One Phase 3 CABP study:

Data

The objectives of these analyses were the following:

• Two additional Phase 1 studies:
  - A healthy volunteer study comparing the pharmacokinetics of 300, 450, and 600 mg oral doses of oral omadacycline administered daily over 5 days.
  - A single-center study using existing data from Phase 1 volunteers to validate the model.

• The model was able to characterize the impact of different oral formulations as well as the impact of weight on the oral absorption of omadacycline.

• Since the development of this population PK model, pharmacokinetic data from additional studies, including studies in infected patients, have become available.

METHODS

OBJECTIVES

• To characterize relationships between patient-specific covariates and omadacycline PK parameters.
• To refine the previously-developed population PK model using data from additional Phase 1 studies in healthy volunteers.

• The ability of subject demographics (i.e., age, sex, various body size measures, renal function, presence of cirrhosis, and presence of various infections) to explain a portion of the interindividual variability (IV) in selected omadacycline PK parameters was then explored using univariate forward selection (α = 0.10) and backward elimination (α = 0.001) procedures.

• A combined additive plus constant coefficient of variation (CCV) error model was used to describe both residual variability and interindividual variability, and comparison of the objective function values demonstrated the superiority of the CCV model.

RESULTS

The final analysis dataset consisted of 11331 plasma PK samples collected from a total of 613 subjects. Of the 613 subjects, 180 (29.4%) were enrolled in Phase 3 studies, 31 (5.1%) were enrolled in phase 1 studies, and 262 (42.6%) were enrolled in phase 2 studies. A combined additive plus constant coefficient of variation (CCV) error model was used to describe both residual variability (σ) and interindividual variability (ω) for each PK parameter. Interindividual variability for each PK parameter was described, where possible, using an exponential error model assuming a log-normal distribution.

CONCLUSIONS

A combined additive plus constant coefficient of variation (CCV) error model was used to describe both residual variability and interindividual variability, and comparison of the objective function values demonstrated the superiority of the CCV model.