Study design.

Objective

• During the study was prohibited except in a medical emergency

• Hydromorphone is a particularly sought after drug of abuse, and severe pain

• Non-oral routes of abuse (i.e., intranasal, intravenous) are commonly reported (Butler 2011)

• Hydromorphone products are commonly prescribed for the treatment of moderate to severe pain

• In a human pharmacokinetic study, KP511 administrated intravenously showed markedly reduced bioavailability compared with intravenous hydromorphone (data on file, KemPharm, Inc.)

• One subject withdrew consent prior to the second dosing period and two subjects were excluded due to protocol deviations

• Subjects underwent a 21-day screening and washout period prior to the study

Methods

Study participants

• Healthy adults, 18 to 55 years of age (inclusive), with a body mass index (BMI) between 18 and 32 kg/m² and a minimum weight of 50 kg (110 lb) who have previously been taken and tolerated opioids

• Female subjects were required to use an acceptable form of birth control

• The administration of concomitant medications other than ibuprofen during the study was prohibited except in a medical emergency

Study design

• This was an open-label, randomized, single-dose, four-treatment, four-period, crossover study that consisted of a screening period followed by a four treatment periods that were separated by a minimum 7-day washout period

• Twenty-four (24) eligible subjects were scheduled to receive separate, single oral doses of 4 mg, 8 mg, and 16 mg of KP511 liquid, and 4 mg of hydromorphone HCl (Ondansetron); Liquid, equivalent to 8 mg of KP511 according to a randomization schedule, under fasted conditions

• All eligible subjects also received naltrexone HCl (50 mg) tablets with according to a randomization schedule, under fasted conditions

• Twenty-four (24) eligible subjects were scheduled to receive separate, single oral doses of 4 mg, 8 mg and 16 mg of KP511 liquid, and 4 mg of hydromorphone HCl (Ondansetron); Liquid, equivalent to 8 mg of KP511 according to a randomization schedule, under fasted conditions

• Subjects underwent a 21-day screening and washout period prior to the study

• All eligible subjects also received naltrexone HCl (50 mg) tablets with glucagon

Results

A total of 24 subjects participated in the study, 23 completed at least two periods of the study and 22 completed all four treatment periods. One subject withdrew consent prior to the second dosing period and therefore was excluded from the analysis

• Mean (SD) age was 35.3 (6.0) years, mean (SD) weight was 72.6 (18.0) kg and mean (SD) height was 170.0 (7.9) cm

Pharmacokinetic Findings

• Plasma concentrations of intact KP511 were below the limit of quantitation in all subjects

• Figure 1 shows that for hydromorphone and all doses of KP511, plasma concentrations were low and peaked at approximately 30 min, and were below the limit of quantitation in most subjects at the end of the sampling period

Conclusions

• The lack of systemic exposure of the produg KP511 indicates that KP511 effectively releases active hydromorphone into systemic circulation after oral administration

• KP511, 8 mg was bioequivalent to hydromorphone HCl, 4 mg with respect to overall hydromorphone exposure, while plasma concentrations were approximately 19% lower

• KP511 produced dose-proportional increases in peak hydromorphone plasma concentrations over the 4 mg – 16 mg dose range

References


4. KemPharm, Inc., Corkhill, JA, USA. Design support was provided by Research Triangle Graphics LLC

Support

This study was funded by KemPharm, Inc., Corkhill, JA, USA. Design support was provided by Research Triangle Graphics LLC

Disclosures

Rene Braeckman, Travis Mickle and Sven Guenther are employees of KemPharm, Inc., Corkhill, Michael Nutti and Cynthia Zamos are employees of Worldwide Clinical Trials.

Support

This study was funded by KemPharm, Inc., Corkhill, JA, USA. Design support was provided by Research Triangle Graphics LLC.