

Supplementary Table 1. Changes in rectal sensory thresholds in the two groups

			N	mean	SD	median	IQR	P-value
DDV (mL)	elobixibat	Observation period	9	115.8	36.1	103.0	93.0 – 143.0	
		Treatment period	9	100.6	40.8	75.0	74.0 – 138.0	
		Difference	9	-15.2	19.0	-11.0	-29.0 – -5.0	0.0433
	placebo	Observation period	8	117.9	54.7	121.0	72.5 – 170.0	
		Treatment period	8	118.6	64.0	138.0	50.0 – 174.5	
		Difference	8	0.8	18.8	3.0	-6.0 – 13.5	0.9131
FCSV (mL)	elobixibat	Observation period	9	89.2	41.2	71.0	69.0 – 83.0	
		Treatment period	9	63.2	27.4	55.0	51.0 – 65.0	
		Difference	9	-26.0	16.9	-19.0	-36.0 – -16.0	0.0017
	placebo	Observation period	8	77.9	48.1	80.5	32.0 – 111.0	
		Treatment period	8	84.9	61.9	94.0	18.5 – 131.5	
		Difference	8	7.0	24.1	-1.5	-11.0 – 27.0	0.4385
MTV (mL)	elobixibat	Observation period	9	161.9	43.6	167.0	125.0 – 175.0	
		Treatment period	9	141.4	58.3	105.0	100.0 – 202.0	
		Difference	9	-20.4	30.2	-12.0	-36.0 – -8.0	0.0767
	placebo	Observation period	8	159.3	50.7	174.5	131.5 – 197.0	

Treatment	8	148.1	56.9	163.0	104.5 –	
period					196.0	
Difference	8	-11.1	23.4	-2.0	-9.5 –	0.2209
					-0.5	

DDV, defaecatory desire volume; FCSV, first constant sensation volume; MTV, maximum tolerable volume.

Supplementary Table 2. Faecal BA concentrations

			N	mean	SD	median	IQR	difference	95% CI	P-value
CA ($\mu\text{mol/g}$)	Observation period	elobixibat	8	0.000	0.000	0.000	0.000 – 0.000	–0.961	–2.9474	0.3169
		placebo	8	0.961	2.619	0.000	0.000 – 0.125		–1.0249	
	Treatment period	elobixibat	9	1.790	2.910	0.390	0.000 – 1.880	1.414	–0.8213	0.1976
		placebo	8	0.376	0.546	0.000	0.000 – 0.820	–3.6488		
	Difference	elobixibat	8	1.011	1.856	0.225	0.000 – 1.155	1.596	–0.7616	0.1685
		placebo	8	–0.585	2.495	0.000	0.000 – 0.295	–3.9541		
CDCA ($\mu\text{mol/g}$)	Observation period	elobixibat	8	0.000	0.000	0.000	0.000 – 0.000	–0.404	–1.2395	0.3177
		placebo	8	0.404	1.102	0.000	0.000 – 0.050		–0.4320	
	Treatment period	elobixibat	9	1.262	1.938	0.110	0.000 – 1.860	0.940	–0.6098	0.2157
		placebo	8	0.323	0.710	0.000	0.000 – 0.270	–2.4892		
	Difference	elobixibat	8	0.790	1.414	0.080	0.000 – 1.120	0.871	–0.5730	0.2166
		placebo	8	–0.081	1.276	0.000	0.000 – 0.005	–2.3155		
DCA ($\mu\text{mol/g}$)	Observation period	elobixibat	8	1.423	0.991	1.135	0.955 – 1.620	–0.228	–1.513 – 1.0584	0.7100
		placebo	8	1.650	1.376	1.380	0.610 – 2.580			
	Treatment period	elobixibat	9	7.318	4.557	7.850	3.150 – 9.980	5.927	2.3924 – 9.4607	0.0028
		placebo	8	1.391	1.102	1.255	0.435 – 2.385			

	Difference	elobixibat	8	5.563	4.565	5.115	1.985 – 8.145	5.821	2.2060 – 9.4365	0.0039
		placebo	8	-0.259	1.376	-0.100	-0.885 – -0.640			
UDCA ($\mu\text{mol/g}$)	Observation period	elobixibat	8	0.000	0.000	0.000	0.000 – 0.000	-0.134	-0.394 – 0.1266	0.2892
		placebo	8	0.134	0.343	0.000	0.000 – 0.045			
	Treatment period	elobixibat	9	0.861	1.322	0.000	0.000 – 1.090	0.684	-0.3493 – -1.7165	0.1788
		placebo	8	0.178	0.367	0.000	0.000 – 0.180			
	Difference	elobixibat	8	0.509	0.848	0.000	0.000 – 0.860	0.465	-0.1814 – -1.1114	0.1452
		placebo	8	0.044	0.084	0.000	0.000 – 0.055			
HDCA ($\mu\text{mol/g}$)	Observation period	elobixibat	8	0.0	0.0	0.0	0.0 – 0.0	0.0	0.0 – 0.0	-
		placebo	8	0.0	0.0	0.0	0.0 – 0.0			
	Treatment period	elobixibat	9	0.0	0.0	0.0	0.0 – 0.0	0.0	0.0 – 0.0	-
		placebo	8	0.0	0.0	0.0	0.0 – 0.0			
	Difference	elobixibat	8	0.0	0.0	0.0	0.0 – 0.0	0.0	0.0 – 0.0	-
		placebo	8	0.0	0.0	0.0	0.0 – 0.0			
LCA ($\mu\text{mol/g}$)	Observation period	elobixibat	8	2.005	1.638	1.420	1.065 – 2.165	0.728	-0.7412 – -2.1962	0.3060
		placebo	8	1.278	1.330	1.330	0.335 – 2.045			
	Treatment period	elobixibat	9	2.202	2.410	2.410	1.270 – 2.630	0.811	-0.4680 – -2.0899	0.1966
		placebo	8	1.391	0.910	0.910	0.335 – 2.610			

	Difference	elobixibat	8	0.031	0.105	0.105	-0.290	-0.083	-1.5831	0.9078
							-0.870		-1.4181	
		placebo	8	0.114	0.095	0.095	-0.470			
							-0.690			
DA ($\mu\text{mol/g}$)	Observation period	elobixibat	8	0.0	0.0	0.0	0.0 – 0.0	0.0	0.0 – 0.0	-
		placebo	8	0.0	0.0	0.0	0.0 – 0.0			
	Treatment period	elobixibat	9	0.0	0.0	0.0	0.0 – 0.0	0.0	0.0 – 0.0	-
		placebo	8	0.0	0.0	0.0	0.0 – 0.0			
	Difference	elobixibat	8	0.0	0.0	0.0	0.0 – 0.0	0.0	0.0 – 0.0	-
		placebo	8	0.0	0.0	0.0	0.0 – 0.0			
isoUDCA ($\mu\text{mol/g}$)	Observation period	elobixibat	8	0.0	0.0	0.0	0.0 – 0.0	0.0	0.0 – 0.0	-
		placebo	8	0.0	0.0	0.0	0.0 – 0.0			
	Treatment period	elobixibat	9	0.0	0.0	0.0	0.0 – 0.0	0.0	0.0 – 0.0	-
		placebo	8	0.0	0.0	0.0	0.0 – 0.0			
	Difference	elobixibat	8	0.0	0.0	0.0	0.0 – 0.0	0.0	0.0 – 0.0	-
		placebo	8	0.0	0.0	0.0	0.0 – 0.0			
Total BAs ($\mu\text{mol/g}$)	Observation period	elobixibat	8	3.428	2.536	2.360	2.225 – 3.350	-0.999	-4.4137 – -2.4162	0.5406
		placebo	8	4.426	3.722	4.120	1.610 – 5.645			
	Treatment period	elobixibat	9	13.433	9.839	11.880	4.090 – 19.530	9.775	2.1275 – 17.2416	0.0157
		placebo	8	3.659	2.486	3.940	1.160 – 6.100			

	Difference	elobixibat	8	7.904	7.901	5.945	1.695 –	8.671	2.2249 –	0.0120
							13.330		15.1176	
		placebo	8	-0.768	3.137	-0.055	-1.710			
							-0.925			
primary BAs ($\mu\text{mol/g}$)	Observation period	elobixibat	8	0.000	0.000	0.000	0.000 –	-1.365	-4.1869	0.3171
							0.000		-1.4569	
		placebo	8	1.365	3.721	0.000	0.000 –			
							0.175			
	Treatment period	elobixibat	9	3.052	4.837	0.540	0.000 –	2.353	-1.4028	0.2016
							3.740		-6.1097	
		placebo	8	0.699	1.203	0.000	0.000 –			
							1.090			
secondary BAs ($\mu\text{mol/g}$)	Observation period	elobixibat	8	3.428	2.536	2.360	2.225 –	0.500	-2.0805	0.6840
							3.350		-3.0805	
		placebo	8	2.928	2.269	2.710	0.945 –			
							5.195			
Treatment period	elobixibat	9	9.520	5.591	10.480	4.090 –	6.738	2.1931 –	0.0065	
						13.510		11.2819		
		placebo	8	2.783	2.353	2.525	0.885 –			
							4.545			
Difference	elobixibat	8	5.594	5.530	3.475	1.695 –	5.739	1.2522 –	0.0158	
						9.015		10.2253		
		placebo	8	-0.145	2.103	-0.350	-1.710			
							-1.545			

N, number; SD, standard deviation; IQR, interquartile range; CI, confidence interval; CA, cholic acid; CDCA, chenodeoxycholic acid; DCA, deoxycholic acid; UDCA, ursodeoxycholic acid; HDCA, hyodeoxycholic acid; LCA, lithocholic acid; DA, dehydrocholic acid; BAs, bile acids. Primary BAs = CA + CDCA; secondary BAs = DCA + LCA + UDCA.

Supplementary Table 3. Summary of DDV in the participants with CC

Subgroup				N	median	IQR	P-value
Presence or absence of complications	presence	elobixibat	Baseline	4	98.0	77.0 – 123.0	0.1511
			Post-treatment	4	74.0	68.0 – 106.0	
			Difference	4	-12.0	-24.0 – 2.0	
		placebo	Baseline	2	104.5	41.0 – 168.0	
			Post-treatment	2	113.0	42.0 – 184.0	
			Difference	2	8.5	1.0 – 16.0	
	absence	elobixibat	Baseline	5	143.0	94.0 – 153.0	0.1892
			Post-treatment	5	126.0	75.0 – 146.0	
			Difference	5	-11.0	-40.0 – 7.0	
		placebo	Baseline	6	121.0	96.0 – 172.0	
			Post-treatment	6	138.0	58.0 – 172.0	
			Difference	6	1.0	-9.0 – 11.0	
Age classification < 65 years	elobixibat	Baseline	2	159.5	153.0 – 166.0	0.3897	
		Post-treatment	2	136.0	126.0 – 146.0		
		Difference	2	-23.5	-40.0 – 7.0		
	placebo	Baseline	2	132.0	96.0 – 168.0		

			Post-treatment	2	121.0	58.0 – 184.0	
			Difference	2	-11.0	-38.0 – 16.0	0.7537
	≥65 years	elobixibat	Baseline	7	103.3	86.0 – 143.0	
			Post-treatment	7	90.4	62.0 – 138.0	
			Difference	7	-11.0	-38.0 – 16.0	0.7537
		placebo	Baseline	6	121.0	49.0 – 172.0	
			Post-treatment	6	138.0	42.0 – 172.0	
			Difference	6	3.0	-3.0 – 11.0	0.3571
Presence or absence of defecation desire	presence	elobixibat	Baseline	9	103.0	93.0 – 143.0	
			Post-treatment	9	75.0	74.0 – 138.0	
			Difference	9	-11.0	-29.0 – 5.0	0.0433
		placebo	Baseline	7	98.0	49.0 – 172.0	
	Post-treatment		7	109.0	42.0 – 177.0		
		Difference	7	1.0	-9.0 – 11.0	0.7301	
	absence	placebo	Baseline	1	144.0	144.0 – 144.0	
			Post-treatment	1	167.0	167.0 – 167.0	
	Difference	1	23.0	23.0 – 23.0	-		
Sex	Men	elobixibat	Baseline	5	143.0	93.0 – 143.0	

			Post-treatment	5	126.0	75.0 – 138.0	
			Difference	5	-11.0	-19.0 – 5.0	0.2523
	placebo		Baseline	4	156.0	120.0 – 171.5	
			Post-treatment	4	169.5	112.5 – 178.0	
			Difference	4	6.5	-20.5 – 19.5	0.9731
Women	elobixibat		Baseline	4	98.5	77.5 – 128.0	
			Post-treatment	4	68.0	57.0 – 110.0	
			Difference	4	-18.0	-35.5 – 3.0	0.1467
	placebo		Baseline	4	73.5	45.0 – 135.0	
			Post-treatment	4	75.5	41.0 – 143.0	
			Difference	4	3.0	-4.0 – 8.0	0.6667
Duration of CC	< 5 years	elobixibat	Baseline	2	118.0	93.0 – 143.0	
			Post-treatment	2	106.0	74.0 – 138.0	
			Difference	2	-12.0	-19.0 – 5.0	0.3362
		placebo	Baseline	2	135.5	96.0 – 175.0	
			Post-treatment	2	115.0	58.0 – 172.0	
			Difference	2	-20.5	-38.0 – 3.0	0.4498
	≥ 5 years	elobixibat	Baseline	6	123.0	94.0 – 153.0	

			Post-treatment	6	100.0	62.0 – 146.0	
			Difference	6	-18.0	-40.0 – 1.0	0.1357
		placebo	Baseline	6	121.0	49.0 – 168.0	
			Post-treatment	6	138.0	42.0 – 177.0	
			Difference	6	8.0	1.0 – 16.0	0.1519
History of treatment for CC	positive	elobixibat	Baseline	3	143.0	61.0 – 153.0	
			Post-treatment	3	138.0	62.0 – 146.0	
			Difference	3	-5.0	-7.0 – 1.0	0.2667
		placebo	Baseline	2	133.0	98.0 – 168.0	
			Post-treatment	2	146.5	109.0 – 184.0	
			Difference	2	13.5	11.0 – 16.0	0.1166
	negative	elobixibat	Baseline	6	98.5	93.0 – 143.0	
			Post-treatment	6	74.5	74.0 – 126.0	
			Difference	6	-24.0	-40.0 – 11.0	0.0604
		placebo	Baseline	6	120.0	49.0 – 172.0	
			Post-treatment	6	112.5	42.0 – 172.0	
			Difference	6	-1.0	-9.0 – 5.0	0.6871

DDV, defaecatory desire volume; CC, chronic constipation; IQR, interquartile range. Change in DDV = DDV after 7 days of treatment – DDV before the treatment. Between-group difference = value for elobixibat group – value for placebo group.