Food Effect and Absolute Bioavailability Study of WCK 2349 and WCK 771 in Healthy Adult Human Volunteers in US

R. Chugh1, F. Lakdavala1, S. Bhagwat2, M. Patel2, A. Bhatia1; 1Wockhardt, Mumbai, India, 2Wockhardt, Aurangabad, India

Background: WCK 771 (IV) and WCK 2349 (PO) are L-arginine salt and L-alanine ester prodrug, respectively, of levonadifloxacin (active moiety), a benzoquinolizine quinolone. These agents are being developed for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and hospital-acquired bacterial pneumonia (HABP) caused by methicillin-resistant Staphylococcus aureus (MRSA). This study was conducted to evaluate the effect of food on the pharmacokinetics of levonadifloxacin administered as oral WCK 2349 and determine the absolute bioavailability of WCK 2349 1000 mg (QD dose) with respect to WCK 771 800 mg (QD dose) in healthy volunteers. Methods: This was a randomized, crossover, food-effect and absolute bioavailability study conducted in three parts i.e., Period 1 and Period 2 (food-effect study) and Period 3 (absolute bioavailability study). In Period 1 and 2, 12 subjects were randomly assigned (1:1) to receive 1000 mg of WCK 2349 (oral dose) as QD dose for one day either in fed state or fasting state (Period 1). After a wash out period of 3 days, subjects were crossed over to the other arm (Period 2). In Period 3, all 12 subjects from the food-effect study were administered WCK 771 800 mg intravenously as QD dose for one day in fasting state after a wash out period of 3 days. Results: The mean $\text{AUC}_{0-\infty}$ of levonadifloxacin after single oral dose of WCK 2349 in fasting state was 147.31 $\mu\text{g}\cdot\text{hr}/\text{ml}$. The mean $\text{AUC}_{0-\infty}$ of levonadifloxacin after 800 mg intravenous dose of WCK 771 in fasting state was 131.89 $\mu\text{g}\cdot\text{hr}/\text{ml}$. The absolute bioavailability of WCK 2349 as compared to WCK 771 was 89.35%. In the fed state, the mean levonadifloxacin $C_{\text{max}}$ was reduced by approximately 27% relative to the fasted state with a 2-hour delay in median time to maximum concentration ($T_{\text{max}}$). Conclusion: Based on high oral bioavailability, a switch over therapy (WCK 771 to WCK 2349) is possible for the treatment of ABSSSI and HABP patients. Lack of a significant food effect would facilitate WCK 2349 administration irrespective of fed status.

R. Chugh,
Wockhardt Role(s): Employee.
F. Lakdavala,
Wockhardt Role(s): Employee.
S. Bhagwat,
Wockhardt Role(s): Employee.
M. Patel,
Wockhardt Role(s): Employee.
A. Bhatia,
Wockhardt Role(s): Employee.