Systemic Safety Profile of Solithromycin in Phase 1 & 2 Clinical Trials

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Background:

Solithromycin (soli), a fluoroketolide with potent activity against azi-resistant (R-) CABP pathogens and *N. gonorrhoeae,* is under study for CABP and STD treatment. The prototype ketolide, telithromycin, was notably associated with liver injury and visual disturbance. A macrolide with activity against R-pathogens and an improved safety profile is desirable.

Methods:

Phase 1 & 2 safety data summary.

Results:

171 healthy subjects (Phase 1 trials) and 64 patients (Phase 2 CABP) have received oral soli, with total exposure up to 4200 mg administered over 7 days. Across all oral dosing studies, the most common AEs were diarrhea (12.8%), headache (12.8%), and nausea (10.2%), most of mild severity; rates among placebo (PBO) or comparator treated subjects were 3.6, 11.4 and 12.9%, respectively. In Phase 2 CABP, AEs occurred more frequently with levofloxacin than soli. Across all trials, SAEs have been reported for 2 soli recipients; in both, not drug related (chest pain; fall with bone fracture and subsequent SAEs; CABP patients). Among all subjects receiving oral soli, ALT elevation >3x ULN was observed once, in a CABP patient with baseline (BL) elevated ALT due to HCV infection and peak ALT < 3x BL. In comparison, 2 levofloxacin treated patients in the CABP trial experienced ALT elevation > 3x ULN. No treatment limiting ECG abnormalities or reports of visual disturbance occurred.

91 healthy adults have received IV soli in a Phase 1 trial, with max single dose exposure of 1000 mg (additional single dose oral soli in 12). Among single dose recipients (n=60), diarrhea, nausea and headache were reported in 0, 6.7, and 8.3%, vs 0, 0 and 20.8% among PBO recipients, respectively. Among multiple dose recipients (n=31), diarrhea, nausea and headache were reported in 0, 0, and 12.9% vs 3.6, 3.6, and 7.1% among PBO recipients, respectively. No SAEs, no ALT elevation >3x ULN, no visual disturbance and no treatment limiting ECG abnormalities were observed.

Conclusions:

Among 314 soli recipients to date, no significant safety concern or signal has emerged. These data support ongoing study of solithromycin, a promising new fluoroketolide.

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