EARLIER KNOWLEDGE FOR EARLIER INTERVENTION

THE IMPORTANCE OF MONITORING PATIENTS WITH FABRY DISEASE

Fabrazyme®
agalsidase beta

INDICATION AND USAGE

Fabrazyme® is indicated for the treatment of adult and pediatric patients 2 years of age and older with confirmed Fabry disease.

SANOFI GENZYME

Please see Important Safety Information and full Prescribing Information.

FABRY DISEASE: PROGRESSIVE. OFTEN LIFE THREATENING.[1-5]

Progressive accumulation of GL-3 and lyso-GL-3 is the hallmark of Fabry disease.[2]

- Fabry disease is caused by pathogenic variants in the *galactosidase-alpha (GLA)* gene that lead to complete or partial deficiency in α-galactosidase (α-GAL A) enzyme activity[6]
- This results in progressive accumulation of glycolipids—globotriaosylceramide (GL-3) and globotriaosylsphingosine (lyso-GL-3)—in lysosomes throughout the body[6,7]
- Accumulation of GL-3 and lyso-GL-3 starts in utero, causing cellular damage that can progress silently before overt clinical signs, often leading to organ damage and premature death[6,8]

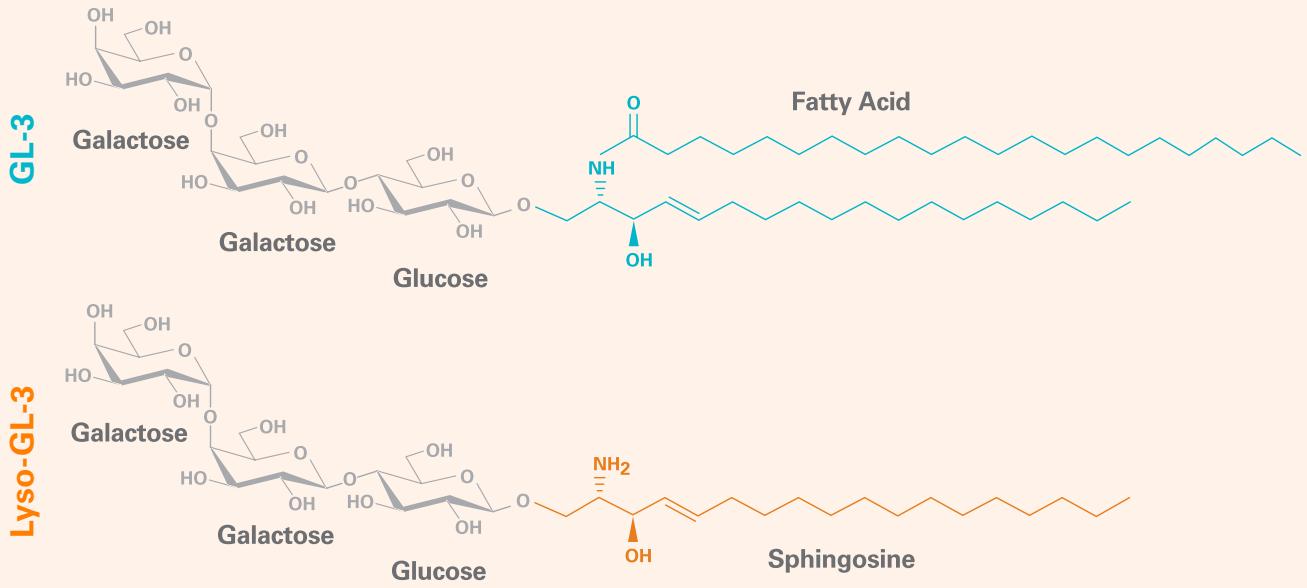
Charles, Heather, and Amanda, *Fabry patients*

LYSO-GL-3 IS AN IMPORTANT BIOMARKER IN EVALUATING FABRY DISEASE BURDEN.[9]

Lyso-GL-3 may correlate with disease severity and organ involvement.[2]

- Along with GL-3, lyso-GL-3 is involved in the pathogenesis of Fabry disease
- Monitoring lyso-GL-3 levels may assist in clinical decision making

Lyso-GL-3, the deacylated form of GL-3, is structurally similar to GL-3[9,10]



Monitor glycolipid levels to help identify early symptoms and manage previously identified symptoms—before they lead to life-threatening conditions.[11]

New Symptoms

Uncover symptoms just starting to emerge

Worsening Symptoms

Track the deterioration of previously identified symptoms

REGULAR ASSESSMENTS ARE IMPORTANT FOR EVALUATING AND MANAGING FABRY DISEASE.

Assessment Recommendations

The following assessments are based on published guidelines and recommendations developed by the Fabry Registry Board of Advisors, a group of physicians who have experience in managing patients with Fabry disease. The Fabry Registry is sponsored by Sanofi Genzyme. This schedule consists of recommendations only. Treating physicians should use their medical judgment to determine the appropriate schedule of assessments based upon an individual patient case[12]

Disease-related assessments for patients <18 years of age[11-13*†]

	Upon diagnosis	Every 6–12 months[a]	Every 24–36 months	At time of an event or therapy change
Overall glycolipid burden				
Plasma GL-3/Lyso-GL-3	Monitor plasma GL-3/Lyso-GL-3 to track glycolipid burden			
General				
Medical history, with a particular focus on:	●	●		●
Gastrointestinal symptoms				
Pain				
Sweating				
Heat & cold intolerance				
Family history	●		●	
Physical exam	●	●		●
Vital signs, height and weight	●	●		●
Blood pressure[b]	●	●		●
Enzyme activity and genotype	●			
Concomitant medication assessment	●	●		●
Pediatric quality of life assessment – PedsQL™ Pediatric Quality of Life Inventory	●	●		●
Pediatric quality of life assessment – PedsQL™ Multidimensional Fatigue Scale	●	●		●
Pediatric pain assessment – PedsQL™ Pediatric Pain Questionnaire™	●	●		●
Renal				
Glomerular filtration rate (GFR)[c]	●		●	●
Albuminuria and proteinuria[d]	●	●		●
Cardiac				
Electrocardiogram[e]	●		●	●
Echocardiogram[f]	●		●	●
Cardiac MRI[g]	●		●	●
Brain				
Cranial MRI –T1, T2 and FLAIR	●		●[h]	●[h1]
Eye				
Slit lamp exam[i]	●		●	
Hearing				
Audiologic evaluation[j]	●		●	●

Heather and Charles, Fabry Patients

Monitor Young Fabry Patients for New or Progressing Symptoms[13]

- Boys and girls with Fabry disease begin developing symptoms at an early age (median age of 6 years for boys and 9 years for girls)[13]

Treatment-related assessments[12*†]

	Specialized laboratory tests	
	Plasma GL-3	Plasma samples for GL-3 testing should be drawn prior to the first infusion, then every 3 months for the first 18 months of treatment, then every 6 months thereafter.
	Antibody testing	Serum samples for IgG testing should be drawn prior to the first infusion, then every 3 months for the first 18 months of treatment, then every 6 months until 2 consecutive negative results are confirmed.
!	**Adverse events**	
	Adverse event monitoring[k]	Continuous monitoring is necessary

* Initiation of Laboratory Tests, Imaging, and Other Studies: There is variability in the clinical complications and progression of Fabry disease. Children are at risk for life-threatening complications. There are no biomarkers available to discern mildly affected from severely affected patients. In children with a family history of early presenting or severe disease, complete evaluations should be done at the time of diagnosis. Other patients should be completely evaluated at no later than 5 years of age.

† Frequency of assessment information is from the Fabry Registry Schedule of Assessments.

[a] Patients receiving ERT are recommended to undergo these evaluations every 6 months; for those not on ERT or with milder disease, once per year may be sufficient.

[b] Blood pressure should be measured 3 times at each assessment; only the last 2 measurements should be recorded.

[c] GFR should be measured directly every 24–36 months until age 15, and annually thereafter. If direct measurement is not possible, serum creatinine levels should be obtained at the recommended intervals for an estimation of GFR, which is a less sensitive method.

[d] First morning voided urine for protein, albumin, and creatinine in order to calculate a protein/creatinine ratio and albumin/creatinine ratio. Protein, albumin, and creatinine measurements can also be performed on timed samples (eg, 24 hours).

[e] Electrocardiogram should be performed starting at ages 10–12 years. If abnormal and/or clinical symptoms arise, Holter monitoring is recommended.

[f] Echocardiogram should be performed starting at ages 10–12 years.

[g] Cardiac MRI is recommended to be performed in patients under age 25 if cardiac hypertrophy or significant arrhythmia is present.

[h] Cranial MRIs should be performed at ages 10, 15, and 18 years.

[h1] At the time of a cerebrovascular event, a cranial MRI should also include diffused, weighted images and apparent diffusion coefficient (DWI/ADC).

[i] Monitor yearly if retinal vessel tortuosity noted.

[j] Audiologic evaluation should be performed at the earliest age that is practical.

[k] Adverse events relating to Fabrazyme should be reported to Sanofi Genzyme Medical Information at 800-745-4447, Option 2.

Assessment Recommendations

Disease-related assessments for patients ≥18 years of age[12,15*]

	Upon diagnosis	Every 6 months	Every 12 months	Every 24–36 months	At time of an event or therapy change
Overall glycolipid burden					
Plasma GL-3/Lyso-GL-3	●		●		
General					
Medical history	●	●			●
Family history	●			●	
Physical exam	●	●			●
Vital signs, height, and weight	●	●			●
Enzyme activity and genotype	●				
Concomitant medication assessment	●	●			●
Quality of life (SF-36®, BPI)	●	●			●
Renal					
Serum creatinine[a] and BUN	●	●			●
Urine protein excretion[b]	●	●			●
Cardiac					
Electrocardiogram[c]	●		●		●
Echocardiogram	●		●		●
24-hour Holter monitoring[d]	●		●		●
Cardiac MRI[e]	●		●[e1]	●[e1]	●[e2]
Lipid panel	●		●		
Respiratory					
Spirometry exam[f]	●			●	
Brain					
Cranial MRI –T1, T2, and FLAIR	●			●	●[g]
Eye					
Slit lamp exam[h]	●				
Hearing					
Audiologic evaluation	●			●	●

Cindy and Amanda, *Fabry Patients*

Monitor Adult Patients at Time of an Event or Therapy Change

Treatment-related assessments[12]*

Specialized laboratory tests	
Plasma GL-3	Plasma samples for GL-3 testing should be drawn prior to the first infusion, then every 3 months for the first 18 months of treatment, then every 6 months thereafter.
Antibody testing	Serum samples for IgG testing should be drawn prior to the first infusion, then every 3 months for the first 18 months of treatment, then every 6 months until 2 consecutive negative results are confirmed.
Adverse events	
Adverse event monitoring[i]	Continuous

*Frequency of assessment information is from the Fabry Registry Schedule of Assessments.

[a] Directly measuring glomerular filtration rate (GFR) is recommended if a more precise evaluation is desired.

[b] 24 hour or first morning void urine for protein, creatinine, and albumin.

[c] If electrocardiogram is abnormal and/or clinical symptoms arise, Holter monitoring is recommended.

[d] Annual 24-hour Holter monitoring is recommended for males 30 years of age or older and females 40 years of age or older.

[e] Cardiac MRI is recommended at Fabry diagnosis for patients ages 25 and older. It is recommended to be performed under age 25 if cardiac hypertrophy or significant arrhythmia is present.

[e1] If first MRI is abnormal: 1) patients with moderate or severe left ventricular hypertrophy (LVH) receiving ERT should have MRI annually; 2) patients with significant arrhythmia should have MRI at least every 2 years or at frequency factoring cardiac disease severity and the physician's clinical judgment; 3) males with no or mild LVH receiving ERT should have MRI every 2 years.

[e2] If first MRI is normal, repeat every 5 years or earlier if ECG/ECHO results are abnormal on annual exam.

[f] If spirometry is abnormal, perform yearly.

[g] At the time of an event, a cranial MRI should also include diffused, weighted images and DWI/ADC.

[h] Monitor yearly if retinal vessel tortuosity noted.

[i] Adverse events relating to Fabrazyme should be reported to Sanofi Genzyme Medical Information at 800-745-4447, Option 2.

COUNT ON FABRAZYME.

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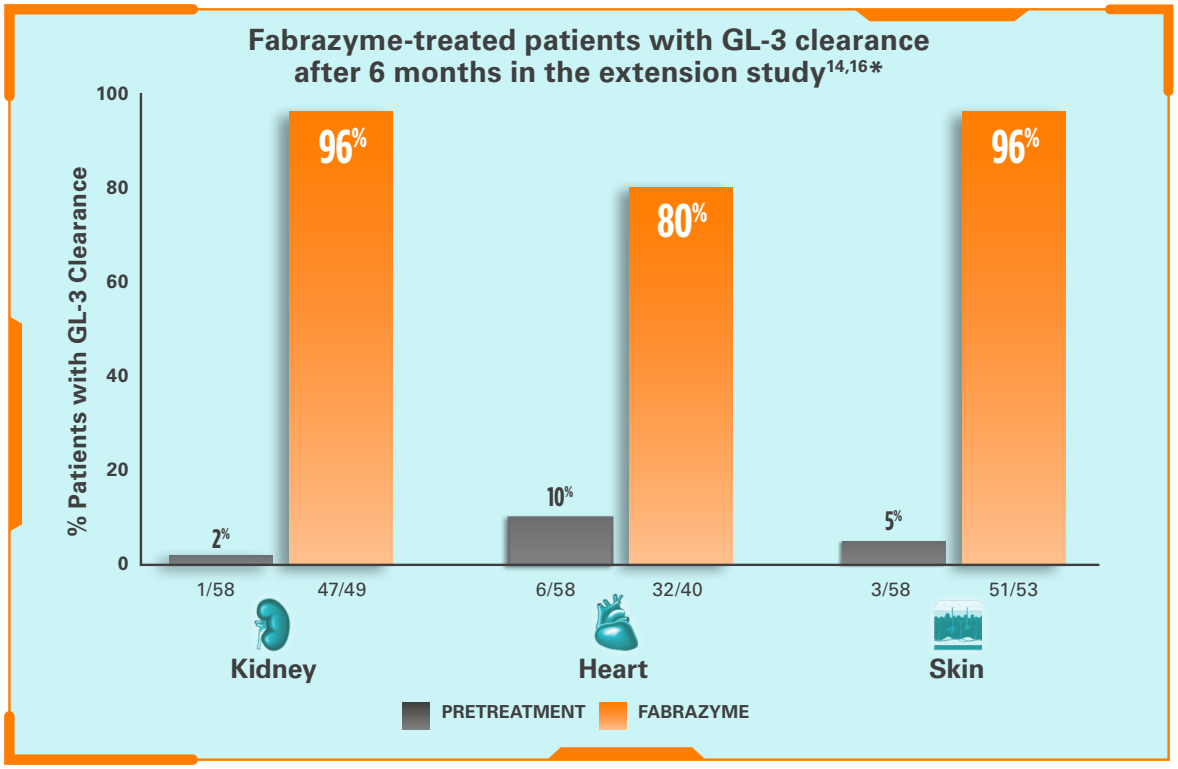
FABRAZYME was proven to clear GL-3 in as quickly as 5 months in the capillary endothelium of the kidney, heart, and skin.[14]

- **Study 1:** At 5 months, a GL-3 inclusion score of 0 was achieved in the capillary endothelium of the: **Kidney:** 20/29 (69%) Fabrazyme patients compared with 0 (0%) placebo patients; **Heart:** 21/29 (72%) Fabrazyme patients compared with 1 (3%) placebo patient; **Skin:** 29/29 (100%) Fabrazyme patients compared with 1/29 (3%) placebo patient[14]
- **Study 1 open-label extension:** After 6 months, the majority of patients treated with Fabrazyme had a GL-3 inclusion score of 0 in the capillary endothelium of the kidney, heart, and skin[14]



*Study 1: Randomized, 1:1, double-blind, placebo-controlled study. 58 patients with Fabry disease (56 males, 2 females), 16 to 61 years, all naive to enzyme replacement therapy. Patients received either 1 mg/kg of Fabrazyme or placebo every 2 weeks for 5 months. GL-3 inclusions were graded on a scale of 0 (trace or nearly none) to 3 (severe). All 58 patients in Study 1 participated in the Study 1 extension, a 54-month, open label extension trial.[14]

Placebo patients began Fabrazyme treatment at entry into the open-label extension. This graph represents pooled results from all patients in the study (Fz/Fz and Pl/Fz).[14]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Anaphylaxis and Hypersensitivity Reactions: In clinical trials and postmarketing safety experience with Fabrazyme, approximately 1% of patients developed anaphylactic or severe hypersensitivity reactions during Fabrazyme infusions. Life-threatening anaphylactic and severe hypersensitivity reactions have been observed in patients during Fabrazyme infusions..

- Reactions have included localized angioedema (including swelling of the face, mouth, and throat), bronchospasm, hypotension, generalized urticaria, dysphagia, rash, dyspnea, flushing, chest discomfort, pruritus, and nasal congestion.

COUNT ON FABRAZYME.

FABRAZYME rapidly normalized plasma GL-3 and maintained it for up to 5 years.[14,17]

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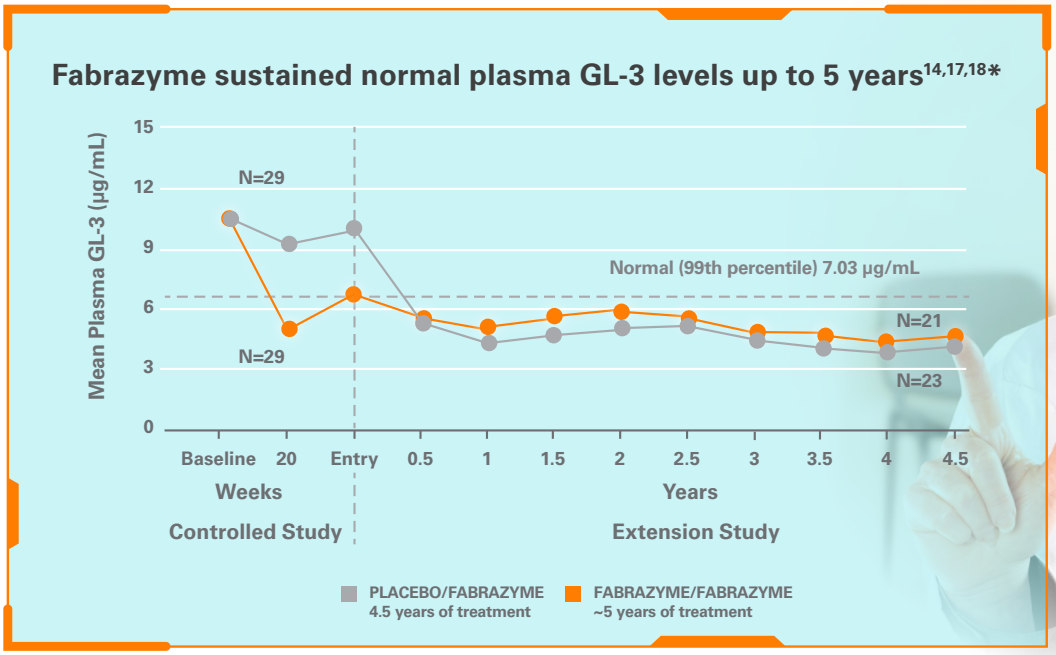

*Study 1: Randomized, 1:1, double-blind, placebo-controlled study. 58 patients with Fabry disease (56 males, 2 females), 16 to 61 years, all naive to enzyme replacement therapy. Patients received either 1 mg/kg of Fabrazyme or placebo every 2 weeks for 5 months. GL-3 inclusions were graded on a scale of 0 (trace or nearly none) to 3 (severe). All 58 patients in Study 1 participated in the Study 1 extension, a 54-month, open-label extension trial.[14]

- Similar long-term responses were seen in a majority of patients, with sustained GL-3 clearance in the capillary endothelium of the kidney (8/8) and heart (6/8) at 4.5 years[14]

IMPORTANT SAFETY INFORMATION

- Interventions have included cardiopulmonary resuscitation, oxygen supplementation, IV fluids, hospitalization, and treatment with inhaled beta-adrenergic agonists, antihistamines, epinephrine, and IV corticosteroids.
- If anaphylactic or severe hypersensitivity reactions occur, immediately discontinue administration of Fabrazyme and provide necessary emergency treatment. Because of the potential for severe hypersensitivity reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.

FABRAZYME WAS EVALUATED FOR OUTCOMES IN CLINICALLY SIGNIFICANT EVENTS.*

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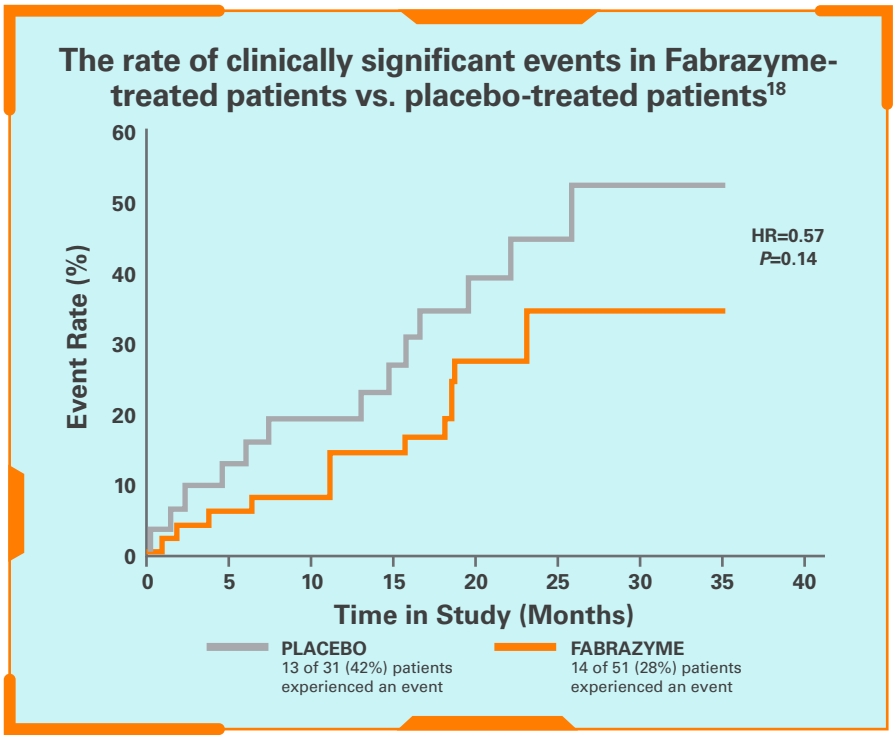
A smaller percentage of patients in the FABRAZYME treatment group experienced a clinically significant event.[14]



VS

HAD RENAL, CARDIAC, CEREBROVASCULAR EVENTS, OR DEATH*

28% (14 of 51) of Fabrazyme-treated patients versus 42% (13 of 31) of placebo-treated patients experienced a clinically significant event (HR† 0.57, 95% CI: 0.27, 1.22, *P*=0.14)[14]

- The primary efficacy endpoint was the time to first occurrence of a clinically significant event (renal, cardiac, or cerebrovascular event, or death)[14]

The study included patients aged 20 to 72 years (median age: 45), with a baseline median plasma αGAL level of 1.5 nmol/hour/mL (range: 0 to 1.5). Patients included had advanced Fabry disease with mild-to-moderate kidney dysfunction at baseline (median eGFR=52 mL/min/1.73m^2 [range: 25 to 113]).[14]

Study 2 design: A randomized, double-blind, placebo-controlled, multinational, multicenter study of 82 patients (72 males and 10 females) with Fabry disease, all naive to enzyme replacement therapy. Patients were randomly assigned to Fabrazyme 1 mg/kg or placebo every 2 weeks for up to 35 months (median follow-up 18.5 months).[14]

eGFR=estimated glomerular filtration rate.
*Clinically significant event is defined as renal, cardiac, or cerebrovascular event or death.
†The hazard ratio is a comparison between the probability of events in a treatment group, compared to the probability of events in a control group.

IMPORTANT SAFETY INFORMATION

In clinical trials with Fabrazyme, some patients developed IgE antibodies or skin test reactivity specific to Fabrazyme.

- Higher incidences of hypersensitivity reactions were observed in adult patients with persistent anti-Fabrazyme antibodies and in adult patients with high antibody titer compared to that in antibody negative adult patients.

FABRAZYME IN PEDIATRIC POPULATIONS.

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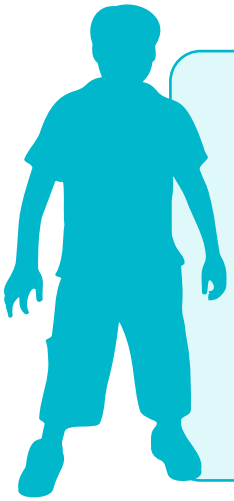
The overall efficacy and safety profile of FABRAZYME in pediatric patients was consistent with that seen in adults.



- This pediatric study evaluated 16 pediatric patients with Fabry disease (14 males, 2 females), aged 8 to 16 years (median 12 years)[14]
- In 14 male patients, Fabrazyme normalized plasma GL-3 levels at 24 weeks and sustained levels at 48 weeks[14]
- The two female patients' plasma GL-3 levels remained normal through week 48[14]
- 12 of the 14 males had GL-3 inclusions at baseline, and all 12 male patients achieved GL-3 inclusion scores of 0 at 24 and 48 weeks of treatment[14]

Study Design: Open-label, single-arm, multinational, multicenter study in 16 pediatric patients with Fabry disease (14 males, 2 females), aged 8 to 16 years (median 12 years). Histological evaluation of the capillary endothelium, deep vessel endothelium, deep vessel smooth muscle cells, and perineurium of biopsied skin was conducted using histochemistry with light microscopy. Scoring was on a scale of 0 (defined as none) to 3 (severe).[14]

Study Dose: Fabrazyme 1 mg/kg every 2 weeks for up to 48 weeks.[14]

Baseline Characteristics: All 14 males had elevated plasma GL-3 levels (ie, >7.03 µg/mL), whereas the two female patients had normal plasma GL-3 levels. 12 of the 14 males had GL-3 inclusions present on skin biopsy (scores 1, 2, or 3), whereas the two females had no GL-3 inclusions at baseline.[14]

Safety: The most common adverse reactions (>20%) were headache, abdominal pain, pharyngitis, fever, nausea, vomiting, rhinitis, diarrhea, arthralgia, and dizziness.[14]

IMPORTANT SAFETY INFORMATION

- Physicians should consider testing for IgE antibodies in patients who experienced suspected hypersensitivity reactions and consider the risks and benefits of continued treatment in patients with anti-Fabrazyme IgE antibodies. Rechallenge of these patients should only occur under the direct supervision of qualified personnel, with appropriate medical support measures readily available.

FABRAZYME IN PEDIATRIC POPULATIONS.

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FABRAZYME is THE ONLY ENZYME REPLACEMENT THERAPY indicated for patients 2 years of age and older.[14]

- In an analysis of 24 Fabrazyme-treated pediatric patients with Fabry disease aged 2 to <8 years, plasma GL-3 levels were normalized[14]
- At baseline, all patients had elevated plasma GL-3 (ie, >7.03 µg/mL)[14]
- After treatment, plasma GL-3 levels fell within the normal range (ie, ≤7.03 µg/mL) in 91% (20/22), 95% (18/19), and 92% (12/13) of patients at 6, 12, and 24 months, respectively[14]

IMPORTANT SAFETY INFORMATION

Infusion-Associated Reactions: In clinical trials with Fabrazyme, 59% of patients experienced infusion-associated reactions, some of which were severe. Infusion-associated reactions are defined as adverse reactions occurring on the same day as the infusion. The incidence of infusion-associated reactions was higher in patients who were positive for anti-Fabrazyme antibodies than in patients who were negative for anti-Fabrazyme antibodies.

THE RATE OF KIDNEY FUNCTION DECLINE WAS STUDIED IN FABRAZYME-TREATED PATIENTS.

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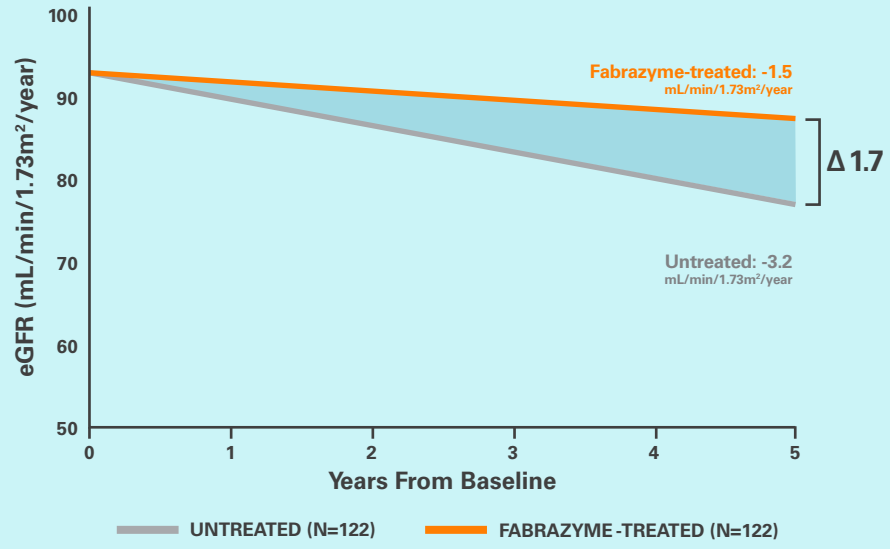
Long-term observational study results show a difference in the mean eGFR slope between the FABRAZYME-treated and untreated patients.*

Five-year observational study comparing eGFR slopes[14]

1:1 matching based on age at Fabrazyme initiation, sex, phenotype, and baseline eGFR



1.7 mL/MIN/1.73M²/YEAR

ESTIMATED DIFFERENCE IN MEAN SLOPE OF eGFR

- Estimated difference in mean slope of eGFR was 1.7 mL/min/1.73m²/year (95% CI: 0.5, 3.0)[14]
- The mean slopes of eGFR of the 2 groups were[14]:
  - Fabrazyme-treated group: -1.5 mL/min/1.73m²/year
  - Untreated group: -3.2 mL/min/1.73m²/year
- The median follow-up time was 3 years in the untreated group and 4.5 years in the treated group (maximum follow-up time was 5 years in both groups)[14]

Study design: In a long-term observational study, the rate of decline in renal function (eGFR slope) was assessed in Fabry disease patients aged ≥16 years, treated with Fabrazyme (n=122) and matched to a historical cohort of untreated patients (n=122).[14]

Patient Baseline Characteristics[14]:

- The median age at Fabrazyme initiation was 35 years. Proportion of male patients=72%. The proportion of patients with a classic phenotype=84%
- The median baseline eGFR was 93 mL/min/1.73m²
- The median age at symptom onset was 10 years and median age at diagnosis was 26 years

*eGFR slope is a measurement of kidney function over time.

IMPORTANT SAFETY INFORMATION

- In patients experiencing infusion-associated reactions, pretreatment with an antipyretic and antihistamine is recommended. Infusion-associated reactions occurred in some patients after receiving pretreatment.
- If an infusion-associated reaction occurs, decreasing the infusion rate, temporarily stopping the infusion, and/or administrating additional antipyretics, antihistamines, and/or steroids may ameliorate the symptoms.

COUNT ON THE WELL-ESTABLISHED SAFETY PROFILE OF FABRAZYME.

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The safety of FABRAZYME has been assessed in **4 clinical trials** involving **162 patients** with over **473 patient-years** of experience.[14,18]

- In clinical trials and postmarketing safety experience with Fabrazyme, approximately 1% of patients developed anaphylactic or severe hypersensitivity reactions during Fabrazyme infusion
- In clinical trials with Fabrazyme, 59% of patients experienced infusion-associated reactions, some of which were severe. Infusion-associated reactions are defined as adverse reactions occurring on the same day as the infusion
- In patients experiencing infusion-associated reactions, pretreatment with an antipyretic and antihistamine is recommended. Infusion-associated reactions occurred in some patients after receiving pretreatment
- Higher incidences of hypersensitivity reactions were observed in adult patients with persistent anti-Fabrazyme antibodies and in adult patients with high antibody titer compared to that in antibody negative adult patients
- Patients with advanced Fabry disease may have compromised cardiac function, which may predispose them to a higher risk of severe complications from infusion-associated reactions. These patients should be monitored closely if Fabrazyme is administered

***Cisneros Family,** Fabry Patients*

SUMMARY OF COMMON ADVERSE REACTIONS IN CLINICAL TRIALS (STUDIES 1 AND 2).

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Reported at a rate of at least 5% in FABRAZYME-treated patients and >2.5% compared with placebo-treated patients.[14]

Adverse Reaction	Fabrazyme (n=80) %	Placebo (n=60) %
Upper respiratory tract infection[a]	53	42
Chills[b]	49	13
Pyrexia	39	22
Headache	39	28
Cough	33	25
Paresthesia	31	18
Fatigue	24	17
Peripheral edema	21	7
Dizziness	21	8
Rash	20	10
Pain in extremity	19	8
Myalgia[c]	18	7
Lower respiratory tract infection	18	7
Pain	16	13
Back pain	16	10
Hypertension	14	5

Adverse Reaction	Fabrazyme (n=80) %	Placebo (n=60) %
Pruritus	10	3
Tachycardia	9	3
Excoriation	9	2
Increased blood creatinine	9	5
Tinnitus	8	3
Dyspnea	8	2
Fall	6	3
Burning sensation	6	0
Anxiety	6	3
Depression	6	2
Wheezing	6	0
Hypoacusis	5	0
Chest discomfort	5	2
Fungal infection	5	0
Viral infection	5	0
Hot flush	5	0

a Includes reports of upper respiratory infection, nasal congestion, sinusitis, respiratory tract congestion, and pharyngitis.
b Includes reports of chills and feeling cold
c Includes reports of myalgia and muscle spasms.

CareConnectPSS®

DEDICATED SUPPORT FOR PATIENTS AND FAMILIES

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- Dedicated CareConnectPSS Case Managers and Patient Education Liaisons
- Disease-specific information and resources
- Genetic education, information on testing, and diagnostics
- Care coordination for treatment
- Help with handling insurance issues

CONTACT A CASE MANAGER

1-800-745-4447, Option 3

Info@CareConnectPSS.com

ONLINE PATIENT RESOURCES

www.CareConnectPSS.com

Patients on treatment with Fabrazyme will also receive additional content, based on their preferences:

- Regular emails on topics of interest to people living with Fabry disease
- Mobile text messages with helpful tips

Whether your patients' needs are large or small, **CareConnectPSS** is here to help them.

careconnect PSS® Personalized Support Services

Visit Fabrazyme.com/HCP to learn more about Fabrazyme safety and efficacy

For questions about Fabry disease, contact Sanofi Genzyme Medical Information at 1-800-745-4447, Option 2, or visit Fabrazyme.com/HCP

IMPORTANT SAFETY INFORMATION

- If severe infusion-associated reactions occur, immediate discontinuation of the administration of Fabrazyme should be considered, and appropriate medical treatment should be initiated. Severe reactions are generally managed with administration of antihistamines, corticosteroids, intravenous fluids, and/or oxygen when clinically indicated. Because of the potential for severe infusion-associated reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.

INDICATION AND USAGE

Fabrazyme® is indicated for the treatment of adult and pediatric patients 2 years of age and older with confirmed Fabry disease.

Fabrazyme® agalsidase beta

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Anaphylaxis and Hypersensitivity Reactions

In clinical trials and postmarketing safety experience with Fabrazyme, approximately 1% of patients developed anaphylactic or severe hypersensitivity reactions during Fabrazyme infusion. Life-threatening anaphylactic and severe hypersensitivity reactions have been observed in patients during Fabrazyme infusions.

- Reactions have included localized angioedema (including swelling of the face, mouth, and throat), bronchospasm, hypotension, generalized urticaria, dysphagia, rash, dyspnea, flushing, chest discomfort, pruritus, and nasal congestion.
- Interventions have included cardiopulmonary resuscitation, oxygen supplementation, IV fluids, hospitalization, and treatment with inhaled beta-adrenergic agonists, antihistamines, epinephrine, and IV corticosteroids.
- If anaphylactic or severe hypersensitivity reactions occur, immediately discontinue administration of Fabrazyme and provide necessary emergency treatment. Because of the potential for severe hypersensitivity reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.

In clinical trials with Fabrazyme, some patients developed IgE antibodies or skin test reactivity specific to Fabrazyme.

- Higher incidences of hypersensitivity reactions were observed in adult patients with persistent anti-Fabrazyme antibodies and in adult patients with high antibody titer compared to that in antibody negative adult patients.
- Physicians should consider testing for IgE antibodies in patients who experienced suspected hypersensitivity reactions and consider the risks and benefits of continued treatment in patients with anti-Fabrazyme IgE antibodies. Rechallenge of these patients should only occur under the direct supervision of qualified personnel, with appropriate medical support measures readily available.

Infusion-Associated Reactions

In clinical trials with Fabrazyme, 59% of patients experienced infusion-associated reactions, some of which were severe. Infusion-associated reactions are defined as adverse reactions occurring on the same day as the infusion. The incidence of infusion-associated reactions was higher in patients who were positive for anti-Fabrazyme antibodies than in patients who were negative for anti-Fabrazyme antibodies.

- In patients experiencing infusion-associated reactions, pretreatment with an antipyretic and antihistamine is recommended. Infusion-associated reactions occurred in some patients after receiving pretreatment.
- If an infusion-associated reaction occurs, decreasing the infusion rate, temporarily stopping the infusion, and/or administrating additional antipyretics, antihistamines, and/or steroids may ameliorate the symptoms.

- If severe infusion-associated reactions occur, immediate discontinuation of the administration of Fabrazyme should be considered, and appropriate medical treatment should be initiated. Severe reactions are generally managed with administration of antihistamines, corticosteroids, intravenous fluids, and/or oxygen when clinically indicated. Because of the potential for severe infusion-associated reactions, appropriate medical support measures should be readily available when Fabrazyme is administered.
- Patients with advanced Fabry disease may have compromised cardiac function, which may predispose them to a higher risk of severe complications from infusion-associated reactions. Monitor closely patients with compromised cardiac function if Fabrazyme is administered to these patients.

ADVERSE REACTIONS

- Common adverse reactions reported (≥20% and >2.5% compared to placebo) were upper respiratory tract infection (44% vs 30%), headache (39% vs 28%), cough (33% vs 25%), paresthesia (31% vs 18%), fatigue (24% vs 17%), dizziness (21% vs 8%), peripheral edema (21% vs 7%), and rash (20% vs 10%).

REFERENCES

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REGULAR MONITORING IS ESSENTIAL TO HELP MANAGE PROGRESSION OF FABRY DISEASE.

Fabrazyme® agalsidase beta

- Accumulation of glycolipids begins in utero and continues silently, which can result in debilitating symptoms, organ damage, and early death[6,8]
- Monitoring is important to identify new or worsening symptoms and should also be done after an event or therapy change[11]
- GL-3 and lyso-GL-3 play a role in disease pathogenesis and are important biomarkers of disease burden[2,9]
- It is important to regularly monitor lyso-GL-3, as well as GL-3, in patients[2,9,12]

CHOOSE THE PROVEN THERAPY FOR FABRY DISEASE WITH OVER 17 YEARS OF REAL-WORLD EXPERIENCE.

- Long-term observational study (maximum follow-up time of 5 years) results show a difference in the mean eGFR slope between the Fabrazyme-treated and untreated patients. The mean slope of eGFR was -1.5 mL/min/1.73m^2/year in the Fabrazyme-treated group and -3.2 mL/min/1.73m^2/year in the untreated group with an estimated difference in mean slope of eGFR of 1.7 mL/min/1.73m^2/year (95% CI: 0.5, 3.0)[14]
- A smaller percentage of Fabrazyme-treated patients experienced a renal, cardiac, or cerebrovascular event, or death. In a randomized, placebo-controlled trial over 35 months (median follow-up 18.5 months), a total of 14/51 (28%) Fabrazyme-treated patients and 13/31 (42%) placebo-treated patients experienced a clinically significant event. The estimated hazard ratio for the risk of clinically significant events was 0.57 (95% CI: 0.27, 1.22)[14]
- Can be used in patients regardless of genotype or disease severity
- Has a well-established safety profile

FABRAZYME IS THE ONLY ERT INDICATED FOR PATIENTS 2 YEARS OF AGE AND OLDER AND HAS PROVEN LONG-TERM EFFICACY AND SAFETY

IMPORTANT SAFETY INFORMATION

- Patients with advanced Fabry disease may have compromised cardiac function, which may predispose them to a higher risk of severe complications from infusion-associated reactions. Monitor closely patients with compromised cardiac function.

ADVERSE REACTIONS

- Common adverse reactions reported (≥20% and >2.5% compared to placebo) were upper respiratory tract infection (53% vs 42%), chills (49% vs 13%), pyrexia (39% vs 22%), headache (39% vs 28%), cough (33% vs 25%), paresthesia (31% vs 18%), fatigue (24% vs 17%), peripheral edema (21% vs 7%), dizziness (21% vs 8%), and rash (20% vs 10%).

INDICATION AND USAGE

Fabrazyme® is indicated for the treatment of adult and pediatric patients 2 years of age and older with confirmed Fabry disease.

SANOFI GENZYME

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