Clinical Characteristics of MDD Responders to V1b Receptor Antagonist ANC-501

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Poster M74

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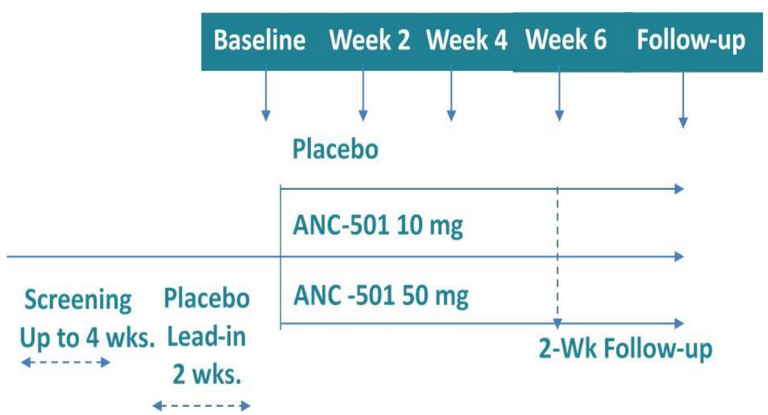
Background

- Repeated or excessive psychosocial stress or trauma, particularly during childhood, can lead to lasting HPA axis impairment, which has been implicated in the pathophysiology of depression and other neuropsychiatric disorders through environmental, genetic, and epigenetic mechanisms [1,2]
- Modulating HPA axis function with HPA axis–targeted therapies may be a promising treatment approach for patients with depression and other neuropsychiatric disorders
- The hormone arginine vasopressin (AVP) plays a key role in HPA axis regulation and cortisol release during stress and exerts its effects via the vasopressin 1b (V1b) receptor [3]
- Blocking the V1b receptor has demonstrated antidepressant-like activities in rodent models of depression, particularly in stressful situations, and has reduced symptoms of depression in patients with elevated HPA axis activity [4]
- We report here the results of MADRS responders and placebo-adjusted MADRS change scores as well as a post-hoc analysis of individual change from baseline MADRS item scores in the high cortisol group (defined as >22.7 nmol/L) in a Phase 2 study in patients with Major Depressive Disorder [5]

Objectives

- To evaluate the change from baseline in MADRS item scores in patients with high urine cortisol
- To determine which MADRS item scores correlated with response at the end of 6-weeks of treatment with ANC-501 and at follow-up in patients with high urine cortisol (>22.7 nmol/L)

Figure 1. Trial Design



Trial Design (cont.)

- Male and female patients between 18 and 65 years of age
- Current DSM-5 diagnosis of MDD confirmed through the MINI-International Neuropsychiatric Interview and SAFER interview administered by expert clinicians from the Massachusetts General Hospital Clinical Trials and Network Institute
- Screening period of up to 4 weeks, 2-week single-blind PBO lead-in, followed by 6-week randomized, double-blind, placebo-controlled treatment period with a 2-week follow-up period
- Patients were required to have remained on the same single SSRI, SNRI or bupropion for at least 6 weeks prior to screening, with a fixed dose for at least 4 weeks prior to screening, and to have had an inadequate response
- Patients remained on a fixed dose of their current ADT for the duration of the study

Methods

- Analysis of combined ANC-501 10 mg and 50 mg MADRS scores in all patients and in patients with high urine cortisol to determine the following:
  - MADRS responders (> 50% improvement vs. baseline) over the double-blind 6-week treatment period and at follow-up (week-8) (Figure 2)
  - PBO-adjusted MADRS change over the double-blind 6-week treatment period (Figure 2)
  - MADRS responders and placebo-adjusted change in MADRS at the end of follow-up (week 8) (Figure 2)
- Analysis of MADRS individual items that correlated with subsequent response at the end of 6 weeks and at follow-up (wk 8) in patients with high urine cortisol (> 22.7 nmol/L) (Table 1)

Figure 2. MADRS - Responders and MADRS Change

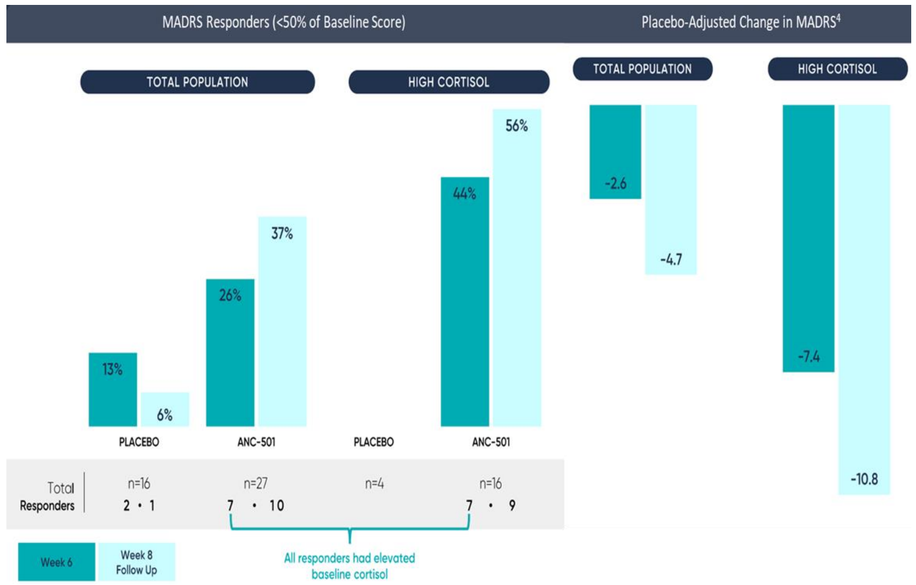


Table 1. Analysis of Individual MADRS Items*

Week 6 n=11 MADRS ITEM	Correlation (r) p value	Week 8 n=11 MADRS ITEM	Correlation (r) p value
Apparent Sadness	—	Apparent Sadness	r(9) = .71 p = .014
Reported Sadness	—	Reported Sadness	—
Inner Tension	—	Inner Tension	r(9) = .73 p = .011
Reduced Sleep	r(9) = .61 p = .046	Reduced Sleep	—
Reduced Appetite	—	Reduced Appetite	r(9) = .72 p = .012
Concentration Difficulties	—	Concentration Difficulties	—
Lassitude	r(9) = .55 p = .078	Lassitude	r(9) = .71 p = .014
Inability to Feel	—	Inability to Feel	r(9) = .66 p = .026
Pessimistic Thoughts	r(9) = .60 p = .049	Pessimistic Thoughts	r(9) = .77 p = .005
Suicidal Thoughts	—	Suicidal Thoughts	—

*Patients with High Urine Cortisol (>22.7 nmol/L)

Discussion

- **Patients with elevated urinary cortisol showed markedly better separation from placebo on MADRS scores at the end of the 6-week treatment period (Figure 2)**
- **MADRS response (> 50% improvement vs. baseline) and MADRS placebo-adjusted change from baseline continued to improve in the high cortisol group at week 8 (Figure 2)**
- **Post-hoc analysis of individual baseline MADRS item scores in the high cortisol ANC-501 group correlated with response at 6 and 8 weeks, including apparent sadness, inner tension, reduced sleep, reduced appetite, lassitude, inability to feel, and pessimistic thoughts (Table 1)**

References

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4. Kamiya M, et al. Efficacy and safety of TS-121, a novel vasopressin V1B receptor antagonist, as adjunctive treatment for patients with major depressive disorder: A randomized, double-blind, placebo-controlled study. J Psychiatr Res. 2020 Sep;128:43-51
5. Data on File Ancora Bio/EmbarkNeuro

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