Pharmacokinetics of Intravenous Levonadifloxacin Administered as WCK 771 in Healthy US Adults

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Background: WCK 771 is an L-arginine salt of benzoquinolizine quinolone levonadifloxacin with enhanced activity against methicillin resistant Staphylococcus aureus (MRSA) and quinolone-resistant staphylococci. It is being developed as a parenteral anti- MRSA agent for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and hospital acquired bacterial pneumonia (HABP).

The primary objective of this analysis was to characterize the pharmacokinetics of multiple doses of 600, 800 and 1000 mg of WCK 771 administered twice daily for 5 days by IV infusion in healthy adult human subjects. Methods: Intensive venous blood samples were collected per protocol, and WCK 771 plasma concentrations were measured with either HPLC or LC-MS/MS. Non-compartmental analysis was performed on data obtained from 10 subjects on 600 mg BID, 9 subjects on 800 mg BID and 10 subjects on 1000 mg BID WCK 771. A total of 10 doses over 5 days were administered as 1 hr IV infusion. The analysis was performed using Phoenix WinNonlin. Results: The mean Cmax,ss (at day 5) was 16.67, 19.57 and 22.09 µg/ml for 600, 800 and 1000 mg BID doses respectively. With a 1.66 fold increase in dose from 600 mg to 1000mg, the Cmax,ss and AUC(0-24),ss increased 1.32 and 1.42 fold at Day 5, respectively. The volume of distribution (Vz) ranged from 145.34 to 172.0 L while the CL,ss ranged from 6.7 to 8.2 L/hr. The terminal half-life was calculated to be 8.5 to 12.0 hrs. Based on the observed profiles at day 1 and 5 and also based on Cmax comparison at day 1 and day 5, the accumulation factor ranged from 0.99 to 1.10 representing no or minimal accumulation. Conclusions: With a 1.66 fold increase in dose from 600 mg to 1000 mg, there was 1.32 fold and 1.42 fold increase in Cmax and AUC, respectively. The terminal half-life was found to be similar between doses. The doses were well tolerated at all levels.

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Wockhardt Role(s): Research Contractor.
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Wockhardt Role(s): Research Contractor.
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