Pharmacokinetics of Intravenous WCK 771 in Healthy Indian Male Adults

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Background & Objective

- WCK 771, a novel broad-spectrum fluoroquinolone with enhanced activity against MRSA and quinolone-resistant staphylococci, is being developed by Wockhardt as a parenteral anti- MRSA agent[1-3].
- The primary objective of this analysis was to characterize the pharmacokinetics (PK) of intravenous (IV) WCK 771 in healthy adult Indian male volunteers.

Methods

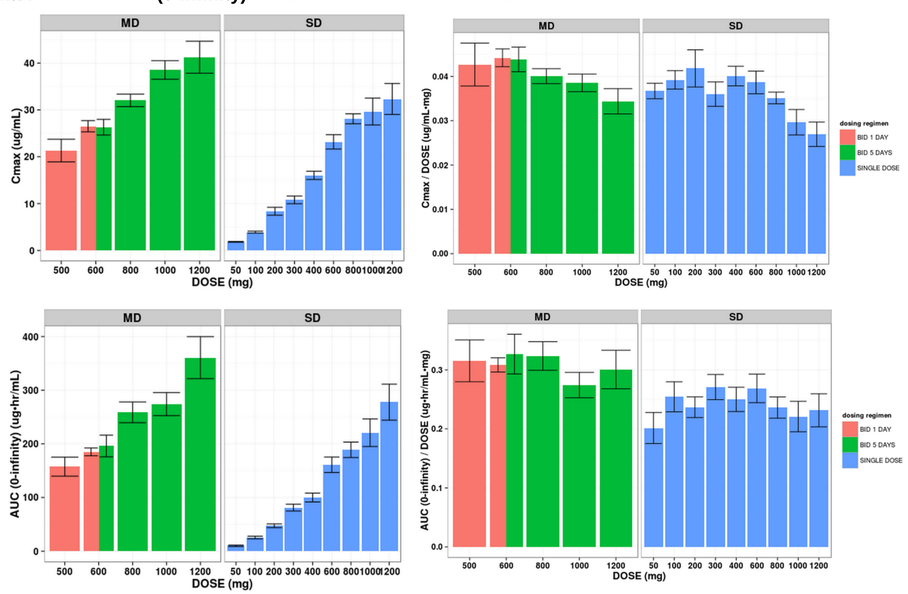
- Intensive venous blood samples were collected per protocol, and WCK 771 plasma concentrations were measured with either HPLC or LC-MS/MS.
- Data from escalating single doses (50 mg, 100 mg, 200 mg, 300 mg, 400 mg, 600 mg, 800 mg, 1000 mg and 1200 mg) and multiple doses (500 mg and 600 mg twice daily (BID) for 1 day; 600 mg, 800 mg, 1000 mg and 1200 BID for 5 days) was analyzed using a non-compartmental approach with Pheonix WinNonlin.

Results

Table 1: Mean Pharmacokinetic Parameters of WCK 771 for all dose levels

			C_{max} (ug/mL)		$t_{1/2}$ (hr)		Vd (L)		CL (L/hr)		$AUC_{(tau)}$ (ug·hr/mL)		$AUC_{(0\text{-}infinity)}$ (ug·hr/mL)	
STUDY	DOSE (mg)	N	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
S.D.	50	6	1.84	0.21	3.60	1.55	24.78	1.72	5.39	1.66			10.07	3.22
S.D.	100	6	3.92	0.51	5.60	1.17	28.16	2.47	4.09	0.80			25.43	6.23
S.D.	200	6	8.36	2.05	5.69	0.39	29.80	4.95	4.35	0.87			47.34	8.61
S.D.	300	6	10.80	2.02	7.45	0.86	32.14	2.94	3.80	0.68			81.25	15.68
S.D.	400	6	16.03	2.17	7.82	1.08	28.65	4.53	4.13	0.82			99.99	20.17
S.D.	600	6	23.19	3.77	6.69	3.05	31.37	7.29	3.87	0.81			161.09	35.46
S.D.	800	6	28.11	2.58	6.77	0.97	34.07	3.34	4.37	0.85			188.89	35.30
S.D.	1000	6	29.66	7.03	6.38	0.40	36.98	12.38	4.92	1.73			220.87	63.08
S.D.	1200	6	32.33	8.08	7.23	2.10	41.27	8.96	4.67	1.44			277.66	82.21
BID×1D	500	6	21.33	5.93	6.13	1.20	36.18	7.81	4.48	1.17			157.62	43.39
BID×1D	600	6	26.52	2.96	5.47	0.77	31.31	3.65	4.17	0.30			185.04	17.80
BID×5D	600	7	26.30	4.42	6.83	1.97	36.00	5.07	4.32	0.70	142.97	30.08	195.89	53.44
BID×5D	800	8	32.04	3.80	6.80	1.86	32.70	3.21	4.18	0.72	195.96	31.03	258.80	54.76
BID×5D	1000	5	38.54	4.43	7.03	1.26	36.08	6.55	4.80	0.89	213.30	34.26	274.15	48.12
BID×5D	1200	6	41.26	8.37	7.19	1.32	40.02	4.05	4.72	0.92	263.15	54.29	360.68	96.02

Figure 1: Mean (±SE) C_{max} and $AUC_{(0\text{-}infinity)}$ (left panel) and dose normalized C_{max} and $AUC_{(0\text{-}infinity)}$ (right panel) in single and multiple dose studies



Results/Discussion

- Linear increase in C_{max} and $AUC_{(0\text{-}infinity)}$ was observed from 50 – 1200 mg single doses. The ranges for dose normalized C_{max} and $AUC_{(0\text{-}infinity)}$ were 0.027-0.042 ug/mL/mg and 0.20-0.27 ug·hr/mL/mg, respectively.
- For BID for 5 days, the $AUC_{(tau)}$ at steady state was not significantly different to the $AUC_{(0\text{-}infinity)}$ after respective single doses at all four dose levels. Accumulation can be observed after multiple doses.
- Terminal elimination half-life ($t_{1/2}$) remained constant at around 6 – 8 hrs throughout single and multiple doses.

Conclusions

Conclusions: Single and multiple dose PK studies for WCK771 show that the drug was well tolerated and the PK are linear across all dose levels.

References

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