

## Supplemental Material

# Cystinosis-associated metabolic bone disease across ages and CKD stages 1-5D/T

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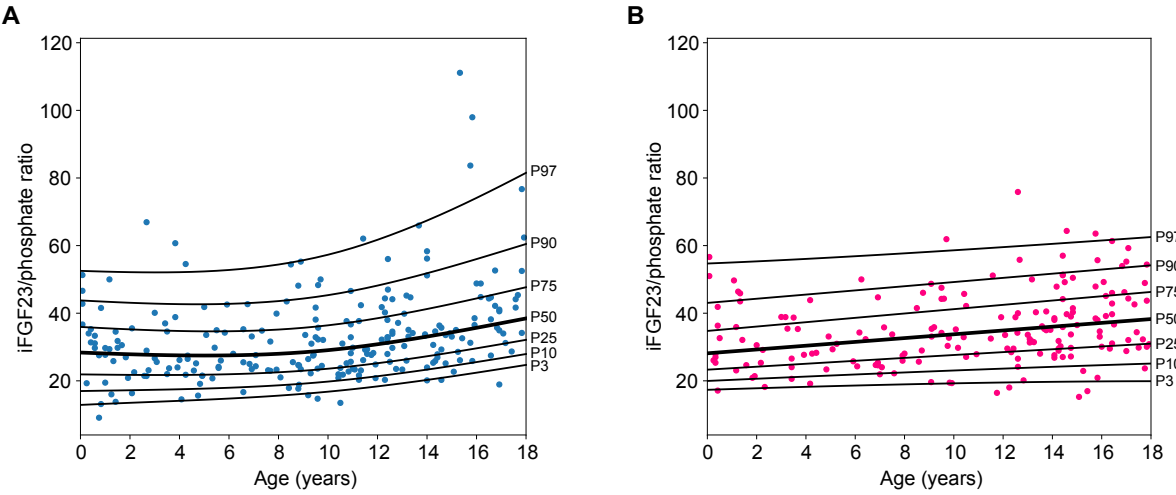
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**Supplemental Figure 1**



**Supplemental Figure 1.** LMS percentiles for the ratio of plasma iFGF23 to serum phosphate ratio in male (A) and female (B) from the HARP cohort according to age. The 3<sup>rd</sup>, 10<sup>th</sup>, 25<sup>th</sup>, 50<sup>th</sup> (bold line), 75<sup>th</sup>, 90<sup>th</sup>, and 97<sup>th</sup> percentiles are given. *iFGF23*, intact fibroblast growth factor 23; *HARP*, HANNOVER Reference values for Pediatrics.

**Supplemental Table 1.** Age-specific percentile limits and LMS values for the ratio of iFGF23 to phosphate in boys and girls

Age (yrs)	Male					Female				
	3 <sup>rd</sup>	50 <sup>th</sup> (M)	97 <sup>th</sup>	L	S	3 <sup>th</sup>	50 <sup>th</sup> (M)	97 <sup>th</sup>	L	S
0	12.88	28.37	52.53	0.355	0.366	17.34	28.14	54.70	-0.557	0.295
0.5	13.04	28.23	52.41	0.320	0.364	17.46	28.42	54.85	-0.527	0.295
1	13.20	28.10	52.30	0.285	0.361	17.58	28.70	55.01	-0.498	0.295
1.5	13.35	27.97	52.21	0.250	0.359	17.69	28.99	55.17	-0.468	0.295
2	13.50	27.86	52.14	0.214	0.357	17.80	29.27	55.34	-0.439	0.295
2.5	13.64	27.75	52.10	0.179	0.354	17.91	29.55	55.51	-0.409	0.295
3	13.79	27.67	52.08	0.144	0.352	18.02	29.83	55.69	-0.380	0.296
3.5	13.94	27.59	52.09	0.109	0.350	18.12	30.11	55.87	-0.350	0.296
4	14.09	27.54	52.14	0.074	0.348	18.22	30.39	56.06	-0.321	0.296
4.5	14.24	27.50	52.23	0.039	0.345	18.32	30.67	56.25	-0.291	0.296
5	14.40	27.49	52.36	0.004	0.343	18.42	30.95	56.45	-0.262	0.296
5.5	14.57	27.50	52.55	-0.031	0.341	18.52	31.24	56.65	-0.232	0.296
6	14.76	27.54	52.79	-0.066	0.339	18.61	31.52	56.86	-0.203	0.296
6.5	14.95	27.60	53.09	-0.101	0.336	18.70	31.80	57.07	-0.174	0.296
7	15.15	27.70	53.46	-0.136	0.334	18.79	32.08	57.28	-0.144	0.296
7.5	15.38	27.83	53.89	-0.172	0.332	18.87	32.36	57.49	-0.115	0.296
8	15.62	28.00	54.40	-0.207	0.330	18.96	32.64	57.71	-0.085	0.296
8.5	15.88	28.21	54.99	-0.242	0.328	19.04	32.92	57.93	-0.056	0.296
9	16.16	28.45	55.67	-0.277	0.326	19.11	33.20	58.15	-0.026	0.296
9.5	16.46	28.74	56.44	-0.312	0.324	19.19	33.49	58.38	0.003	0.296
10	16.79	29.07	57.30	-0.347	0.321	19.26	33.77	58.61	0.033	0.296
10.5	17.14	29.44	58.26	-0.382	0.319	19.33	34.05	58.84	0.062	0.296
11	17.53	29.86	59.32	-0.417	0.317	19.39	34.33	59.07	0.092	0.296
11.5	17.93	30.32	60.48	-0.452	0.315	19.45	34.61	59.31	0.121	0.296
12	18.36	30.82	61.72	-0.487	0.313	19.51	34.89	59.55	0.151	0.296
12.5	18.81	31.35	63.04	-0.522	0.311	19.56	35.17	59.79	0.180	0.296
13	19.28	31.91	64.43	-0.558	0.309	19.61	35.45	60.03	0.210	0.296
13.5	19.77	32.48	65.89	-0.593	0.307	19.66	35.74	60.27	0.239	0.296
14	20.27	33.09	67.41	-0.628	0.305	19.70	36.02	60.51	0.269	0.296
14.5	20.78	33.71	68.99	-0.663	0.303	19.74	36.30	60.76	0.298	0.296
15	21.31	34.35	70.64	-0.698	0.301	19.78	36.58	61.01	0.328	0.296
15.5	21.86	35.01	72.35	-0.733	0.299	19.81	36.86	61.26	0.357	0.296
16	22.41	35.69	74.10	-0.768	0.297	19.84	37.14	61.51	0.387	0.296
16.5	22.97	36.37	75.91	-0.803	0.295	19.86	37.42	61.76	0.416	0.296
17	23.55	37.06	77.75	-0.838	0.293	19.88	37.70	62.02	0.445	0.296
17.5	24.12	37.76	79.62	-0.873	0.292	19.89	37.99	62.27	0.475	0.296
18	24.70	38.46	81.52	-0.908	0.290	19.89	38.27	62.53	0.504	0.296

To calculate the age-related z-score for the iFGF23 to phosphate ratio, the ratio  $x$  of the determined concentrations for iFGF23 in pg/mL and phosphate in mmol/L together with the corresponding age and sex-related values for L, M, and S are used according to the formula  $z = [(x/M)^L - 1]/S \times L$ . L, skewness; M, median; S, coefficient of variation.

**Supplemental Table 2.** Medication in pediatric and adult subjects with nephropathic cystinosis at the time of evaluation

Characteristics	All patients			Patients pre-transplant			Patients post-transplant		
	Children (n=63)	Adults (n=40)	<i>P</i>	Children (n=54)	Adults (n=19)	<i>P</i>	Children (n=9)	Adults (n=21)	<i>P</i>
Cysteamine, n	63 (100.0)	37 (92.5)	0.024	54 (100.0)	18 (94.7)	0.075	9 (100.0)	19 (90.5)	0.908
IR-cysteamine, n	29 (46.0)	31 (77.50)	<0.01	29 (53.7)	16 (84.2)	0.046	0 (0.0)	15 (71.4)	<0.01
IR-cysteamine dosage, mg/m <sup>2</sup>	1375 (362)	1177 (364)	0.046	1375 (362)	1073 (435)	0.031	-	1280 (251)	n.a.
DR-cysteamine, n	38 (60.3)	8 (20.0)	<0.01	29 (53.7)	4 (21.1)	0.025	9 (100.0)	4 (19.1)	<0.01
DR-cysteamine dosage, mg/m <sup>2</sup>	1096 (387)	858 (246)	0.043	1132 (416)	912 (202)	0.126	971 (238)	804 (304)	0.382
WBC cystine levels, μmol/g protein	0.46 (0.30-0.80)	0.57 (0.34-1.51) <sup>a</sup>	0.097	0.41 (0.28-0.65)	0.57 (0.31-1.15) <sup>a</sup>	0.137	0.89 (0.65-1.00)	0.63 (0.34-2.28) <sup>a</sup>	0.713
Phosphate, n	39 (61.9)	12 (30.0)	0.002	39 (72.2)	12 (63.2)	0.649	0 (0.0)	0 (0.0)	n.a.
Phosphate <sup>b</sup> dosage, mg/kg/d	32.6 (23.1-55.1)	16.0 (11.0-41.0)	0.023	32.6 (23.1-55.1)	16.0 (11.0-41.0)	0.023	-	-	-
Calcium, n	9 (14.3)	2 (5.0)	0.194	9 (16.7)	1 (5.3)	0.302	0 (0.0)	1 (4.8)	0.547
Active vitamin D, n	18 (28.6)	9 (22.5)	0.407	18 (33.3)	7 (36.8)	0.882	0 (0.0)	2 (9.5)	0.975
Active vitamin D dosage, ng/kg/d	5.82 (3.97-14.62)	5.97 (4.72-7.32)	0.887	5.82 (3.97-14.62)	5.97 (4.58-8.41)	0.919	-	5.75 (5.0-6.49)	n.a.
Cholecalciferol, n	42 (66.7)	34 (85.0)	0.074	37 (68.5)	18 (94.7)	0.036	5 (55.6)	16 (79.2)	0.682
Cholecalciferol dosage, IU/d	1000 (1000-2000)	1429 (1000-2000)	0.842	1000 (1000-2000)	1214 (1000-2000)	0.424	3000 (2000-4502)	1429 (1000-2875)	0.036
Bicarbonate, n	26 (41.3)	21 (52.5)	0.341	23 (42.6)	11 (57.9)	0.262	3 (33.3)	10 (47.6)	0.753
rhGH, n	21 (33.3)	n.a.	n.a.	20 (37.0)	n.a.	n.a.	1 (11.1)	n.a.	n.a.

Data are presented as mean (SD), median (IQR), or n (%). IR, immediate release; DR, delayed release; WBC, white blood cells; n.a., not applicable; rhGH, recombinant human growth hormone; <sup>a</sup>, only patients on cysteamine treatment; <sup>b</sup>, based on elemental phosphorus.

**Supplemental Table 3.** Skeletal findings in pediatric and adult subjects with nephropathic cystinosis at the time of evaluation

Characteristics	All patients			Patients pre-transplant			Patients post-transplant		
	Children (n=63)	Adults (n=40)	<i>P</i>	Children (n=54)	Adults (n=19)	<i>P</i>	Children (n=9)	Adults (n=21)	<i>P</i>
Short stature, n	27 (42.9)	12 (30.0)	0.192	22 (40.7)	5 (26.3)	0.199	5 (55.6)	7 (33.3)	0.527
Fractures, n	7 (11.1)	4 (10.0)	0.832	7 (13.0)	3 (15.8)	0.717	0 (0.0)	1 (4.8)	0.455
Surgery, n	9 (14.3)	17 (42.5)	<0.01	8 (14.8)	11 (57.9)	<0.01	1 (11.1)	6 (28.6)	0.617
Skeletal deformities, n	26 (41.3)	27 (67.5)	0.013	23 (42.6)	14 (73.7)	0.023	3 (33.3)	13 (61.9)	0.340
Scoliosis, n	4 (6.3)	16 (40.0)	<0.01	4 (7.4)	9 (47.4)	<0.01	0 (0.0)	7 (33.3)	0.176
Genu valgum, n	24 (38.1)	16 (40.0)	0.905	21 (38.9)	7 (36.8)	0.939	3 (33.3)	9 (42.9)	0.696
Genu varum, n	1 (1.6)	2 (5.0)	0.560	1 (1.9)	2 (10.5)	0.243	0 (0.0)	0 (0.0)	n.a.

Data are presented as n (%). n.a., not applicable.