This single-center, randomized, double-dummy, double-blind, two-part study comprised Dose Selection (Part A) and Main Study (Part B). Part A was designed to identify the maximum tolerated dose (MTD) of KP201/APAP. Study participants included experienced opioid users, male or female, 18 to 55 years of age, including those who had not yet been dependent on opioids. Participants were screened and qualified to be enrolled into sequential parallel groups (4 subjects each) for each of 8 tablets, with 40 patients randomized with 60 planned completions.

Methods

The study was registered, double-blind, double-dummy, four-arm study comprising a Dose Selection (Part A) and Main Study (Part B). Part A was designed to identify the maximum tolerated dose of both KP201/APAP and HB/APAP. Subjects were categorized as opioid abusers, and the study was blinded. Study participants included experienced opioid users, male or female, aged 18 to 55 years of age, including those who had not yet been dependent on opioids. Participants were screened and qualified to be enrolled into sequential parallel groups (4 subjects each) for each of 8 tablets, with 40 patients randomized with 60 planned completions.

Results

Study Participants. Of 50 subjects admitted to the qualification criteria (Part A), 40 subjects participated in the Dose Selection Study and 46 subjects completed the Main Study. Of 50 subjects admitted to the qualification criteria (Part A), 40 subjects participated in the Dose Selection Study and 46 subjects completed the Main Study.

Drug Liking effect curve was calculated for time zero to 0.5 hours across treatments post-dose up to 2 hours for oral and IN HB/APAP and IN KP201/APAP. The LS geometric mean ratios for C max and AUCs were calculated.

Pharmacokinetic (PK) Analyses. During Part B, plasma hydrocodone concentration was assessed in blood samples obtained pre-dose and 0.083, 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours post-dose. Descriptive statistics were calculated for parameters including maximum observed concentration (C max), area under the curve (AUC), and other PK parameters. The plasma hydrocodone concentration-time curve from time zero to 2 hours post-dose was log-transformed and analyzed using a linear mixed-effects model (EXTRA and ACU). The least square (LS) geometric mean and 90% CI were calculated using the SAS conditional confidence interval confidence level.

Pharmacodynamic Analyses. During Part B, all post-dose Drug Liking scores were evaluated. Adverse events, especially for Drug Liking effect curve was calculated for time zero to 0.5 hours across treatments post-dose up to 2 hours for oral and IN HB/APAP and IN KP201/APAP. The LS geometric mean ratios for C max and AUCs were calculated.

Relative Bioavailability, Intranasal Abuse Potential, and Safety of Benzhydrocodone/Acetaminophen, a Novel Immediate-Release Hydrocodone Prodrug Combination, Compared With Oral Hydrocodone Bitartrate/Acetaminophen in Recreational Drug Abusers

Sven Guenther, Travis Mickle, Kathryn Roupe, Jing Zhou, Beatrice Setnik, Vincent Lam, Talar Hopyan, Catherine Mills

KemPharm, Coralville, IA; Worldwide Clinical Trials, Austin, TX; INC Research, Raleigh, NC; INC Research, Toronto, ON

Background

Immediate-release (IR) hydrocodone combination products are the most commonly prescribed opioid abusers. KP201/APAP was formulated as 6.67/325 mg tablets, relative to equimolar doses of hydrocodone bitartrate plus aspirin (30/1000 mg capsules). Relative bioavailability, intranasal abuse potential, and safety of KP201/APAP were compared to that of IR hydrocodone combination products designed to deter non-oral abuse, has been combined with acetaminophen, benzhydrocodone hydrobromide, and hydrocodone bitartrate.

Objectives

To compare the bioavailability, intranasal (IN) abuse potential, and safety of KP201/APAP, formulated as 6.67/325 mg tablets, relative to equimolar doses of hydrocodone bitartrate plus aspirin (30/1000 mg capsules) in non-dependent, non-chronically

Methods

A peak difference of at least 15 points on the bipolar visual analog scale (VAS) for Drug Liking effect curve was calculated for time zero to 0.5 hours across treatments post-dose up to 2 hours for oral and IN HB/APAP and IN KP201/APAP. The LS geometric mean ratios for C max and AUCs were calculated.

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