Supplementary Materials

Long-Term Add-On Use of a Fixed Multicomponent Formulation Containing Palmitoylethanolamide and Acetyl-L-Carnitine in Fibromyalgia Syndrome: A 15-Month Retrospective Single-Cohort Study of 150 Patients

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Table S1. Number and proportion of missing values for each outcome at each scheduled visit (N = 150), with the breakdown between patients lost to follow-up and patients who had discontinued treatment.

Visit	Observed, n	Missing, n (%)	Lost to follow-up	Discontinued
Pain VAS (0–100)				
Baseline	150	0 (0.0%)	0	0
Month 1	128	22 (14.7%)	22	0
Month 2	111	39 (26.0%)	35	4
Month 3	92	58 (38.7%)	35	23
Month 6	80	70 (46.7%)	37	33
Month 9	71	79 (52.7%)	40	39
Month 12	64	86 (57.3%)	41	45
Month 15	64	86 (57.3%)	41	45
FIQR (0–100)				
Baseline	150	0 (0.0%)	0	0
Month 1	127	23 (15.3%)	23	0
Month 2	111	39 (26.0%)	35	4
Month 3	91	59 (39.3%)	35	24
Month 6	80	70 (46.7%)	37	33
Month 9	71	79 (52.7%)	40	39
Month 12	64	86 (57.3%)	41	45
Month 15	64	86 (57.3%)	41	45
PSQI (0–21)				
Baseline	150	0 (0.0%)	0	0
Month 3	91	59 (39.3%)	35	24
Month 6	80	70 (46.7%)	37	33
SF-12 PCS				
Baseline	150	0 (0.0%)	0	0
Month 3	91	59 (39.3%)	35	24
Month 6	80	70 (46.7%)	37	33
SF-12 MCS				
Baseline	150	0 (0.0%)	0	0
Month 3	91	59 (39.3%)	35	24
Month 6	81	69 (46.0%)	36	33

VAS, visual analogue scale; FIQR, revised Fibromyalgia Impact Questionnaire; PSQI, Pittsburgh Sleep Quality Index; SF-12 PCS and MCS, Physical and Mental Component Summary of the 12-item Short Form Health Survey. Missing values are counted among patients without an observed assessment at the visit; "lost to follow-up" denotes patients with no documented treatment status whose last visit preceded the one considered (n = 41 overall), and "discontinued" denotes patients with a documented discontinuation before the visit (n = 45 overall). Values carried forward in the source dataset after a documented discontinuation are not counted as observed. No patient who completed treatment (n = 64) has a missing value at any visit. The PSQI and the SF-12 were administered at baseline, 3 and 6 months only. Adverse events were recorded for every patient (an empty field denoting no event), whereas the treatment satisfaction score is missing for 35 patients, all of them non-completers.

Table S2. Sensitivity of the mean change from baseline in VAS and FIQR at 6 and 12 months to assumptions about missing data.

Scenario	n (6 / 12 months)	VAS, 6 months	VAS, 12 months	FIQR, 6 months	FIQR, 12 months
Observed cases at the visit	80 / 64	−25.5 [−29.0, −22.0]	−30.5 [−34.0, −27.1]	−19.5 [−22.7, −16.3]	−22.1 [−25.9, −18.4]
LOCF for discontinued patients	113 / 109	−18.2 [−21.7, −14.7]	−19.4 [−23.1, −15.8]	−13.3 [−16.2, −10.3]	−13.2 [−16.4, −10.1]
Delta-adjusted LOCF, δ = 5	113 / 109	−17.2 [−20.8, −13.5]	−18.0 [−21.9, −14.1]	−12.1 [−15.2, −8.9]	−11.6 [−15.0, −8.1]
Delta-adjusted LOCF, δ = 10	113 / 109	−16.2 [−20.0, −12.3]	−16.6 [−20.8, −12.4]	−10.9 [−14.3, −7.4]	−10.0 [−13.7, −6.2]
Delta-adjusted LOCF, δ = 15	113 / 109	−15.4 [−19.4, −11.3]	−15.4 [−19.8, −11.0]	−9.7 [−13.5, −6.0]	−8.4 [−12.5, −4.4]
Delta-adjusted LOCF, δ = 20	113 / 109	−14.6 [−18.8, −10.4]	−14.3 [−19.0, −9.6]	−8.8 [−12.8, −4.8]	−7.1 [−11.5, −2.7] (p = 0.004)
Delta-adjusted LOCF, δ = 25	113 / 109	−14.1 [−18.4, −9.7]	−13.5 [−18.4, −8.7]	−7.9 [−12.1, −3.7]	−5.8 [−10.5, −1.2] (p = 0.034)
Delta-adjusted LOCF, δ = 30	113 / 109	−13.6 [−18.1, −9.1]	−12.8 [−17.9, −7.8]	−7.2 [−11.6, −2.8] (p = 0.003)	−4.9 [−9.8, 0.1] (p = 0.109)
BOCF for all discontinued patients	113 / 109	−18.1 [−21.3, −14.8]	−17.9 [−21.4, −14.4]	−13.8 [−16.6, −11.0]	−13.0 [−16.0, −10.0]
BOCF for all non-completers (worst case)	150 / 150	−13.6 [−16.4, −10.8]	−13.0 [−15.9, −10.2]	−10.4 [−12.7, −8.1]	−9.4 [−11.8, −7.1]

Observed cases at the visit: all patients with an assessment at that visit (6 months: n = 80; 12 months: the 64 completers). Mean change from baseline with 95% CI (t-based); Wilcoxon signed-rank $p < 0.001$ unless stated. LOCF, last observation carried forward (the last value recorded before discontinuation); δ, number of points added to the carried-forward value of each patient who discontinued for lack of perceived efficacy (n = 36), the other discontinued patients keeping their carried-forward value; BOCF, baseline observation carried forward. Patients lost to follow-up (n = 41) contribute only the assessments actually performed, except in the worst-case scenario, in which they are assumed to have returned to baseline. For VAS and FIQR the tipping point, i.e. the smallest δ at which the mean change was no longer statistically significant, was not reached for VAS at either visit, nor for FIQR at 6 months, and was reached at δ = 30 for FIQR at 12 months. Imputation applies only to patients without an observed value at the visit considered; patients who discontinued after that visit contribute their observed value.

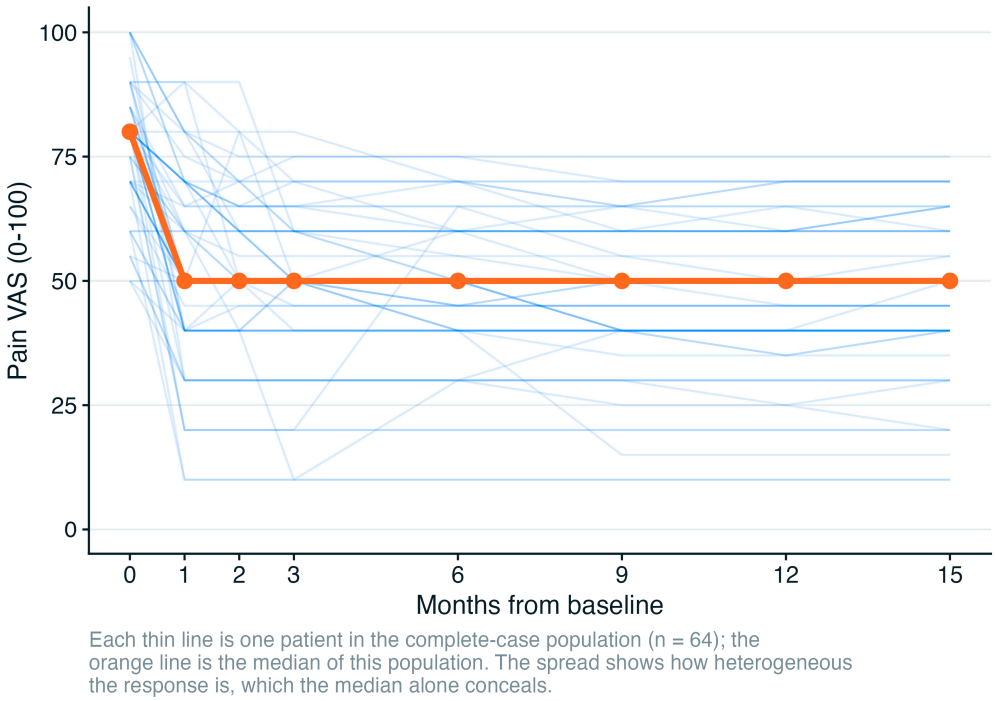


Figure S1. Individual pain trajectories in the complete-case population (n = 64). Each thin line is one patient; the orange line is the cohort median. The dispersion shows how heterogeneous the individual response is, which the median alone conceals.