INPLASY PROTOCOL

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None declared.

Efficacy and Safety of PRC-063 for Attention-deficit/hyperactivity disorder: A systematic review and meta-analysis from randomized controlled trials

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Review question / Objective: **We conducted a systematic review and meta-analysis from randomized controlled trials to evaluate the efficacy and safety of PRC-063 for Attention-deficit/hyperactivity disorder.**
Condition being studied: **Attention-deficit/hyperactivity disorder (ADHD) is diagnosed with the core symptoms including inattention, hyperactivity and/or impulsivity.Current treatment options for ADHD include pharmacological treatment, behavioral therapy, and combination therapy of the two treatments above. Methylphenidate (MPH) and the extended-release formulation, as a first-line pharmacological treatment of ADHD, have been widely researched in the world.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 December 2022 and was last updated on 18 December 2022 (registration number INPLASY2022120073).

INTRODUCTION

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inattention, hyperactivity and/or impulsivity. Current treatment options for ADHD include pharmacological treatment, behavioral therapy, and combination therapy of the two treatments above. Methylphenidate (MPH) and the extended-release formulation, as a first-line pharmacological treatment of ADHD, have been widely researched in the world.

METHODS

Participant or population: 1215 patients (663 male, 552 female) from U.S. and Cananda were involved into this systematic review and meta-analysis.

Intervention: The intervention is PRC-063.

Comparator: The comparative intervention is placebo.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: Studies were included if they met the following criteria: (i)Study type: only RCT; (ii)Population: ADHD patients 6 years or older; (iii)Intervention: PRC-063 at any dose versus placebo; (iv)Outcomes: reporting the efficacy and safety endpoints. Exclusion criteria were defined as follow: conference abstracts, reviews, case reports, observation studies, long-term extension studies and reports about pharmacokinetics.

Information sources: We searched articles from inception to October 2022 in PubMed, EMBASE and Cochrane Library databases, using keywords related to ADHD, PRC-063 and randomized controlled trials (RCT). Our research was based on published data and data from ClinicalTrials.gov.

Main outcome(s): ADHD-5-RS was used to assess participants' ADHD symptoms. It was an 18-question scale (0 = not present; 3 = severe; total score of 0 to 54) based on the 18-item DSM-5 diagnostic criteria for ADHD(DuPaul et al. 2016). We applied SKAMP, a scale designed to evaluate the drug effect during 16 hours, to assess inattention and behavior problems in a classroom environment(Wigal et al. 1998). CAARS-S was a 26-item tool completed by participants that measures outcome in the following domains: inattention and memory problems, hyperactivity and restlessness, impulsivity and emotional liability, and problems with self-concept(Conners et al. 1999). For PERMP, the subjects were asked to complete as many of the math problems given as possible in 10 minutes. Permanent Product Measure of Performance – Total (PERMP-T) score was the summation of problems attempted (PERMP-A) and problems correct (PERMP-C) in a 10-min session(Swanson et al. 2000). CGI-I was used to grade improvement compared with baseline on a scale of 1 (very much improved) to 7 (very much worse)(Guy and 76 1976). PSQI was utilized to assess sleep habits and quality with 19 self-rating items(Buysse et al. 1989). It supports the efficacy of the drug with a low score in the scales mentioned above.
Treatment-emergent adverse events (TEAEs) involved serious TEAEs, treatment-related TEAEs, drug withdrawal due to TEAEs and several TEAEs. To be specific, TEAEs included headache, insomnia, nausea, irritability, dry mouth, decreased appetite, abdominal pain upper and upper respiratory tract infection.

Quality assessment / Risk of bias analysis: Review Manager 5.4 software was used to measure the risk of bias. We referred uniform criteria of the Cochrane collaboration to evaluate the risk of bias RCTs, including selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias. The result of each aspect was divided into low risk, unknown risk, or high risk.

Strategy of data synthesis: The information was extracted from included trials:1) trial characteristics: first authors, published year, country, National Clinical Trial (NCT) number, study period, number of participants; 2) patient characteristics and baseline data: the specific statistics of intervention and control groups, age, gender, Body-mass index(BMI), ADHD subtype; 3) study design and intervention

characteristics: include RCT, different dose of PRC-063 as intervention group and placebo as control group; 4) data of outcomes: ADHD DSM-5 Rating Scale (ADHD-5-RS), Clinical Global Impressions-Improvement Score (CGI-I), Conners' Adult ADHD Rating Scale–Self: Short Form (CAARS-S), Swanson, Kotkin, Agler, M-Flynn, and Pelham Scale (SKAMP),Permanent Product Measure of Performance (PERMP), and number of treatment-emergent adverse events (TEAEs), serious TEAEs, drug withdrawal due to TEAEs, treatment-related TEAEs, each reported TEAE.

Subgroup analysis: To answer the question about safety of types of intervention (different dosages), we conducted subgroup analysis among 25mg/d, 45mg/d, 70mg/d, 100mg/d. Similarly, considering the age factor, we compared the effects of PRC-063 when divided into adult (≥18) and minor (6-18) subgroups.

Sensitivity analysis: Sensitivity analysis was conducted by removing each RCTs one by one to estimate effectiveness of individual study on pooled effect size.

Country(ies) involved: China (The First Affiliated Hospital of Soochow University).

Keywords: PRC-063; Methylphenidate; Attention-Deficit/Hyperactivity Disorder; Meta-analysis.

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