ELFABRIO® (pegunigalsidase alfa-iwxj)

for Fabry Disease

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GENERAL UNIVERSITY HOSPITAL IN PRAGUE

FIRST FACULTY OF MEDICINE
Charles University

June 26, 2024

Disclaimer

- Speaker´s and consultancy honoraria
  - Chiesi; Sanofi; Takeda; Amicus Therapeutics
- Research grant
  - Sanofi
- Board member
  - Fabry Registry, FollowMe Next Registry
- Clinical trials
  - Protalix / Chiesi, Sanofi
- Imaging from files of the General University Hospital, Prague, CZ; patients gave their consent for data and imaging use for teaching and research

Prof. Aleš Linhart, MD, DrSc., FESC

Graduated in Medicine at Charles University in Prague, Czech Republic

Training in cardiology and vascular medicine at General University Hospital in Prague and Broussais Hospital in Paris, France

Board certified specialist in Cardiology, Vascular Medicine, Internal Medicine

Research focusing mainly on metabolic cardiomyopathies, noninvasive cardiac imaging, and atherosclerosis

Author or co-author of > 450 scientific papers, 80 book chapters and 3 monographs

In 2004 appointed Professor at Charles University in Prague

Since 2005 - Head 2nd Department of Internal Cardiovascular Medicine, First Faculty of Medicine, Charles University, Prague, Czech Republic

Immediate past president of the Czech Society of Cardiology

Past President of Myocardial and Pericardial Working Group of the European Society of Cardiology

Disclaimer

The data discussed in this presentation are not intended to establish noninferiority or superiority to any other marketed drug product on the basis of safety or efficacy. The FDA has indicated that the magnitude of drug effect of agalsidase beta in a study population similar to that of BALANCE cannot be sufficiently quantified and as such, a non-inferiority margin cannot be determined for the BALANCE study. Additionally, the FDA relied on the estimated mean eGFR slope and concluded the two arms were comparable (-2.4 for PRX-102 and -2.3 for agalsidase beta), and the estimated treatment difference was -0.1 (95% CI: -2.3, 2.1) mL/min/1.73 m^2/year.

Elfabrio® was approved by the FDA with a boxed warning for hypersensitivity reactions/anaphylaxis, consistent with Enzyme Replacement Therapy (ERT) class labeling, and Warnings/Precautions providing guidance on the signs and symptoms of hypersensitivity and infusion-associated reactions seen in the clinical studies as well as treatments to manage such events should they occur. The Warnings/Precautions for membranoproliferative glomerulonephritis (MPGN) alert prescribers to the possibility of MPGN and provide guidance for appropriate patient management. Overall, the FDA review team concluded that in the context of Fabry disease as a rare, serious disease with limited therapeutic options that may not be suitable to all individual patients, the benefit-risk of Elfabrio is favorable for the treatment of adults with confirmed Fabry disease.

Clinical studies have not shown that a long half-life results in a medicine working better or more safely.

Approval Package
Information regarding the FDA's approval of Elfabrio is available on the FDA's website. For more information see the FDA Approval Package:

- Multi-discipline Review issued by the FDA's Center for Drug Evaluation and Research, https://www.accessdata.fda.gov/drugsatfda_docs/nda/2023/761161Orig1s000MultidisciplineR.pdf
- Other Reviews issued by the FDA's Center for Drug Evaluation and Research, https://www.accessdata.fda.gov/drugsatfda_docs/nda/2023/761161Orig1s000OtherR.pdf

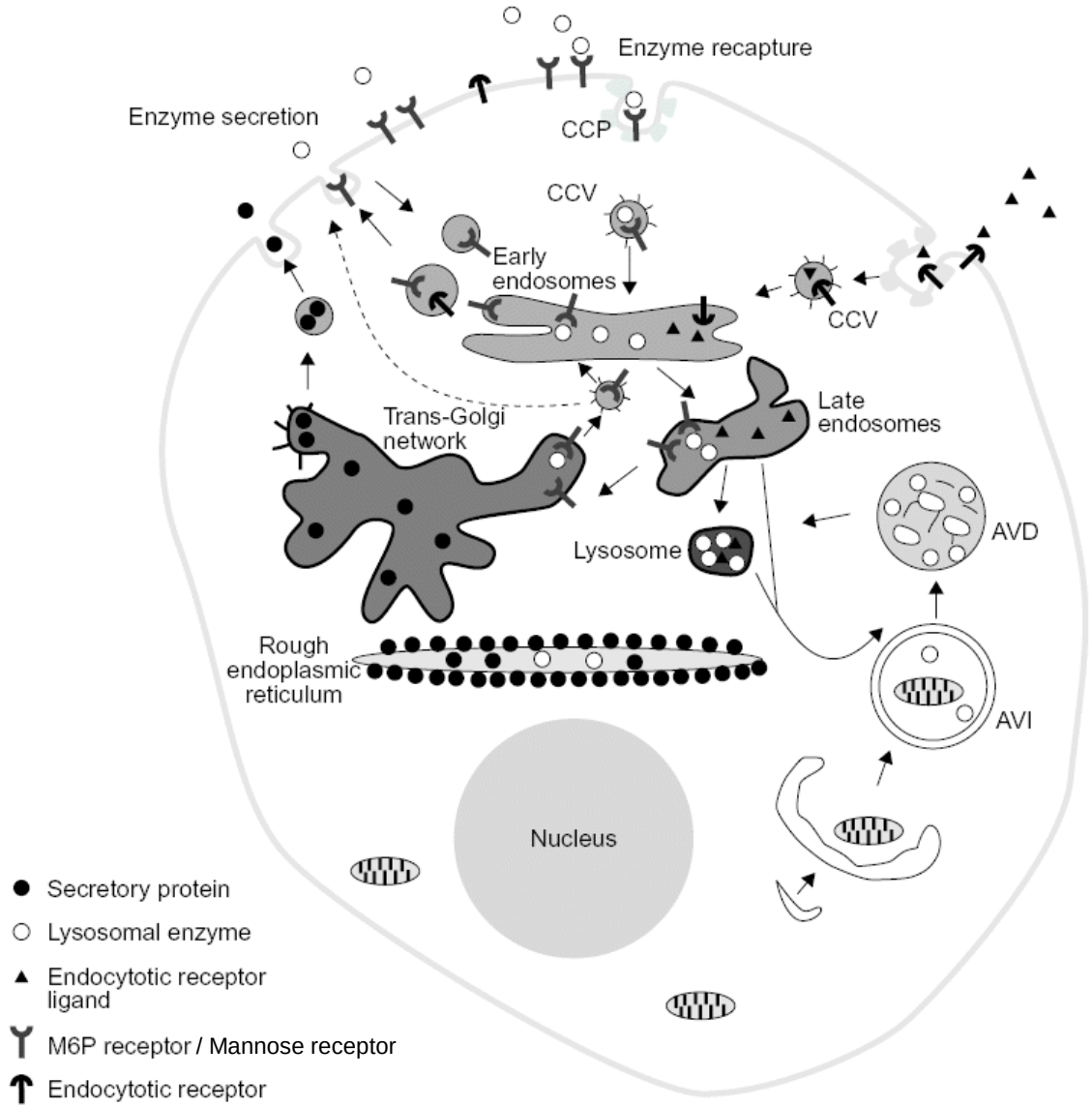
Refer to the Full Prescribing Information for Elfabrio for more information, https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761161s000lbl.pdf.

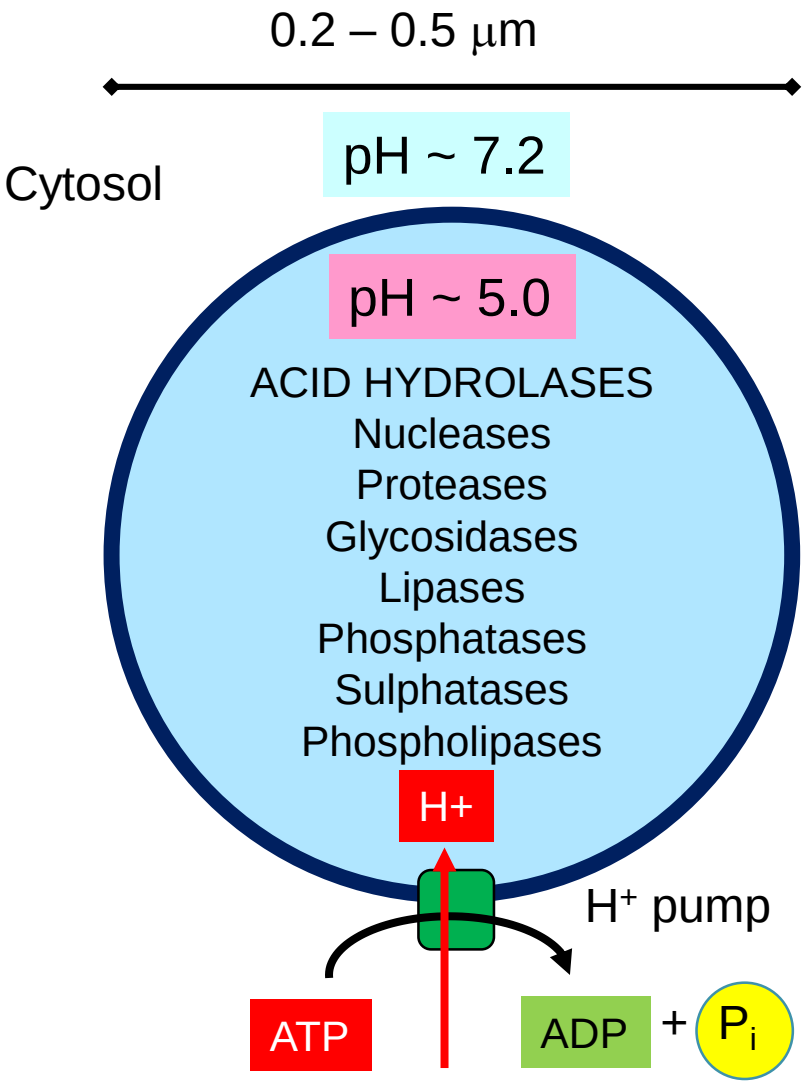
Note Regarding Forward-Looking Statements

This presentation contains forward-looking statements that involve risks and uncertainties within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements are neither historical facts nor assurances of future performance. Forward-looking statements can be identified by the use of words such as “anticipate,” “believe,” “estimate,” “expect,” “can,” “continue,” “could,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” and other words or phrases of similar import, as they relate to Protalix, its subsidiaries or its management, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements are subject to many risks and uncertainties that could cause our actual results to differ materially from any future results expressed or implied by the forward-looking statements, including, but not limited to: risks related to the commercialization of Elfabrio® (pegunigalsidase alfa-iwxj); the inherent risks and uncertainties in developing drug platforms and products of the type Protalix is developing; the impact of development of competing therapies and/or technologies by other companies and institutions; potential product liability risks, and risks of securing adequate levels of product liability and other necessary insurance coverage; and other factors described in Protalix’s filings with the U.S. Securities and Exchange Commission. In addition, new risk factors and uncertainties may emerge from time to time, and it is not possible to predict all risk factors and uncertainties. Given these uncertainties, investors should not place undue reliance on these forward-looking statements. Except as required by law, no obligation has been undertaken to update or revise the information contained in this presentation whether as a result of new information, future events or circumstances or otherwise.

Fabry Disease

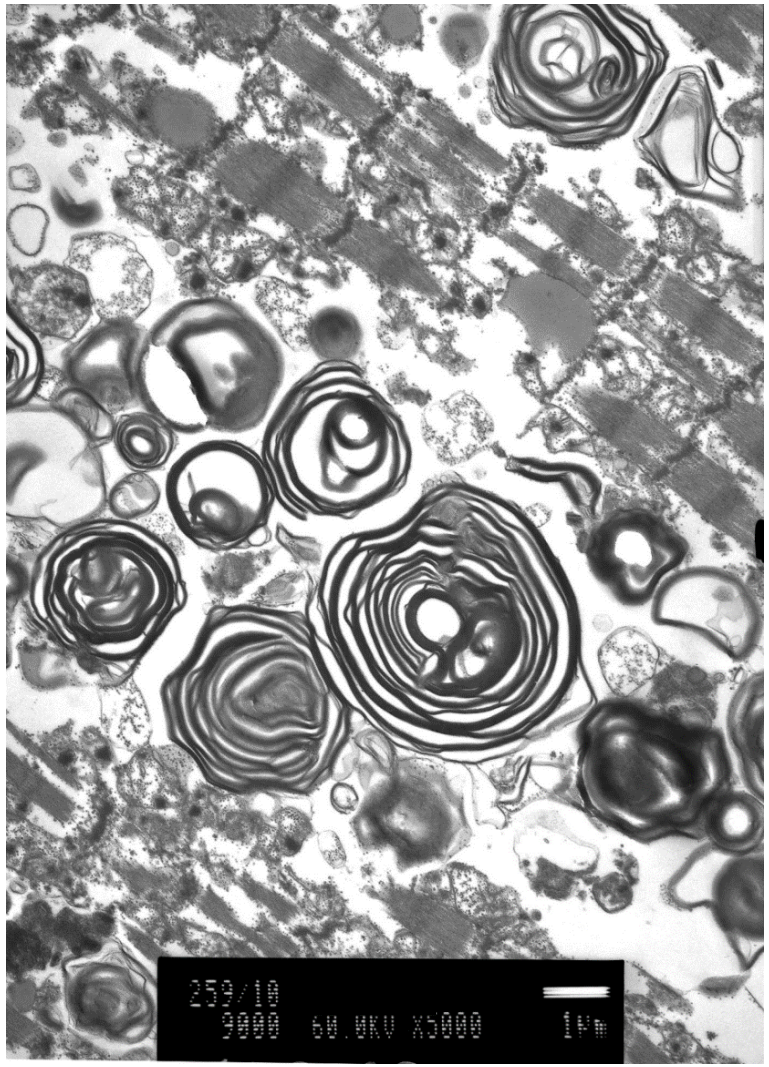
Lysosomal function in cells



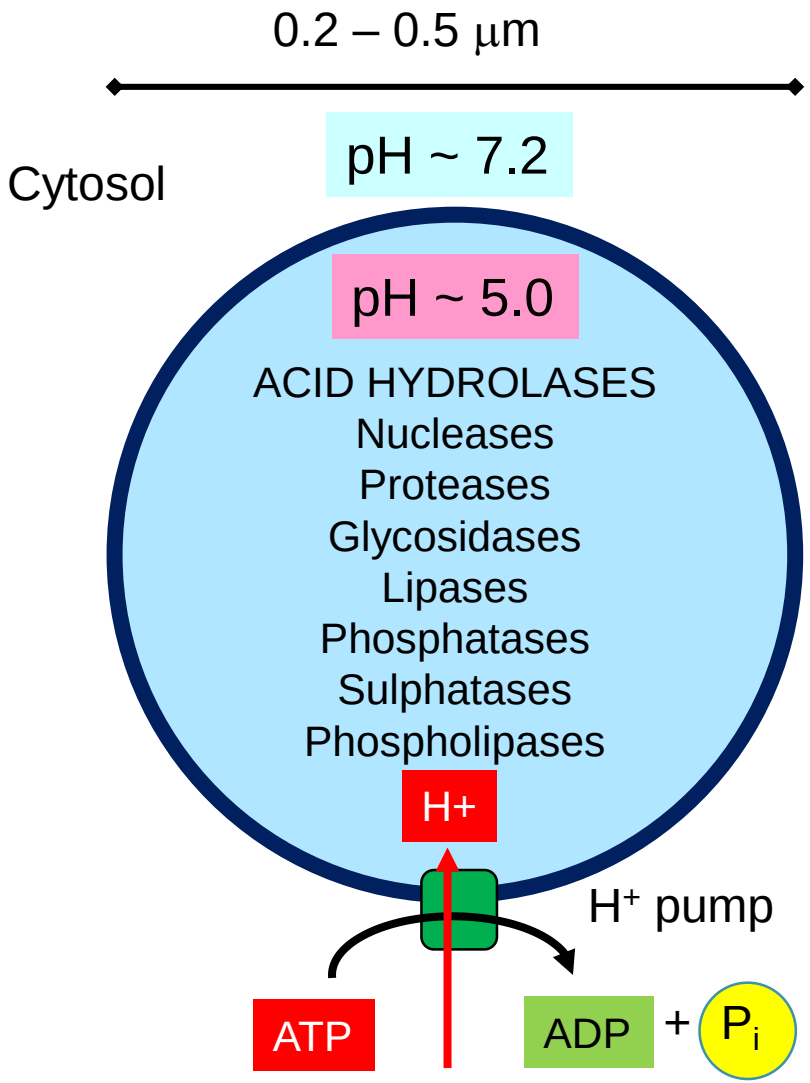


Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell, 4th edition New York: Garland Science; 2002.

Lysosomal function in cells



Electron microscopy: Charles University, Prague



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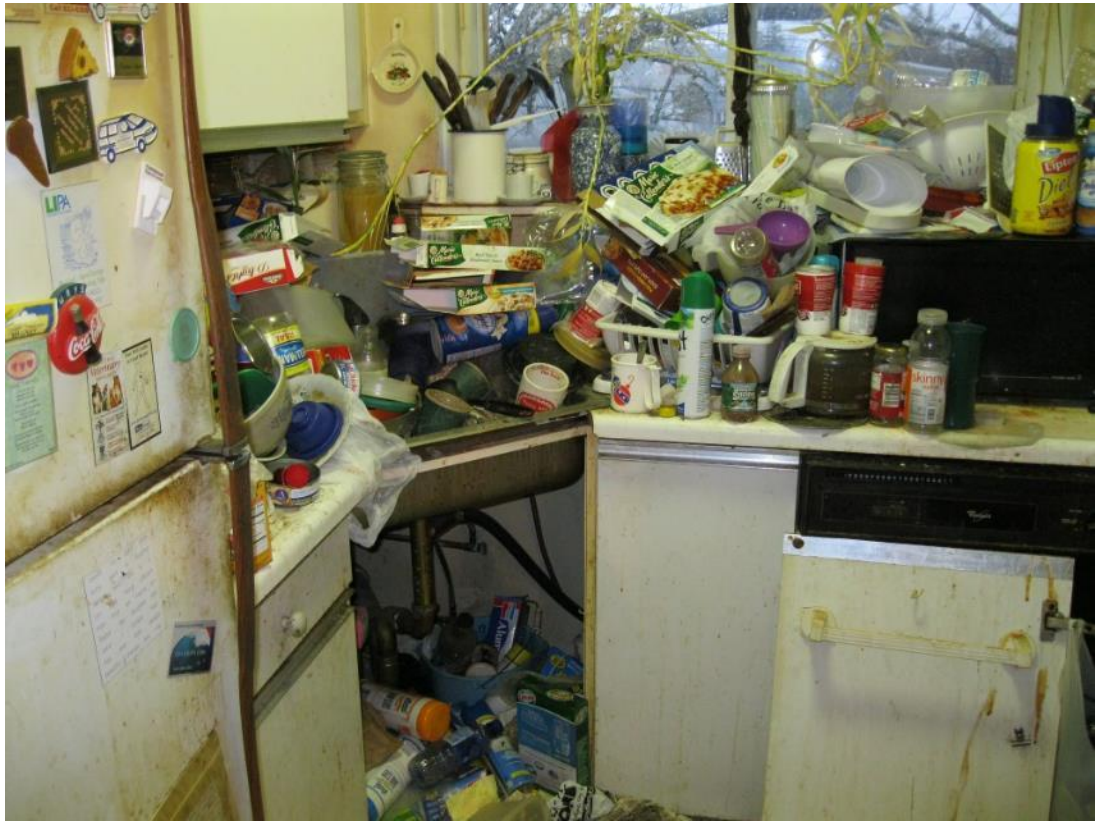
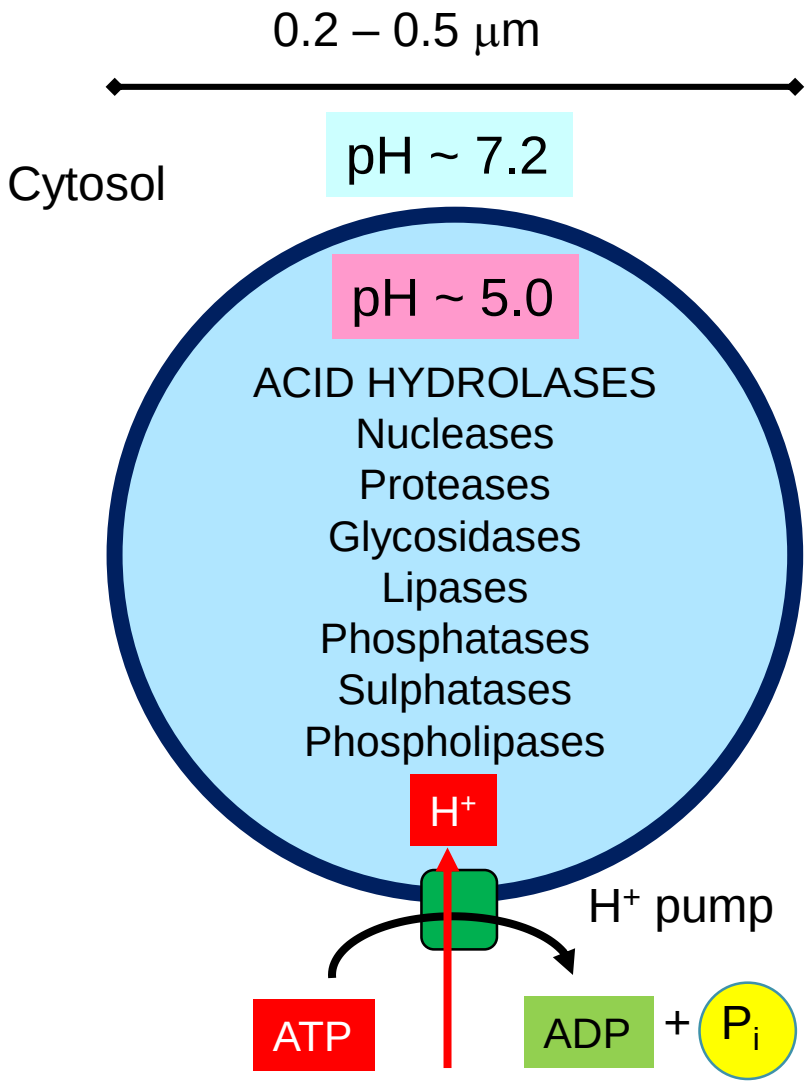
Lysosomal function in cells

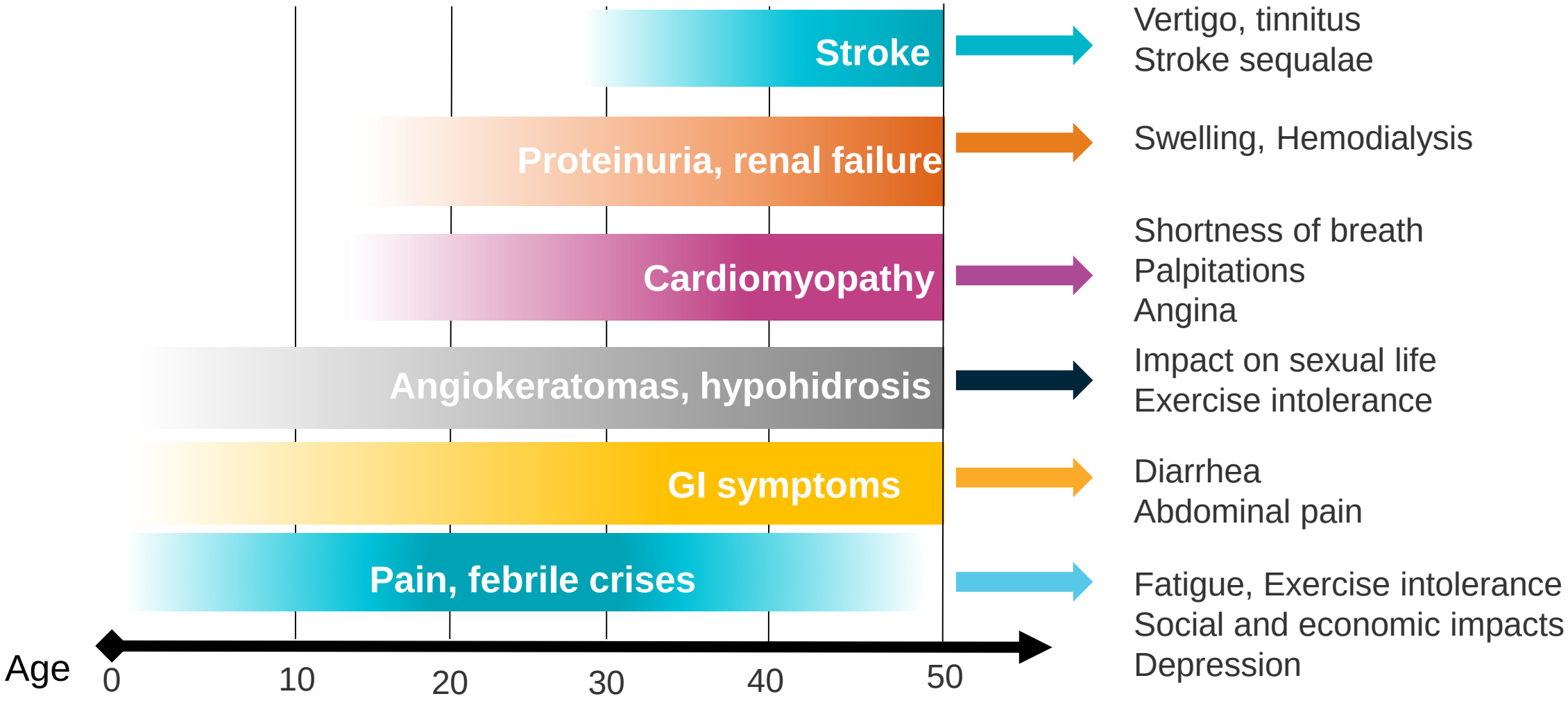


http://www.trashitman.com/



Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular Biology of the Cell, 4th edition New York: Garland Science; 2002.

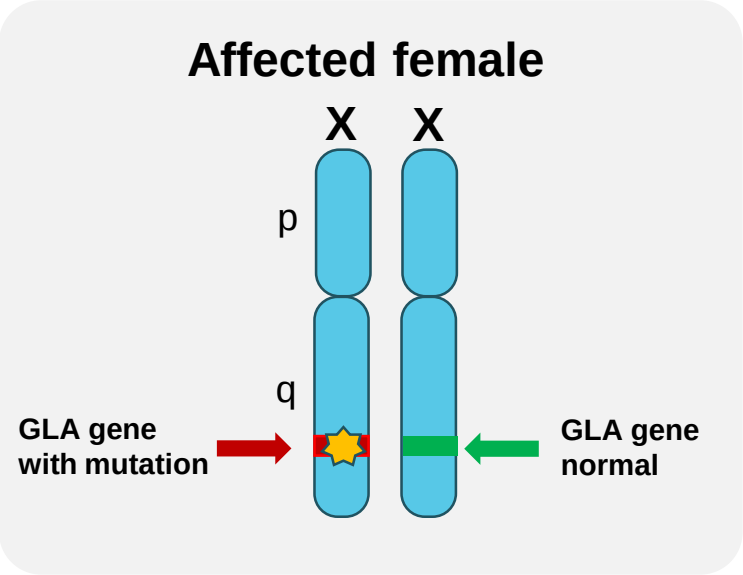
Timeline of Fabry disease manifestations in hemizygous male patients

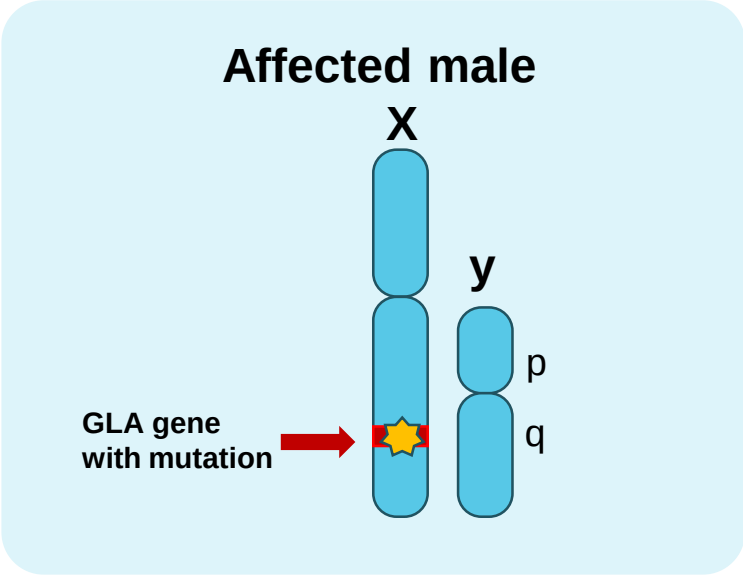


GI, gastrointestinal

Linhart A and Elliott PM. *Heart*. 2007;93(4):528–35

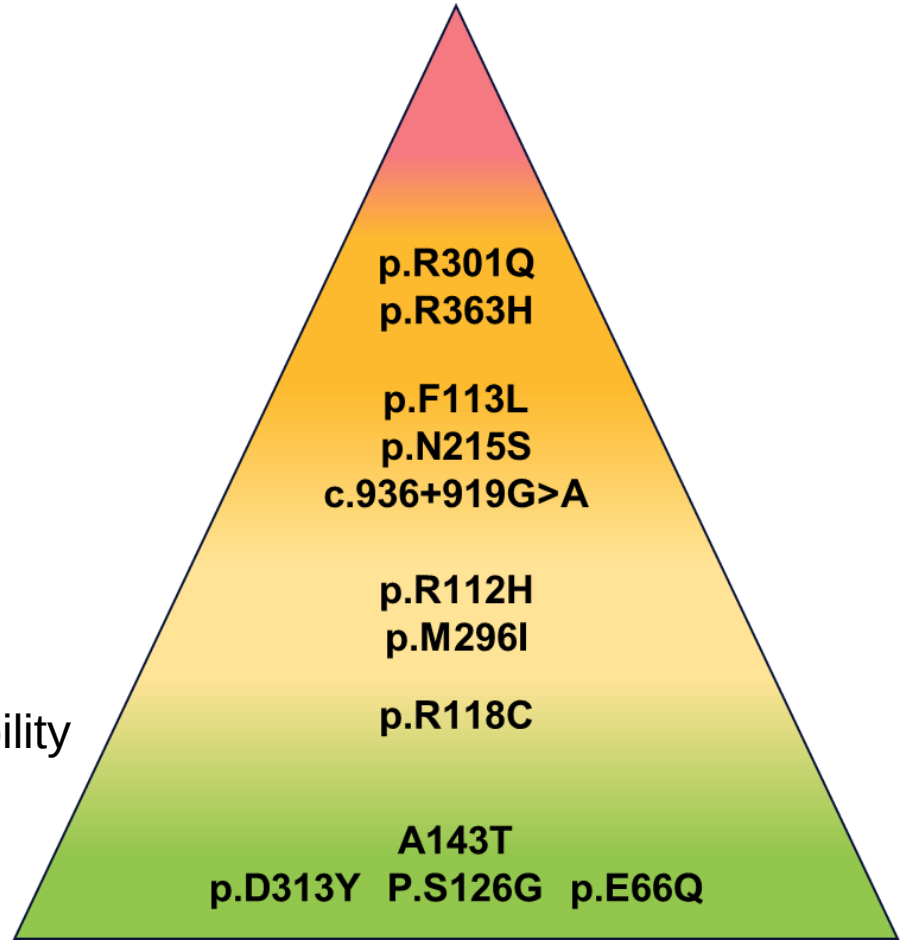
Fabry disease – Genetic disease with X-linked inheritance





- Males are usually more affected than females
- In females, the disease is highly variable
- The type and severity of mutations represents another source of variability

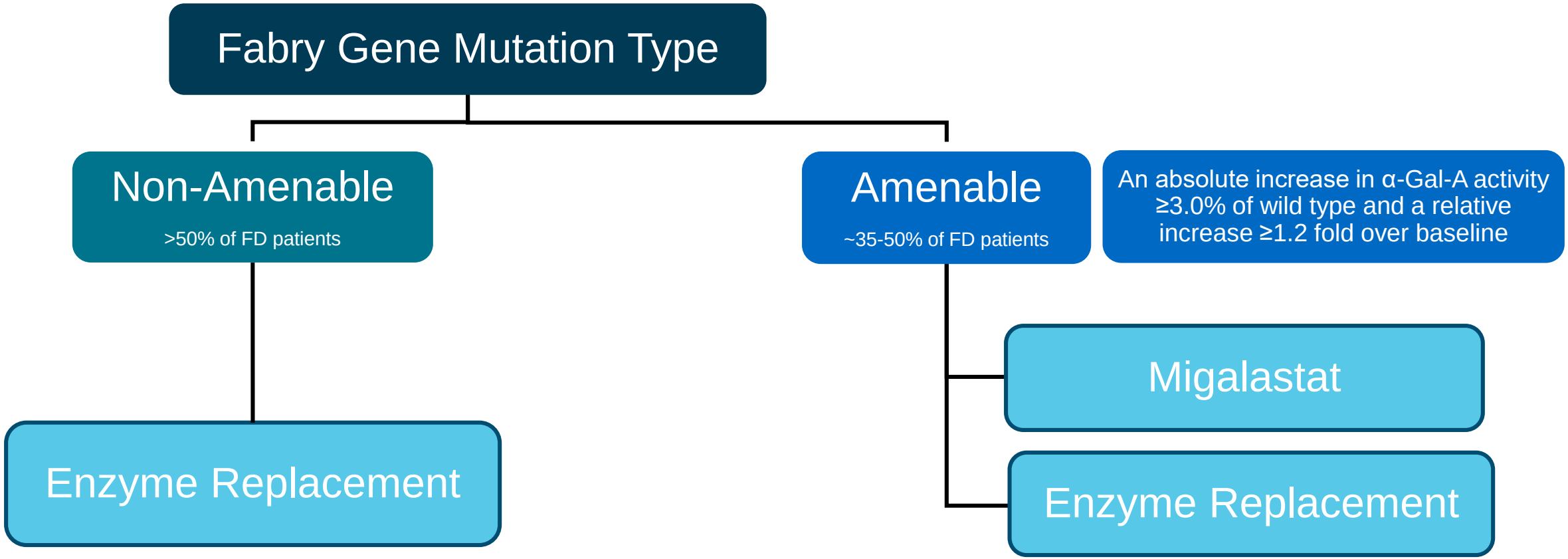
>1000 gene variants known



Ortiz A. et al. Molecular Genetics and Metabolism 2018;123:416–427

Fabry Disease – Specific Therapies

Fabry disease treatment options

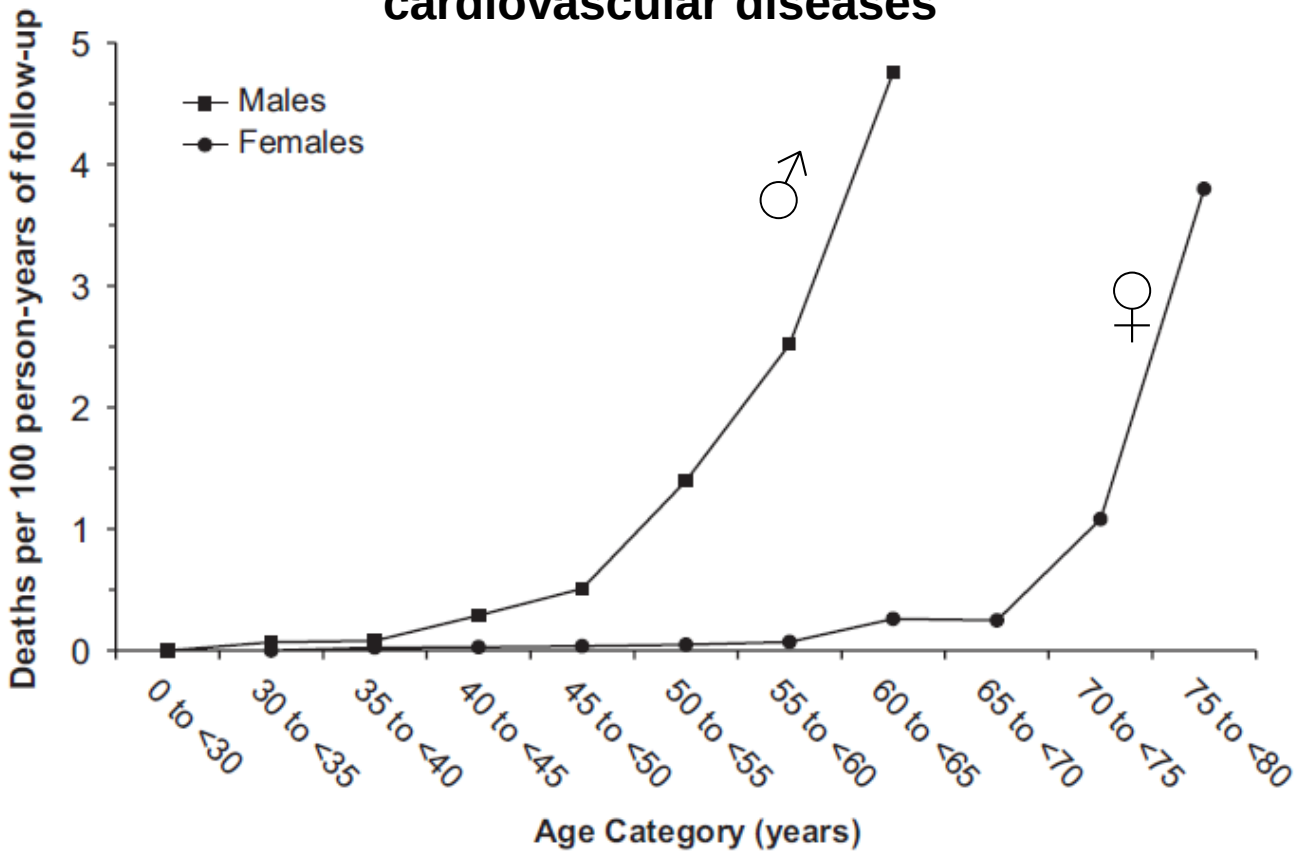


Hughes et al. 2017 Apr;54(4):288-296. doi: 10.1136/jmedgenet-2016-104178. Epub 201 Nov 10.
Germain et al. Molecular Genetics and Metabolism 137 (2022) 49–61
Bichet et al. Front Med (Lausanne). 2023; 10: 1220637.
https://www.ema.europa.eu/en/documents/overview/elfabrio-epar-medicine-overview_en.pdf

Life expectancy in untreated patients with Fabry disease (FD): Fabry registry

2,848 patients with FD (1,422 males)

The most common cause of death: cardiovascular diseases



Life expectancy in untreated FD patients:

- Males - 58 years
  (vs. 75 years in the general population)
- Females - 75 years
  (vs. 80 years in the general population)

Waldek S, et al., Genet Med 2009

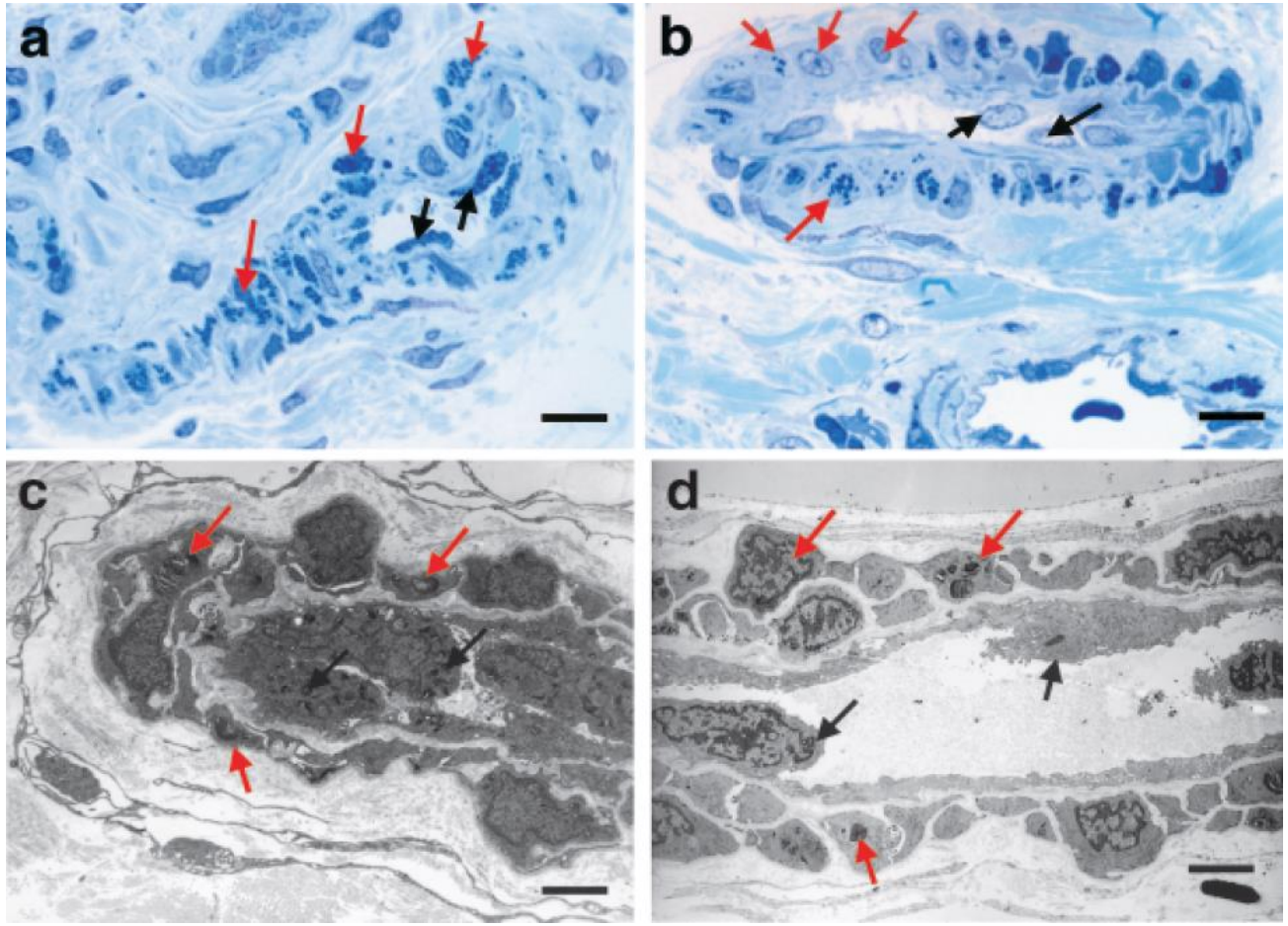
Proof of concept: After ERT – Gb_3 is cleared from endothelial cells and reduced in smooth muscle cells

Enzyme Replacement Therapy (ERT) = agalsidase beta – 36 months

Skin biopsy

Red arrows = endothelial cells
Black arrows = smooth mucle cells

* Pegunigalsidase alfa data – is presented in slide # 22



pre-treatment

post-treatment

(a and b – magnification x100, scale bar = 10 μm).
(c - electron microscopy magnification x 3000, scale bar = 2.43 μm).
(d - electron microscopy -magnification x 2000, scale bar = 2.95 μm)

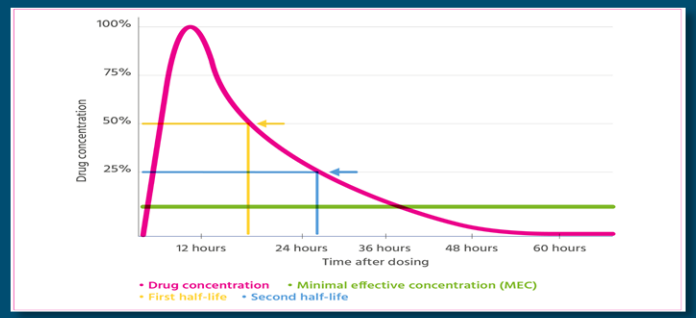
Thurberg BL et al. J Invest Dermatol. 2004 Apr;122(4):900-8.

Key Issues with Classical Enzyme Replacement Therapies

Infusion (IV) frequency
Every second week

Duration depends on dosing and tolerability

Infusion related reactions



Short plasma half-life

Limited coverage of the dosing interval

Instability in neutral pH

Potential impact on efficacy[1]

Antidrug antibodies (ADA) formation
Infusion-related reactions

Neutralizing ADA (nAb)
Potential threat to efficacy

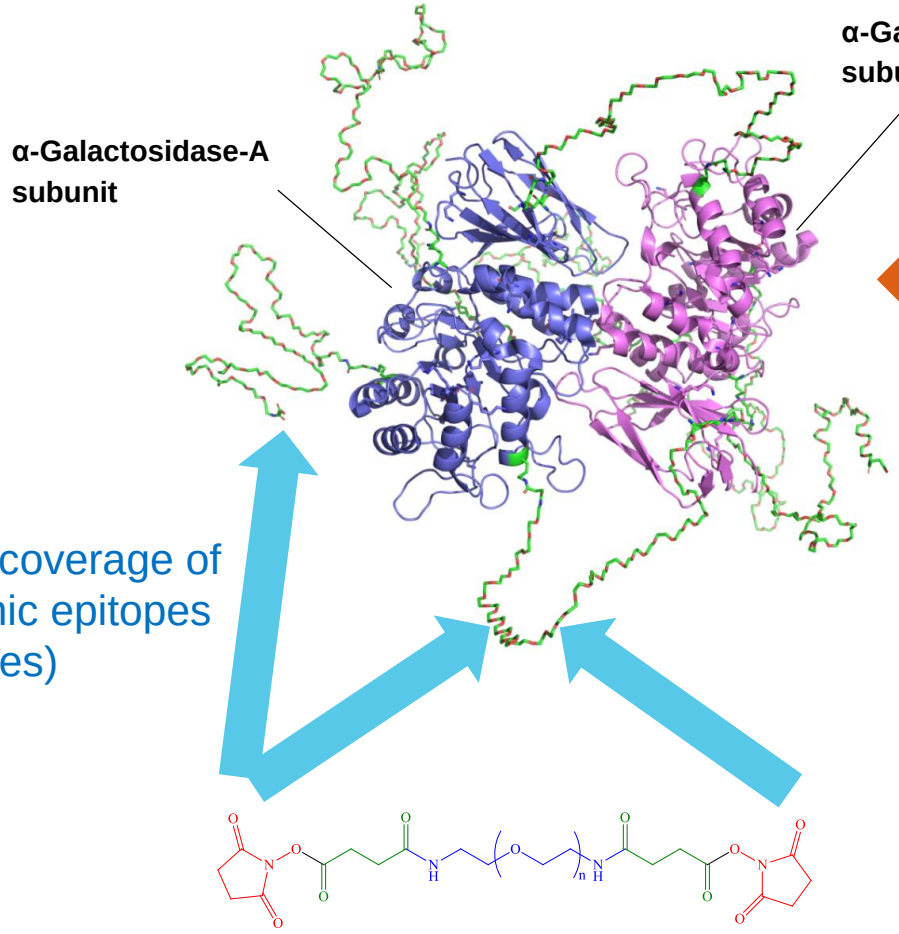
[1]exposure-response relationship is unknown.

Germain DP. and Linhart A. Front Genet. 2024 Apr 12:15:1395287

Innovations Addressing Several Critical Limitations

pegunigalsidase alfa (Elfabrio®) – new ERT option in Fabry

Elfabrio is a recombinant human α-Galactosidase-A enzyme approved in the United States and Europe for the treatment of adult patients with Fabry disease



Plant-based production (ProCellEx®)

PEGylation leads to coverage of potential immunogenic epitopes (hiding from antibodies)

2.3 kDa polyethylene glycol (PEG)

Covalently binding together the two subunits

- ↑↑ **Half-life**
- **High stability at the lysosomal-like conditions**
- **Coverage of epitopes**

Kizhner T. et al. Mol Genet Metab. 2015 114, 259–267
Ruderfer I., et al. Bioconjugate Chem. 2018. 29, 5, 1630–1639
Schiffmann R., et al. J Inherit Metab Dis. 2019. 42:534–544
Lenders MI, et al. Mol Ther Methods Clin Dev. 2022. 26:323-330

Elfabrio® Clinical Development Program

Elfabrio® Clinical Program Overview

Mechanism of action
- Delivered to lysosome to reduce accumulated substrate
- Prolonged drug presence in the circulation due to a long half-life
- Low immunogenicity

Phase 1/2
- Safety
- Reduction of Gb_3 and lyso-Gb_3
- eGFR

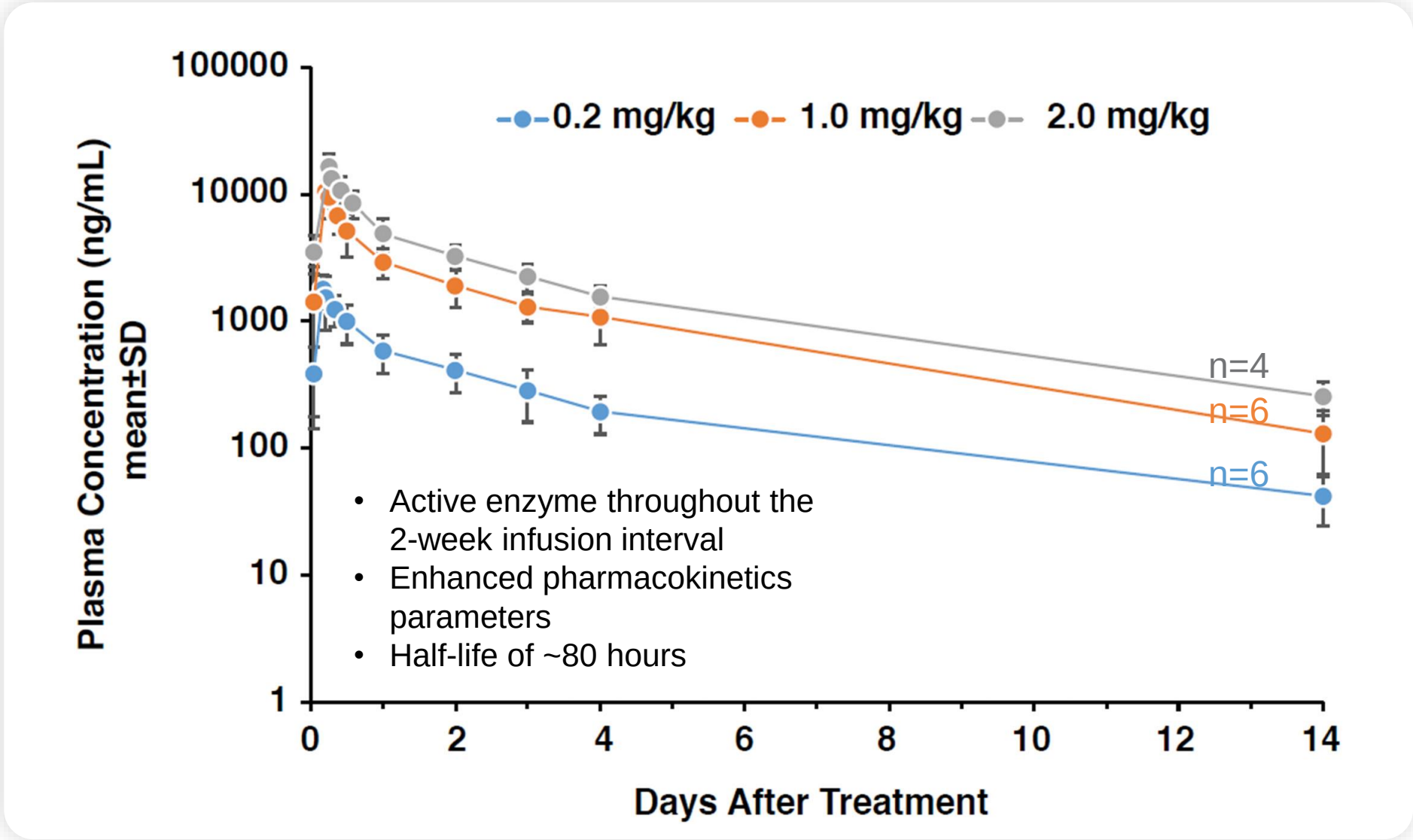
	bridge (a Fabry clinical study)	balance (a Fabry clinical study)	bright
Endpoints	• Safety • eGFR slope	• Safety • Noninferiority in eGFR slope	• Safety • eGFR slope
Study design	• 1 mg/kg every 2 weeks • Open label • Switch over from Replagal® • 12 months	• 1 mg/kg every 2 weeks • Randomized, double-blind, head-to-head vs Fabrazyme® • 24 months	• 2 mg/kg **every 4 weeks** • Open label • Switch over from Fabrazyme® and Replagal® • 12 months
Status	✓ **Completed[1]**	✓ **Completed[2]**	✓ **Completed**

The 2 mg/kg every four weeks dosage has not been approved by the EMA, FDA or any other jurisdiction.

Gb_3, globotriaosylsphingosine
https://clinicaltrials.gov/ NCT01678898, NCT03018730, NCT03180840, NCT02795676, NCT01981720, NCT03566017, NCT03614234

1) Linhart A, et al. Orphanet J Rare Dis. 2023 Oct 21;18(1):332.
2) Wallace EL, et al. J Med Genet. 2023 Nov 8:jmg-2023-109445.

Pegunigalsidase alfa exhibits prolonged half-life in Fabry patients in Phase 1/2 Study

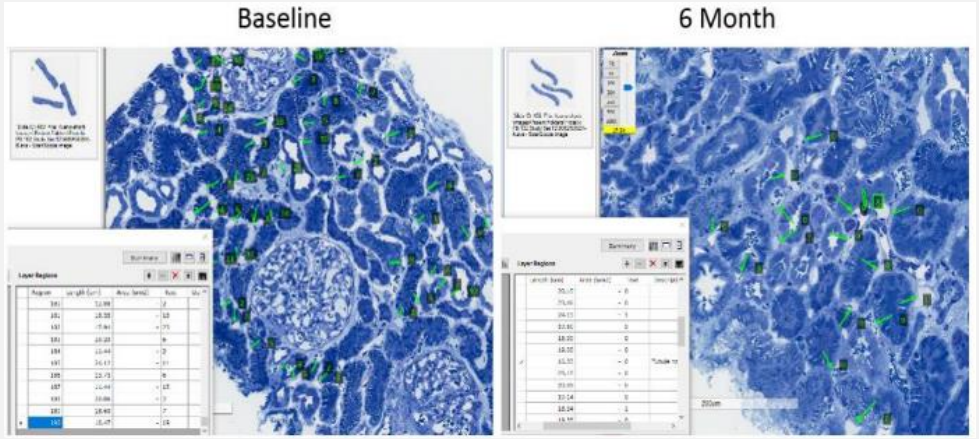


Pegunigalsidase alfa exposure-response relationship is unknown.

Schiffmann R, et al. J Inherit Metab Dis. 2019 May;42(3):534-544

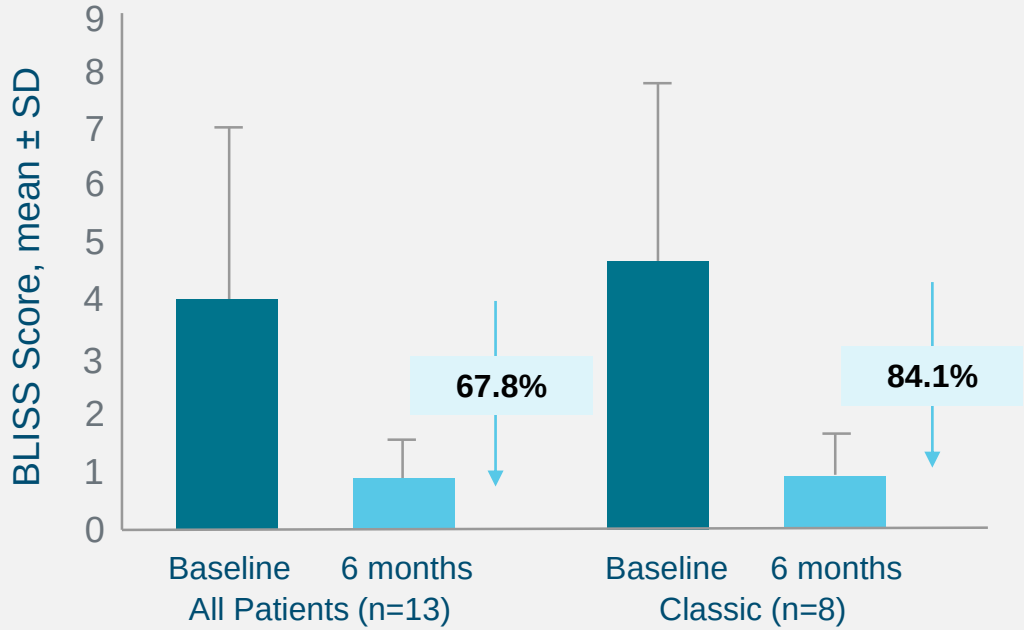
Phase 1/2 Study Histology[1,2]

- In the overall population at **6 months** there was **67.8% reduction in GL-3** from baseline in peritubular capillaries (n=13)
  - Patients with classic Fabry disease (n=8) exhibited a mean reduction in GL-3 of 84.1%



Analysis includes all three dosing groups

Change in BLISS Score* with pegunigalsidase alfa



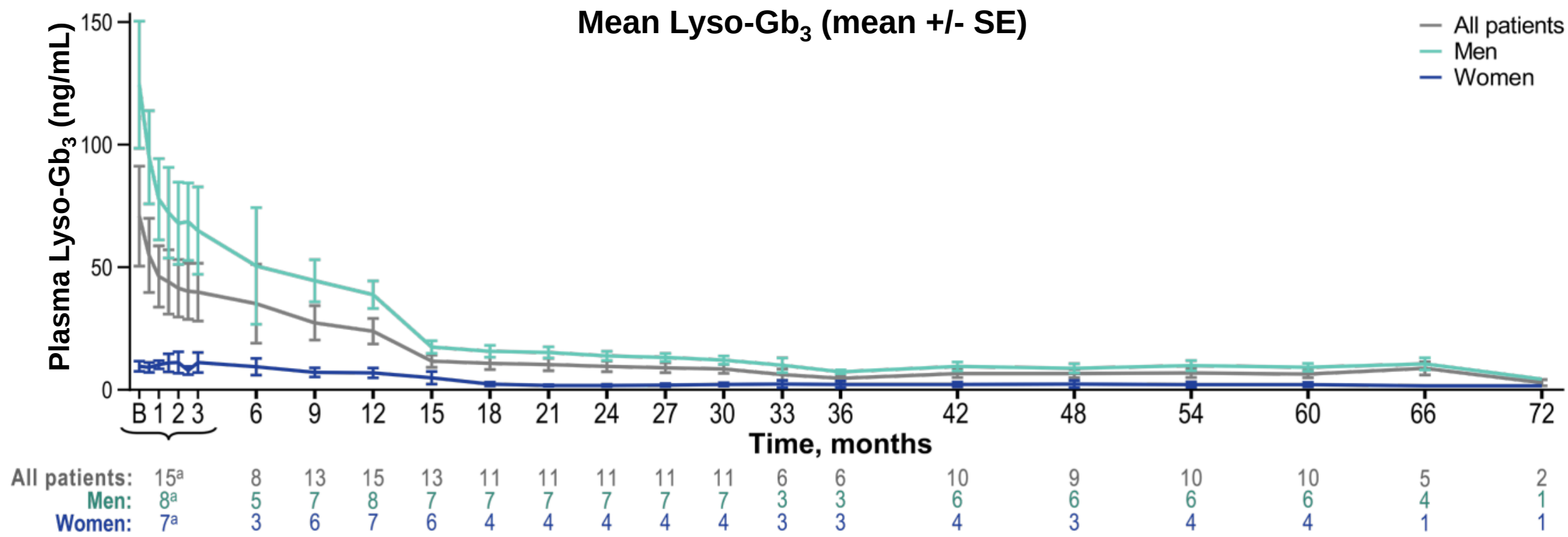
*The BLISS score requires two pathologists to each independently count GL-3 inclusions per peritubular capillary across multiple vessels and record the average number; the final BLISS score is then the average of the two pathologists' scores[3]

agalsidase beta phase 3 evidence shows "0" scores clearance 20 weeks post therapy for 20 patients (69%) and "1 score" for 8 of the remaining patients[4]

BLISS, Barisoni lipid inclusion scoring system; GL-3, globotriaosylceramide; SD, standard deviation

1. Schiffmann R, et al. J Inherit Metab Dis 2019;42:534–544; 2. Barisoni L, et al. Arch Pathol Lab Med 2012;136:816–824; 3. Germain DP, et al. J Am Soc Nephrol 2007;18:1547–1557; 4 Eng CM, et al. N Engl J Med. 2001 Jul 5;345:9-16.

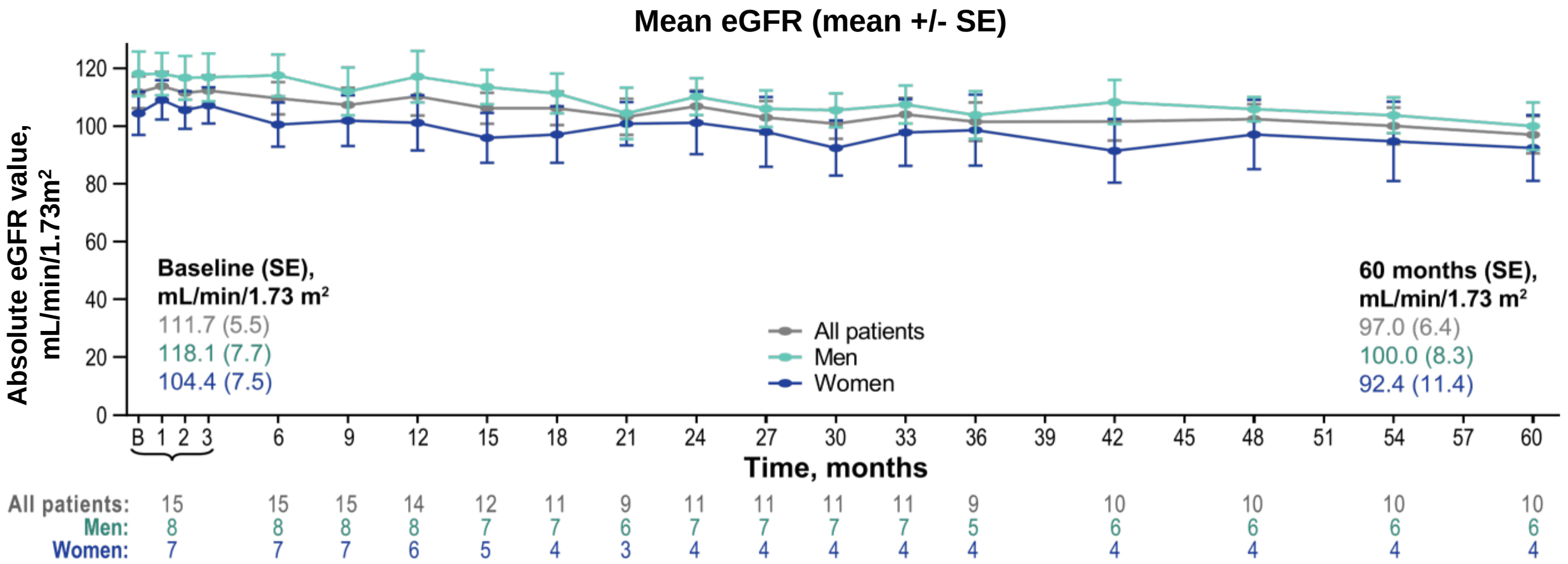
Long-term extensions of Phase 1/2 Study



[a]At month 1.5, n = 13 for all patients, n = 7 men, and n = 6 women.
B, baseline; Lyso-Gb_3, plasma Globotriaosylsphingosine

1. Hughes et al., Long-term safety and efficacy of pegunigalsidase alfa: A multicenter 6-year study in adult patients with Fabry disease. Genet Med. 2023 Dec;25(12)

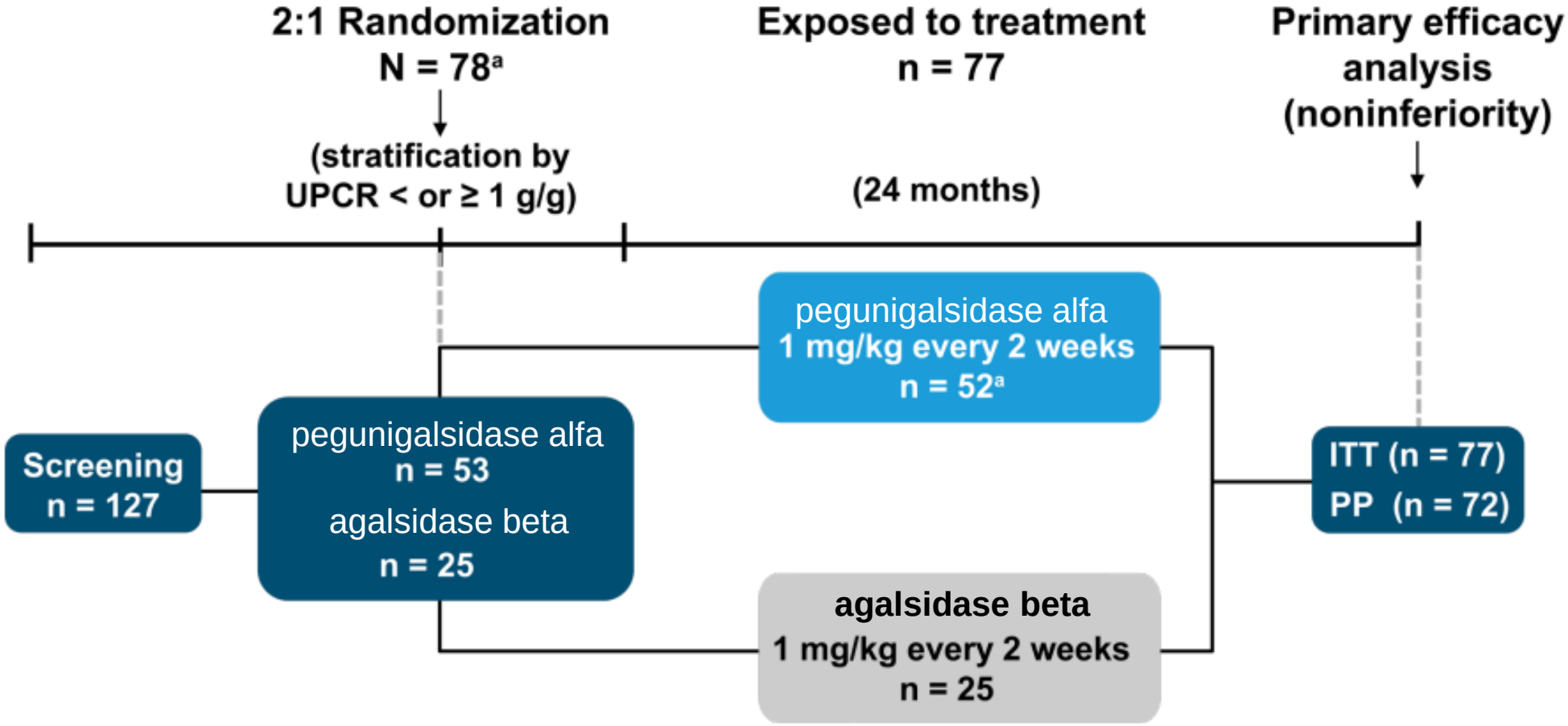
Long-term extensions of Phase 1/2 Study



[a]Baseline values are from either Visit 1 or screening if Visit 1 is not available.
A small number of patients (n = 2) had values at 72 months and are not included in the graph.
B, baseline; eGFR, estimated glomerular filtration rate; SE, standard error.

1. Hughes et al., Long-term safety and efficacy of pegunigalsidase alfa: A multicenter 6-year study in adult patients with Fabry disease. Genet Med. 2023 Dec;25(12)

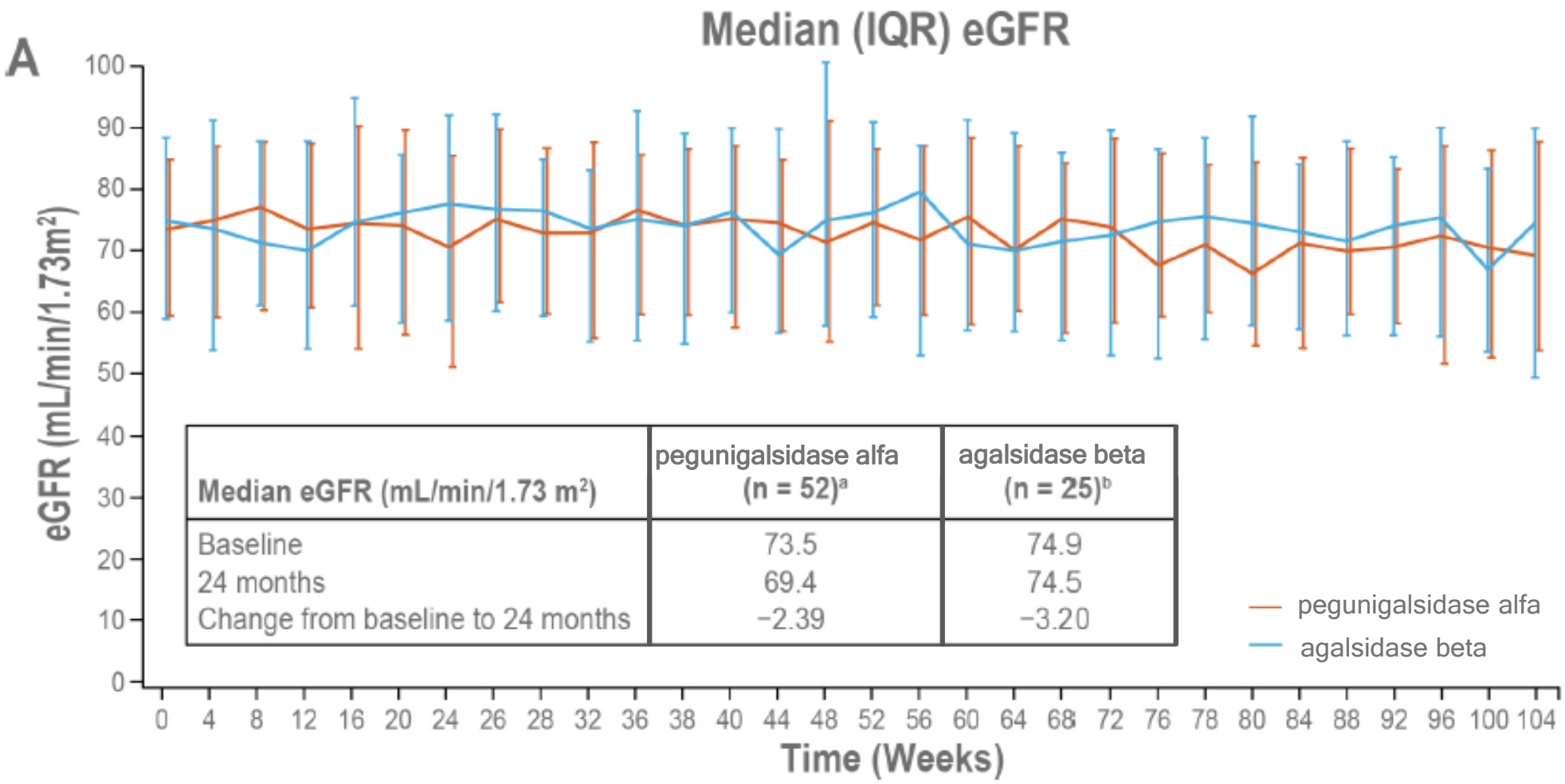
BALANCE Study - design



[a]1 Patient withdrew consent prior to the first dose.
ITT, intent-to-treat; PP, per protocol; UPCR, urinary protein-to-creatinine ratio.

Wallace EL, Goker-Alpan O, Wilcox WR, Holida M, Bernat J, Longo N, Linhart A, Hughes DA, Hopkin RJ, Tøndel C, Langeveld M, Giraldo P, Pisani A, Germain DP, Mehta A, Deegan PB, Molnar MJ, Ortiz D, Jovanovic A, Muriello M, Barshop BA, Kimonis V, Vujkovac B, Nowak A, Geberhiwot T, Kantola I, Knoll J, Waldek S, Nedd K, Karaa A, Brill-Almon E, Alon S, Chertkoff R, Rocco R, Sakov A, Warnock DG. Head-to-head trial of pegunigalsidase alfa versus agalsidase beta in patients with Fabry disease and deteriorating renal function: results from the 2-year randomised phase III BALANCE study. J Med Genet. 2023 Nov 8:jmg-2023-109445.

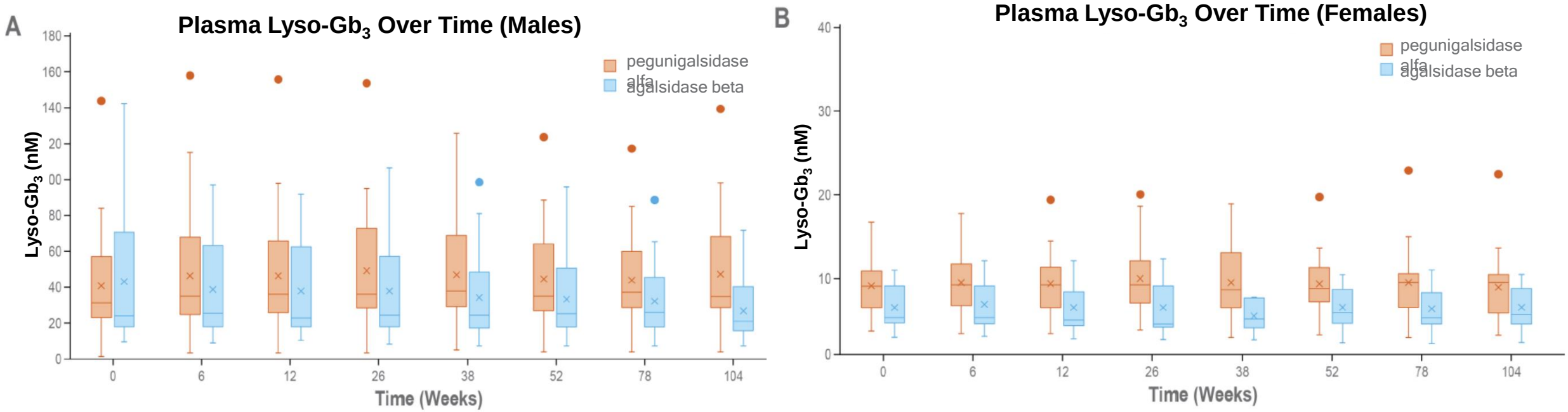
BALANCE Study - Key Results



Median eGFR (mL/min/1.73 m²)	pegunigalsidase alfa (n = 52)[a]	agalsidase beta (n = 25)[b]
Baseline	73.5	74.9
24 months	69.4	74.5
Change from baseline to 24 months	−2.39	−3.20

Wallace EL, Goker-Alpan O, Wilcox WR, Holida M, Bernat J, Longo N, Linhart A, Hughes DA, Hopkin RJ, Tøndel C, Langeveld M, Giraldo P, Pisani A, Germain DP, Mehta A, Deegan PB, Molnar MJ, Ortiz D, Jovanovic A, Muriello M, Barshop BA, Kimonis V, Vujkovac B, Nowak A, Geberhiwot T, Kantola I, Knoll J, Waldek S, Nedd K, Karaa A, Brill-Almon E, Alon S, Chertkoff R, Rocco R, Sakov A, Warnock DG. Head-to-head clinical trial of pegunigalsidase alfa versus agalsidase beta in patients with Fabry disease and deteriorating renal function: results from the 2-year randomised phase III BALANCE study. J Med Genet. 2023 Nov 8:jmg-2023-109445.

BALANCE Study - Key Results



Increase in lyso-Gb_3 more prominent in patients with high UPCR and ADA positive

Patients with baseline UPCR ≥1 g/g and ADA positive status were all male and more frequently assigned to the pegunigalsidase alfa arm (of 18 ADA-positive patients, 6 had UPCR ≥1 g/g) than agalsidase beta (of 8 ADA-positive patients, 1 had UPCR ≥1 g/g)

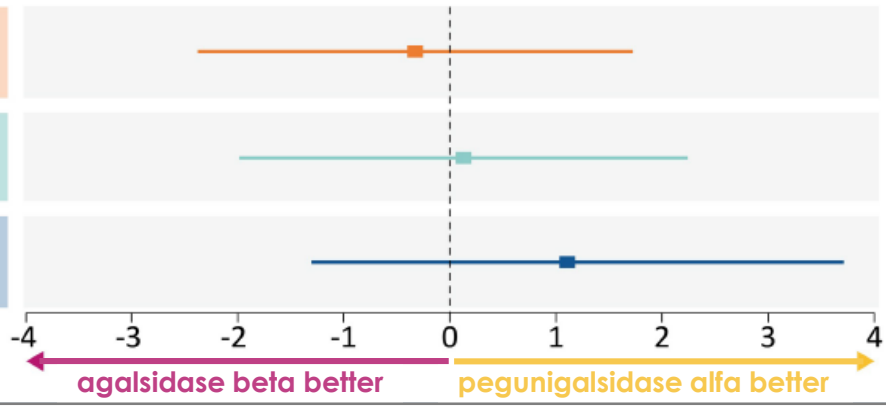
Wallace EL, Goker-Alpan O, Wilcox WR, Holida M, Bernat J, Longo N, Linhart A, Hughes DA, Hopkin RJ, Tøndel C, Langeveld M, Giraldo P, Pisani A, Germain DP, Mehta A, Deegan PB, Molnar MJ, Ortiz D, Jovanovic A, Muriello M, Barshop BA, Kimonis V, Vujkovac B, Nowak A, Geberhiwot T, Kantola I, Knoll J, Waldek S, Nedd K, Karaa A, Brill-Almon E, Alon S, Chertkoff R, Rocco R, Sakov A, Warnock DG. Head-to-head trial of pegunigalsidase alfa versus agalsidase beta in patients with Fabry disease and deteriorating renal function: results from the 2-year randomised phase III BALANCE study. J Med Genet. 2023 Nov 8:jmg-2023-109445.

The Impact of Baseline Proteinuria on Renal Outcomes in the BALANCE Study of pegunigalsidase alfa vs. agalsidase beta in Fabry Disease

Post-hoc analysis

Difference in Annualized eGFR Slope for pegunigalsidase alfa vs agalsidase beta in Overall Patient Population

Analysis/2-stage model	eGFR Slope (mL/min/1.73 m²/year) pegunigalsidase alfa n = 51	eGFR Slope (mL/min/1.73 m²/year) agalsidase beta n = 25	Treatment Difference (95% CI)
Primary / Quantile regression Median	−2.5	−2.2	−0.4 (−2.4, 1.7)
Post hoc / Quantile regression Median	−1.2	−1.3	0.1 (−2.0, 2.2)
Post hoc / ANCOVA Mean	−2.0	−3.1	1.1 (−1.3, 3.7)



eGFR slopes adjusted for baseline UPCR as continues variable

Effect of proteinuria on eGFR slope

- In the prespecified primary analysis, eGFR slope was analyzed by quantile regression
- In post hoc analyses, eGFR slope was adjusted for baseline UPCR as a continuous variable and analyzed by both quantile regression and ANCOVA
- In all models, the 95% CI included 0

Wallace E.L., et. al., 8th Fabry Disease Update, June 2–4, 2024, Hamburg, Germany

BALANCE Study - rates of Adverse Events and Infusion-Related Reactions

	pegunigalsidase alfa		agalsidase beta	
	ADA negative (n=34)	ADA positive (n=18)	ADA negative (n=17)	ADA positive (n=8)
Number of related TEAEs (rate*)	13 (20.08)	29 (87.18)	28 (83.64)	48 (295.80)
Total number of IRRs (rate†)	5 (0.3)	8 (0.9)	19 (2.2)	32 (7.5)

The related treatment-emergent adverse event rate was at least 3x higher for agalsidase beta than pegunigalsidase alfa

The infusion-related reaction rate was at least 7x higher for agalsidase beta than pegunigalsidase alfa‡

In the whole clinical program, 3% of pegunigalsidase alfa -treated patients experienced anaphylaxis reactions that occurred within 5 to 40 minutes of the start of the initial infusion. The signs and symptoms of hypersensitivity reactions and anaphylaxis included headache, nausea, vomiting, throat tightness, facial and oral edema, truncal rash, tachycardia, hypotension, rigors, urticaria, intense pruritus, moderate upper airway obstructions, macroglossia, and mild lip edema.

The most common adverse reactions for Elfabrio® (≥15%) are: infusion-associated reactions, nasopharyngitis, headache, diarrhea, fatigue, nausea, back pain, pain in extremity, and sinusitis.

In the Elfabrio Prescribing Information, BALANCE is referred to as Trial 2.

*A TEAE was defined as related if it was reported as possibly, probably, or definitely related to the study drug. Rate is calculated as the adjusted number of events per 100 years of exposure.

†IRRs are not injection site reactions. TEAEs occurred during the infusion or within 2 hours after the completion of the infusion, and causality was assessed as definitely, probably, or possibly related. Rate is presented as the number of IRRs per 100 infusions.

‡The data discussed are not intended to establish noninferiority or superiority to any other marketed drug product on the basis of safety or efficacy.

IRR = infusion reaction rates; TEAEs = treatment-emergent adverse events.

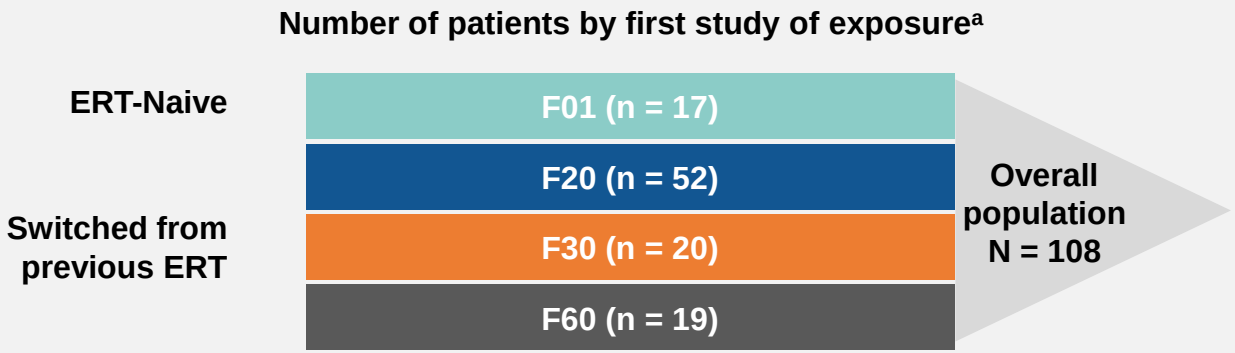
US Food and Drug Administration. Drug approval package: Elfabrio; Multi-discipline Review. May 8, 2023. Accessed July 14, 2023

pegunigalsidase alfa Immunogenicity

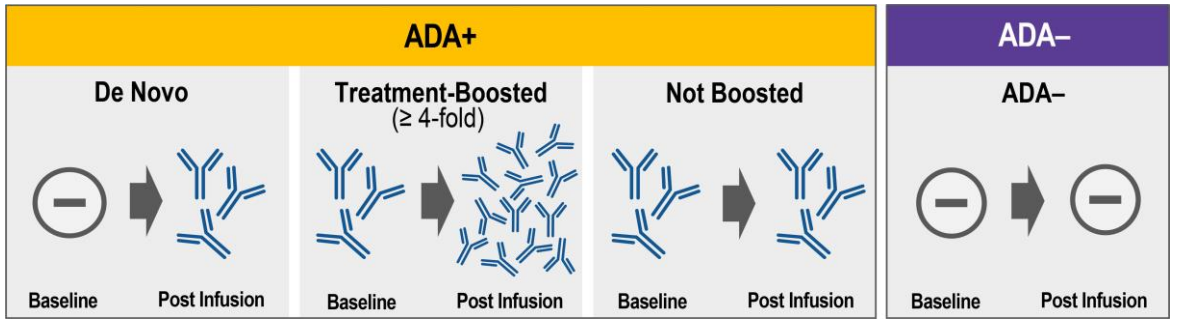
Assessment of immunogenicity from the pegunigalsidase alfa clinical program

Integrated analysis of de novo and pre-existing anti-drug antibodies

Number of Patients Receiving pegunigalsidase alfa E2W in Clinical Trials included in this Pooled Analysis



Patient Subgroups by ADA Status



De novo ADA: patients who were ADA− at baseline and **seroconverted** in at least 1 evaluation following the first pegunigalsidase alfa administration;

Treatment boosted: patients who were ADA+ at baseline and developed **≥ 4-fold increase in antibody** titer in at least 1 evaluation following the first pegunigalsidase alfa administration;

ADA+ (not boosted): patients who were ADA+ at baseline but were not treatment boosted;

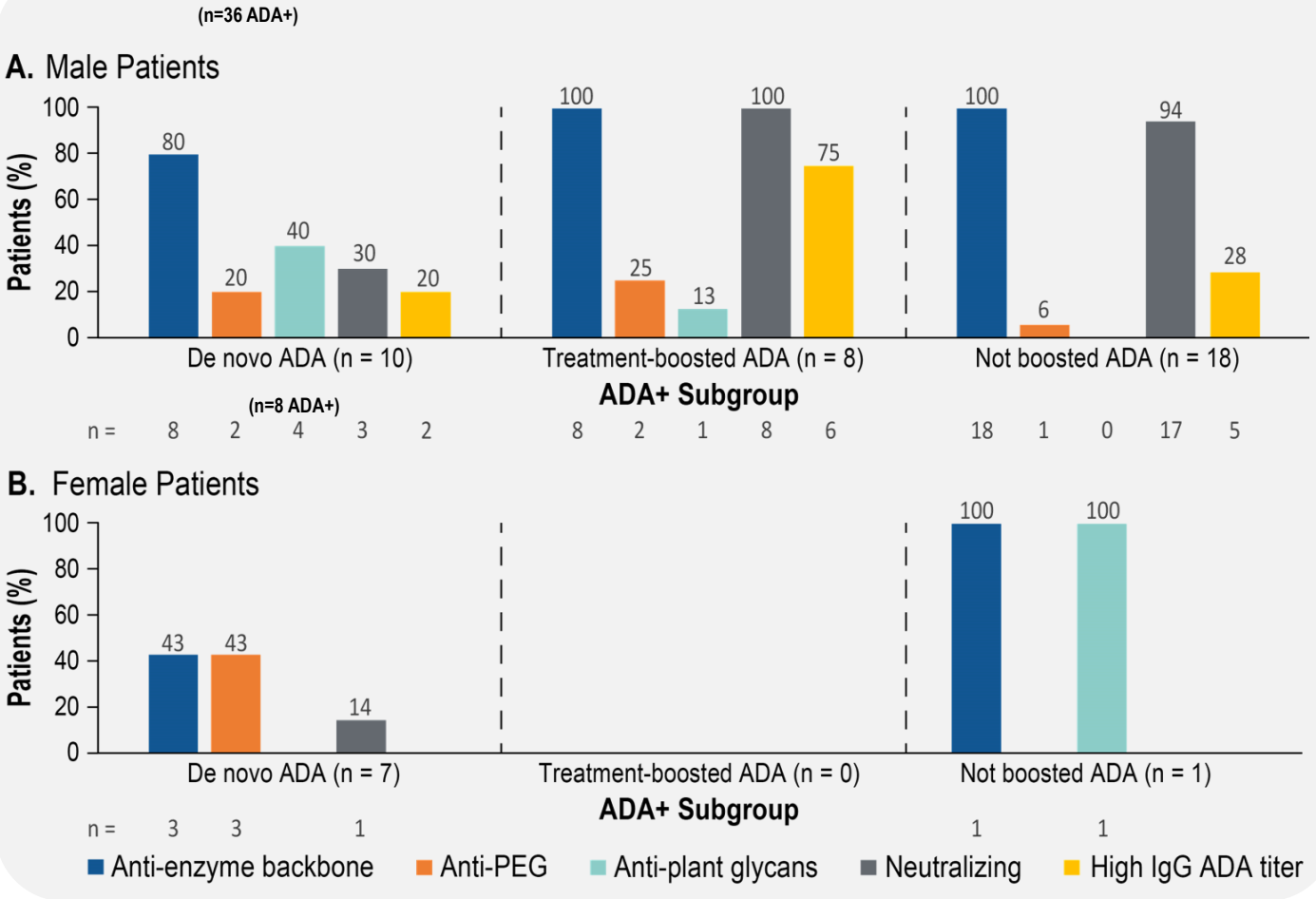
ADA−: patients who were ADA− at all evaluations.

Hopkin R.J., et al., 8th Fabry Disease Update, June 2–4, 2024, Hamburg, Germany

Assessment of immunogenicity from the pegunigalsidase alfa clinical program - Antibody characteristics

27/108 (25%) of FD recruited to pegunigalsidase alfa studies were ADA+ and the rest 81 (75%) patients were ADA-

- **17/81 (21%) patients who were ADA– at baseline developed de novo ADAs (10/41 males, 7/40 females), and 64 (79%) remained ADA-.**
- 8/27 (30%, all male) patients who were ADA+ at baseline had treatment-boosted ADAs; the other 19 patients (70%) remained positive but were not boosted.



Includes any patient who tested positive at least once for the characteristic during the study. High IgG ADA titer was defined as > 75th percentile of all observed titers (> 1:14,000) in at least one sample.

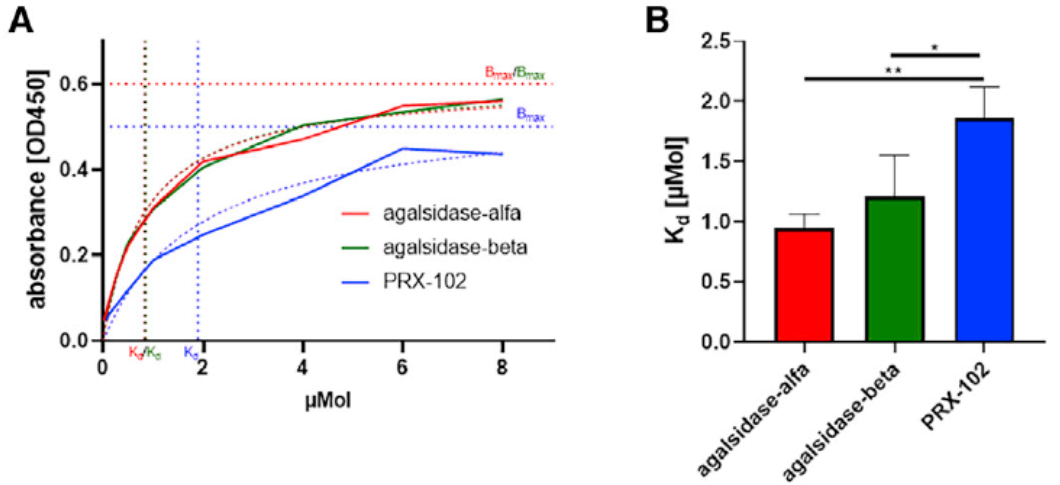
ADA, anti-drug antibody; IgG, immunoglobulin G; PEG, pegylated.

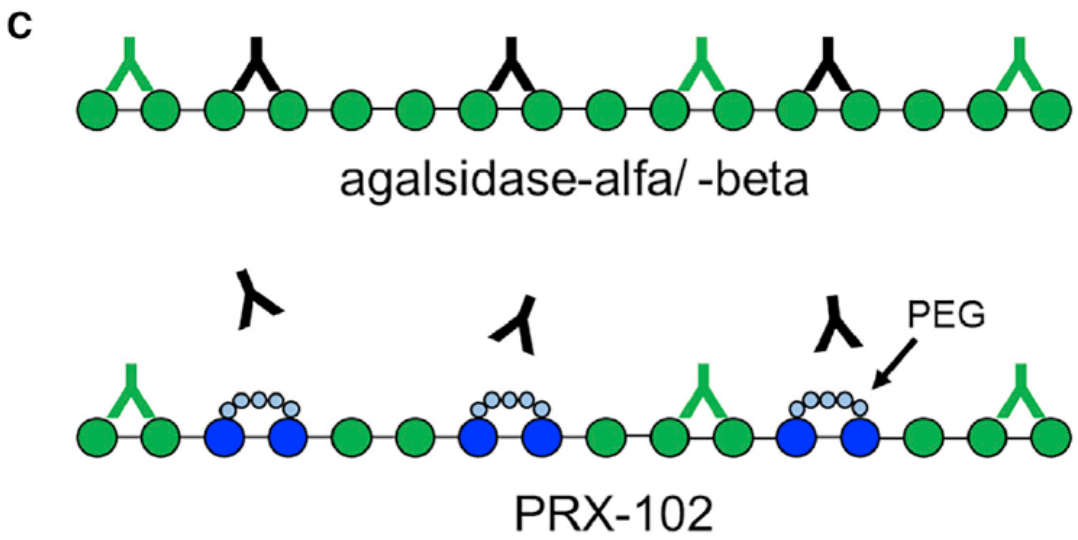
Hopkin R.J., et al., 8th Fabry Disease Update, June 2–4, 2024, Hamburg, Germany

Lower affinity of anti-drug antibodies to pegunigalsidase alfa

- Analysis of the cross-reactivity of ADAs against agalsidase alfa and agalsidase beta from 49 patients with Fabry disease against the novel PEGylated enzyme pegunigalsidase alfa (PRX-102).

- Affinities of ADAs of individual patients against PRX-102 (Kd: 3.55 ± 2.72 mmol) were significantly lower compared to agalsidase alfa (Kd: 1.99 ± 1.26 mmol) and agalsidase beta (Kd: 2.18 ± 1.51 mmol) (both $p < 0.0001$).





Lenders et al. Molecular Therapy: Methods & Clinical Development Vol. 26 September 2022

Conclusions

Main conclusions from the overall clinical program of Elfabrio®

Elfabrio is now approved in the EU and US, based on clinical program included >140 patients who received at least 1 infusion of pegunigalsidase alfa; some patients have been treated with pegunigalsidase alfa for >7.5 years

Pharmacokinetics and pharmacodynamics

- **Significantly prolonged plasma half-life (~80 hr) and in-vitro stability in plasma and in lysosomal pH**
- **Reduction in plasma lyso-Gb_3 in ERT-naïve** FD patients demonstrated a pharmacologic effect of Elfabrio in humans

Efficacy

- Substantial **reduction in Gb_3 deposits** in ERT-naïve FD patients (Phase 1/2), as assessed in kidney biopsies at 6 months vs. baseline
- Comparable **annualized eGFR slope** between ERT-experienced patients randomized to Elfabrio or to agalsidase beta was shown in the BALANCE study
- **eGFR over time** show stability and high similarity between treatment arms in BALANCE study, and stability in the Phase 1/2 study and their extension studies
- Positive mean change in eGFR slopes from pre- to post-switch in patients switching from agalsidase alfa (BRIDGE study)

Immunogenicity

- Low ADA prevalence and potential to become ADA negative when treated with Elfabrio
- Lower affinity of pre-existing ADAs towards Elfabrio
- Most pre-existing ADAs in ERT pre-treated patients enrolled in the ERT experienced studies were neutralizing

Safety

- Overall, in the active-control trial similar % of patients with ADRs were observed between the treatment arms (BALANCE study)
- Lower rates of TEAEs and IRRs as compared to agalsidase beta (BALANCE study)

Indication and Important Safety Information

Indication: Elfabrio® (pegunigalsidase alfa-iwxj) is a prescription infusion medicine used to treat adults with confirmed Fabry disease.

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

Patients treated with ELFABRIO® have experienced hypersensitivity reactions, including anaphylaxis. Appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available during ELFABRIO® administration. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue ELFABRIO® immediately and initiate appropriate medical treatment. In patients with severe hypersensitivity reaction, a desensitization procedure to ELFABRIO® may be considered.

Prior to Elfabrio administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids. Inform patients and caregivers of the signs and symptoms of hypersensitivity reactions and infusion-associated reactions (IARs) and instruct them to seek medical care immediately if such symptoms occur.

- If a severe hypersensitivity reaction (including anaphylaxis) or severe IAR occurs, immediately discontinue Elfabrio administration and initiate appropriate medical treatment.
- If a mild to moderate hypersensitivity reaction or IAR occurs, consider slowing the infusion rate or temporarily withholding the dose.

In clinical trials, 20 (14%) Elfabrio-treated patients experienced hypersensitivity reactions.
Four Elfabrio-treated patients (3%) experienced anaphylaxis reactions that occurred within 5 to 40 minutes of the start of the initial infusion. The signs and symptoms of hypersensitivity reactions and anaphylaxis included headache, nausea, vomiting, throat tightness, facial and oral edema, truncal rash, tachycardia, hypotension, rigors, urticaria, intense pruritus, moderate upper airway obstructions, macroglossia, and mild lip edema.

In clinical trials, 41 (29%) Elfabrio-treated patients experienced one or more infusion-associated reactions, including hypersensitivity, nausea, chills, pruritus, rash, chest pain, dizziness, vomiting, asthenia, pain, sneezing, dyspnea, nasal congestion, throat irritation, abdominal pain, erythema, diarrhea, burning sensation, neuralgia, headache, paresthesia, tremor, agitation, increased body temperature, flushing, bradycardia, myalgia, hypertension, and hypotension.

A case of membranoproliferative glomerulonephritis with immune depositions in the kidney was reported during clinical trials. Monitor serum creatinine and urinary protein-to-creatinine ratio. If glomerulonephritis is suspected, discontinue treatment until a diagnostic evaluation can be conducted.

When switching to Elfabrio from a prior enzyme replacement therapy, the risk of hypersensitivity reactions and infusion-associated reactions may be increased in certain patients with pre-existing anti-drug antibodies (ADAs). Consider monitoring IgG and IgE ADAs and clinical or pharmacodynamic response (eg, plasma lyso-Gb_3 levels).

The most common adverse reactions (≥15%) were infusion-associated reactions, nasopharyngitis, headache, diarrhea, fatigue, nausea, back pain, pain in extremity, and sinusitis.

Please see Full Prescribing Information for Elfabrio

1. Chiesi (2023). *ELFABRIO® Prescribing Information*.