Background

Previous studies with long-acting cabotegravir (CAB LA, GSK1265744) demonstrated protection against repeated multi-exposure intravaginal challenge. In addition, the data acquired from the use of three dose levels (10, 30, and 50 mg/kg; n = 9) at days -7 and -1 prior to initiation of weekly intravaginal SIVmac251 twenty-seven Chinese rhesus macaques were injected intramuscularly with CAB LA at three dose intervals throughout the virus challenge period. In one study, evaluation of the "window of protection" levels (10, 30, and 50 mg/kg; n = 9) at days -7 and -1 prior to initiation of weekly intravaginal SIVmac251 infections, a total of 30 macaques were administered a loading dose of CAB LA and a second dose just before the first SIVmac251 challenge. All macaques were cycling, but Depo-Provera was not used to synchronize their menstrual cycles. Study design depicting the timing of CAB LA administration, weekly virus challenges, and sample collections is shown in Figure 1.

Methods

For quantitation of plasma CAB concentrations, a Waters 50 x 2.1 mm XBridge C18 3.5 µm column was coupled with API 4000 MS system; lower limit of detection is 5 ng/mL. For quantitation of plasma CAB concentrations, a Waters 50 x 2.1 mm XBridge C18 3.5 µm column was coupled with API 4000 MS system; lower limit of detection is 5 ng/mL. In one study, evaluation of the "window of protection" levels (10, 30, and 50 mg/kg; n = 9) at days -7 and -1 prior to initiation of weekly intravaginal SIVmac251 infections, a total of 30 macaques were administered a loading dose of CAB LA and a second dose just before the first SIVmac251 challenge. All macaques were cycling, but Depo-Provera was not used to synchronize their menstrual cycles. Study design depicting the timing of CAB LA administration, weekly virus challenges, and sample collections is shown in Figure 1.

Results

The CAB plasma concentrations demonstrated a significant correlation between plasma CAB concentration and virus acquisition (P = 0.0004). A CAB plasma concentration of 0.70 µg/mL (~4x PA-IC90) was predicted to provide a 90% probability of no infection after 15 HIV challenges (Figure 2).

Conclusions

This study demonstrated that 30 and 50 mg/kg of CAB LA were equally potent and provided similar efficacy following multi-exposure intravaginal challenge. In addition, the data acquired from the use of three dose levels (10, 30, and 50 mg/kg; n = 9) at days -7 and -1 prior to initiation of weekly intravaginal SIVmac251 infections, a total of 30 macaques were administered a loading dose of CAB LA and a second dose just before the first SIVmac251 challenge. All macaques were cycling, but Depo-Provera was not used to synchronize their menstrual cycles. Study design depicting the timing of CAB LA administration, weekly virus challenges, and sample collections is shown in Figure 1.

Acknowledgments

This study was supported by NIH DAIDS contract: "This project has been funded in whole or in part with Federal funds from the National Institutes of Health, Department of Health and Human Services. " The long-acting integrase inhibitor GSK744 protects macaques from repeated intravaginal SHIV challenge. Sci Transl Med. 2015;7(270):270ra5.

References
