The novel compound BNC210 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 and but with a broader therapeutic window.

A phase I 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 (ARC19) (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 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 Tmax).

TRIAL SCHEDULE

RESULTS:

Reduction in Panic Symptom Scale (PSS) Scores

<table>
<thead>
<tr>
<th>Treatment</th>
<th>T0+6h</th>
<th>T0+8h</th>
<th>T0+7h</th>
<th>T0+12h</th>
<th>T0+30'</th>
<th>T0+7h 30'</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>BNC210</td>
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</tbody>
</table>

Reduction in Mood Symptoms

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean Change from baseline</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-0.5</td>
<td></td>
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<tr>
<td>BNC210</td>
<td>-0.8</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

DISPOSITION OF SUBJECTS

99 SUBJECTS SCREENED
77 SUBJECTS ELIGIBLE
59 SUBJECTS RANDOMIZED AND COMPLETED STUDY
15 SUBJECTS PANICKED

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 ARC49.

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 beta activity which has been associated with the anxiolytic activity of benzodiazepines (5).

REFERENCES


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