



THE JOURNAL OF  
**CLINICAL PSYCHIATRY**

THE OFFICIAL JOURNAL OF THE AMERICAN SOCIETY OF CLINICAL PSYCHOPHARMACOLOGY

## **Supplementary Material**

**Article Title:** Omega-3 Fatty Acids for Major Depressive Disorder With High Inflammation: A Randomized Dose-Finding Clinical Trial

**Authors:** David Mischoulon, MD, PhD; Boadie W. Dunlop, MD; Becky Kinkead, PhD; Pamela J. Schettler, PhD; Stefania Lamon-Fava, MD, PhD; Jeffrey J. Rakofsky, MD; Andrew A. Nierenberg, MD; Alisabet J. Clain, MS; Tanja Mletzko Crowe, BA; Andrea Wong, BA; Jennifer C. Felger, MD; Lisa Sangermano, BA; Thomas R. Ziegler, MD; Cristina Cusin, MD; Lauren B. Fisher, MD; Maurizio Fava, MD; and Mark Hyman Rapaport, MD

**DOI Number:** 10.4088/JCP.21m14074

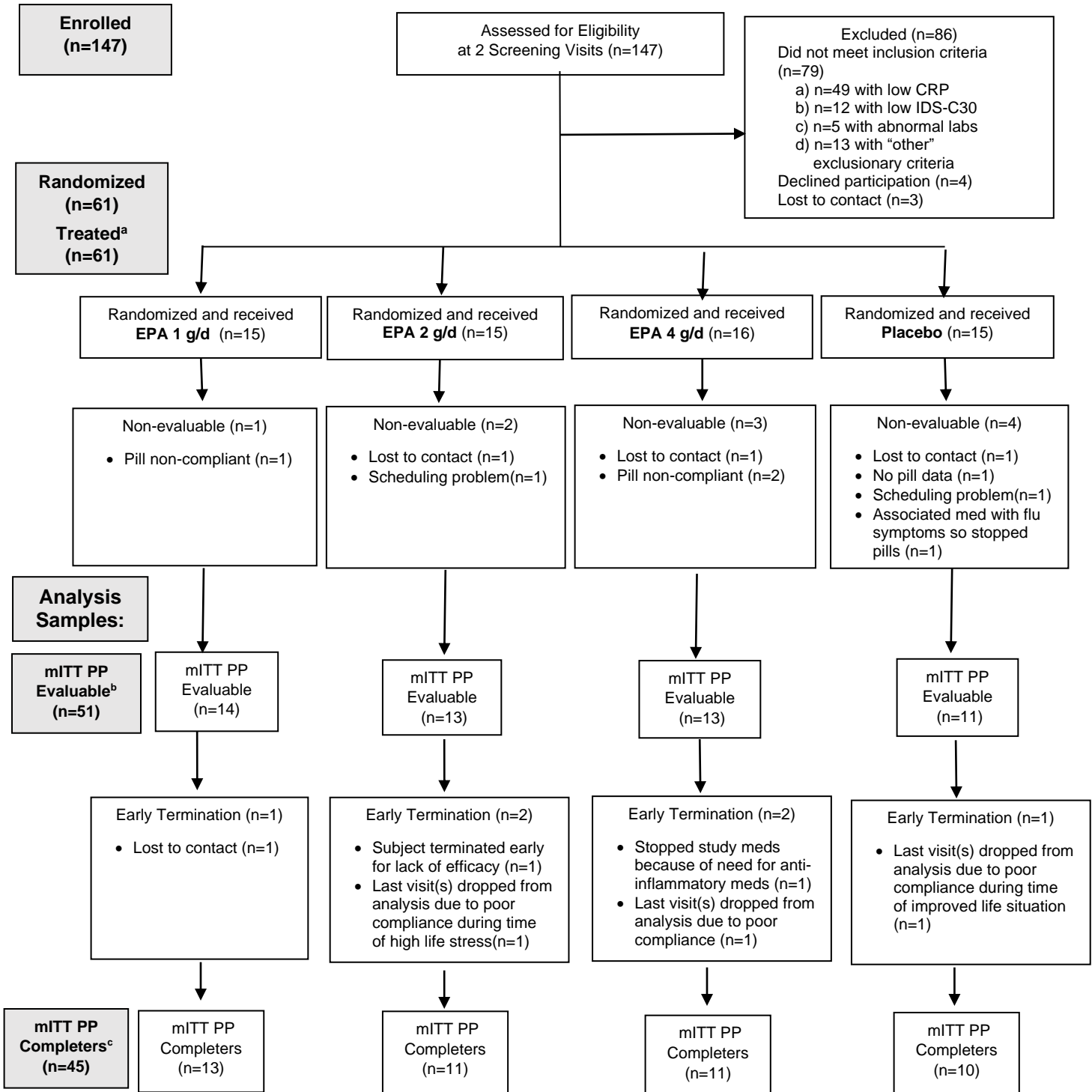
### **List of Supplementary Material for the article**

1. [Figure 1](#) CONSORT Statement Flow Diagram
2. [Figure 2](#) Spearman's Rho Correlation Between Percent Changes in hsCRP and IDS-C Scores, by Treatment Arm
3. [Table 1](#) Adverse Events (AEs) Reported by n=61 Randomized Subjects, by Treatment Group

### **Disclaimer**

This Supplementary Material has been provided by the authors 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.

**Supplementary Figure 1: CONSORT Statement Flow Diagram**



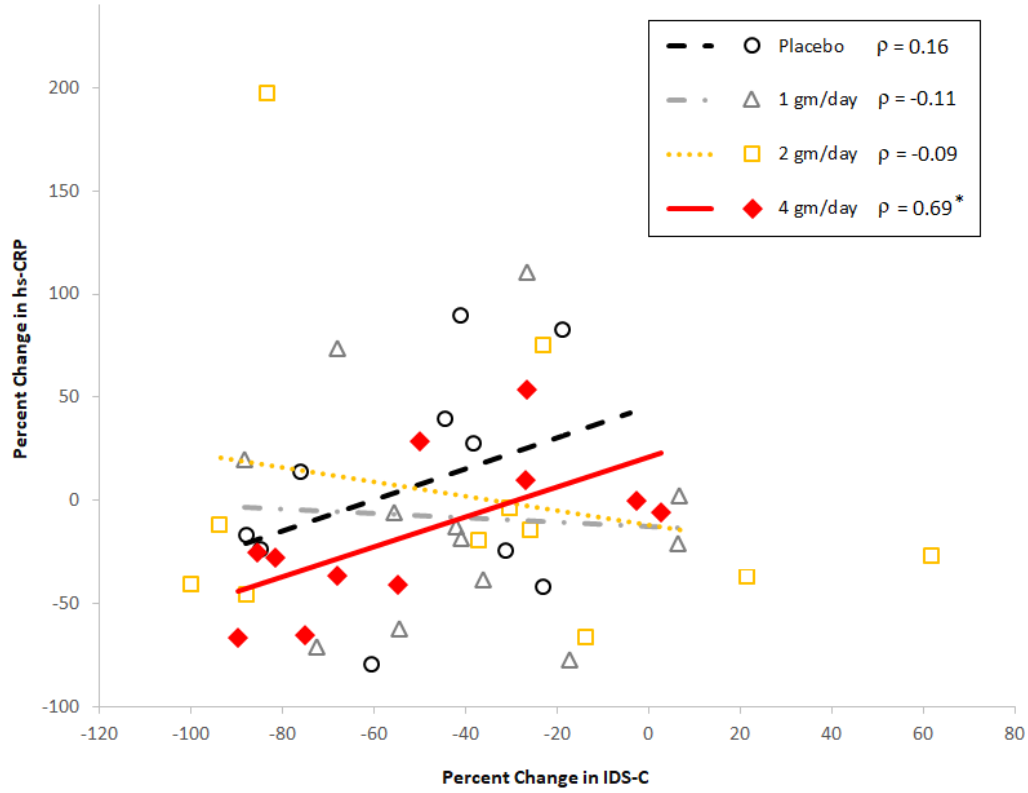
a. Used for safety analysis

b. Randomized subjects who had baseline and at least one post-baseline per protocol (PP) assessment of IDS-C30

c. Randomized subjects who had PP data at baseline and treatment week 12 (end of treatment)

Abbreviations: EPA: Eicosapentaenoic Acid; CRP: C-Reactive Protein; IDS-C30: Inventory of Depressive Symptomatology, Clinician-Rated version; mITT: modified Intent-to-Treat; PP: Per Protocol

**Supplementary Figure 2: Spearman's Rho Correlation Between Percent Changes in hsCRP and IDS-C Scores, By Treatment Arm**



\* Statistically significant correlation,  $p=0.019$ .

Abbreviations: hsCRP: high-sensitivity C-Reactive Protein; IDS-C: Inventory of Depressive Symptomatology.

**Supplementary Table 1: Adverse Events (AEs) Reported by n=61 Randomized Subjects, by Treatment Group**

	<b>EPA 1 g/day</b>	<b>EPA 2 g/day</b>	<b>EPA 4 g/day</b>	<b>Placebo</b>
	<b>Affected / Total (%)</b>	<b>Affected / Total (%)</b>	<b>Affected / Total (%)</b>	<b>Affected / Total (%)</b>
<b>Total</b>	<b>8/15 (53.33%)</b>	<b>8/15 (53.33%)</b>	<b>9/16 (56.25%)</b>	<b>11/15 (73.33%)</b>
<b>Gastrointestinal System</b>				
Abnormal Propulsive movement of large bowel	0/15 (0%)	0/15 (0%)	0/16 (0%)	1/15 (6.67%)
Acute vomiting	0/15 (0%)	0/15 (0%)	1/16 (6.25%)	1/15 (6.67%)
Belching	0/15 (0%)	0/15 (0%)	1/16 (6.25%)	0/15 (0%)
Bloating	0/15 (0%)	0/15 (0%)	0/16 (0%)	1/15 (6.67%)
Constipation alternating with diarrhea	0/15 (0%)	0/15 (0%)	0/16 (0%)	1/15 (6.67%)
Diarrhea/Loose stool	1/15 (6.67%)	0/15 (0%)	0/16 (0%)	2/15 (13.33%)
Flatulence	0/15 (0%)	1/15 (6.67%)	0/16 (0%)	0/15 (0%)
Gastric reflux	2/15 (13.33%)	1/15 (6.67%)	1/16 (6.25%)	2/15 (13.33%)
Gastroenteritis	1/15 (6.67%)	0/15 (0%)	0/16 (0%)	0/15 (0%)
Increased frequency of bowel movements	0/15 (0%)	0/15 (0%)	1/16 (6.25%)	1/15 (6.67%)
Nausea	1/15 (6.67%)	1/15 (6.67%)	0/16 (0%)	0/15 (0%)
Constipation	2/15 (13.33%)	0/15 (0%)	0/16 (0%)	1/15 (6.67%)
Increased appetite	1/15 (6.67%)	0/15 (0%)	0/16 (0%)	0/15 (0%)
<b>Renal and Urinary Tract</b>				
Increased Urination	0/15 (0%)	0/15 (0%)	0/16 (0%)	1/15 (6.67%)
Acute Urinary Tract Infection	1/15 (6.67%)	1/15 (6.67%)	0/16 (0%)	0/15 (0%)
<b>Nervous System</b>				
Headache	0/15 (0%)	1/15 (6.67%)	0/16 (0%)	2/15 (13.33%)
Dizziness of unknown cause	0/15 (0%)	0/15 (0%)	0/16 (0%)	2/15 (13.33%)
<b>General</b>				
Increased thirst	0/15 (0%)	1/15 (6.67%)	0/16 (0%)	0/15 (0%)
Tiredness	0/15 (0%)	0/15 (0%)	0/16 (0%)	1/15 (6.67%)
Weight loss	0/15 (0%)	0/15 (0%)	0/16 (0%)	1/15 (6.67%)
<b>Eye related</b>				
Acute conjunctivitis	0/15 (0%)	0/15 (0%)	1/16 (6.25%)	0/15 (0%)
<b>Immune System</b>				
Allergy symptoms (environmental)	1/15 (6.67%)	0/15 (0%)	0/16 (0%)	1/15 (6.67%)
Hives	0/15 (0%)	0/15 (0%)	1/16 (6.25%)	0/15 (0%)
<b>Musculoskeletal</b>				
Back pain	2/15 (13.33%)	0/15 (0%)	0/16 (0%)	0/15 (0%)
Knee pain	0/15 (0%)	0/15 (0%)	0/16 (0%)	1/15 (6.67%)
Ligament strain	0/15 (0%)	0/15 (0%)	1/16 (6.25%)	0/15 (0%)
Muscle strain	1/15 (6.67%)	1/15 (6.67%)	1/16 (6.25%)	0/15 (0%)
Lower limb numbness	1/15 (6.67%)	0/15 (0%)	0/16 (0%)	0/15 (0%)
Hematoma (toe)	0/15 (0%)	0/15 (0%)	0/16 (0%)	1/15 (6.67%)
Hand laceration	0/15 (0%)	1/15 (6.67%)	0/16 (0%)	0/15 (0%)

<b>Dermatological</b>				
Burn injury (right thumb)	1/15 (6.67%)	0/15 (0%)	0/16 (0%)	0/15 (0%)
<b>Reproductive System</b>				
Ovarian cyst exacerbation	0/15 (0%)	0/15 (0%)	1/16 (6.25%)	0/15 (0%)
Vaginal discharge	0/15 (0%)	1/15 (6.67%)	0/16 (0%)	0/15 (0%)
<b>Cardiovascular System</b>				
Palpitations	0/15 (0%)	0/15 (0%)	1/16 (6.25%)	0/15 (0%)
<b>infections</b>				
Influenza	0/15 (0%)	1/15 (6.67%)	0/16 (0%)	0/15 (0%)
Shingles	0/15 (0%)	1/15 (6.67%)	0/16 (0%)	0/15 (0%)
Upper Respiratory Infection	3/15 (20%)	1/15 (6.67%)	4/16 (25%)	2/15 (13.33%)
<b>Ear related</b>				
Tinnitus	0/15 (0%)	0/15 (0%)	0/16 (0%)	1/15 (6.67%)
<b>Respiratory</b>				
Cough	0/15 (0%)	0/15 (0%)	0/16 (0%)	1/15 (6.67%)

Abbreviations: AE: Adverse Event; EPA: Eicosapentaenoic acid.