Results of a Phase 2a Clinical Trial of Inhaled Mebufotenin (GH001) in Patients with Postpartum Depression

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Submitter Claus Bo Svendsen

Affiliation GH Research, Dublin, Ireland

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Abstract Background: Postpartum depression (PPD) is a debilitating mood disorder occurring during pregnancy or within four weeks of delivery. PPD represents a substantial perinatal complication that can have serious consequences for both the mother's well-being and the long-term development of the child. Current treatment options are limited, particularly for patients with more severe disease. GH001 is an inhalation formulation of synthetic mebufotenin (5-MeO-DMT) that has been shown to exert ultra-rapid antidepressant effects in patients with treatment-resistant depression. This study investigated the safety and potential antidepressant effects of GH001 in adult patients with PPD.
Methods: This Phase 2a, proof-of-concept, open-label trial enrolled women aged 18-45 years who met the Mini-International Neuropsychiatric Interview diagnostic criteria for major depressive disorder with peripartum onset. Patients were required to have received no other antidepressant therapy for 14 days prior to dosing and have a Montgomery–Åsberg Depression Rating Scale (MADRS) score of ≥28 at pre-dose. GH001 was administered as an individualized dosing regimen (IDR) of at least one and up to three escalating doses (6, 12, and 18 mg) on a single day (Day 1). This trial was conducted under the supervision of a psychiatrist who provided a standard psychiatric assessment during the screening window but did not provide any planned psychotherapeutic intervention intended to enhance the efficacy of GH001 treatment before, during, or after administration. The primary endpoint was the change in MADRS from baseline to Day 8, and MADRS remission (MADRS total score ≤10) was also assessed. The safety and tolerability of GH001 were evaluated up to Day 8.
Results: A total of 10 patients were enrolled in this trial. Mean MADRS total score at baseline was 36.7 (standard deviation [SD]=4.8). Mean change from baseline to Day 8 in the MADRS total score was -35.4 points (SD=5.5; P <0.0001). All patients were in remission 2 hours after their final dose on Day 1, and this was sustained up to Day 2 and Day 8. Inhalation of GH001 was well tolerated and no serious adverse events were reported. All treatment-emergent adverse events were mild or moderate in severity, with the most commonly reported event being headache (n=5), and all other events were only reported once.
Conclusion: In this trial, GH001 demonstrated rapid and significant improvements in depressive symptoms with an acceptable safety profile and remission of PPD.

Author Listing

* Presenting Author

First Name	Last Name	Affiliation
Claus Bo *	Svendsen *	GH Research, Dublin, Ireland
Emilio	Arbe	St. Pancras Clinical Research, London, United Kingdom
Sem E.	Cohen	Department of Psychiatry, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands
Kristina M.	Deligiannidis	Institute of Behavioral Science; Feinstein Institutes for Medical Research; Manhasset, New York
William	Gann	Department of Psychiatry, Sheffield Health and Social Care NHS Foundation Trust, Sheffield, United Kingdom
Sarah	Keady	GH Research, Dublin, Ireland
Rachael	MacIsaac	GH Research, Dublin, Ireland
Stuart	Ratcliffe	St. Pancras Clinical Research, London, United Kingdom
David R.	Rubinow	University of North Carolina, Department of Psychiatry
Dan	Tully	Department of Psychiatry, Sheffield Health and Social Care NHS Foundation Trust, Sheffield, United Kingdom
Velichka	Valcheva	GH Research, Dublin, Ireland
Jasper B.	Zantvoord	Department of Psychiatry, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands
Martin	Johnson	St. Pancras Clinical Research, London, United Kingdom

Signature Claus Bo Svendsen