

Supplemental Table S1. Levels of serum bile acid in patients with non-truncating BSEP following 72 weeks of maralixbat treatment compared with baseline

BA Hydrophobicity	BA species	Nonresponders			Responders		
		Baseline conc. (μM ; n=8)	Week 72 conc. (μM ; n=6)	p- value ^a	Baseline conc. (μM ; n=11)	Week 72 conc. (μM ; n=9)	p-value ^a
Hydrophilic	TCA	36.80 \pm 19.87	60.48 \pm 29.46	NS	48.38 \pm 35.60	29.07 \pm 49.14	NS
	TUDCA	14.63 \pm 6.88	22.26 \pm 15.07	NS	10.16 \pm 8.25	6.70 \pm 15.32	NS
	TCDC A	16.15 \pm 10.30	34.62 \pm 32.67	NS	18.14 \pm 14.03	17.27 \pm 32.10	NS
	GCA	144.64 \pm 59.79	154.33 \pm 41.41	NS	134.47 \pm 82.70	64.06 \pm 71.16	0.06
	GUDCA	108.72 \pm 38.62	140.63 \pm 83.33	NS	63.80 \pm 57.55	28.19 \pm 27.91	0.09
	GCDCA	81.87 \pm 42.15	119.62 \pm 57.63	NS	71.29 \pm 47.69	49.15 \pm 45.59	NS
	CA	0.08 \pm 0.05	0.08 \pm 0.04	NS	0.08 \pm 0.04	0.06 \pm 0.00	NS
	UDCA	2.13 \pm 2.18	2.74 \pm 2.46	NS	2.20 \pm 3.18	1.17 \pm 2.11	NS
	CDCA	0.06 \pm 0.00	0.07 \pm 0.02	NS	0.06 \pm 0.00	0.13 \pm 0.09	0.06
	TOTAL	405.09 \pm 134.96	534.83 \pm 155.37	NS	348.58 \pm 183.29	195.79 \pm 202.11	0.098
Hydrophobic	TDCA	0.05 \pm 0.00	0.06 \pm 0.02	NS	0.62 \pm 1.21	0.12 \pm 0.17	NS
	TLCA	0.05 \pm 0.00	0.06 \pm 0.01	NS	0.05 \pm 0.00	0.05 \pm 0.00	NS
	GDCA	0.06 \pm 0.00	0.07 \pm 0.03	NS	1.34 \pm 3.02	0.23 \pm 0.36	NS
	GLCA	0.06 \pm 0.00	0.07 \pm 0.02	NS	0.06 \pm 0.00	0.06 \pm 0.00	NS
	DCA	0.06 \pm 0.00	0.07 \pm 0.02	NS	0.07 \pm 0.02	0.13 \pm 0.18	NS
	LCA	0.06 \pm 0.00	0.07 \pm 0.02	NS	0.06 \pm 0.00	0.06 \pm 0.00	NS
	TOTAL	0.35 \pm 0.00	0.41 \pm 0.10	NS	2.20 \pm 4.19	0.65 \pm 0.49	NS

^ap < 0.10 was considered to be statistically significant given dataset limitations

BA, bile acid; BSEP, bile salt export pump; CA, cholic acid; CDCA, chenodeoxycholic acid;

DCA, deoxycholic acid; LCA, lithocholic acid; GCA, glycine-conjugated cholic acid;

GCDCA, glycochenodeoxycholic acid; GDCA, glycodeoxycholic acid;

GLCA, glycolithocholic acid; GUDCA, glyoursodeoxycholic acid; NS, non-significant;

TCA, taurine-conjugated cholic acid; TCDC A, taurochenodeoxycholic acid;

TDCA, taurodeoxycholic acid; TLCA, tauroolithocholic acid; TUDCA, taurooursodeoxycholic acid; UDCA, ursodeoxycholic acid

Data are mean \pm standard deviation. The two-tailed Student's t-test was used to compare groups.

Supplemental Table S2. Total BA as biomarker – model optimization

Fix effect	Random effect	AIC	BIC	Random effect residual variance
1 + Week + Age + Gender + Predictor_baseline +Total_BA	1 + Week Subject_ID	203.1	231.0	0.1279
1 + Week + Gender + Predictor_baseline +Total_BA	1 + Week Subject_ID	200.3	225.4	0.1278
1 + Week + Age + Predictor_baseline +Total_BA	1 + Week Subject_ID	200.1	225.3	0.1279
1 + Week + Age + Gender + Total_BA	1 + Week Subject_ID	201.1	226.3	0.1278

Supplemental Table S3. Likelihood-ratio test for reduced model excluding age, gender, and pre-dose baseline vs. full model

LMM model	npar	AIC	BIC	logLik	deviance	Chisq	Df	Pr(>Chisq)
`ItchRO Weekly Average Score` ~ 1 + Week + Total_BA + (1 + Week Subject_ID)	7	197.81	217.38	-91.905	183.81			
`ItchRO Weekly Average Score` ~ 1 + Week + Age + Predictor_baseline + Gender + Total_BA + (1 + Week Subject_ID)	10	202.06	230.02	-91.030	182.06	1.751	3	0.6257

Supplemental Table S4. Summary of linear mixed model (LMM) of pruritus ItchRO score ~ UDCA (%)

Predictors	ItchRO_score		
	Estimates	CI	p-value
(Intercept)	1.79	1.46 – 2.12	< 0.001
Week	-0.01	-0.01 – -0.00	0.001
UDCA	-0.03	-0.05 – -0.01	0.002
Random Effects			
σ^2		0.14	
τ_{00} Patient_id		0.47	
τ_{11} Patient_id.Week		0.00	
Q_{01} Patient_id		-0.13	
ICC		0.80	
N Patient_id		19	
Observations		121	
Marginal R ² / Conditional R ²		0.139 / 0.828	

*Significant p-values, i.e. at 0.05 level, are highlighted in bold.

Supplemental Table S5. Summary of linear mixed model (LMM) of pruritus ItchRO score ~ GCA (%)

Predictors	ItchRO_score		
	Estimates	CI	p-value
(Intercept)	0.97	0.54 – 1.40	< 0.001
Week	-0.01	–0.01 – –0.00	0.006
GCA	0.02	0.01 – 0.03	< 0.001
Random Effects			
σ^2		0.12	
τ_{00} Patient_id		0.45	
τ_{11} Patient_id.Week		0.00	
Q_{01} Patient_id		–0.33	
ICC		0.81	
N Patient_id		19	
Observations		121	
Marginal R ² / Conditional R ²		0.229 / 0.853	

*Significant p-values, i.e. at 0.05 level, are highlighted in bold.

Supplemental Table S6. Summary of linear mixed model (LMM) of pruritus ItchRO score ~ TCA (%)

Predictors	ItchRO_score		
	Estimates	CI	p-value
(Intercept)	1.32	0.93 – 1.71	<0.001
Week	-0.01	-0.02 – -0.00	<0.001
TCA	0.04	0.02 – 0.06	<0.001
Random Effects			
σ^2		0.14	
τ_{00} Patient_id		0.44	
τ_{11} Patient_id.Week		0.00	
Q_{01} Patient_id		-0.37	
ICC		0.76	
N Patient_id		19	
Observations		121	
Marginal R ² / Conditional R ²		0.226 / 0.815	

*Significant p-values, i.e. at 0.05 level, are highlighted in bold.

Supplemental Table S7. Summary of general linear mixed model (GLMM) of pruritus responder class ~ GCA (%)

Pruritus responder			
Predictors	Odds Ratios	CI	p-value
(Intercept)	0.00	0.00 – 973.31	0.274
Week	0.93	0.74 – 1.16	0.527
GCA	0.88	0.58 – 1.33	0.548
Random Effects			
σ^2		3.29	
τ_{00} Patient_id		375.26	
τ_{11} Patient_id.Week		24.83	
ρ_{01} Patient_id		−0.84	
ICC		1.00	
N Patient_id		19	
Observations		121	
Marginal R ² / Conditional R ²		0.000 / 1.000	

Supplemental Table S8. Summary of general linear mixed model (GLMM) of pruritus responder class ~ ratio of total cholic acids/total chenodeoxycholic acids

Predictors	Pruritus_responding		
	Odds Ratios	CI	p-value
(Intercept)	0.00	0.00 – 0.75	0.044
Week	0.94	0.75 – 1.17	0.564
Total CA/CDCA ratio	0.22	0.01 – 8.12	0.411
Random Effects			
σ^2		3.29	
τ_{00} Patient_id		429.46	
τ_{11} Patient_id.Week		27.69	
Q_{01} Patient_id		-0.85	
ICC		1.00	
N Patient_id		19	
Observations		121	
Marginal R^2 / Conditional R^2		0.000 / 1.000	

*Significant p-values, i.e. at 0.05 level, are highlighted in bold.