic and intracellular expression of GCase85, providing sustained enzyme exposure beyond what is achievable with ERT

Background

- In the firts-in-human GALILEO-1 trial (NCT05324943) and its long-term extension study GALILEO-2 (NCT06545136), **FLT201** provided durable long-term GCase85 expression out to at least **two years**, **enabling continuous intracellular enzyme activity and sustained glucosylsphingosine (lyso-Gb1) clearance following a single low dose (4.5 x 1011 vg/kg) IV administration in all participants who discontinued ERT/SRT**
- These subjects continue to remain off their background therapy. No treatment-related serious adverse events occurred and only mild (<2 x ULN) transient elevations in alanine aminotransferase considered related to therapy were observed in the 6 participants treated with FLT201

Study Design and Methods

- Study Design and Methods GALILEO-3 (EU CT 2025-520765-50) is an open label, non-randomized, global, multicenter, phase 3 study designed to evaluate the safety and efficacy of **FLT201**
- The study will enroll approximately **45 adults** with GD1 who have been on **stable ERT/SRT treatment for at least 2 years.**
- Participants will receive a **single IV infusion of FLT201 at a dose of 4.5 x 1011 vg/kg, discontinue ERT/SRT treatment after week 4, and will be followed for a period of 5 years**
- A primary analysis will occur at Week 52 with the option for an interim analysis to occur at Week 24 and a final analysis at the end of study

Inclusions and Exclusions criteria

- Key inclusion criteria: diagnosis of GD1, age ≥18, stable Hb and PLTs count at baseline, and receiving ERT or SRT without interruption for at least 2 years
- Key exclusion criteria: Gaucher disease type 2 or 3, positivity for AAVS3 neutralizing antibodies, positive pregnancy test, lactating, hematopoietic stem cell transplantation or solid organ transplant, previous gene or cell therapy, splenectomy

Endpoints

- **Primary endpoint: proportion of participants with stable Hb g/dL (decrease from baseline not <1.5 g/dL) at Week 52**
- **Secondary endpoints:** change from baseline in Lyso-Gb1 levels and the proportion of participants with stable platelet count, spleen volume, and liver volume at Week 52
- Further efficacy endpoints: bone health, quality of life (PROMs, Reported Outcome Measures), Gaucher disease severity (DS3), and fatigue; change from baseline in vital signs and laboratory assessments, and incidence of clinically significant abnormalities upon physical examination and 12-lead ECG
- Safety endpoints: adverse events (AE) and serious adverse events (SAE)

Conclusions

GALILEO-3 is a pivotal phase 3 switch study that is designed to evaluate the safety and efficacy of FLT201 in adult GD1 participants on stable ERT/SRT therapy. This study is intended to support the registration of FLT201 in the adult GD1 patients

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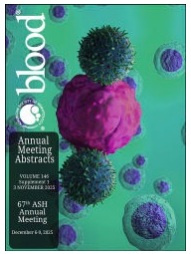

801. GENE THERAPIES

Safety and activity of gene therapy with AAV8 GBA1 (LY-M001)on type I adults gaucher disease

Yishan Ye[1,2,3,4], *Xueping Luo*[1,2,3,4], *Jingwen Li*[1,2,3,4], *Yixiong Chen*[5], *Qin Lin*[5], *He Huang*[1,2,3,4], *Weiyan Zheng*[1,2,3,4]

: This pilot study suggests that LY-M001 is well tolerated up to 21 months post-infusion, with encouraging biochemical and clinical responses observed in the medium-dose cohort. LY-M001 holds potential as a promising gene therapy alternative to current GD treatments, addressing key unmet clinical needs.

Background

LY-M001 is a novel rAAV8-based gene therapy delivering a codon-optimized GBA1 transgene under a liver-specific promoter to express a modified GCase (GCaseLY)

This investigator-initiated trial evaluates the safety and therapeutic potential of LY-M001 in type 1 GD

Methods

- **Single-center, single-arm, dose-escalation study** conducted at the First Affiliated Hospital of Zhejiang University School of Medicine (Hangzhou, China) to evaluate the safety and preliminary efficacy of LY-M001, an AAV8-based GBA1 gene therapy, in adults with type 1 Gaucher disease
- **Eligible participants (aged 18–60)** had confirmed GBA1 mutations; no prior use of GCase inhibitors, and low anti-AAV8 neutralizing antibody titers (1:10)
- **After one week of prophylactic prednisone (1 mg/kg/day), participants received a single intravenous infusion of LY-M001 at either 5 x 10^12 vg/kg (Cohort 1, n=1) or 1.5 x 10^12 vg/kg (Cohort 2, n=2)**
- Primary endpoints included treatment-related adverse events (AEs), changes in ALT/AST, and development of anti-capsid antibodies over 12 months (ClinicalTrials.gov: NCT06162338)

Results

- 6 patients screened, and 3 females enrolled; 3 screened patients were excluded due to high neutralizing antibody titers
- **Follow-up of 76 weeks (IQR 69–85), all participants showed increased peripheral GCase levels and activity**
- **Both participants in cohort 2 reduced peripheral Lyso-GL1 level**
- **The sole participant in cohort 1 also reduced Lyso-GL1 level after combining ERT therapy**

Results

- **Hemoglobin and platelet counts improved** in Cohort 2, and both patients remained off ERT for 19 months
- **Liver and spleen volumes decreased** within 6 months across all patients
- No serious adverse events (SAEs) reported
- The sole Cohort 1 patient experienced mild infusion-related symptoms (diarrhea, abdominal pain, headache), managed with symptomatic treatment
- In Cohort 2, one patient had transient ALT elevations (peak 96 IU/L) and delayed mild elevation (ALT 73 IU/L), managed with oral tacrolimus
- The other participant reported transient left lower lip numbness, also managed with symptomatic treatment
- All patients developed anti-AAV8 neutrilizing antibodies post-infusion
- Pharmacodynamic data collection is ongoing

Conclusions

This pilot study suggests that LY-M001 is well tolerated up to 21 months post-infusion, with encouraging bio-chemical and clinical responses observed in the medium-dose cohort. **LY-M001 holds potential as a promising gene therapy alternative to current GD treatments, addressing key unmet clinical needs**

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Grazie!