구연 5

Evaluation of the Pharmacokinetics and Safety/Tolerability of Avanafil, a Novel Phosphodiesterase Type 5 Inhibitor in Healthy Korean Subjects

JA Jung, SM Choe, SH Cho, JL Ghim, UJ Kim, HS Lim, KS Bae

Clinical Pharmacology & Therapeutics, Asan Medical Center

Background/Aims: This study assessed the pharmacokinetics and safety/tolerability of avanafil, a fast-acting highly selective phosphodiesterase type 5 (PDE5) inhibitor, in Korean male subjects.

Methods: A double blinded, randomized, placebo-controlled, dose-escalation study was conducted in Asan Clinical Research Center. Thirty healthy subjects were randomly allocated into 3 dose groups (avanafil:placebo = 8:2 in each dose groups) and they received once daily oral doses of either 50, 100, 200 mg of avanafil or placebo for 7 days. Safety assessments including Farnsworth-Munsell 100-Hue test were also performed. Blood samples were obtained at predose and predefined time points after dosing. Pharmacokinetics of avanafil on day 1 and day 7 were analyzed by noncompartmental methods and compared among three dose groups. The observed accumulation index (AI_{obs}) was calculated as day 7 Cmax/day 1 Cmax.

Results: Avanafil was rapidly absorbed reaching peak plasma concentrations 0.33~0.5 hours (Tmax) and then declined bi-exponentially with terminal elimination half-life ($t_{1/2\beta}$,) of 5-11 hours, irrespective of doses, or single vs. multiple administrations. Cmax and AUC increased proportionally with increment of doses. Accumulation on multiple dosing was little in that AIobs were below 1. There were no serious adverse events and the incidence of adverse events was not related to doses. There were no significant difference in Hue test scores, changes in QTc intervals, and the frequency of adverse events between placebo and avanafil.

Conclusion: Avanafil were well tolerated and showed linear PK on dosing 50~200 mg/day over 7 days.