[Title] Impact of P-glycoprotein-mediated active efflux on drug distribution into lumbar cerebrospinal fluid in nonhuman primates

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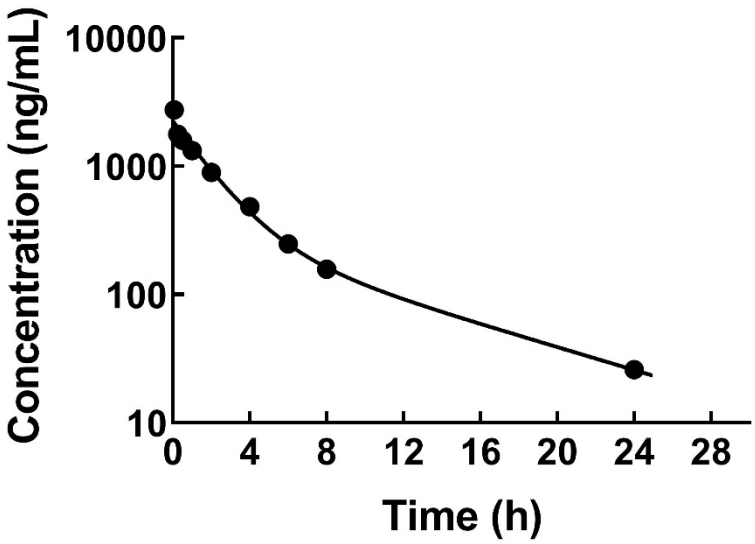

Supplemental Figure 1. Plasma concentration-time profile of zosuquidar in monkey after a single intravenous administration

One male cynomolgus monkey (4 years old, 4 kg) was used. A single intravenous bolus dose of zosuquidar (10 mg/kg) was given to monkey via the saphenous vein to measure the drug concentrations in plasma. Blood samples (0.5 mL per sampling point) were collected using heparinized syringes via the cephalic vein at 5, 15, 30 minutes, and 1, 2, 4, 6, 8, and 24 hours after dosing. The blood samples were centrifuged to prepare plasma. The plasma samples were stored below –20°C until analysis. Closed circles represent observed total plasma concentrations and the solid line represents the fitted curve that was obtained by 2-compartment model with a weighting factor 2 using Phoenix WinNonlin Ver8.1 (Certara USA Inc., Princeton, NJ). The plasma concentration was described as follows:

$$C_{plasma}=A\times e^{-\alpha t}+B\times e^{-\beta t}$$

The A, α, B, and β were estimated to be 1950 ng/mL, 0.525 h^{-1}, 303 ng/mL, and 0.103 h^{-1}, respectively.