A Phase I Study to Determine Safety, Tolerability and Pharmacokinetics (PK) of Finafloxacin (FIN) in Healthy Subjects

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Methods

The study was an open, randomized, double-blind, placebo-controlled, dose-escalating study to evaluate the safety, tolerability, pharmacokinetics and urinary excretion of finafloxacin. Healthy male and female subjects aged 18-55 years were recruited. Eligible subjects had to be non-smokers, non-vegan, alcohol-free and caffeine-free within 24 hours of dosing. Finafloxacin hydrochloride administered orally to healthy male and female subjects aged between 18 and 55 years.

Results and Discussion

FIN is a novel fluoroquinolone (FQ) under early clinical development. FIN exhibits optimal activity at slightly acidic pH (pH 5.0-6.0). A combined Phase I study protocol was designed to evaluate safety, tolerability and pharmacokinetic profiles of single and multiple doses of FIN.

FIN absorption was rapid, with t<sub>max</sub> values of 0.5-2 hours. C<sub>tmax</sub> and AUC<sub>0→inf</sub> increased almost linearly with dose. The median value of total body clearance was 28.0 and 53.0 L/hr for 400 mg and 800 mg, respectively.

Finafloxacin plasma concentration vs. time curve for multiple dose of FIN.

- No clear difference of AEs experienced by subjects taking FIN or placebo was observed.
- The tolerability of FIN/Placebo tablets given as a single dose revealed a favorable safety profile.
- FIN was well tolerated following single dose and when given for 7 consecutive days (part B).
- The tolerability of FIN as compared with placebo.
- FIN contains a novel base component which confers improved bactericidal activity at slightly acidic pH (pH 5.0-6.0) under which other marketed FQs exhibit significantly reduced activity.
- FIN exhibited superior activity to comparator FQs against multidrug-resistant strains.

Results and Discussion

Finafloxacin (FIN) Phase I study in healthy subjects revealed a favorable pharmacokinetic profile with high C<sub>tmax</sub> and zero/off halflife.

- FIN was well tolerated following single dose and when given for seven days in a range of doses up to 800 mg.
- Human safety data do not suggest any quantitatively higher or qualitatively different toxicity for FIN as compared with placebo.
- Overall, these findings indicate that the risk of serious adverse reactions to finafloxacin hydrochloride can be expected to be very low. Given the possible therapeutic effects of FIN, further clinical development of the drug appears justified and can be recommended.

Conclusion

- The FIN Phase I study in healthy subjects revealed a favorable pharmacokinetic profile with high C<sub>tmax</sub> and zero/off halflife.

Literature

7 Naber et al., 48th ICAAC, Washington DC 2008.