Subjects with Fabry Disease Treated with Migalastat HCl Continue to Demonstrate Stable Renal Function in a Phase 3 Extension Study

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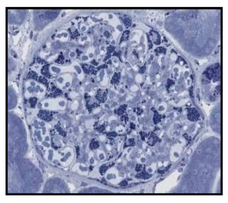
Introduction

Fabry Disease

- Progressive X-linked lysosomal storage disorder with an estimated incidence of 1 in 100,000. Actual incidence is thought to be higher.
- Mutations in the *GLA* gene lead to a paucity or absence of α-galactosidase A (α-Gal A) activity.
- More than 800 disease-causing mutations in *GLA* have been identified (~60% missense).
- Affects males and females; females have mosaic of healthy and diseased cells.
- Globotriaosylceramide (GL-3) and other substrates of α-Gal A accumulate in multiple tissues including the kidney, heart, brain, GI, skin leading to the symptoms and sequelae of Fabry disease.

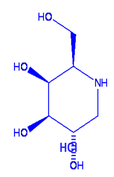


Kidney GL-3

Coronary GL-3

Migalastat HCl for Fabry Disease

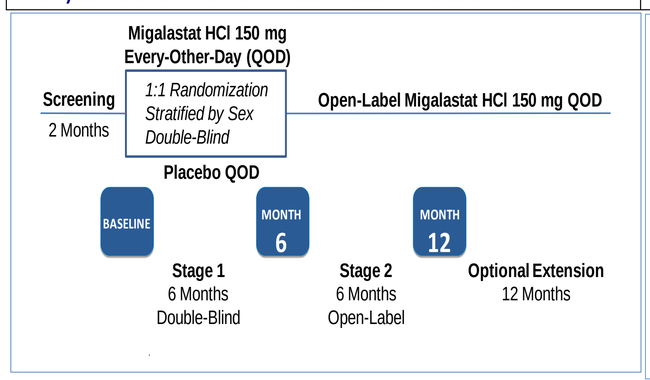
- Orally administered investigational pharmacological chaperone for specific patients.
- Designed to selectively and reversibly bind and stabilize endogenous α-Gal A in specific patients.
- Facilitates proper folding and cellular trafficking of specific mutant forms of α-Gal A from the endoplasmic reticulum to lysosomes where the breakdown of GL-3 and related substrates can proceed.
- In development for treatment of patients that express mutant forms of α-Gal A identified as amenable to this chaperone in an *in vitro* GLP-validated assay (estimated 30-50% of patients with Fabry disease).



Deoxygalactonojirimycin (DGJ)
AT1001

DESIGNS of AT1001-011 (FACETS, NCT00925301) and AT1001-041 (NCT01458119)

Study 011: A Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy, Safety and Pharmacodynamics of Migalastat HCl in Patients With Fabry Disease and Amenable *GLA* Mutations	Study 041: Open-label Extension



Key Inclusion and Exclusion Criteria for Study 011:

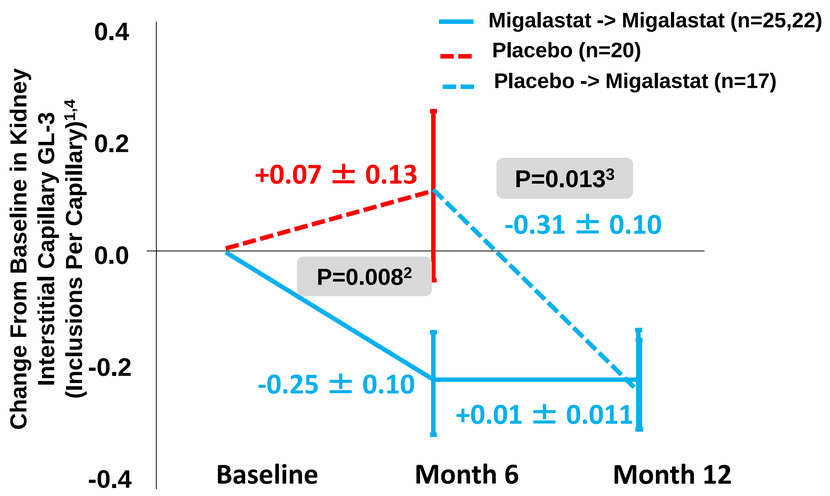
- Males and females, 16 to 74 years, diagnosed with Fabry disease.
- Responsive *GLA* mutations using the "Clinical trial" human embryonic kidney-293 (HEK) assay.
- Naïve to ERT or have not received ERT for ≥6 months before screening,
- Estimated GFR (MDRD) (eGFR) at screening ≥30 ml/min/1.73 m^2.
- Urine GL-3 at screening ≥4 times the upper limit of normal (24-hour collection),
- Patients taking angiotensin converting enzyme inhibitors or angiotensin receptor blockers had been on a stable dose for at least 4 weeks before screening.

Baseline Characteristics of the Intent-to-treat Population from Study 011

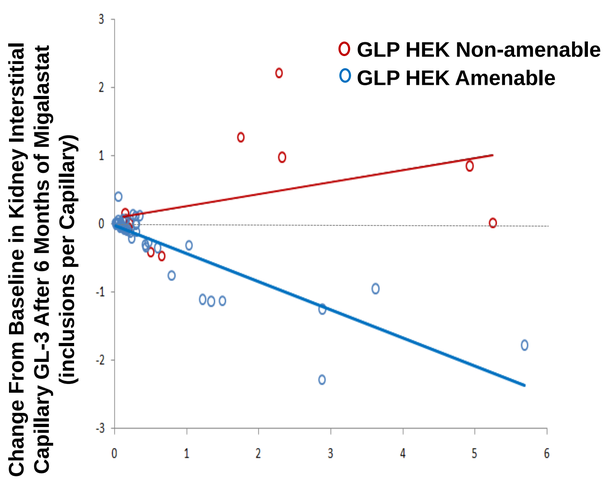
	Placebo n=33	Migalastat n=34
Sex Female n (%) Male n (%)	 21 (64) 12 (36)	 22 (65) 12 (35)
Age Median (range)	37 (24, 64)	46 (16, 68)
Years since diagnosis Mean (SD)	7.1 (7.8)	5.7 (6.8)
eGFR (CKD-EPI) mL/min/1.73 m^2 Mean (SD)	94 (21)	95 (29)
24-hr Urine Protein (mg) Mean (SD)	452 (626)	342 (459)
ACEi/ARB /RI Use: n (%)	13 (39)	6 (18)
Previously on ERT: n (%)	12 (36)	5 (15)
GLP HEK Amenable: n (%)	22 (67)	28 (82)

- Patients were randomized based on *GLA* mutations classified with the clinical trial HEK assay.
- During the conduct of Study 011, the clinical trial HEK assay was analytically validated in compliance with GLP regulations (GLP HEK assay).
- 17 of 67 randomized patients were re-categorized as having non-amenable mutations based on the GLP HEK assay.
- Renal findings presented in this poster were based on the 41 of 50 patients with amenable mutations using on the GLP HEK assay that completed Study 011,
- Safety results were based on all 67 randomized patients.

Kidney Interstitial Capillary GL-3 Results from Study 011



*All patients with evaluable paired biopsies and amenable mutations in GLP-validated HEK assay – post hoc at month 6 and pre-specified at month 12. [1]Data points are baseline corrected; represent mean ± standard error (SEM) change from baseline in the mean number of GL-3 inclusions per capillary after 6 months of treatment with migalastat or placebo. [2]Analysis of covariance (ANCOVA) model with covariate adjustment for baseline value and factors for treatment group and treatment by baseline interaction. P-value corresponds to least-square mean difference between migalastat and placebo. [3]MMRM Placebo change: M6 to M12. [4]Baseline IC GL-3: 0.61 (Migalastat) and 0.59 (Placebo).



Baseline Kidney Interstitial Capillary GL-3 (Inclusions Per Capillary)

*All patients with evaluable paired biopsies. Combines change from baseline to month 6 for Migalastat > Migalastat arm with change from month 6 to month 12 for Placebo > Migalastat arm. Results presented based on GLA mutation classification in in GLP-validated HEK assay.

Annualized eGFR Over an Average of 32 Months on Migalastat in Studies 011 and 041 Compared to Natural History

Annualized eGFR (ml/min/1.73m^2/yr) BL (Migalastat-Migalastat) or M6 (Placebo-Migalastat) to Last Available		Male			Female			All		
Migalastat (011 + 041)	Baseline 24 Hr Urine Protein (mg)	N	Mean	(SEM)	N	Mean	(SEM)	N	Mean	(SEM)
eGFR (CKD-EPI)	<100	–	–	–	7	0.5	(0.6)	7	0.5	(0.6)
	100-1000	12	0.4	(0.7)	18	-0.2	(1.2)	30	0.0	(0.8)
	>1000	2	-4.1	(0.1)	2	-2.0	(2.1)	4	-3.1	(1.1)
	ALL	14	-0.3	(0.6)	27	-0.2	(0.8)	41	-0.2	(0.6)
eGFR (MDRD)	<100	–	–	–	7	0.6	(0.5)	7	0.6	(0.5)
	100-1000	12	1.4	(0.2)	18	0.9	(1.7)	30	1.1	(1.1)
	>1000	2	-3.6	(1.1)	2	-1.5	(1.9)	4	-2.6	(1.0)
	ALL	14	0.6	(1.0)	27	0.7	(1.1)	41	0.6	(0.8)
Untreated (Literature)[1]	24 Hr Urine Protein (mg)	N	Mean	(SEM)	N	Mean	(SEM)	N	Mean	(SEM)
eGFR (MDRD)	<100	18	-1.6	(1.5)	7	-0.6	(2.6)	Not reported		
	100-1000	21	-3.3	(1.8)	17	-2.2	(2.2)			
	>1000	22	-6.9	(1.5)	5	-4.6	(2.3)			
	All	128[2]	-2.9[2]		51[2]	-1.0[2]				

[1]Schiffmann et al., Nephrol Dial Transplant (2009) | [2]For patients not developing ESRD |

Renal Function (To-Date)

- As previously reported for Study 011, GFR in subjects with amenable mutations remained stable over 18-24 months of treatment, with mean annualized eGFR changes of -0.30 ± 0.66 (CKD-EPI eGFR) and +0.79 ± 1.03 (MDRD eGFR) mL/min/1.73m^2/yr.
- The current preliminary analysis indicates that renal function has continued to remain stable in subjects with amenable mutations over an average of 32 months in Studies 011 and 041, with mean annualized eGFR changes of -0.20 ± 0.60 (CKD-EPI eGFR) and +0.63 ± 0.08 (MDRD eGFR) mL/min/1.73m^2/yr.

Safety (All Randomized Patients) (To-Date)

- Migalastat was generally safe and well tolerated.
- No patient met the mandatory stopping criteria: 30% decrease from baseline in serum creatinine, 25% decrease from baseline in cardiac ejection fraction, or cerebrovascular event with significant sequelae,
- There were no withdrawals due to treatment-related AEs or SAEs.
- In Study 011, two SAEs, fatigue and paresthesia (reported in the same patient) were deemed possibly related to migalastat by the Principal Investigator. These SAEs resolved, the patient completed Study 011 and enrolled in Study 041.
- In Study 041, one death, unrelated to treatment, was reported in a 63-year old male. Significant medical history included obesity, hypertension, type 2 diabetes mellitus and CAD (myocardial infarction, stent placement and triple bypass surgery).
- There were no treatment-related SAEs in Study 041.

Conclusions

- Treatment with migalastat over an average of 32 months was associated with stable renal function in Fabry disease patients with amenable mutations.
- Mean annualized change in eGFR (mL/min/1.73m^2/yr) was: -0.20 ± 0.60 (CKD-EPI) and +0.63 ± 0.08 (MDRD).
- Migalastat was generally safe and well tolerated.