Supplemental Information

1. Key Assessment Tools
   a. PTSD Checklist for DSM IV/V (PCL-5): A 20-item self-report measure that assesses the 20 DSM-IV/V. The PCL-5 serves to monitor symptoms change during and after treatment, screen individuals for PTSD, and diagnose PTSD. Other versions are PCL-S (specific), PCL-M (military), PCL-C (civilian). Interpretation should be completed by clinician.
      i. Assessment Areas:
         1. Symptom change during and after treatment
         2. Screening individuals for PTSD
         3. Provisional PTSD diagnosis
      ii. Scoring:
         1. 0 – not at all
         2. 1 – A little bit
         3. 2 – Moderately
         4. 3 – Quite a bit
         5. 4 – Extremely
   b. Clinician-Administered PTSD Scale (CAPS): The gold standard in PTSD assessment, a 30-item structured interview. Can be used to make current (past month) diagnosis of PTSD, make lifetime diagnosis of PTSD, and assess PTSD symptoms over the past week.
      i. Assessment:
         1. 20 DSM-5 PTSD symptoms
         2. Onset and duration of symptoms
         3. Subjective distress
         4. Impact of symptoms on social and occupational functions
         5. Overall PTSD severity, and specifications for the dissociative subtype
      ii. Scoring:
         1. 0 – Absent
         2. 1 – Mild / subthreshold diagnosis
         3. 2 – Moderate / clinically significant
         4. 3 – Severe / Markedly elevated, difficult to manage
         5. 4 – Extreme / incapacitating, pervasive and unmanageable
   c. Post-traumatic Diagnostic Scale (PDS): A 49-item self-report measure recommended for clinical or research settings to measure severity of PTSD symptoms related to a single identified traumatic event. Assesses all of DSM-IV criteria for PTSD (i.e. Criteria A-F) and inquires about the past month. In addition, measures the severity of PTSD symptoms (Criteria B, C, and D).
      i. Assessment:
         1. Trauma checklist
         2. Respondents description of traumatic event
         3. Assessment of the 17 PTSD symptoms by rating 0 to 3.
         4. Assessment of interference of the symptoms
ii. Scoring: PTSD diagnosis through algorithm that rates individual’s responses to meet the following criteria:
   a. Traumatic event involves injury or life threat
   b. Person felt helpless or terrified during event
   c. Endorsement (rating > 1) of at least one re-experiencing symptoms, three avoidance symptoms, and two arousal symptoms
   d. Duration at least one month
   e. Impairment in at least one area of functioning

2. Assessment of the 17 PTSD symptoms by rating 0 to 3.
   a. 0- “not at all or only one time”
   b. 1- Once a week or less/once in a while
   c. 2- 2 to 4 times a week
   d. 3- “5 or more times a week/always”

3. Global Assessment of Functioning Scale (GAF):Clinician administered and assigns a clinical judgment in numerical fashion to the individual’s overall functioning level in psychological, social, school, and occupational.
   i. Assessment:
      1. Psychological
      2. Social
      3. Occupational
   ii. Scoring:
      1. 100 to 0 in increments of 10-points, higher scores describe higher level of functioning and less risk of harm to self or others
      2. 100-91: Superior Functioning, no distress over life’s problems
      3. 60-51: Moderate symptoms: flat circumstantial speech, occasional panic attacks OR moderate difficulty in social occupations, or social functioning
      4. 30-21: Behavior considerably influenced by delusions or hallucinations OR serious impairment in communication or judgment, acts grossly inappropriately
      5. 10-1: Persistent danger of severely hurting self or others (e.g., recurrent violence) OR persistent inability to maintain minimal personal hygiene OR serious suicidal act
      6. 0: inadequate information

4. Clinical Global Impressions (CGI): severity and improvement of illness and global improvement on a 7-point rating scale.
   i. Assessment: Each component of the CGI is rated separately; the instrument does not yield a global score
      1. Illness severity (CGI-S)
      2. Global improvement or change (CGI-C)
      3. Therapeutic response
   ii. Scoring: severity scale
      1. 1 – very much improved
2. 7 – very much worse

f. **PHQ-9**: Patient reported for monitoring the severity of depression and response to treatment

g. **Pittsburgh Sleep Quality Index (PSQI)**: sleep quality and sleep disturbances

h. **Nightmare Frequency Questionnaire (NFQ)**: Self-reported, number of nightmares experienced on a nightly basis

2. **Appendix B**: McAllister et al. 2015

   a. Patient demographics
      i. n=75, aged 18-55 years
      ii. 47% civilian participants vs military experienced in study groups

   b. Inclusion
      i. diagnosis of PTSD and/or traumatic brain injury (TBI)

   c. Exclusion
      i. sensitivity or adverse reaction to study drugs
      ii. pregnant women or planning to become pregnant
      iii. history of glaucoma
      iv. cardiac conditions
      v. seizure disorders

   d. Intervention
      i. Week 0 – initiated GAL 4 mg BID, increased to 12 mg BID at week 4
      ii. Week 0 – initiated MPH 5 mg BID, increased to 10 mg BID at week 4, then 20 mg BID at week 8
e. Results

i. MPH treatment demonstrated an overall reduction of PTSD symptoms assessed by PCL-S
3. **Appendix C**: Cameron et. al 2016

![Graph showing N=104, Mean 4.4 Axis I Diagnoses (SD 1.6)
Maximum of one diagnosis credited for alcohol and/or substance abuse

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol/Substance Abuse</td>
<td>10.0%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>9.0%</td>
</tr>
<tr>
<td>Mood</td>
<td>7.0%</td>
</tr>
<tr>
<td>PTSD &amp; similar</td>
<td>6.0%</td>
</tr>
<tr>
<td>Dysthymia</td>
<td>5.0%</td>
</tr>
<tr>
<td>Bipolar</td>
<td>4.0%</td>
</tr>
<tr>
<td>Schizophrenia/Schizoaffective</td>
<td>3.0%</td>
</tr>
<tr>
<td>ADHD</td>
<td>2.0%</td>
</tr>
<tr>
<td>Depressive</td>
<td>1.0%</td>
</tr>
</tbody>
</table>

a. Intervention
   i. Mean initial dose – 1.4 mg daily (0.5-2.0 mg)
   ii. Mean final dose – 4.0 mg daily (0.5-6.0 mg)
   iii. Mean length of use - 11.2 weeks (1 day-36 weeks); total 1229.9 weeks for total-cohort

b. Adverse effects
   i. 27.8% experienced at least of the following – sedation, dry mouth, feeling “stoned”, orthostatic hypotension, agitation, headache
   ii. 1.9% - most serious reported adverse effect of psychosis, but patient had pre-existing psychotic illness


   a. Patient demographics:
      i. Initial Global Impression of Severity of PTSD of 3.3 ± 0.9

   b. Intervention
      i. Dosage initiated at 0.5mg, titrated weekly to max 3.0mg based on efficacy (nightmare suppression) and tolerability

   c. Inclusion
      i. PTSD diagnosis of operational origin at least 2 years prior to screening
      ii. History of distressing nightmares; CAPS > 5 recurrent distressing dreams and difficulty falling asleep

   d. Exclusion
      i. Significant cognitive impairment
      ii. Positive illicit drug screen, including tetrahydrocannabinol (THC)

   e. Methods
i. Randomized 1:1 ratio to NAB vs PBO for two separate 7-week periods (1 and 2)

ii. Dosage started at 0.5mg given 1 hour before bedtime and titrated weekly to max 3.0 mg based on efficacy (nightmare suppression) and tolerability

iii. Dose achieved at week 5 was maintained, continued for final 2 weeks

iv. 2-week washout separated periods 1 and 2

5. **Appendix E**: Roitman et al (2014)

   a. Rating Scales
      i. Review Appendix A

   b. Concurrent psychotropic use for PTSD (n/mean dose, mg)
      i. Duloxetine - 3/70
      ii. Escitalopram – 3/13.3
      iii. Mirtazapine – 2/45
      iv. Bupropion – 2/225
      v. Clonazepam – 5/2
      vi. Lorazepam – 3/3

   c. Inclusion
      i. Diagnosis of PTSD per DSM-IV Criteria A through F

   d. Exclusion
      i. Prior cannabis use or no use for last 6 months
      ii. Patients with frequent dissociative episodes
      iii. Women who were currently pregnant or nursing
      iv. Patients not using reliable method of contraception
      v. Patients with suicidal ideation
      vi. Patients with concurrent psychosis, alcohol, or drug abuse

   e. Methods
      i. 1 week - Clinical Assessment 1 (CA1) – 2.5 mg (0.1cc) sublingually BID, 1 hour after waking and 2 hours before bed
      ii. Tolerated doses were increased to 5 mg (0.2 cc) BID until end of trial

   f. Adverse effects
      i. Dry mouth, n=2
      ii. Headache, n=1
      iii. Tremor, n=1
Sources


