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## **Supplementary Material**

**Article Title:** A Double-Blind, Randomized Controlled Clinical Trial Comparing Eicosapentaenoic Acid Versus Docosahexaenoic Acid for Depression

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1. [eTable 1](#) Current Anxiety Disorders in the Study Sample, and Change from Baseline to Treatment Week 8 for N=170 Evaluable Subjects Based on Mixed Model Repeated Measures Analysis For Groups Defined by Any vs. No Current Anxiety Diagnosis

### **Disclaimer**

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplemental Table 1  
Current Anxiety Disorders in the Study Sample, and Change from Baseline to Treatment Week 8 for N=170 Evaluable Subjects<sup>a</sup>  
Based on Mixed Model Repeated Measures Analysis<sup>b</sup>  
For Groups Defined by Any vs. No Current Anxiety Diagnosis

Diagnosis		All Evaluable Subjects (N=170) <sup>a</sup>	EPA (N = 59)	DHA (N = 53)	Placebo (N = 58)	Significance		
						χ <sup>2</sup>	df	P
Current Anxiety Disorders								
Panic Disorder	N (%)	7 (4.1)	1 (1.7)	4 (7.6)	2 (3.4)	2.52 <sup>b</sup>	2	0.283
Agoraphobia	N (%)	4 (2.4)	0 (0.0)	2 (3.8)	2 (3.4)	2.19 <sup>b</sup>	2	0.334
Social Phobia	N (%)	16 (9.4)	5 (8.5)	7 (13.2)	4 (6.9)	1.39	2	0.500
Obsessive-Compulsive Disorder	N (%)	3 (1.8)	1 (1.7)	2 (3.8)	0 (0.0)	2.28 <sup>b</sup>	2	0.320
Generalized Anxiety Disorder	N (%)	24 (14.1)	6 (10.2)	10 (18.9)	8 (13.8)	1.75	2	0.417
PTSD	N (%)	9 (5.3)	4 (6.8)	2 (3.8)	3 (5.2)	0.51 <sup>b</sup>	2	0.776
Hamilton Depression Rating Scale - 17-Item Version (HAM-D <sub>17</sub> )	Least-Square Means (se) of Change at Treatment Week 8 <sup>b</sup>			Significance of Treatment-by-Time Interaction		Standardized Effect Size at Week 8 <sup>e</sup>		
Analyzed by These Groups	EPA	DHA	Placebo			EPA vs. Placebo	DHA vs. Placebo	EPA vs. DHA
	LS-Mean <sup>c</sup> (se) [N]	LS-Mean <sup>c</sup> (se) [N]	LS-Mean <sup>c</sup> (se) [N]	F	df <sup>d</sup>	P		
<u>All Evaluable Subjects</u>	- 10.34 (0.62) [60]	- 9.26 (0.62) [58]	- 9.49 (0.61) [59]	0.23	2, 687	0.794	- 0.179	+ 0.049 - 0.228
<u>Current Anxiety Disorder<sup>a</sup></u>								
Yes	- 9.66 (1.08) [15]	- 9.81 (0.99) [17]	- 7.83 (1.19) [13]	0.72	2, 162	0.489	- 0.431	- 0.474 + 0.036
No	- 10.68 (0.64) [44]	- 9.06 (0.70) [36]	- 9.80 (0.60) [45]	0.09	2, 575	0.916	- 0.213	+ 0.180 - 0.382
Hamilton Depression Rating Scale - 17-Item Version (HAM-D <sub>17</sub> )	Mean Baseline, Last Visit, and Change (Baseline to Last Visit) <sup>f</sup>			Significance of Treatment				
<u>by Current Anxiety Disorder<sup>a</sup></u>								

	EPA	DHA	Placebo			
	[N] Mean (sd)	[N] Mean (sd)	[N] Mean (sd)	F	df	P
Yes	[15]	[17]	[13]			
Baseline	21.20 (4.93)	20.35 (3.57)	19.15 (2.19)	1.02	2, 42	0.369
Last Visit	11.93 (5.57)	11.12 (4.76)	12.69 (7.51)	0.26	2, 42	0.770
Change (Baseline to Last Visit)	- 9.27 (6.60)	- 9.24 (5.78)	- 6.46 (7.15)	0.86	2, 42	0.431
No	[44]	[36]	[45]			
Baseline	18.45 (2.62)	19.58 (3.07)	19.16 (3.31)	1.45	2, 122	0.239
Last Visit	9.48 (6.58)	11.64 (6.49)	9.96 (5.08)	1.36	2, 122	0.261
Change (Baseline to Last Visit)	- 8.98 (6.91)	- 7.94 (6.34)	- 9.20 (5.52)	0.44	2, 122	0.644

Abbreviations: EPA: Eicosapentaenoic acid; DHA: docosahexaenoic acid; HAM-D-17: 17-item Hamilton Depression Rating Scale; CGI: Clinical Global Improvement scale; se: standard error; df: degrees of freedom; PTSD: Post-Traumatic Stress Disorder.

- N=7 subjects have no SCID data, so comorbid disorder information is missing.
- HAM-D was administered at Baseline and at 2-week intervals during the 8-week study. A full-model MMRM was performed on change from Baseline to Week 8, testing the significance of effects of treatment, visit, and treatment-by-visit interaction, as well as the covariates of site, baseline score and baseline score-by-visit interaction.
- Change at 8 weeks is significantly different from zero for each treatment group, by every breakdown of evaluable cases shown in the table, at  $P \leq 0.001$ .
- Degrees of freedom are determined using the Satterthwaite approximation method.
- By Cohen's  $d$  effect size = (difference between LS-Mean change) / pooled sd for each pair of treatments (sd per group computed from se of LS-Mean from MMRM). A negative effect size indicates that the 1<sup>st</sup> group improved more than the 2<sup>nd</sup> one (has a lower negative LS-mean change).
- Mean baseline, last visit, and change HAM-D scores by treatment group. NOTE: The last visit and change scores do not reflect time in treatment for subjects who terminated early.