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Paper Poster Session
Omadacycline in vitro and in vivo

Effect of age and gender on the pharmacokinetics of the oral and IV omadacycline, a new class of aminomethylcyclines

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Background: Omadacycline is the first of a new class of antibiotics, the aminomethylcyclines, currently in phase 3 clinical development as a once daily oral and intravenous (IV) formulation for CABP and ABSSSI. Two phase 1 studies were undertaken to evaluate the effect of age and gender on the pharmacokinetic (PK) of omadacycline after oral and IV administration in healthy volunteers.

Material/methods: Both were double-blind and placebo-controlled studies of single oral doses of omadacycline in subjects randomized in a 3:1 ratio to omadacycline or placebo. Study 1 included 4 subject groups: A) young males; B) young females; C) elderly males; D) elderly females. After an 8-hour overnight fast, each group received placebo or omadacycline 200 mg. Study 2 included healthy young male and female subjects who received a single 200 mg oral or IV dose of omadacycline or placebo. Blood samples were obtained pre-dose, and 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 18, 24, 48, 72 and 96 hours post-dose to determine PK parameters.

Results: In Study 1 (23 subjects), a high degree of consistency was observed for the PK characteristics of a single 200 mg oral dose. No significant difference in drug exposure was observed between fasting young and elderly subjects. Both young and elderly females exhibited greater mean AUC_{inf} values than corresponding young and elderly male subjects (14.6 mcg*h/mL vs. 9.4 mcg*h/mL for all female and all male subjects; ratio 0.64, 90% CI: 0.52, 0.80). For elderly vs. young subjects, the mean ratio was 1.13 (90% CI: 0.91, 1.41). In Study 2 (24 subjects), evaluation of PK profiles showed a high degree of consistency between males and females who received a 200 mg oral dose of omadacycline. The AUC_{inf} ratio of males to females was 1.02 (2-sided 90% CI 0.69, 1.50). The geometric mean half-life was 17.2 hours for the males and 11.4 hours for the females. The $AUCi_{nf}$ for IV omadacycline exhibited more variability in female (18.4%) than in male subjects (4.9%) but the 90% CI for mean AUC_{inf} ratio for males to females was within the specified range (ratio 0.77, 90% CI: 0.67, 0.89). Omadacycline oral and IV formulations were well tolerated with no unexpected safety or tolerability adverse events.

Conclusions: After a single oral administration of 200 mg of omadacycline, female subjects demonstrated higher mean AUC_{inf} compared to male subjects. However, the exposure in females did not differ significantly after a single IV dose. No effect of age on omadacycline absorption and PK profile was observed. Thus, no dosage adjustment on the basis of patient age or gender is necessary.