

Additional file 4 Mean values and standard error or the mean (SEM) calculated for the questionnaires PAC-QOL and PSS at visits 1, 2 and 3.

Instrument	GI symptoms		Total cohort		Severe		Moderate	
			EpiCor	Placebo	EpiCor	Placebo	EpiCor	Placebo
PAC-QOL	PhD_V1	Mean	1.51	1.39	1.69	1.65	1.10	0.87
		SEM	±0.12	±0.10	±0.14	±0.10	±0.17	±0.13
	PhD_V2	Mean	1.05	1.17	1.22	1.33	0.65	0.83
		SEM	±0.12	±0.12	±0.15	±0.14	±0.14	±0.19
	PhD_V3	Mean	1.04	1.12	1.21	1.32	0.67	0.69
		SEM	±0.12	±0.11	±0.15	±0.14	±0.16	±0.16
	PhD	<i>p</i> -value (ANOVA)	<b>&lt;0.0001</b>	<b>0.005</b>	<b>0.001</b>	<b>0.007</b>	<b>0.017</b>	<b>0.435</b>
	PsD_V1	Mean	0.68	0.65	0.78	0.78	0.45	0.38
		SEM	±0.08	±0.08	±0.11	±0.09	±0.11	±0.11
	PsD_V2	Mean	0.45	0.45	0.50	0.50	0.33	0.35
		SEM	±0.07	±0.06	±0.09	±0.08	±0.09	±0.07
	PsD_V3	Mean	0.38	0.39	0.46	0.48	0.17	0.19
		SEM	±0.07	±0.07	±0.09	±0.09	±0.06	±0.07
	PsD	<i>p</i> -value (ANOVA)	<b>&lt;0.0001</b>	<b>0.001</b>	<b>0.001</b>	<b>0.002</b>	<b>0.027</b>	<b>0.129</b>
	W&C_V1	Mean	1.05	1.03	1.17	1.22	0.78	0.64
		SEM	±0.09	±0.08	±0.11	±0.09	±0.16	±0.14
	W&C_V2	Mean	0.79	0.77	0.83	0.87	0.67	0.57
		SEM	±0.08	±0.09	±0.09	±0.11	±0.17	±0.13
	W&C_V3	Mean	0.69	0.63	0.81	0.72	0.43	0.45
		SEM	±0.08	±0.08	±0.10	±0.09	±0.09	±0.13
	W&C	<i>p</i> -value (ANOVA)	<b>0.000</b>	<b>&lt;0.0001</b>	<b>0.002</b>	<b>&lt;0.0001</b>	<b>0.090</b>	<b>0.112</b>
	SAT_V1	Mean	2.62	2.50	2.69	2.65	2.45	2.19
		SEM	±0.13	±0.10	±0.15	±0.12	±0.25	±0.16
	SAT_V2	Mean	2.13	2.28	2.26	2.41	1.84	2.03
		SEM	±0.16	±0.14	±0.19	±0.17	±0.27	±0.23
	SAT_V3	Mean	1.99	2.04	2.13	2.18	1.64	1.75
		SEM	±0.14	±0.14	±0.16	±0.15	±0.22	±0.27
	SAT	<i>p</i> -value (ANOVA)	<b>0.000</b>	<b>0.004</b>	<b>0.010</b>	<b>0.027</b>	<b>0.013</b>	<b>0.166</b>
ITS_V1	Mean	1.27	1.23	1.39	1.40	1.01	0.86	
	SEM	±0.08	±0.07	±0.10	±0.07	±0.14	±0.10	
ITS_V2	Mean	0.96	1.00	1.04	1.10	0.77	0.79	
	SEM	±0.08	±0.07	±0.09	±0.09	±0.13	±0.12	
ITS_V3	Mean	0.88	0.88	1.00	1.00	0.60	0.64	
	SEM	±0.08	±0.07	±0.09	±0.08	±0.10	±0.11	
ITS	<i>p</i> -value (ANOVA)	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>	<b>0.022</b>	<b>0.040</b>	
PSS	ITS_V1	Mean	11.92	11.98	11.96	13.44	11.83	8.92
		SEM	±1.05	±0.99	±1.26	±1.26	±1.96	±1.26
ITS_V2	Mean	11.68	11.58	11.36	12.67	12.42	9.31	
	SEM	±0.99	±1.07	±1.26	±1.29	±1.56	±1.84	
ITS_V3	Mean	10.13	11.95	10.43	12.41	9.42	11.00	
	SEM	±1.19	±1.00	±1.46	±1.07	±2.12	±2.18	
ITS	<i>p</i> -value (ANOVA)	<b>0.016</b>	<b>0.846</b>	<b>0.044</b>	<b>0.555</b>	<b>0.197</b>	<b>0.379</b>	

**Legend:** The enlisted Patient Assessment of Constipation Quality of Life (PAC-QOL) items are PhD (physical discomfort), PsD (psychosocial discomfort), W&C (worries and concerns) and SAT (satisfaction). An instrument total score (ITS) calculated as the average of all 28 items recorded at each visit is also shown. The Perceived stress scale

(PSS) instrument only includes a total score (ITS) calculated as the sum of all 10 items recorded at each visit. Both instruments were filled in during visits 1 (V1, baseline), V2 and V3. A lower score is concomitant with a better quality of life and lower perceived stress for PAC-QOL and PSS, respectively. A one-way repeated measures ANOVA was used to test for significant changes over time within each group ( $p$ -values  $\leq 0.05$  are depicted in bold text).