Pharmacokinetics and Abuse Potential of KP511, a Novel Prodrug of Hydromorphone, after Intranasal Administration in Recreational Drug Users

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Objective
The objective of this study was to assess the pharmacokinetics and abuse potential of a prodrug of hydromorphone (KP511), following intranasal administration to recreational drug users in an inpatient controlled setting.

Methods
Study participants were recreational opioid users who were not currently physically dependent on opioids (based on DSM-5 criteria), but who used opioids for non-treatment purposes (i.e., for psychoactive effects) within the last 12 months.

Experience with intranasal opioid use was collected through a cross-sectional survey. Only those who reported no prior opioid use were selected for enrollment in the study.

Statistical Analyses
The primary comparison of interest was performed for hydromorphone pharmacokinetic parameters (Cmax, AUC0-t, t1/2) using a mixed-effects model. Treatment comparisons were evaluated using the Wilcoxon Signed-Rank Test. Least-squares (LS) means geometric means provided a measure of relative bioavailability for the Test (16.1 mg KP511 API) to Reference (8 mg HM HCl API) ratios of geometric LS Means were used to assess the exploratory endpoints.

Results
A total of 26 subjects were randomized, of whom all completed the study (KP511: n = 13, HM HCl: n = 13). The mean (SD) weight was 77.1 (11.6) kg and 75.2 (12.1) kg for KP511 and HM HCl, respectively. Subsequent analysis of the randomized treatment revealed no significant differences between the two groups.

Safety Results
Overuse effects were assessed using validated and novel scales, including nasal discomfort, respiratory, thoracic and mediastinal disorders, general disorders and adverse events, and non-specific safety parameters (Nasal Care) study. No significant adverse effects were reported.

Pharmacodynamic Assessments
The primary endpoint was pharmacokinetic withdrawal of HM from the blood following intranasal administration of KP511 compared with KP511.

Conclusions
These collective findings suggest that KP511 may have reduced intranasal abuse potential relative to HM HCl API.

References

Disclosures
Sven Guenther, Travis Mickie, Andrew Barrett, Adam Smith, Rene Braeckman, Debra Kelsh, Bradley Vinson are employees of VinciPharm, Inc., Coralville, IA. USA. Design support was provided by Research Triangle Graphics, LLC.