

Utilizing Biological Noise to Optimize Outcomes, and Its Relevance as a Disease-Modifying Intervention for Alzheimer's Disease (AD)

Agus S., Fuerst O., Ilan Y.

Oberon Sciences · Faculty of Medicine, Hebrew University & Hadassah Medical Center, Jerusalem, Israel

KEY TAKEAWAY *Life Lever* — a condition-agnostic AI/ML platform that introduces personalized, label-bounded variability in dose and timing — produced consistent improvements across five treatment-resistant conditions. A proof-of-concept study now applies it to curcumin in early-symptomatic AD, using plasma biomarkers as the primary endpoint.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Setting a strategy to prevent or slow progression of a chronic disease such as Alzheimer's disease (AD) is challenging: progression is non-linear, varies between patients, and newly available AD therapies show low response rates with a high-risk profile. The Constrained Disorder Principle (CDP) provides a framework for understanding the function of biological systems. A growing body of evidence shows that CDP-based interventions — which introduce personalized biological <i>noise</i> — can improve response even when treatment resistance is present. <i>Life Lever</i> is an AI/ML-powered tool that acts as a reminder with controlled variance in dose and timing, within the approved label. It is agnostic to condition or remedy and uses pre-defined measures (e.g., a lab or performance test, or patient-reported outcomes) to guide the variance pattern and optimize outcomes.	A set of open-label studies was conducted in individuals who had experienced a significant degree of treatment resistance. <i>Life Lever</i> guided the the medical treatment to which resistance was experienced. Outcome measures: - Biomarkers - Function tests - Disease scales Follow-up: 6–12 weeks. Conditions tested: - Congestive heart failure (CHF) - Multiple sclerosis (MS) - Gaucher disease - Metastatic cancer - Chronic pain, treated with cannabionoids (real-world study)	In most participants, consistent improvements were observed across all the measures: - Dose reduction — e.g., diuretics in the CHF study - Improved biomarkers — e.g., natriuretic peptides in CHF; imaging in MS and cancer - Improved function — e.g., the 10-metre walk test - Good adherence — >80% engagement in a real-world setting for >3 months <i>Improvements were seen even where prior treatment resistance had limited response — consistent with the CDP hypothesis that bounded, personalized variability restores responsiveness.</i>	<i>Life Lever</i> can be combined with remedies that were tested in AD and showed positive signals but failed in pivotal studies — or were not pursued — due to dosing uncertainties or lack of proprietary position. Planned AD proof-of-concept: - Life Lever combined with curcumin - Population: individuals with early-symptomatic AD - Primary endpoint: plasma biomarkers - Additional endpoints: cognitive and functional tests This positions a CDP-based, label-bounded variability approach as a potential disease-modifying intervention for AD.	- Ilan Y. The constrained-disorder principle defines the functions of systems in nature. <i>Front Netw Physiol.</i> 2024;4:1361915. - Gelman R, et al. A second-generation AI-based regimen improves diuretic resistance in heart failure: a feasibility open-label trial. <i>Biomed Pharmacother.</i> 2023;161:114334. - Lehmann H, et al. A feasibility open-label trial of CDP-based second-generation AI in Parkinson's disease. <i>IBRO Neurosci Rep.</i> 2026. - Sigawi T, et al. Improving response to lenvatinib in partial responders using a CDP-based second-generation AI regimen. <i>Front Oncol.</i> 2024;14:1426426. - Hurvitz N, et al. A feasibility open-label trial of second-generation AI in Gaucher disease on enzyme replacement therapy. <i>J Clin Med.</i> 2024;13(11):3325.

CONTACT

Dr. Shmuel (Sam) Agus, MD

Oberon Sciences

sam.agus@samagus.com

