Table e-1. Plasma concentrations of CBD and metabolites after single and multiple dosing of CBD

	CBD dose																
	5 mg/kg/day (N = 10)						10 mg/kg/day (N = 8)						20 mg/kg/day (N = 9)					
	CBD		6-OH-CBD		7-COOH-CBD		CBD		6-OH-CBD		7-COOH-CBD		CBD		6-OH-CBD		7-COOH-CBD	
Parameter Time	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
Plasma concentration on Day 1 at starting CBD dose (1.25 mg/kg), ng/mL																		
Pre-dose	10	0	10	0	7	0	8	0	8	0	7	0	8	0	7	0	6	0
2.5 hours	9	37.6 (53.7)	9	0.960 (1.36)	9	157 (151)	8	34.4 (32.1)	8	0.993 (0.956)	7	207 (236)	8	29.3 (28.5)	7	1.43 (1.36)	7	159 (171)
5 hours	7	10.0 (5.74)	7	0.233 (0.368)	7	103 (64.9)	8	11.3 (11.7)	8	0.243 (0.222)	6	120 (113)	9	25.3 (42.4)	9	1.04 (1.42)	8	131 (141)
Plasma concentration on Day 22 at target CBD dose, ng/mL																		
Pre-dose	10	23.0 (11.5)	10	1.53 (0.727)	10	1150 (777)	7	62.1 (44.7)	7	4.10 (2.28)	6	3440 (3460)	7	121 (81.3)	6	9.88 (8.08)	6	5630 (3890)
2.5 hours	10	130 (170)	10	4.18 (3.19)	9	1180 (761)	7	242 (159)	7	8.05 (4.46)	6	3550 (3680)	7	380 (370)	6	20.2 (14.6)	6	6090 (4110)
5 hours	9	72.1 (49.0)	8	3.01 (1.87)	9	1200 (837)	7	288 (345)	7	9.49 (8.03)	5	3630 (4400)	7	308 (321)	6	18.4 (14.6)	6	4920 (3170)

All data are given to 3 significant figures.

Table e-2. CBD and metabolite exposures and metabolite:parent ratios (based on AUC_{0-t}) after single and multiple dosing of CBD

Parameter Day	CBD dose								
	5 mg/kg/day (N = 10)			10 mg/kg/day (N = 8)			20 mg/kg/day (N = 9)		
	CBD	6-OH-CBD	7-COOH-CBD	CBD	6-OH-CBD	7-COOH-CBD	CBD	6-OH-CBD	7-COOH-CBD
	n / Geometric mean (%CV)	n / Geometric mean (%CV)	n / Geometric mean (%CV)	n / Geometric mean (%CV)	n / Geometric mean (%CV)	n / Geometric mean (%CV)	n / Geometric mean (%CV)	n / Geometric mean (%CV)	n / Geometric mean (%CV)
AUC_{0-t}, h·ng/mL									
Day 1 at starting CBD dose (1.25 mg/kg)	5 / 70.6 (20.4)	3 / 3.27 (132)	6 / 297 (97.3)	7 / 66.4 (121)	5 / 2.79 (87.7)	6 / 125 (1750)	7 / 73.7 (96.6)	5 / 5.16 (57.2)	6 / 195 (573)
Day 22 at target CBD dose	9 / 241 (101)	8 / 9.33 (119)	9 / 4190 (81.2)	7 / 722 (79.9)	7 / 26.3 (82.9)	5 / 9220 (178)	7 / 963 (93.4)	6 / 58.6 (90.1)	5 / 15500 (148)
Metabolite:parent ratio for AUC_{0-t}									
Day 1 at starting CBD dose (1.25 mg/kg)	- / -	3 / 0.0417 (141)	5 / 5.03 (96.0)	- / -	5 / 0.0393 (50.3)	5 / 2.29 (448)	- / -	5 / 0.0519 (41.7)	5 / 3.47 (3570)
Day 22 at target CBD dose	- / -	8 / 0.0391 (85.7)	9 / 17.4 (124)	- / -	7 / 0.0365 (76.0)	5 / 13.1 (286)	- / -	6 / 0.0572 (36.7)	5 / 14.2 (318)

%CV: % coefficient of variation. All data are given to 3 significant figures.

Table e-3. Plasma N-CLB: CLB concentration ratios before and after multiple dosing of CBD or placebo in patients with end of treatment data

Parameter Day	CBD dose							
	5 mg/kg/day (N = 10)		10 mg/kg/day (N = 8)		20 mg/kg/day (N = 9)		Placebo (N = 7)	
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
Pre-dose N-CLB:CLB ratio in all patients taking CLB								
Day 1	6	3.65 (2.83)	6	9.14 (8.04)	5	5.24 (3.95)	5	9.10 (5.65)
Day 22 at target CBD dose	6	10.9 (5.94)	6	14.7 (7.52)	5	9.83 (2.79)	5	7.06 (3.95)
Percentage change	6	271 (139)	6	186 (261)	5	166 (172)	5	−14.3 (23.8)
Pre-dose N-CLB:CLB ratio in patients taking CLB but not stiripentol								
Day 1	5	2.64 (1.51)	4	4.20 (1.56)	4	3.60 (1.70)	3	6.19 (5.51)
Day 22 at target CBD dose	5	11.3 (6.54)	4	16.0 (9.33)	4	10.0 (3.20)	3	4.46 (2.36)
Percentage change	5	325 (47.7)	4	297 (254)	4	213 (156)	3	−12.3 (30.6)
Pre-dose N-CLB:CLB ratio in patients taking CLB and stiripentol								
Day 1	1	8.73 (N/A)	2	19.1 (4.60)	1	11.8 (N/A)	2	13.5 (2.05)
Day 22 at target CBD dose	1	8.74 (N/A)	2	12.2 (0.92)	1	9.19 (N/A)	2	11.0 (0.92)
Percentage change	1	0.115 (N/A)	2	−34.9 (11.3)	1	−22.0 (N/A)	2	−17.3 (19.2)

All data are given to 3 significant figures.