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EFFECTS OF LONG-TERM MIGALASTAT TREATMENT ON RENAL FUNCTION BY BASELINE PROTEINURIA IN PATIENTS (PTS) WITH FABRY DISEASE

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INTRODUCTION AND AIMS: Fabry disease is an X-linked disorder of α-galactosidase A (α-Gal A) deficiency, leading to substrate accumulation and multiorgan disease. eGFR declines of up to -6.9 mL/min/1.73 m^2/y have been reported in male pts with untreated Fabry disease and high levels of proteinuria. Migalastat, an oral pharmacological chaperone, stabilizes and induces proper folding of specific mutant forms of α-Gal A. In the Phase 3 FACETS study (NCT00925301), migalastat stabilized renal function in enzyme replacement therapy (ERT)-naive pts with Fabry disease and *amenable* mutations. Here, we evaluated renal outcomes by baseline proteinuria.

METHODS: ERT-naive pts who received migalastat during a Phase 2 trial (NCT00526071) or the FACETS study were eligible to continue open-label migalastat 150 mg QOD in a separate Phase 3 extension (NCT01458119). Annualized change rate in $eGFR_{MDRD}$ was calculated based on baseline proteinuria (<100, 100-1000, >1000 mg/24 h); migalastat 150 mg QOD is not intended for use in pts with severe renal impairment. Pts with amenable mutations who entered the Phase 3 extension and received migalastat 150 mg QOD for ≥17 m were analyzed. Results were compared with changes reported in the literature for untreated pts with Fabry disease (natural history cohort; Schiffmann R et al. *Nephrol Dial Transplant.* 2009;24:2102-11).

RESULTS: Median treatment duration ranged from 3.5-4.8 y (max 5.3 y) across proteinuria subgroups. Mean annualized change in eGFR was smaller overall in pts treated with migalastat vs that observed in the natural history cohort across proteinuria categories (**Table**). Although eGFR declined in all untreated subgroups, increases were seen with migalastat in pts with baseline proteinuria <100 (males) and 100-1000 mg/24 h (males and females). Regardless of treatment, eGFR decreased in pts with baseline

proteinuria >1000 mg/24 h; however, pts treated with migalastat had smaller decreases compared to the natural history cohort.

CONCLUSIONS: Long-term migalastat treatment (~3-5 years) was generally associated with stable renal function in pts with Fabry disease and amenable mutations, regardless of baseline proteinuria levels.

		Males		Females	
	Baseline 24 h urine protein, mg/24 h	**n**	**Annualized eGFR Rate of Change, mL/min/1.73 m^2, Mean (SE)**	**n**	**Annualized eGFR Rate of Change, mL/min/1.73 m^2, Mean (SE)**
Migalastat cohort					
	<100	3	+1.2 (1.2)	9	-0.9 (0.5)
	100-1000	16	+0.9 (1.0)	19	+1.3 (1.5)
	>1000	2	-4.3 (0.1)	3	-1.7 (1.1)
Natural history cohort (Schiffmann et al. 2009)					
	<100	18	-1.6 (1.5)	7	-0.6 (2.6)
	100-1000	21	-3.3 (1.8)	17	-2.2 (2.2)
	>1000	22	-6.9 (1.5)	5	-4.6 (2.3)

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