

Brain-Gut Stimulation as a Novel Therapeutic Approach in Alzheimer’s Disease: Updates from the LIGHT4LIFE Pivotal Trial

Julien Delrieu, CHU de Toulouse, Toulouse, France, **Marie-Noëlle Cufi**, CHIC Castres-Mazamet, Castres, France, **Claire Paquet**, Université Paris Cité, GHU APHP Nord, Hôpital Lariboisière, IHU ReConnect, Paris, France, **Hermine Lenoir**, Hôpital Broca AP-HP, Centre-Université Paris Cité, Paris, France, **Louise Naccache**, CH de Lavour, Lavour, France, **Mélodie Fouillen**, RCTs, Lyon, France, **Guillaume Blivet**, REGENLIFE SAS, Paris, France, **Jacques Touchon**, Université de Montpellier, Montpellier, France.

Brain-gut stimulation, using photobiomodulation represents a novel, non-invasive therapeutic strategy targeting the brain–gut axis in Alzheimer’s disease. The LIGHT4LIFE pivotal trial evaluates the safety, efficacy, and health-economic impact of the RGn600 device in patients with mild to moderate Alzheimer’s disease.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS
Chronic neuroinflammation and dysregulation of the brain-gut axis are increasingly recognized as key contributors to Alzheimer’s disease (AD) pathophysiology. Non-pharmacological interventions capable of modulating systemic and central inflammation may offer complementary or alternative therapeutic options to current drug-based approaches. Simultaneous transcranial and transabdominal stimulation using photobiomodulation can reduce brain-gut axis inflammation, leading to cognitive stabilization or improvement in patients with mild to moderate AD.	LIGHT4LIFE (NCT05926011) is a multicenter, randomized, double-blind, sham-controlled pivotal clinical trial conducted in France. A total of 108 patients meeting McKhann (2011) criteria for mild to moderate AD are randomized to active treatment or sham control. Participants receive 84 sessions (20 minutes each) over 26 weeks using the RGn600 medical device (REGENLIFE, Paris, France). The device delivers combined static magnetic fields and red/near-infrared photonic emissions via a cranial helmet and an abdominal belt. The primary endpoint is change in ADAS-Cog score at 26 weeks. Secondary endpoints include cognitive performance, functional autonomy, quality of life, blood, saliva and fecal biomarkers, safety, tolerability, and a medico-economic evaluation. LIGHT4LIFE: Ongoing Pivotal Trial NCT05926011 Multicentric, double-blind, randomized Inclusion of 108 patients with mild-to-moderate Alzheimer’s disease RGn 54 patients RGn SHAM 54 patients 84 sessions of 20 minutes each, spread over 26 weeks Start Treatment by PBM or Placebo-Sham (6 months) 5 sessions/Wk 3 sessions/Wk 2 sessions/Wk 8 weeks8 weeks10 weeks Follow up 6 months Day 0 W8 W10 W26 W52 Evaluation before treatment Evaluation after 8 weeks Evaluation after 26 weeks Evaluation 26 weeks after End of Treatment Primary endpoint Cognition assessed with the ADAS-Cog score at W26 Secondary endpoints • Cognition + autonomy: Neurological scales / neuropsychological tests • Quality of life + medico-economic impact: Questionnaires with caregiver support • Safety: Adverse events + device deficiencies + blood safety labs + clinical exams • Biomarkers (blood, saliva, feces) sub-study (advancement toward mechanism)	Patient recruitment began in June 2023 and is ongoing across soon seven investigational centers in France. The last patient inclusion is planned for end-2026–early 2027. Final analyses will assess outcomes at 6 months of treatment and 6 months of post-treatment follow-up. Analyses will be conducted in Full Analysis Set, Per Protocol, and Treated Set populations.	Brain-gut stimulation using the RGn600 device may offer a safe, well-tolerated, and scalable technological therapeutic option for mild to moderate AD. Deliverable both in hospital and at home, this approach has the potential to address unmet medical needs while reducing healthcare burden. LIGHT4LIFE will provide evidence on cognitive efficacy and overall impact of this innovative medical device. CONTACT Julien Delrieu delrieu.j@chu-toulouse.fr ---- Guillaume Blivet gblivet@regenlife.com www.regenlife.com ALZHEIMER’S ASSOCIATION AAIC>26