Home-Based Neuromodulation In Major Depressive Disorder: Proliv™Rx Pivotal Study Findings

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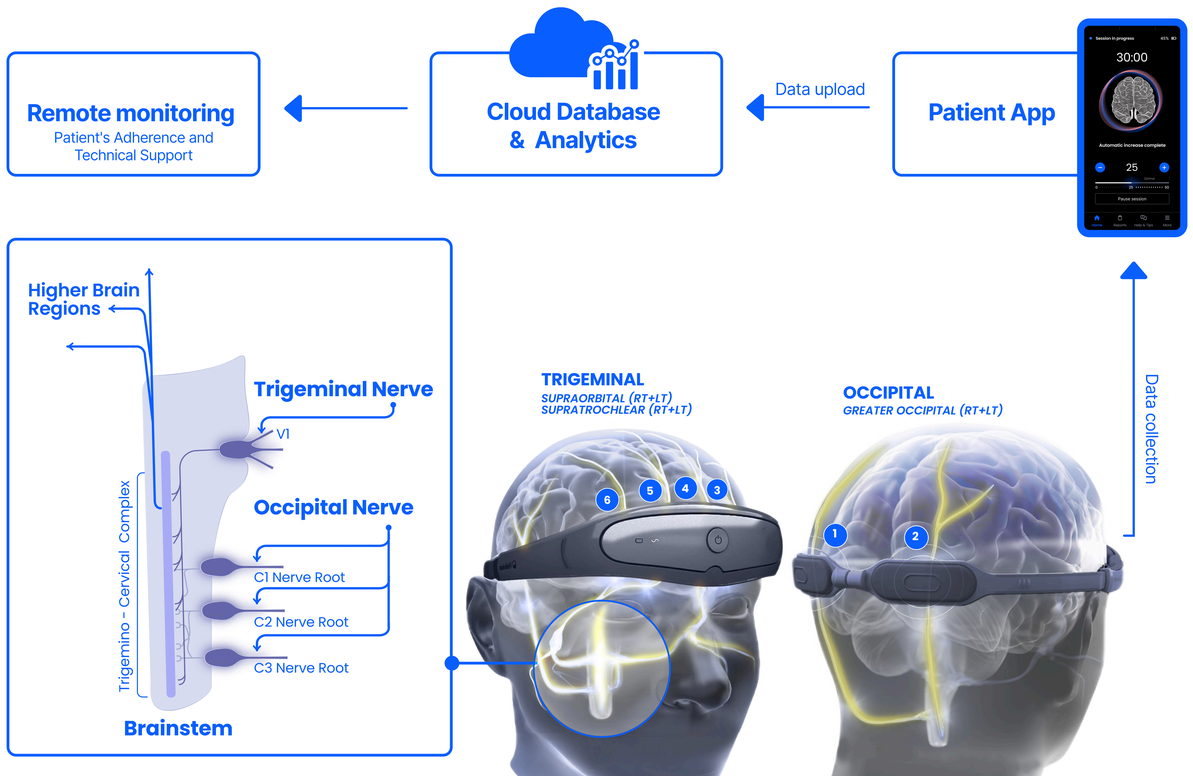
BACKGROUND

- Major Depressive Disorder (MDD) is a leading cause of disability worldwide.
- 20-40% of patients with MDD fail to achieve satisfactory outcomes with antidepressant medications and are left with limited treatment options.
- Neuromodulation therapies such as electroconvulsive therapy (ECT), surgically implanted cervical vagus nerve stimulation (VNS) and transcranial magnetic stimulation (TMS) have shown efficacy in this population, however, each modality presents limitations that restrict accessibility.
- External Combined Occipital and Trigeminal Afferent Stimulation (eCOT-AS) represents a novel, non-invasive neuromodulation approach targeting patients with inadequate response to pharmacotherapy.
- Proliv™Rx is a physician-prescribed, home-based eCOT-AS therapy. It delivers controlled electrical pulses through three output channels and six surface electrodes acting concomitantly on both the occipital and trigeminal nerve branches. These signals are conducted by the target nerves to the brainstem and subsequently to higher brain regions involved in mood regulation and other core symptoms of MDD.
- This pivotal trial was designed to evaluate the safety and efficacy of the Proliv™Rx system in adults with MDD who failed to respond to antidepressant medications.



METHODS

- **Design:** Multicenter, double-blind, randomized, sham-controlled trial conducted across multiple centers.
- **Participants:** 124 adults with moderate to severe MDD (HDRS-21 ≥ 20) and failed to respond to antidepressant medication.
- **Intervention:** Participants were randomized to receive either active or sham Proliv™Rx stimulation, administered as two 40-minute sessions per day for 8 weeks, followed by an additional 8 weeks of active stimulation for all participants.
- **Analysis:** The modified Intent-to-Treat (mITT) analysis included 97 participants.

RESULTS

Outcome	Week 8 (Double Blind)		Week 16 (All Active)	
	Active	Sham	Active (continued)	Cross to active (Initially Sham)
Mean HDRS-17 Reduction (Points)	8.6	6	9.8	9.6
Remission Rate (HDRS-17≤7)	21.3%	6%	32%	22%
50% Responder Rate (HDRS-17 reduction ≥ 50%)	32%	18%	48.8%	48.8%
Clinically Substantial Improvement Rate (HDRS-17 reduction ≥ 7 points)	62%	32%	70.7%	78%

- Other Measures:
  - **Blinding Integrity:** 90% of subjects could not correctly guess their treatment assignment.
  - **Adherence:** Treatment compliance exceeded 96%, demonstrating very high adherence to the daily home treatment.
  - **Safety:** No serious unanticipated adverse events reported.

CONCLUSION

This multicenter, randomized, double-blind, sham-controlled pivotal trial provides evidence that the evaluated home-based, physician-supervised neuromodulation therapy is a safe and effective treatment for patients with major depressive disorder who have failed to respond to antidepressant medications. The study demonstrated a significant reduction in depression severity, high remission rates and excellent adherence.

By extending advanced neuromodulation therapy beyond the clinic, this technology offers a promising solution for patients who currently face barriers to accessing care.