

The novel compound BNC210 partially reduces Panic Symptom Scale scores in a model of CCK-4 induced panic in healthy volunteers.

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INTRODUCTION

BNC210 is a novel compound in development for the treatment of anxiety disorders. In preclinical models it exhibits anxiolytic and antidepressant effects without inducing side effects associated with benzodiazepines and SSRIs. In a rat model of CCK-4 challenge, BNC210 demonstrates equivalent activity to Diazepam but with a broader therapeutic window. A phase Ib clinical trial was conducted in healthy male volunteers to investigate the effects of BNC210 in a human model of CCK-4 induced panic (1, 2).

METHODS

TRIAL DESIGN

Phase I, single-centre, randomized, double blind, placebo-controlled, two-way crossover design.

TRIAL OBJECTIVES

PRIMARY: To assess the effects of a single dose of BNC210 on CCK-4 induced panic-like symptoms using the Panic Symptom Scale (PSS) (1).
SECONDARY: To assess the effects of a single dose of BNC210:

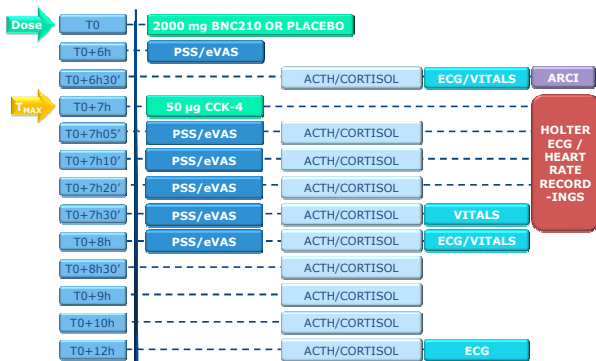
- On CCK-4 induced mood symptoms using the emotional Visual Analog Scale (eVAS) (3);
- On mood parameters using the Addiction Research Center Inventory (ARCI49) (4);
- On CCK-4 induced elevations on heart rate, plasma adrenocorticotrophic hormone (ACTH) and plasma cortisol release.

To assess the safety and tolerability of a single dose of BNC210.

DRUG ADMINISTRATION

Subjects received a single oral dose of 2000 mg BNC210 or vehicle placebo over two consecutive periods one week apart. In each period the subjects received a single i.v. bolus injection of 50 µg CCK-4 at T0+7 hours (BNC210 T_{MAX}).

TRIAL SCHEDULE

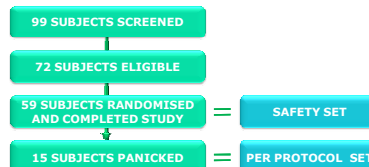


DEFINITION OF A PANICKER

As defined in the protocol:

- ✓ Sudden onset of panic symptoms
- ✓ Endorsement of at least 4 PSS symptoms
- ✓ Score of 2 or higher on Item 15: 'Anxiety or Fear or Apprehension'

DISPOSITION OF SUBJECTS

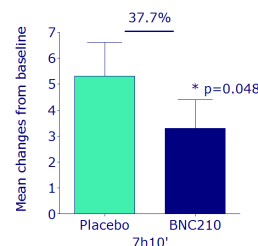


RESULTS:

Reduction in Panic Symptom Scale (PSS) Scores

TOTAL NUMBER OF SYMPTOMS

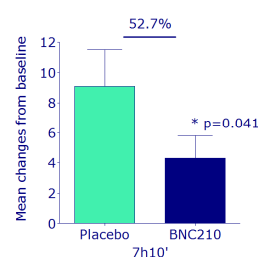
- A single dose of **BNC210 significantly reduced (p=0.048) the total number of symptoms** on the PSS at 10 minutes post CCK-4 injection.



- Subjects on BNC210 experienced **37.7% less symptoms than placebo** treated subjects

TOTAL INTENSITY OF SYMPTOMS

- A single dose of **BNC210 significantly reduced (p=0.041) the intensity of symptoms** on the PSS at 10 minutes post CCK-4 injection.

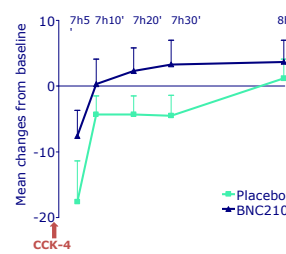


- Symptom intensity was **52.7% less** in BNC210 treated subjects compared to those on placebo

Reduction in Mood Symptoms

EMOTIONAL VISUAL ANALOG SCALE

- A single dose of **BNC210 produced a trend (p=0.104) towards better emotional stability in eVAS scores** at T7h+5 minutes post CCK-4 injection **and a return to baseline levels at T7h+10 minutes.**



- Placebo treated subjects did not return to baseline levels until T0+8h.

RESULTS: SAFETY SET (59 SUBJECTS)

- ACTH and cortisol levels were increased in response to the CCK-4 injection: a single oral dose of **BNC210 significantly reduced the ACTH levels** (p=0.04) at 5 minutes post CCK-4 injection.
- BNC210 treated subjects had 94% probability of having less than 4 symptoms on the PSS** compared to placebo treated subjects.
- A single oral dose of **BNC210 had no effect on subjective feelings associated with drugs of abuse as assessed by the ARCI 49.**
- A single oral dose of **BNC210 was safe and well-tolerated:**
 - No serious adverse events were reported.
 - No clinically significant changes in electrocardiogram, vital signs or laboratory parameters were reported.

CONCLUSIONS

- BNC210 produced a statistically significant reduction of both the Total Number and Total Intensity of the panic-like symptoms induced by a CCK-4 injection in healthy male subjects. This was observed at 10 minutes post CCK-4 injection.
- BNC210 produced a positive trend on the emotional stability of subjects suffering a CCK-4 induced panic attack.
- The reduction of panic symptoms in this study provides evidence for the anxiolytic activity of BNC210 in humans in a challenge setting. This finding is supported by the EEG data presented at ECNP 2011, which shows that BNC210 produces an increase in fast beta activity which has been associated with the anxiolytic activity of benzodiazepines (5).

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