

SUPPLEMENTARY MATERIALS

Anti-Proteinuric Therapy and Fabry Nephropathy; Factors Associated with Preserved Kidney Function During Agalsidase-Beta Therapy

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eTable 1. Study Sites, Investigators; 32 subjects enrolled; 24 subjects completed protocol

Study Site Location	Principal Investigator	Subjects Completing	Subjects not Completing	Reasons for Discontinuation
Atlanta, GA (USA)	A. Guasch	6	1	Moved to Australia (visit 4)
Birmingham, AL (USA)	R. Campbell	4	1	ERT supply issues after visit 6
Boston, MA (USA)	K. Sims	1	1	Kidney transplantation after visit 5
Budapest (Hungary)	G. Fekete	0	1	ERT supply issues after visit 4
Chicago, IL (USA)	J. Charrow	2	2	Ineligible, discontinued after visit 1; withdrew consent after visit 4 (transportation)
Würzburg, Germany	C. Wanner	0	1	Withdrew consent after visit 3 (transportation)
Iowa City, IA (USA)	C. Thomas	6	0	
Los Angeles, CA (USA)	W. Wilcox	1	1	Ineligible, discontinued after visit 1
New York, NY (USA)	M. Velinov	2	0	
Slovenj Gradec, Slovenia	B. Vujkovak	2	0	

Abbreviations: ERT, enzyme replacement therapy; USA, United States of America;

eTable 2. Baseline Renal and Cardiac Status of FAACET Participants; stratified at baseline eGFR \geq or $<$ 60 ml/min/1.73 m²

Baseline eGFR \geq 60 ml/min/1.73 m ²								
ID	Genotype	A/G/R	UPCR	ACR	eGFR	Con_Meds	ECHO	EKG
02	p.R227X	40/F/W	0.97	782	93	Losar 100 mg	SWT 9mm; Regurg	Brady
03	p.R227Q	23/M/W	0.62	7	120		SWT 9mm; Regurg	Brady, NS-STT
04	p.R227X	52/F/W	0.70	261	100	Irbesar 160 mg	LVH, SWT 13 mm, Regurg, Diast_Dys	NS-STT, BBB
05	p.W287C	55/F/W	0.05	49	63	Irbesar 320 mg; HCTZ 25 mg; Metop 25 mg	LVH, SWT 15 mm, Regurg, Diast_Dys	Brady, NS-STT, LVH, Afib
07	p.M43T	46/F/W	0.88	245	89	Lisin 40 mg; HCTZ 25 mg	SWT 9mm; Diast_Dys	NS-STT
08	p.L120P, p.A121T	35/M/W	2.86	1,398	71	Lisin 10 mg	SWT 12mm, LVH, Regurg, Aort_Dil	LVH, Cond_Abnorm
09	1188 insT	42/M/W	0.12	89	62	Lisin 10 mg	SWT 12mm, Regurg	LVH
10	p.W204X	49/W/M	0.10	15	75	Lisin 10 mg	LVH; SWT 16mm; Regurg	LVH
11	821insG	40/M/W	0.40	105	63	Lisin 15 mg	SWT 11mm; Regurg	LVH, PAC, Cond_Abnorm,
13	p.W340X	47/M/B	0.54	22	92	Irbesar 75 mg	LVH; SWT 13mm; Regurg	BBB
14	p.R342Q	37/F/W	0.32	144	117	Ramip 2.5 mg	SWT 9mm; Regurg	Brady
15	p.R342Q	37/M/W	1.08	672	70	Losar 50 mg	LVH; SWT 16mm; Regurg	LVH, Brady
19	p.D264Y, p.V269M	42/M/W	2.49	1,110	82	Losar 100 mg	SWT 12mm, Aort_Dil	NS-STT
20	C717 del3	29/M/W	0.42	114	102	Losar 50 mg	SWT 9mm; Regurg	PAC, Cond_Abnorm
21	p.W277X	49/F/B	0.75	38	69	Lisin 80, Losar 100, Felod 5	LVH; SWT 12mm; Regurg	NS-STT, PAC
22	p.R227X	31/F/W	0.52	555	130	Lisin 20, Losar 50	SWT 10mm; Regurg	Brady, NS-STT, LVH

Baseline eGFR <60 ml/min/1.73 m ²								
ID	Genotype	A/G/R	UPCR	ACR	eGFR	Con_Meds	ECHO	EKG
01	p.T194I	43/M/W	2.04	1,559	42	Irbesar 75 mg	LVH; SWT 15mm; Regurg, Akinesis	Brady, LVH
06	1118 del1	55/M/W	0.11	28	56	Lisin 2.5 mg, Metop 25 mg	LVH, Regurg, Diast_Dys	ICD, Cond_Abnorm
12	1139 delC	44/F/W	1.13	1,468	34	Lisin 20 mg, Nadol 20 mg	LVH; SWT 11mm; Regurg	Brady, Cond_Abnorm
16	p.N272K	41/M/W	1.48	57	38		SWT 11mm; Regurg	Brady, Cond_Abnorm
17	p.R227X	44/M/W	0.40	459	40	Ramip 6.25 mg	LVH; SWT 15mm; Regurg	NS-STT
18	p.N272S	52/M/W	1.40	736	46	Ramip 5 mg	LVH; SWT 13mm; Regurg	NS-STT
23	p.W227X	52/M/B	2.28	2,014	53	Enal 10 mg, Torsem 50 mg, Metop 12.5 mg	LVH; SWT 15mm; Regurg	LVH, PAC, PVC, Cond_Abnorm
24	717 del2	53/M/W	0.33	101	52	Metop 25 mg	LVH; SWT 13mm; Regurg	Afib, PVC, ICD

Abbreviations: ACR, albumin to creatinine ratio (mg/gm); Afib, atrial fibrillation; A/G/R, age, gender, race; B, black; BBB, bundle branch block; Brady, bradycardia; Con_Meds; concomitant medications; Cond_Abnorm, conduction abnormality; Diast_Dys, diastolic dysfunction; ECHO, echocardiogram; EKG, electrocardiogram; eGFR, estimated glomerular filtration rate (ml/min/1.73 m²); Enal, Enalapril; F, female; Felod; Felodipine; HCTZ, hydrochlorothiazide; ICD, intracardiac device; Irbesar, Irbesartan; Lisin, Lisinopril; Losar, Losartan; LVH, left ventricular hypertrophy; M, male; M, Metoprolol; NS-STT, non-specific ST-T wave changes; Nadol, Nadolol; PAC, premature atrial contraction; PVC, premature ventricular contractions; Ramip, Ramipril; SWT, septal wall thickness; Regurg, regurgitation; Toresm, Toresemide; UPCR, urine protein to creatinine ratio (gm/gm); W, white.

eTable 3A. FAACET Participants stratified by UPCR Goal and eGFR slope at -2.0 ml/min/ 1.73 m²/year
N=6: Met UPCR Goal & Slope > -2.0 ml/min/ 1.73 m²/year

ID	Age/Sex Race	Genotype	Slope	Inter- cept	Averaged Values			Max K ⁺	Con_Meds: Last Visit (Medication Score)	Adverse Events
					UPCR	ACR	SBP			
3	23/M/W	p.R227Q	-1.08	125	0.15	24	102	3.8	Losar 12.5 (1)	
4	52/F/W	p.R227X	1.28	98	0.44	220	123	4.0	Irb 160; Enal 10 (2)	
6	55/M/W	1118del	-1.70	70	0.11	18	111	5.2	Losar 37.5, Carv 3.1 (1)	↑K ⁺
11	40/M/W	82insG	0.59	81	0.52	234	102	4.4	Lisin 30 (1)	↓BP ↓Hgb
16	41/M/W	p.N272K	-0.74	30	0.10	11	103	5.4	Lisin 20, HCTZ 25 (2)	
22	31/F/W	p.R227X	1.58	124	1.05	673	104	6.1	Lisin 10, Losar 50 (2)	↑K ⁺
	41±12	Mean±SD or Median	-0.01 ±1.3	88 ±36	0.40 ±0.37	197 ±254	108 ±5	4.9 ±0.9	1.5 (1 - 2)	
	4 M/0 B	Min	-1.7	30	0.1	11	102	3.8	1	
		Max	1.6	126	1.1	673	123	6.1	2	

eTable 3B. N=12: Met UPCR Goal & Slope < -2.0 ml/min/ 1.73 m²/year

ID	Age/Sex Race	Genotype	Slope	Inter- cept	Averaged Values			Max K ⁺	Con_Meds: Last Visit (Medication Score)	Adverse Events
					UPCR	ACR	SBP			
1	43/M/ W	p.T194I	-3.703	41	0.91	618	106	5.7	Irb 80, Ram 10 (2)	↑K ⁺ ↓BP
5	55/F/W	p.W287C	-5.005	52	0.36	233	109	4.8	Irb 160, HCTZ 12.5, Metop 100 (2)	↓BP
7	46/F/W	p.M42T	-4.077	70	1.30	1,200	127	4.7	Lisin 40, Losar 100 HCTZ 25 (3)	↓BP
9	42/M/ W	1188insT	-5.549	56	0.50	323	126	4.1	Losar 100 (3)	Edema
10	49/M/ W	p.W204X	-6.441	85	0.12	39	133	4.9	Lisin 10 (1)	

12	44/F/W	1139delC	-3.470	36	0.50	365	99	4.6	Lisin 40, Nadol 10, Nifed 30 (3)	↓BP, PTCA
13	47/M/B	p.W340X	-2.645	86	0.21	116	131	4.2	Irb 75, Furos 40 (2)	Cardiac Cath
14	37/F/W	p.R342Q	-5.91	104	0.26	81	98	4.9	Ram 2.5, Irb 320 (3)	↓BP
15	37/M/W	p.R112S	-4.22	48	0.34	217	112	5.0	Lisin 20, Losar 200 (3)	↓BP
19	42/M/W	p.D264Y, p.V269M	-2.35	74	1.20	865	130	4.7	Losar 200 (3)	
21	49/F/B	p.W277X	-4.81	60	0.41	276	130	5.3	Lisin 80, Losar 100, Felod 10, Spiro 25 (3)	
24	53/M/W	717del2	-4.13	56	0.26	130	113	5.5	Losar 25, Metop 25 (1)	↑K+
	48 (6) 6 M/2 B	Mean±SD or Median	-4.36 ±1.25	65 ±20	0.53 ±0.39	372 ±352	118 ±13	4.9 ±0.5	3 (2 - 3)	
		Min	-6.44	36	0.12	39	98	4.1	1	
		Max	-2.35	104	1.29	1,200	133	5.7	3	

eTable 3C. N=6: Above UPCR Goal & Slope < -2.0 ml/min/1.73 m²/year

ID	Age/Sex Race	Genotype	Slope	Inter- cept	Averaged Values			Max K+	Con_Meds: Last Visit	Adverse Events
					UPCR	ACR	SBP			
2	40/F/W	p.R227X	-4.48	82	0.75	501	116	4.0	Losar 100, Lisin 10 (3)	
8	35/M/W	p.L120P, p.A121T	-14.4	55	2.40	1,650	108	4.6	Lisin 40, Losar 100 (3)	Polyuria
17	44/M/W	p.R227X	-6.93	43	0.68	454	120	5.6	Ram 7.5 (1)	↑K+
18	52/M/W	p.N272S	-5.59	45	0.96	657	117	5.5	Ram 8.75 (1)	↑K+

20	29/M/W	C717 delAA	-9.02	95	0.53	259	107	4.0	Losar 50 (1)	Fatigue
23	52/M/B	p.W277X	-7.09	56	1.50	733	95	5.2	Enal 10, Torse 60, Metop 12.5 (3)	↓BP ↑K ⁺
	42 (9)	Mean±SD or Median	-7.92 ±3.53	63 ±21	1.14 ±0.70	708 ±489	110 ±9.1	4.8 ±0.7	1.5 (1 - 3)	
	5 M/1 B	Min Max	-14.4 -4.47	43 95	0.53 2.35	259 1,650	96 120	4.0 5.6	1 3	

Continuous variables presented as median (25th – 75th-tile), categorical variables as median (25th –75th-centile); Medication Score defined as: 0, none; 1, ACE Inhibitor or ARB; 2, ACE Inhibitor plus ARB, or Beta Blocker; 3, ACE Inhibitor or ARB at maximum dose. Abbreviations: ACR, albumin to creatinine ratio (mg/g); Afib, atrial fibrillation; A/G/R, age, gender, race; B, black; BP, blood pressure; Cardiac Cath, cardiac catheterization; Carv, Carvedilol; Con_Meds; concomitant medications; eGFR, estimated glomerular filtration rate (ml/min/1.73 m²); Enal, Enalapril; F, female; Felod, Felodipine; HCTZ, hydrochlorothiazide; Irbesar, Irbesartan; K⁺, serum potassium; Lisin, Lisinopril; Losar, Losartan; M, male; M, Metoprolol; Nadol, Nadolol; PTCA, percutaneous transluminal angioplasty; Ramip, Ramipril; Toresm, Toresemide; UPCR, urine protein to creatinine ratio (gm/gm); W, white.