



A Randomized, Placebo-Controlled Trial of the Dopamine-β-Hydroxylase (DBH) Inhibitor, Nopicastat, for the Treatment of PTSD in OIF/OEF Veterans



Traci Dutton, PharmD, Lori Davis, MD, Catherine Ball, LCSW,
Allison Kluz, MS, Ann Mahaney-Price, CRNP, Katherine Muhlstadt, PharmD
Tuscaloosa VA Medical Center (TVAMC), Tuscaloosa, AL

BACKGROUND

Current events have led to an increase in posttraumatic stress disorder (PTSD). A survey of US combat infantry units reported that approximately 20% of those who served in Iraq and 12% of those who served in Afghanistan reported symptoms consistent with PTSD.

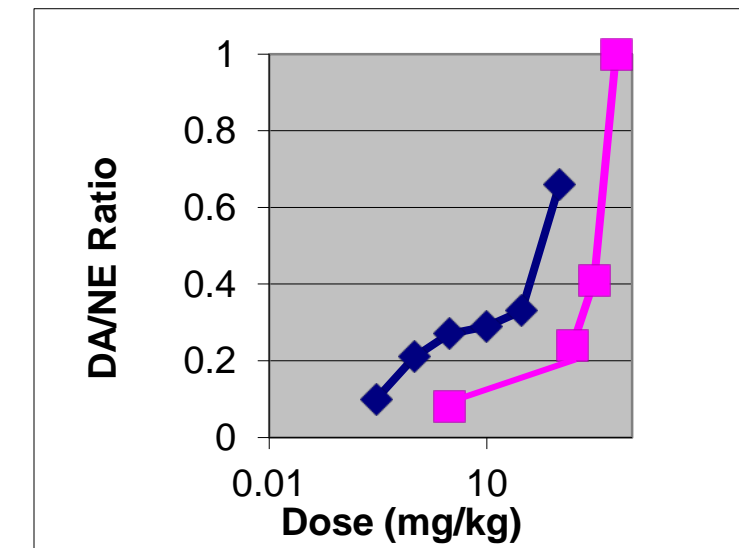
PTSD is a chronic and costly illness that is associated with significant dysfunction, premature death, increased risk of suicide, increased substance abuse/dependence, and long-term disability, especially if left untreated.

Unfortunately, current treatments for PTSD are not very effective and thus, novel treatments for PTSD are needed. Preclinical and clinical research define a substantial increase in norepinephrine (NE) activity associated with PTSD. Recent clinical studies have shown improved PTSD hyperarousal symptoms by reducing the NE hyperactivity using agents like NE post-synaptic antagonists. Key support for the proposed study with nopicastat is based on a similar improvement in PTSD symptoms after a study that reported reduced hyperarousal symptoms after treatment with disulfiram, a weak DBH inhibitor

NEPICASTAT: A dopamine-β-hydroxylase inhibitor

Dopamine (DA) is converted to norepinephrine (NE) by dopamine-β-hydroxylase (DBH). Dopamine-β-hydroxylase inhibitors decrease the amount of norepinephrine by inhibiting DBH conversion of dopamine to norepinephrine.

Nopicastat (pink) is a DBH inhibitor, and increases the DA-to-NE ratio in animal brain more potently than disulfiram (blue).



METHODS

Study Design: A phase II, 6-week, prospective, multi-site, double-blind, placebo-controlled, randomized clinical trial (RCT) of nopicastat monotherapy for PTSD in 120 subjects who have previously served in a combat zone during Operation Iraqi Freedom and Operation Enduring Freedom (OIF/OEF). The RCT will be followed by an 8-week open extension phase in which patients who have a defined positive clinical response to the study medication will continue on open-label nopicastat to evaluate longer-term safety and efficacy.

Clinical Sites: Veterans Affairs Medical Centers: Tuscaloosa VA; Houston VA; Charleston VA; San Diego VA; Bronx VA

OUTCOMES

Hypothesis to be Tested: Subjects treated with nopicastat will have significantly reduced PTSD symptoms than those treated with placebo.

Assessments: Subjects will be assessed at baseline, weekly for 6 weeks, and then every 2 weeks for an additional 8 weeks.

Primary Outcome: Clinician-Administered PTSD Scale (CAPS) hyperarousal subscale D (CAPS-D)

Secondary Outcomes: Clinician-Administered PTSD Scale (CAPS) total and subscales, Montgomery Asberg Depression Rating Scale, Clinical-Global Severity and Improvement, Quality of Life Enjoyment and Satisfaction Questionnaire, Davidson Trauma Scale, and the Sheehan Disability Scale

RESULTS

This study is ongoing. There are no results at this time. Nopicastat is a novel agent seeking FDA approval.

DISCLOSURE

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

Traci Dutton: Nothing to disclose
Lori Davis: Consultant—Eli Lilly; Speaker—AstraZeneca; Research — AstraZeneca
Catherine Ball: Nothing to disclose
Allison Kluz: Nothing to disclose
Ann Mahaney-Price: Nothing to disclose
Katherine Muhlstadt: Nothing to disclose

CDMRP Grant Number: W81CWH-08-2-0071 and W81XWH-09-1-0287. Study medication provided by Synosia Therapeutics.