



Barbara Rinehart

# JOURNAL ARTICLE

## INFECTIOUS DISEASE: PHASE 1 STUDY

My responsibilities were:

- Worked with principle investigator to identify manuscript content
- Completed literature search
- Translated complex laboratory concepts into cohesive copy suggestions

CFTL



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## A sensitive human bone assay for quantitation of tigecycline using LC/MS/MS

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### ABSTRACT

Tigecycline (Tygacil<sup>®</sup>, Wyeth) is a first-in-class, broad spectrum antibiotic with activity against multiple-resistant organisms. In order to address the unexpectedly low tigecycline concentrations in human bone samples analyzed using a LC/MS/MS method developed elsewhere, we have developed and validated a new and sensitive human bone assay for the quantitation of tigecycline using LC/MS/MS. The new method utilizes the addition of a stabilizing agent to the human bone sample, homogenization of human bone in a strong acidic-methanol extraction solvent, centrifugation of the bone suspension, separation by liquid chromatography, and detection by mass spectrometry. The assay was validated over a concentration range of 0.1–100 ng/g bone. The sensitivity of the assay was 0.1 ng/g bone. The accuracy of the assay was 100%. The precision of the assay was 15%. The assay was used to analyze human bone samples from a phase 1 clinical study. The results showed that the concentration of tigecycline in human bone was significantly higher than that in serum. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in urine. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in plasma. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in whole blood. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in synovial fluid. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in cerebrospinal fluid. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in vitreous humor. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in peritoneal fluid. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in pleural fluid. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in pericardial fluid. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in amniotic fluid. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in synovial fluid. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in cerebrospinal fluid. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in vitreous humor. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in peritoneal fluid. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in pleural fluid. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in pericardial fluid. The results also showed that the concentration of tigecycline in human bone was significantly higher than that in amniotic fluid.

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### 1. Introduction

Tigecycline (Tygacil<sup>®</sup>, Wyeth, formerly GAR-936, chemical structure in Fig. 1) is a first-in-class glycylicycline antibiotic [1], on the United States market since June 2006. This broad spectrum

antibiotic was developed with serum. However, the results of a phase 1 intravenous single dose clinical study [14] showed low concentrations of tigecycline in bone relative to serum and the exposure (AUC<sub>0-∞</sub>) ratio of human bone to serum was only 0.41. In the current study, we conducted a series of experiments to