Results

Conclusions

Background

- Posttraumatic stress disorder (PTSD) is a major public health problem, particularly among active military personnel and veterans
- The Veterans Health Administration (VHA) has observed a 60% increase in PTSD diagnosis between 2001 and 2007, with approximately 229,000 of 1.64 million (14%) veterans of Operations Enduring Freedom and Iraqi Freedom meeting diagnostic criteria for PTSD
- While several empirically-supported pharmacological and behavioral interventions are available for individuals with PTSD, a majority of patients continue to experience PTSD following treatment
- Cannabidiol (CBD) has been shown to modulate the endocannabinoid system, which regulates physiological processes including pain sensation, mood, and memory
- In PTSD treatment models, various formulations of CBD have been shown to reduce anxiety, particularly among those with anxiety disorders
- Improve sleep
- A permeation-enhanced synthetic CBD transdermal gel — ZYN002 — is being developed for treatment of PTSD
- As an initial step toward the examination of ZYN002, the objectives of this study were to evaluate the:
  - Safety and tolerability of ZYN002
  - Cognitive effects of ZYN002

Methods

- Single-dose, randomized, double-blind, placebo-controlled trial in healthy volunteers
- Subjects were randomized 3:1 to receive single applications of ZYN002 transdermal gel or placebo
  - The gel was applied to clean, dry, intact skin of the shoulders and/or upper arms by a member of the research facility
  - Subjects were not permitted to wash the application site for at least 12 hours after application
- Study drug treatments were applied as follows:
  - Period 1: ZYN002 50 mg (1% × 5 g)
  - Period 2: ZYN002 100 mg (1% × 10 g)
  - Period 3: ZYN002 125 mg (2.5% × 5 g)
  - Period 4: ZYN002 250 mg (2.5% × 10 g)
- Placebo:
  - Periods 1 and 3 (5 g)
  - Periods 2 and 4 (10 g)
- Outcome measures included:
  - Safety/Tolerability: baseline, 15, 30, 60, and 120 minutes, and 1, 2, 4, 6, 8, 12, 16, 24, 36, 48, 72, and 96 hours post-application
  - Physical exams
  - Application site irritation
  - Vital signs and pulse oximetry
  - Electrocardiograms (EKGs)
  - Safety laboratories
  - Urinalysis
  - Spontaneously reported adverse events
- Cognitive Effects (Trail Making Test [A and B]): baseline and 2, 4, 8, and 24 hours post-application
  - Time to complete each trail
  - Total line length

Results

Table 1. Demographics (N = 32)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), n (%)</td>
<td>25.9</td>
</tr>
<tr>
<td>Min, max</td>
<td>19.0, 52.0</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>21 (65.6)</td>
</tr>
<tr>
<td>Female</td>
<td>11 (34.4)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>25 (78.1)</td>
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<tr>
<td>Asian</td>
<td>2 (6.3)</td>
</tr>
<tr>
<td>Various*</td>
<td>5 (15.6)</td>
</tr>
</tbody>
</table>

*1 subject each was classified as Brazilian, White/Caribbean, White/Black, Latino, White/Asian

Table 2. Treatment-Emergent Adverse Events

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Period</th>
<th>Placebo</th>
<th>Pooled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal discomfort</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Vessel puncture site bruise</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Headache</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Erythema*</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

*93 dressing tape and blood pressure cuff

No effects of Drug Condition or Drug x Time interactions were observed

Safety/Tolerability

- The incidence of treatment-emergent adverse events with ZYN002 was similar to placebo (Table 2)

Figure 1. Time to Completion, Trail A (msec)

Future work — a Phase 2a clinical trial of the effects of ZYN002 in patients with PTSD

Conclusions

- ZYN002 has an acceptable tolerability profile for the treatment of PTSD
- The frequency and severity of adverse events with ZYN002 were comparable to placebo
- There was no evidence of cognitive impairment on the Trail Making task, a validated measure of psychomotor ability and executive function, indicating psychomotor functioning and executive function were not impacted by exposure to ZYN002

Cognitive Effects

- For line length, no main effects of Drug Condition and No Drug x Time interaction were found on Trails A or B
- For time to completion, subjects receiving 50 mg ZYN002 outperformed those in the placebo group on Trail A (Figure 1)

References