

Supplemental Material

I. Pharmacokinetic analyses

Blood samples for pharmacokinetic analyses were drawn on Day 7 at the following time points: 15 minutes prior to dosing (0 hour), and 0.5, 1, 2, 4, 8, 12, and 24 hours post dose. The following pharmacokinetic variables were estimated at steady state (Day 7) using noncompartmental methods: maximum observed plasma concentration (C_{\max}), minimum observed plasma concentration (C_{\min}), average plasma concentration (C_{avg}), time to C_{\max} (T_{\max}), and area under the plasma concentration-time curve from 0 to 24 hours (AUC_{0-24}). C_{\max} , C_{\min} , and T_{\max} were determined directly from the plasma concentration-time data. AUC_{0-24} was calculated by the linear trapezoidal rule. C_{avg} was calculated as the AUC_{0-24} divided by the dosing interval (24 hours).