

PT150 FOR TREATMENT OF “LONG HAUL COVID” FEATURED POSTER AT THE NEUROSCIENCE CLINICAL-TRANSLATIONAL RESEARCH SYMPOSIUM

Palisades Therapeutics' PT150 for symptoms associated with long haul COVID syndrome requested for possible inclusion in the NIH RECOVER COVID Studies

CLIFFSIDE PARK, NJ, UNITED STATES,
September 30, 2022 /

EINPresswire.com/ -- The novel

Coronavirus disease 2019 (COVID-19)

outbreak is a major health threat caused by the Severe Acute Respiratory Syndrome Coronavirus 2 ([SARS-CoV-2](#)). SARS-CoV-2 has caused a wide range of disease severity among the patients.

COVID-19 affects approximately 45 million Americans, out of that 10-30% are estimated to be

“long haulers.” A growing body of clinical and preclinical evidence implicates hypothalamic-pituitary-adrenal (HPA) axis dysfunction as the neurologic and psychological aspects of long COVID-19. PT150 is an oral dose clinical stage glucocorticoid receptor (GR) antagonist with antiviral activity against COVID-19 with an active IND.

“

beneficial results for long haul COVID, & the direct antiviral actions of PT150 are likely to diminish or eliminate potential rebound infections as have been seen following other anti-covid treatments”

Neil Theise, MD (Palisades Therapeutics and NYU)

A multi-center, randomized, double-blind, paroxetine-controlled, flexible dose study with PT150 in patients with major depressive disorder was conducted. The Hamilton Rating Scale for Depression (HDRS), the most widely used clinician-administered depression assessment scale, was administered to determine clinical efficacy. PT150

treatment for 4-weeks equally reduced the symptoms of depression measured by HDRS score compared to the selective serotonin reuptake inhibitor (SSRI) paroxetine. In particular, PT150 showed significantly increased efficacy in subsets of depressed patients displaying HPA-axis dysfunction (as measured by high levels of serum cortisol), compared to paroxetine. Similarly, in



another clinical trial, we also observed that the treatment of PT-150 is particularly effective in depressed patients with HPA-axis dysregulation compared to the antidepressant clomipramine. Importantly, our collaborators have also demonstrated for the first time a significant inhibitory antiviral activity in in vitro COVID-19 model using human bronchial epithelial lining cells (Theise et al., 2020), and in vivo COVID-19 infection model using Syrian hamster (Rocha et al., 2022). These data have been accepted for presentation at the 2022 Neuroscience Clinical-Translational Research Symposium at the University of Kentucky.

Selective glucocorticoid receptor (GR) antagonist, PT150 as a potential therapeutic candidate for depression in long haul COVID-19 patients

Chirayu D. Pandya, PhD^{1,2*}, Neil D. Theise, PhD^{3,4*}, Christopher B. Verrojo, PhD⁵, Deeben Baker, PhD⁶, Christopher J. McLouth, PhD^{6*}, and James Z. Porter-Ford, MD, PhD⁷

¹University of Kentucky Department of Neurosurgery, ²Center for Advanced Translational Studies, ³Spinal cord and Brain Injury Research Center, ⁴Neurology, ⁵Biostatistics, ⁶Microbiology, Immunology, and Molecular Genetics, ⁷Department of Pathology, ⁸Palisades Therapeutics, New Jersey; ⁹Department of Psychiatry & Behavioral Sciences, Baylor College of Medicine, Houston; ¹⁰Department of Psychiatry, School of Medicine, University of California, San Francisco

Introduction

The novel Coronavirus disease 2019 (COVID-19) outbreak is a major health threat caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). COVID-19 affects approximately 45 million Americans, out of that 10-30% are estimated to be "long haulers." A clinical and preclinical evidence implicates hypothalamic-pituitary-adrenal (HPA) axis dysfunction as the neurologic and psychological aspects of long COVID-19. The HPA axis is the body's main stress response system, and cortisol is the major glucocorticoid hormone produced by the adrenal cortex in humans. A negative feedback system involving glucocorticoid receptors (GR) regulates HPA axis activity and cortisol secretion.

A multiple collaboration research team, clinical trial with PT150 in patients with major depressive disorder (MDD) was performed. PT150, formerly known as ORG 34517, is an oral dose clinical stage GR antagonist with anabolic activity. Because selective antagonism of GRs may regulate HPA axis function and depression, we conducted a clinical trial using two flexible dose regimens of PT150 in subjects with MDD, also in comparison with paroxetine (selective serotonin reuptake inhibitor, SSRI). Also the possible association between HPA axis and HAM-D-21 (Paroxetine depression rating scale with 21 item) score in MDD patients were determined in comparison with paroxetine after two and four weeks of PT150 treatment. Moreover, the reported beneficial effects of SSRI for long COVID-19 neuropsychiatric conditions, further support the potential candidature of PT150. Similarly, the therapeutic effects of PT150 in post-COVID-19 depressed patients utilizing our "Kentucky Infection Treatment Excellent" (KITE) research registry is under progress.

Clinical Trial Plan

Previous work: Preclinical studies demonstrated for the first time a significant inhibitory antiviral activity in in vitro COVID-19 model using human bronchial epithelial cells (Theise et al., 2020), and in vivo model using Hamster (Rocha et al., 2022).

The experiment: This was a multi-center, multi-national, randomized, double-blind, paroxetine controlled flexible dose trial of PT150 in subjects with MDD. The total number of subjects was to be 150, of whom at least the first 50 (40 subjects on PT150 and 10 subjects on paroxetine) were to be hospitalized at least for the last three days of the screening period and first seven days of active treatment (Day 3 until Day 7). The dates of hospitalization and discharge were to be recorded in the Drug Accountability forms at baseline and Day 28.

Groups: Group 1: Received a starting dose of 150 mg PT150 (this group will be referred to as L, i.e., low dose, group). Group 2: Received a starting dose of 450 mg PT150 (this group will be referred to as H, i.e., high dose, group) and Group 3: Received a starting dose of 20 mg paroxetine (paroxetine group).

HAM-D-21: It was a reliable questionnaire for assessing depression severity, guilty conscience, suicide idea, sleeping difficulty, weight loss, decline of ability, and cognitive disturbance, etc. A higher score of HAM-D-21 was indicative of a more severe depression (non-depression, <7 points; depression, >7 points).

Conclusions

The results conclude that PT150 treatment for 4 weeks equally reduced the symptoms of depression, compared to the paroxetine. Interestingly, PT150 showed significantly increased efficacy in subjects of MDD patients displaying HPA axis dysfunction compared to the paroxetine.

Results

Table 1: Dosing schedule (approximate)

Time	Group 1 (mg/Day)	Group 2 (mg/Day)	Group 3 (mg/Day)
1-4	150 mg	450 mg	20 mg
In case the starting dose was not tolerated, the dose could be reduced as follows:			
5-8	150 mg	150 mg	20 mg
In case of inadequate response the dose could be increased as follows:			
9-10	150 mg	450 mg	20 mg
In case the dose increase was not tolerated, the dose could be reduced to the previous level:			
11-13	150 mg	150 mg	20 mg
14-15	150 mg	450 mg	20 mg


Table 2: Summary of results with the change from Figure 1-4.

GR antagonist	Assessment	Baseline (n=10)	Post-treatment (n=10)
L (Low dose)	Day 7	24.000	14.000
	Day 14	24.000	14.000
	Day 21	24.000	14.000
	Day 28	24.000	14.000
H (High dose)	Day 7	24.000	14.000
	Day 14	24.000	14.000
	Day 21	24.000	14.000
	Day 28	24.000	14.000
Paroxetine	Day 7	24.000	14.000
	Day 14	24.000	14.000
	Day 21	24.000	14.000
	Day 28	24.000	14.000

Figure 1: Change from baseline in morning cortisol levels (ng/ml). **Figure 2:** Change from baseline in DHEA-S levels (µmol/L). **Figure 3:** Change from baseline in testosterone levels (nmol/L). **Figure 4:** Change from baseline in testosterone levels (nmol/L).

Figure 5: Box plot (joined median) of the HAM-D-21 total score. **Figure 6:** Scatter plot between the change from baseline cortisol and change from baseline in testosterone levels (nmol/L). **Figure 7:** Change from baseline in cortisol by treatment group and responder outcome to the 50% reduction in HAM-D-21 total score.

2022 NEUROSCIENCE CLINICAL-TRANSLATIONAL RESEARCH SYMPOSIUM



UKY Neuroscience Poster

Since, neuroinflammatory changes have been implicated in long haul COVID syndrome, underlying symptoms such as depression, fatigue, memory dysfunction, and "brain fog", it is postulated that cortisol-mediated neuroinflammation can be down regulated by PT150. Pre-clinical data for PT150 strongly supports these findings, with protective effects against models of viral/infectious neuroinflammation (lipopolysaccharide, tumor necrosis factor, poly I:C), decreased pro-inflammatory interleukins (IL-6 and IL-1B), and inhibition of SARS-CoV-2 microgliosis in brains of infected Syrian hamsters. RNA silencing of glucocorticoid receptor in these models mitigates the benefits of PT150 further supporting the HPA-axis modulatory effects as a primary and targeted therapeutic against neuroinflammation underlying long haul COVID-19. Palisades' lead scientist [Dr. Neil Theise](#) states "Not only do we expect beneficial results for symptoms of long haul COVID, but the direct antiviral actions of PT150 are likely to diminish or eliminate potential rebound infections as have been seen following other anti-covid treatments." Moreover, in support of [Palisades Therapeutics](#), University of Kentucky's faculty and Palisades' scientific advisor, Dr. Chirayu D. Pandya and his collaborators are planning to evaluate the therapeutic effects of PT150 in post-COVID-19 depressed patients utilizing "Kentucky Infection Treatment Excellent" (KITE) research registry, University of Kentucky.

In light of the potential of PT150 for therapeutic benefit in patients with long haul COVID neurological and psychological symptoms, PT150 has been requested for possible inclusion in the NIH RECOVER COVID Clinical Studies.

Palisades invites leading companies such as Glaxo Smith Kline (NYSE: GSK), Johnson & Johnson (NYSE: JNJ) and Pfizer Inc. (NYSE: PFE) to review our data.

Randi Altschul
Pop Test Oncology/Palisades Therapeutics
+1 201-943-3770
randi@palisadestherapeutics.com

This press release can be viewed online at: <https://www.einpresswire.com/article/593432985>

EIN Presswire's priority is source transparency. We do not allow opaque clients, and our editors try to be careful about weeding out false and misleading content. As a user, if you see something we have missed, please do bring it to our attention. Your help is welcome. EIN Presswire, Everyone's Internet News Presswire™, tries to define some of the boundaries that are reasonable in today's world. Please see our Editorial Guidelines for more information.

© 1995-2022 Newsmatics Inc. All Right Reserved.