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A PHASE II RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF GLYX-13 FOR THE RAPID TREATMENT OF MAJOR DEPRESSIVE DISORDER USING CENTRAL RATINGS

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Introduction: NMDA receptor ligands have been shown to rapidly treat depression but are associated with psychotomimetic effects. GLYX-13 is an NMDA receptor glycine site functional partial agonist with ~ 25% of the agonist activity of glycine or D-serine. Animal models suggest a single intravenous dose may produce long-term efficacy without psychotomimetic effects.
Objective: A phase II randomized, double-blind, placebo-controlled trial was conducted to assess the efficacy of GLYX-13 with central raters.
Aim: To examine the effects of a single dose of GLYX-13 in subjects with inadequate response to previous treatment for MDD.
Methods: 48 male and 68 female subjects received a single dose of GLYX-13 (1-/5-/10-/30-mg/kg) or placebo. Central raters assessed subjects via telephone using the HDRS-17 at Screening, Baseline, Days 1, 3, 7, 14, 21 and 28.
Results: The *a priori* primary efficacy ANCOVA on pooled drug dose versus placebo was not significant for change from baseline to Day 1 on HDRS-17 total score. MMRM revealed a statistically significant reduction in HDRS-17 total score versus placebo at Day 3 for 5-mg/kg (-4.4; $p < .05$) and a trend at Day 1 for 5-mg/kg (-3.5; $p=.068$) and at Day 7 for 5 and 10-mg/kg (-4.0 for both; p's=.059 and .073). GLYX-13 did not cause psychotomimetic side effects at any dose studied.
Conclusion: This study suggests that GLYX-13, an NMDA receptor glycine site functional partial agonist, rapidly reduces depression scores without eliciting psychotomimetic effects at therapeutic doses as assessed by central raters. Further study is indicated.

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