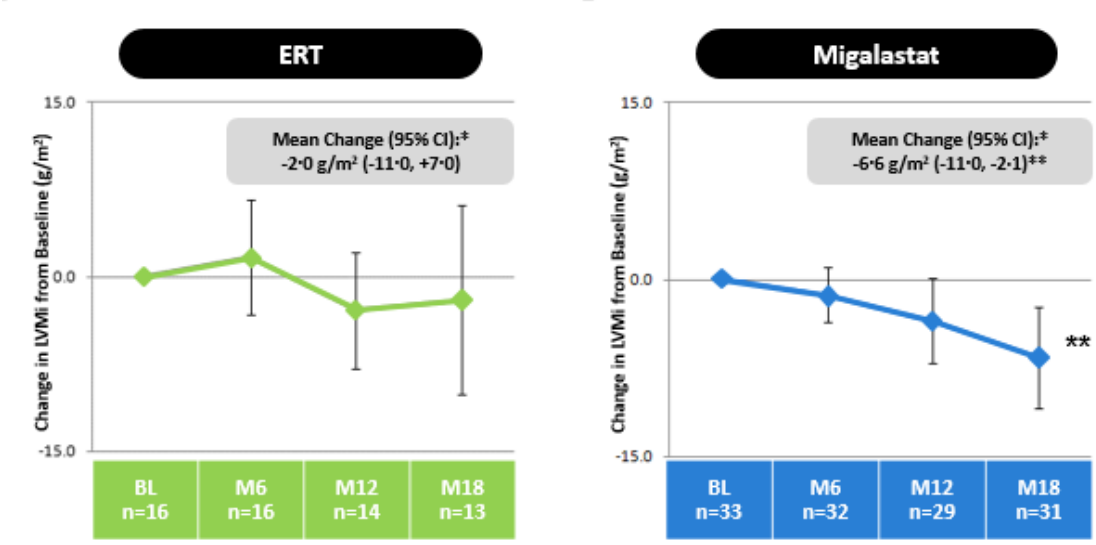
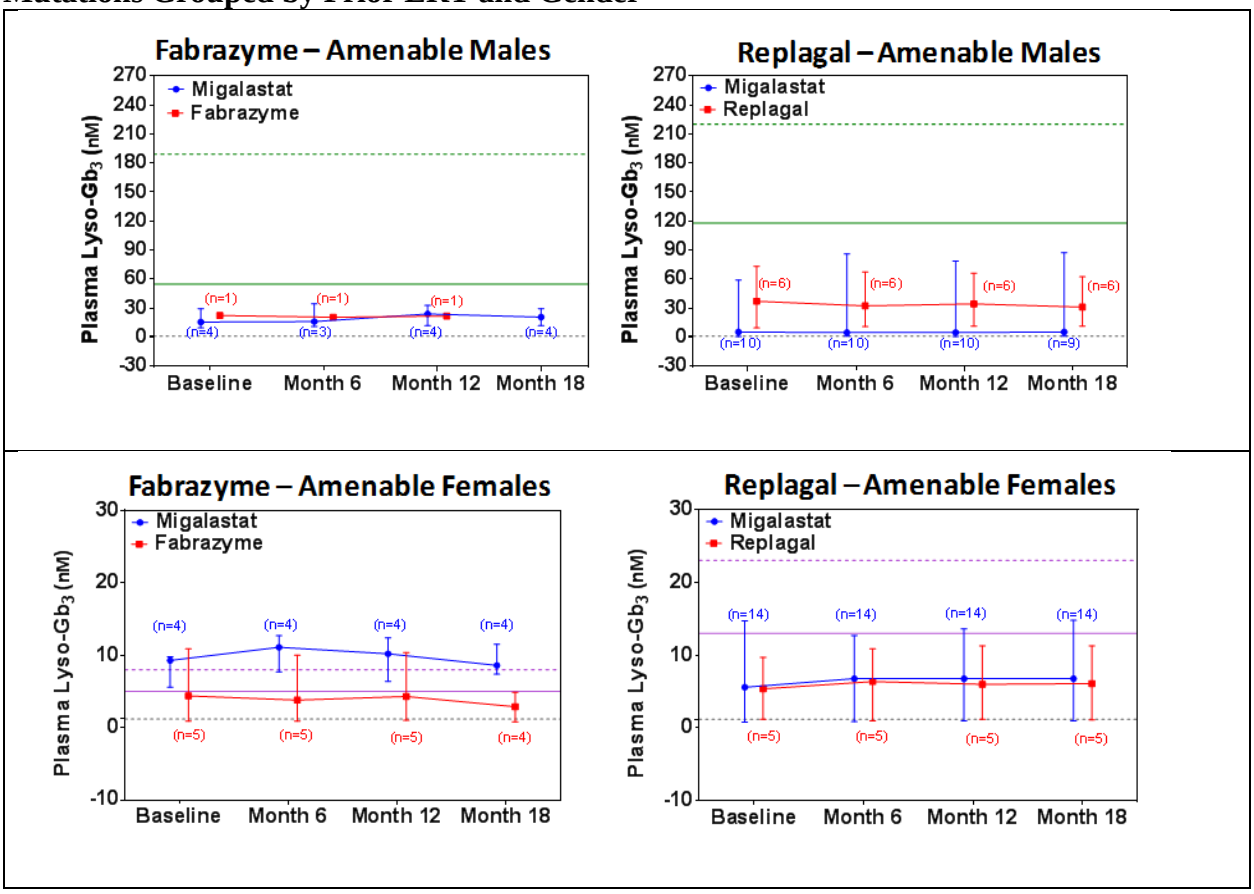
Figure S1. LVMi Change over 18 months on Migalastat and ERT



Mean change to month 18 in mITT patients (all randomized, treated patients with amenable mutations); LVMi decreased significantly (95% CI does not overlap zero) in patients switched to migalastat (-6.6g/m^2 [-11.0,-2.2]); a smaller non-significant change was observed in the ERT group (-2.0 g/m^2 [-11.0, 7.0]). Abbreviations: LVMi, left ventricular mass index; mITT, modified intention-to-treat; CI, confidence interval; B, baseline, M, month.

Figure S2. Change in Lyso-Gb_3 from Baseline to Month 18 in Patients with Amenable Mutations Grouped by Prior ERT and Gender



Data points are median values; error bars represent the range. The blue dotted line represents upper range of the normal plasma lyso-Gb_3 reference range (1·19 nM).
Upper figure (males): Baseline and median values in a cohort of classical phenotype males after 1 year of agalsidase beta treatment were 189 nM and 55 nM, respectively (dotted and solid green lines in graph on left, respectively). Baseline and median values in a cohort of classical phenotype males after 1 year of agalsidase alfa treatment were 220 nM and 118 nM, respectively (dotted and solid green lines in graph on right, respectively).
Lower figure (females): Baseline and median values in a cohort of classical phenotype females after 1 year of agalsidase beta treatment were 8 nM and 5 nM, respectively (dotted and solid purple lines in graph on left, respectively). Baseline and lowest median values in a cohort of classical phenotype females after 1 year of ERT treatment were 23 nM and 13 nM, respectively (dotted and solid purple lines in graph on right, respectively).(1)

Table S1. Baseline Assessment of Disease Severity

Sex	Fabry Disease in ≥ 2 Organ Systems	Angio-keratoma or Corneal Whorling	Cardiac Events	CNS Events	Neuro-pathic Pain	Renal Impairment	Gastro-intestinal Symptoms
Male n (%)	21/23 (87)	13/23 (57)	15/23 (65)	17/23 (74)	14/23 (61)	17/23 (74)	14/23 (61)
Female n (%)	29/33 (88)	16/33 (48)	25/33 (75)	12/33 (36)	22/33 (67)	25/33 (76)	20/33 (61)

Includes randomized patients with amenable mutations. Angiokeratoma, corneal whorling, neuropathic pain, and gastrointestinal symptoms based on medical history finding. Cardiac involvement includes previous cardiac event (based on medical history), LVH, or conduction abnormality (eg, tachycardia, ST-T segment abnormality) based on medical history finding or baseline assessment of LVMi. CNS involvement was based on medical history findings (stroke/TIA, tinnitus/hearing loss). Renal involvement based on medical history finding or baseline eGFR < 90 mL/min/1.73m^2, 24-hr protein ≥ 150 mg.

CNS, central nervous system, LVH, left ventricular hypertrophy, LVMi, left ventricular mass index; TIA, transient ischemic attack; eGFR, estimated glomerular filtration rate.

Table S2. Baseline Characteristics in Study 012 versus ERT Registries

	Male Patients			Female Patients		
	FOS	**FR**	**012**	**FOS**	**FR**	**012**
Age at enrolment	39	40	47/44[1]	44	44	50/47[1]
Body System involvement (%)						
Dermatologic	78	31	38	50	12	21
Cardiac	69	13	67	65	10	75
CNS	69	17	75	74[2]	16[3]	36
Neuroparesthesias	76	62	58	64	41	67
Renal	50	17	75	50	11	76
Gastrointestinal	55	19	58	50	13	61

Abbreviations: CNS = Central Nervous System; FOS = Fabry Outcomes Survey; FR = Fabry Registry; TIA = transient ischaemic attack | [1] Second number reflects age at start of ERT which is more relevant comparison to age at enrolment into ERT registry; [2] Combines auditory and TIA/Stroke; [3]Combines cerebrovascular and neurological: other | Sources: Fabry Outcomes Survey (2); Fabry Registry (3, 4).

Table S3. Amenable Mutations of Enrolled and Treated Patients and the Corresponding Clinical Phenotype with supportive references from the Medical Literature

Amino Acid Change (number of patients with the mutation)	Literature Phenotype / Reference(s)	Amino Acid Change	Literature Phenotype / Reference(s)
p.M96I	Nonclassic	p.G260A	Classic(5)
p.L32P (n = 3)	Unknown*	p.Q279E	Nonclassic(6)
p.G35R	Nonclassic(7)	p.M284T	Classic(8)
p.D55V/Q57L	Unknown*	p.M296I	Nonclassic(9)
p.G85D (n = 4)	Unknown*	p.R301P (n = 3)	Classic(10)
p.A97V	Nonclassical(11)	p.R301Q	Both(6, 12-14)
p.R112G	Unknown*	p.G328A	Classic(15)
p.R112H	Nonclassic(16)	p.Q312R	Nonclassic(17)
p.A143T (n = 3)	Nonclassic(18)	p.D322E (n = 4)	Classic(19)
p.A156T (n = 6)	Classic(20)	p.R356Q	Nonclassic(21)
p.P205T	Classical(22)	p.R363H	Both(23, 24)
p.N215S (n = 10)	Nonclassic(25)	p.L403S	Classic(17)
p.Y216C	Classic(26)	p.P409T	Unknown*
p.I253S	Unknown*		

Number of patients with each mutation is 1 unless indicated otherwise. * Ten of these 11 patients including at least one patient for each of the six unique mutations with an unknown phenotype (3 of 4 for p.G85D) had baseline disease in ≥2 organ systems.
To date, 269 *GLA* mutations have been categorized as amenable to migalastat based on the GLP HEK assay.

Table S4. Echocardiography-Derived Changes in Patients with Amenable Mutations

Parameter	Baseline Mean	Month 18
Migalastat: Left Ventricular Ejection Fraction (%±SEM) (n= 33)	64.0±0.51	-1.07±0.53 (change from baseline)
ERT: Left Ventricular Ejection Fraction (%±SEM) (n= 17)	61.1±1.0	-0.49±1.1 (change from baseline)
Migalastat: Diastolic Grade (n, %) **Normal** **Impaired Relaxation** **Restrictive Filling**	 19 (61%) 3 (10%) 9 (29%)	 20 (65%) 4 (13%) 7 (23%)
ERT: Diastolic Grade (n, %) **Normal** **Impaired Relaxation** **Restrictive Filling**	 9 (53%) 3 (19%) 5 (29%)	 10 (67%) 0 5 (33%)
Migalastat: Systolic Grade (n, %) **Normal** **Mildly Abnormal** **Moderately Abnormal**	 33 (100%) 0 0	 33 (97%) 1 (3%) 0
ERT: Systolic Grade (n, %) **Normal** **Mildly Abnormal** **Moderately Abnormal**	 16 (94%) 1 (6%) 0	 11 (79%) 2 (14%) 1 (7%)

Diastolic grades were based on E/A ratio: impaired relaxation <0.75, normal 0.75-1.5, restrictive filling >1.5. Systolic grades were based on ejection fraction: normal >=55, mildly abnormal 45-54, moderately abnormal 30-44.

Table S5: Patient-Reported Outcomes

Assessment	Baseline (Mean±SEM)		Change from Baseline to Month 18 [Mean (95% CI)]	
	Migalastat	ERT	Migalastat	ERT
SF-36v2				
n	34	16	31	16[1]
Physical component	47.8±1.9	40.4±2.7	0.96 (-1.0, 2.9)	-1.92 (-6.7, 2.8)
Mental component	49.3±1.8	50.6±2.6	0.08 (-3.3, 3.4)	-0.41 (-4.3, 3.5)
BPI-SF (Pain Severity)				
n	34	17	34	17
Score	1.29±0.31	2.12±0.56	0.15 (-0.56, 0.88)	-0.19 (-0.98, 0.59)

Based on all randomized patients with amenable mutations. SF-36v2=Short Form Health Survey with 36 questions, version 2 (higher score represent less disability; range for each component: 0-100) | BPI-SF= Brief Pain Inventory Short Form– pain severity component (higher scores represent more pain; range: 1-10); CI=confidence interval; ERT=enzyme replacement therapy; SEM=standard error of the mean.
[1]For change from baseline in the mental component of SF-36v2, n=17.

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