

International ME/CFS Conference 2025  
Berlin, Germany

# Oxaloacetate CFS

*Anhydrous Enol-Oxaloacetate  
Treatment of ME/CFS*

Terra Biological LLC

May 2025

San Diego, California

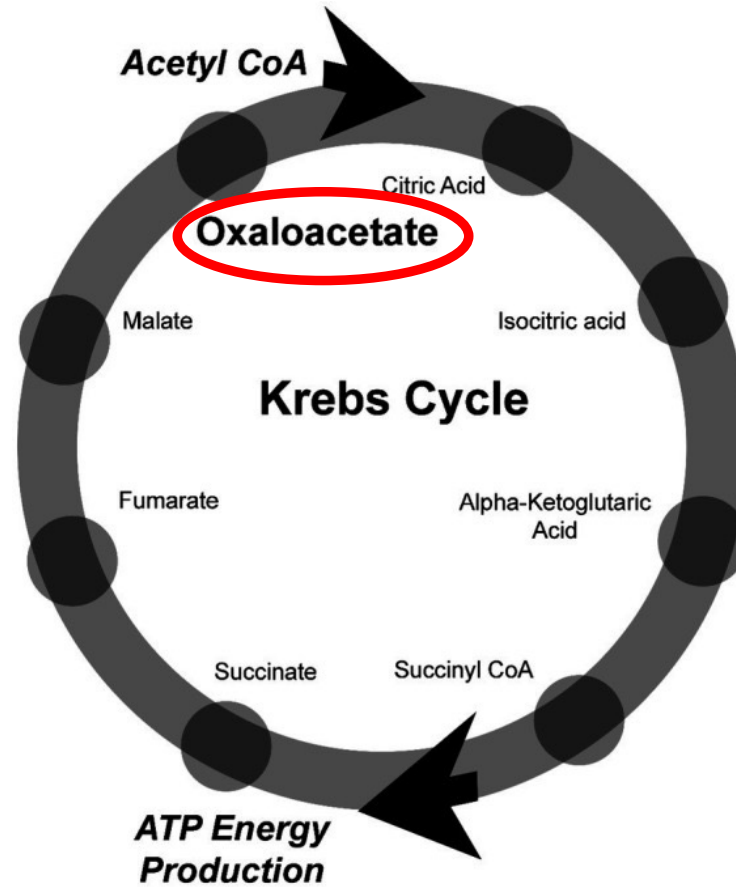
[www.OxaloacetateCFS.com](http://www.OxaloacetateCFS.com)

# Oxaloacetate

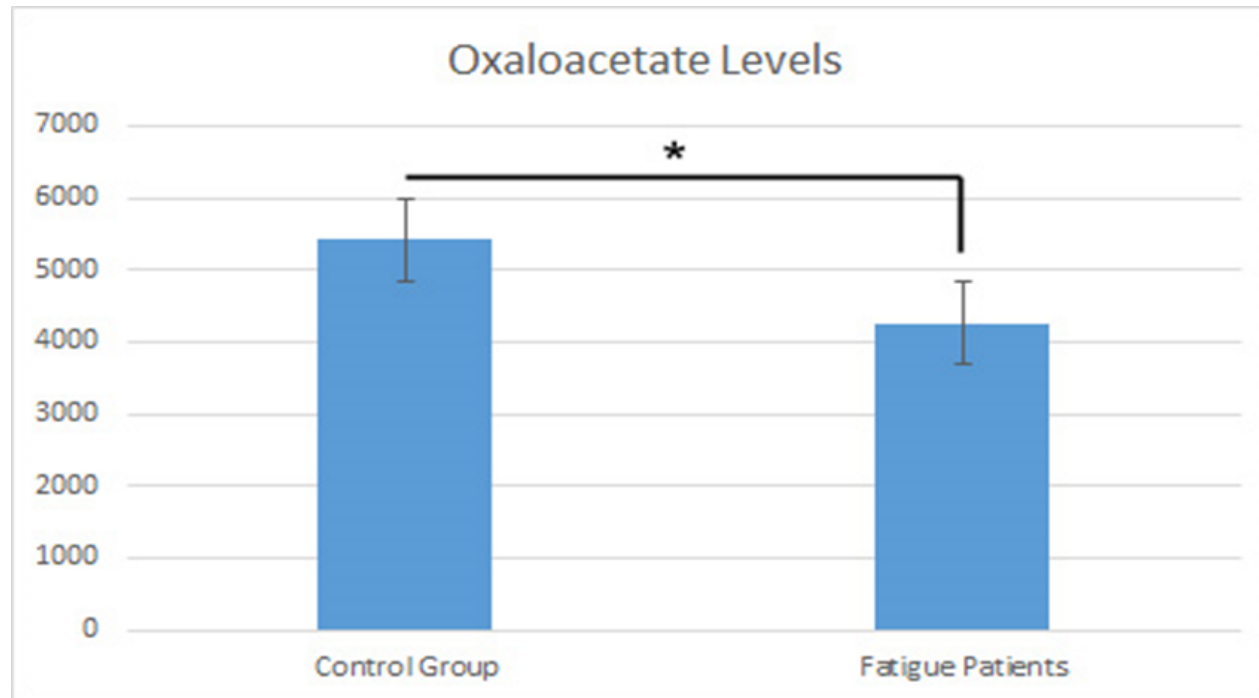
Part of the Krebs Cycle

Found in nearly every cell

Critical for Energy Formation



# Background: Oxaloacetate is depleted in ME/CFS patients



- Cornell University Study
- 2 arm study
- 15 Control Patients
- 17 ME/CFS Patients
- $P < 0.05$
- Females between 42 and 68 years old
- All ME/CFS Pts meet 1994 Fukuda definition For ME/CFS
- QE-MS method for Metabolomics in Blood

Germain A, Ruppert D, Levine SM, Hanson MR. Metabolic profiling of a myalgic encephalomyelitis/chronic fatigue syndrome discovery cohort reveals disturbances in fatty acid and lipid metabolism. Mol Biosyst. 2017 Jan 31;13(2):371-379. doi: 10.1039/c6mb00600k. PMID: 28059425; PMCID: PMC5365380. <https://pubmed.ncbi.nlm.nih.gov/28059425/>

# Cellular/Animal AEO Studies-- Mechanisms of Action?

- Reduction of Chronic Inflammation Activation Via NF-kB Reduction of up to 70%

Wilkins HM, Harris JL, Carl SM, et al. Oxaloacetate activates brain mitochondrial biogenesis, enhances the insulin pathway, reduces inflammation and stimulates neurogenesis. *Hum Mol Genet.* 2014;23(24):6528-6541. doi:10.1093/hmg/ddu371 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4271074/>

- Reduction of Glycolysis/Warburg Effect 48.8% and Increased Mitochondrial Energy Production, Decrease of Lactate Production

Omkar Ijare, David Conway, Alan Cash, David Baskin, Kumar Pichumani, CBMT-49. OXALOACETATE ALTERS GLUCOSE METABOLISM IN GLIOBLASTOMA: <sup>13</sup>C ISOTOPOMER STUDY, *Neuro-Oncology*, Volume 21, Issue Supplement\_6, November 2019, Pages vi43–vi44, <https://doi.org/10.1093/neuonc/noz175.171> [https://academic.oup.com/neuro-oncology/article-abstract/21/Supplement\\_6/vi43/5620031?redirectedFrom=fulltext](https://academic.oup.com/neuro-oncology/article-abstract/21/Supplement_6/vi43/5620031?redirectedFrom=fulltext)

- Increase in the Redox NAD<sup>+</sup>/NADH Ratio by 50%

Wilkins HM, Harris JL, Carl SM, et al. Oxaloacetate activates brain mitochondrial biogenesis, enhances the insulin pathway, reduces inflammation and stimulates neurogenesis. *Hum Mol Genet.* 2014;23(24):6528-6541. doi:10.1093/hmg/ddu371 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4271074/>

- Increase in PGC1 $\alpha$  ratio by 58% to Facilitate Mitochondrial Biogenesis, Providing More Cellular Power Plants.

Wilkins HM, Harris JL, Carl SM, et al. Oxaloacetate activates brain mitochondrial biogenesis, enhances the insulin pathway, reduces inflammation and stimulates neurogenesis. *Hum Mol Genet.* 2014;23(24):6528-6541. doi:10.1093/hmg/ddu371 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4271074/>

- Increase in Cellular Glucose Uptake, Providing More Fuel for the Cell

Yoshikawa K. Studies on the anti-diabetic effect of sodium oxaloacetate. *Tohoku J Exp Med.* 1968 Oct;96(2):127-41. doi: 10.1620/tjem.96.127. PMID: 4884771. <https://pubmed.ncbi.nlm.nih.gov/4884771/>

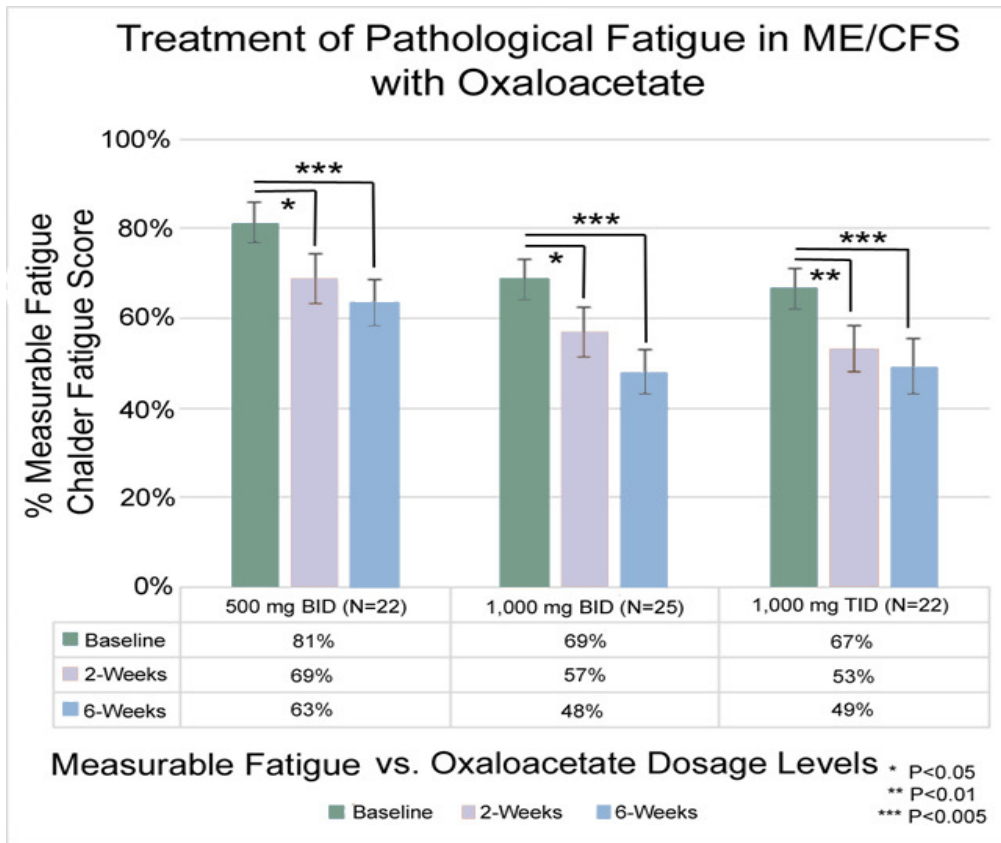


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# Proof of Concept Clinical Trial

## NCT04592354

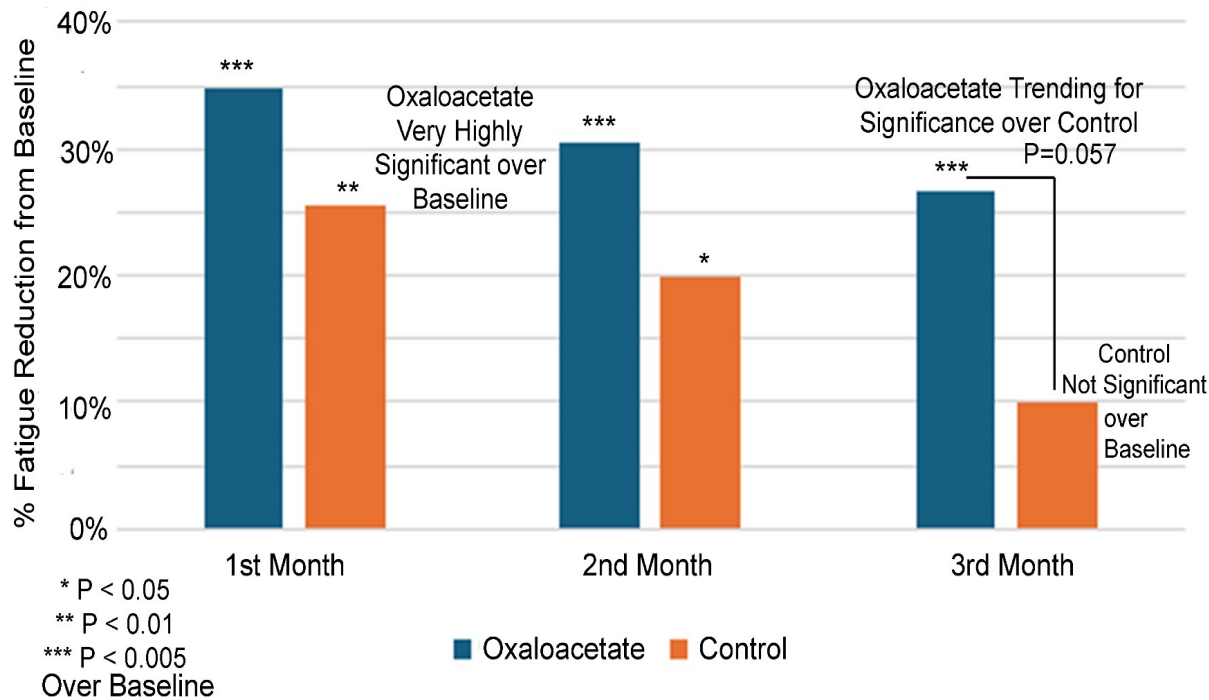
ME/CFS Myalgic Encephalomyelitis / Chronic Fatigue Syndrome



- Proof of Concept Trial
- Dose Ranging Study
- 76 Patients with ME/CFS
- 8.9 Year Average Illness
- **Average Reduction in Fatigue up to 33.3% in 6 weeks**
- Highly Significant Improvement.

# RCT Oxaloacetate for ME/CFS **NCT05273372**

% Reduction In Fatigue From Baseline  
Chlader Fatigue Score -- Completer's Analysis

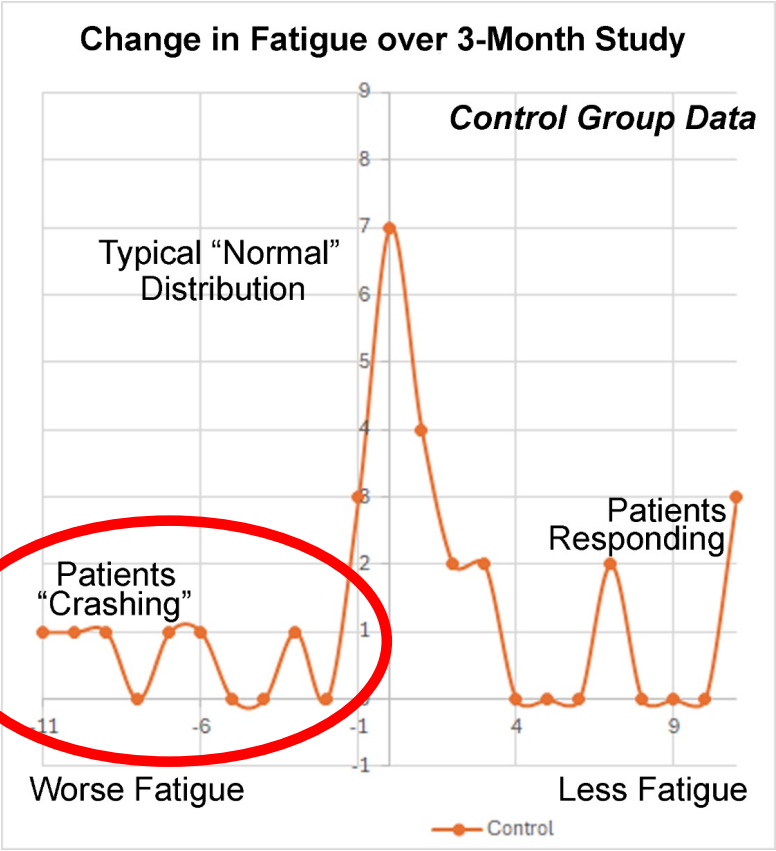


Participants that completed the study  
N= 64, Bimodal Scoring

Oxaloacetate Group maintains highly **significant improvement of 25% to 35%** over baseline fatigue levels throughout the study, and trends over control as the placebo effect drops off.

Control group quickly loses significance and reduces to similar historical levels of response.

# Initial Change in Fatigue From Baseline



## Control Group

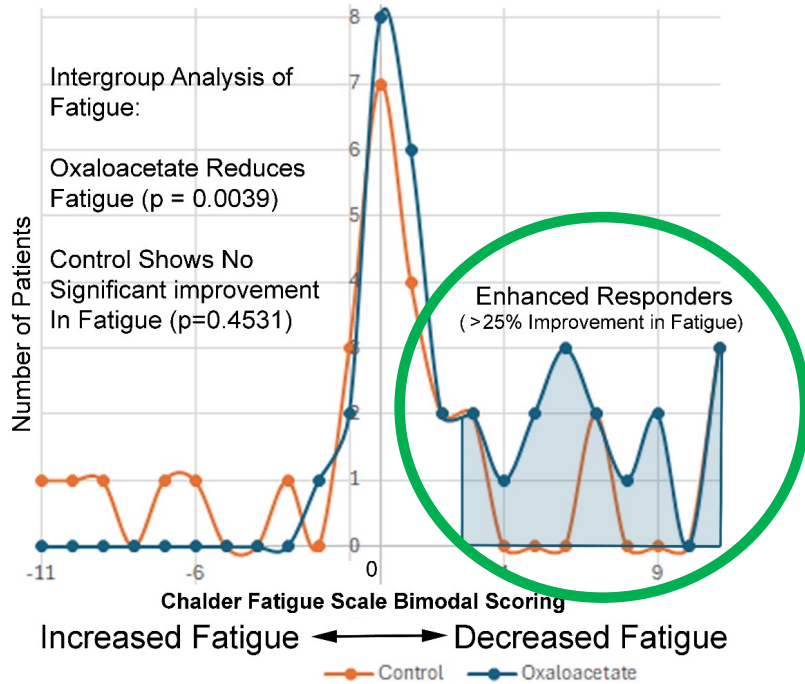
Patients Experience Both

**"Fatigue Crashes" (on left of graph)**

And Improvements in Energy (right side of Graph)– Normal Distribution

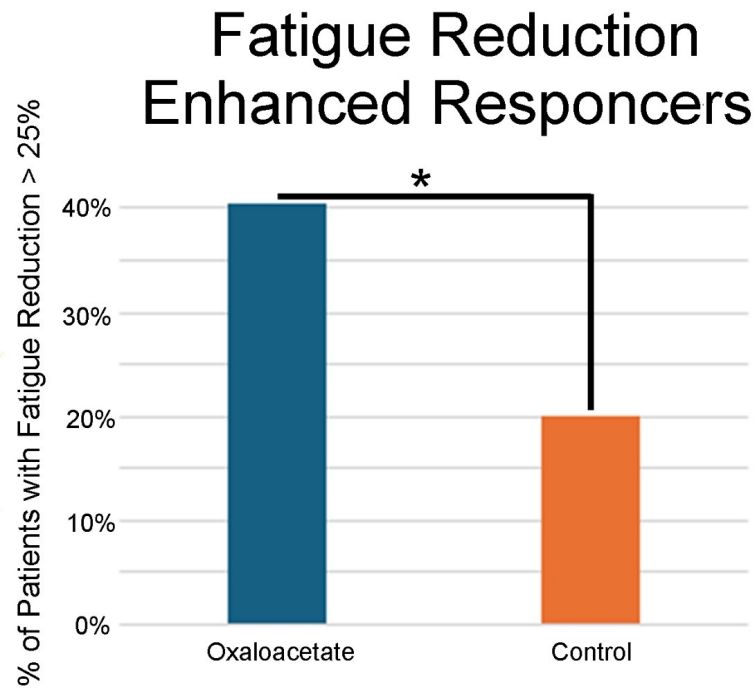
# Significant Shift to Decreased Fatigue

Shift From Day 1 to End of Treatment-- Efficacy Analysis  
Chalder Fatigue Score



- Oxaloacetate Group at 3 months (Trial End) had significant movement to less fatigue which was not seen in the Control Group. (P < 0.005) **Protection against crashes**
- **40.5%** of the Oxaloacetate Patients were **Enhanced Responders** with greater than 25% improvement in fatigue. (P < 0.05)
- **Average Improvement of Enhanced Responders was 63%**

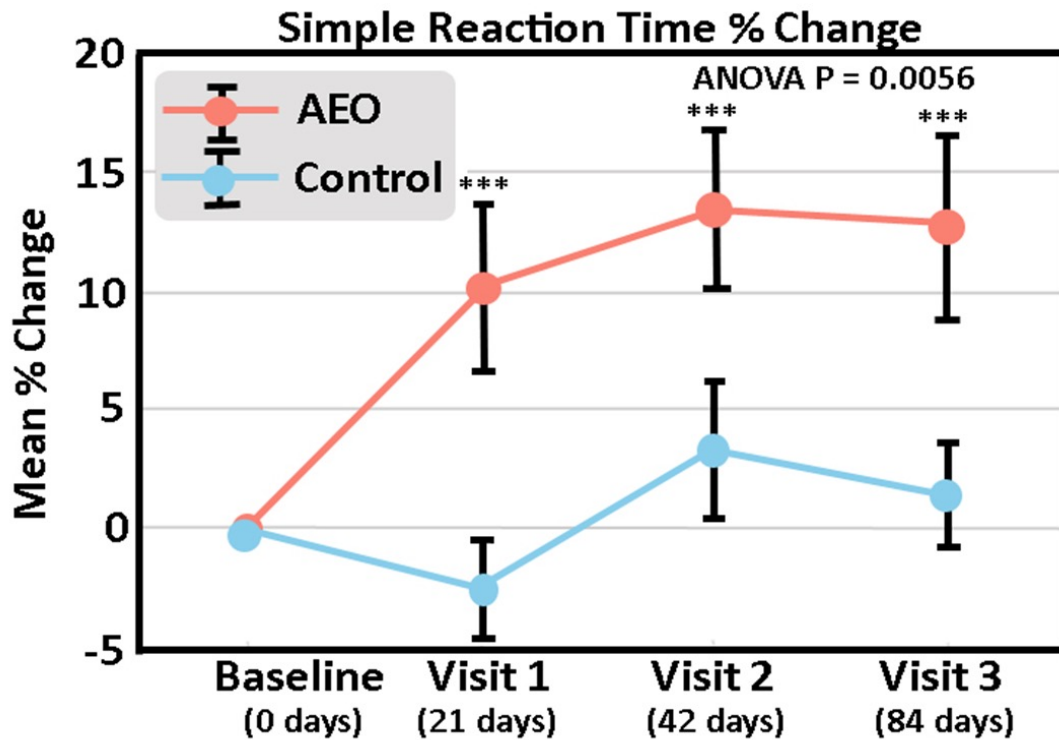
# Oxaloacetate– the right key to unlock fatigue improvement ....For some patients.....



**40.5%** of total patients in the oxaloacetate group were classified as “**Enhanced Responcers**”– (participants with a fatigue reduction of 25% or more from baseline) as compared to 20.0% in the Control group ( $P < 0.05$ )

The Average improvement within the Oxaloacetate Enhanced Responcers Group was a **63% Reduction in Fatigue.**

# DANA Brain Vital– Efficacy Analysis



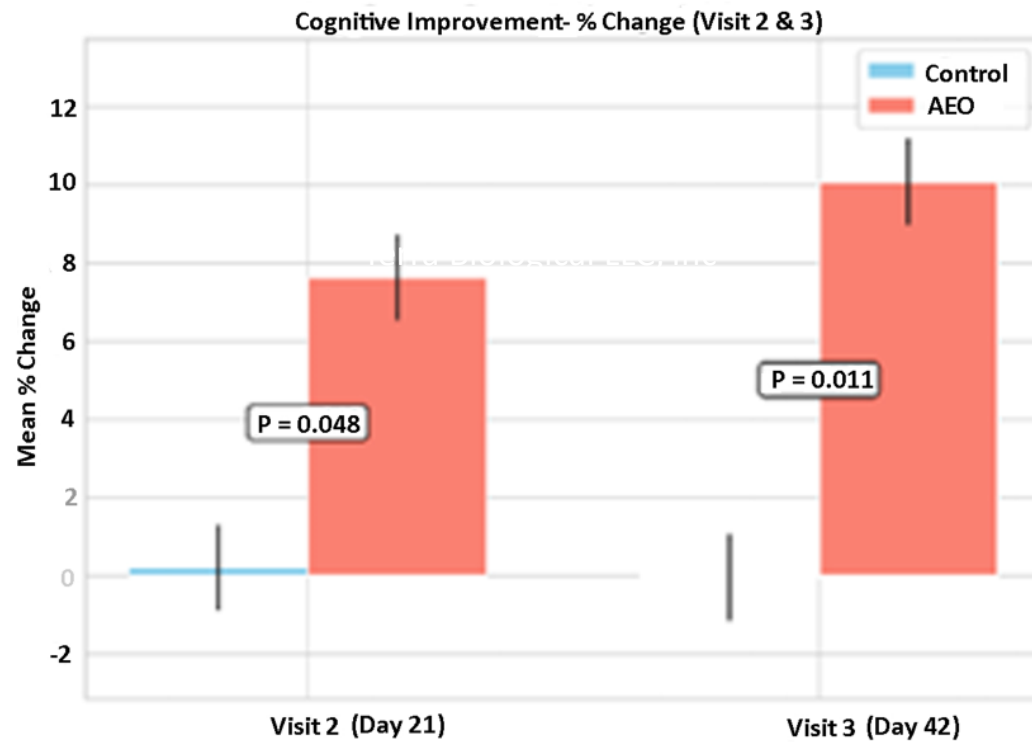
Meta analysis of 50 ME/CFS studies indicated that ME/CFS lowers “Simple Reaction Time”.  
<https://pubmed.ncbi.nlm.nih.gov/20047703/>

***Oxaloacetate Treatment significantly improves “Simple Reaction Time” over the Control Group, by ANOVA test. (P =0.0056)***

The SRT CE test measures “Simple Reaction Time”. The tests are reported as cognitive efficiency calculated accuracy x speed x 60,000. *Increases measure improved cognitive reaction time.*

For more information on DANA Brain Vital:  
Day H, Yellman B, Hammer S, Rond C, Bell J, Abbaszadeh S, Stoddard G, Unutmaz D, Bateman L, Vernon SD. **Cognitive impairment in post-acute sequelae of COVID-19 and short duration myalgic encephalomyelitis patients is mediated by orthostatic hemodynamic changes.** Front Neurosci. 2023 Jun 26;17:1203514. doi: 10.3389/fnins.2023.1203514. PMID: 37434760; PMCID: PMC10330752.

# Other AEO Studies– Cognition in Long COVID

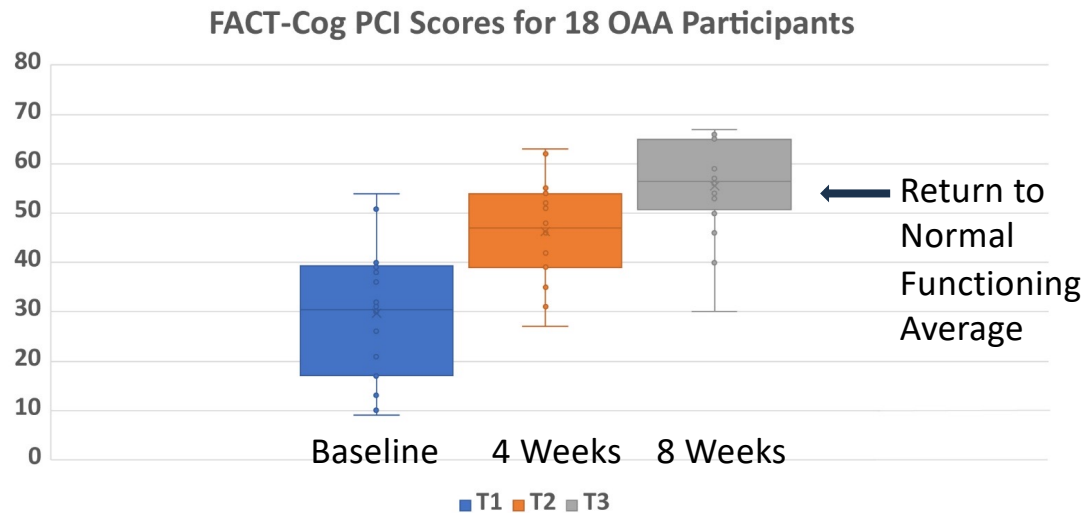


- NCT0540237 REGAIN: RCT of AEO for Fatigue in Long COVID
- 69 Patient Trial
- Significant improvement in Cognition within weeks

# Initial Breast Cancer Survivor Phase 2 Cognitive data is very promising using AEO

## Primary Study Outcome for the Phase II Trial

NCT04290897



- FACT-Cog Functional Assessment of Cancer Therapy- Cognitive Function.

- Mean Change of 26 points SD 14,  $p < 0.001$

- Amelioration of CRCI

- Improvements in secondary Outcomes

- Decreased Fatigue
- Decreased Insomnia
- Improved physical functioning

# Conclusions

- Oxaloacetate is well tolerated in ME/CFS Patients.
- Oxaloacetate helps significantly shift patients to a lower fatigue state, ( $P < 0.005$ ), Reducing energy “Crashes”, increasing Quality of Life.
- Oxaloacetate significantly improves effective Cognitive Function in ME/CFS and Long COVID Patients, decreasing Brain Fog.
- 40.5% of the Oxaloacetate group were “Enhanced Responders” with a clinically significant  $> 25\%$  improvement in fatigue, and 63% average improvement in physical fatigue.



- Oxaloacetate CFS, the first ***medical food*** for the treatment of fatigue in ME/CFS Patients.
- US FDA Allowed Structure/Function Claim:  
***“Oxaloacetate may help alleviate physical and mental fatigue symptoms Associated with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS).”***
- ***“Medical Food”***, does not require a prescription, but does require medical oversight.
- Available at **[OxaloacetateCFS.com](https://OxaloacetateCFS.com)**

