NATIONAL CENTER FOR HIV, VIRAL HEPATITIS, STD, AND TB PREVENTION

EXTENDED POST-EXPOSURE PROTECTION AGAINST SHIV VAGINAL INFECTION WITH TAF/EVG INSERTS

990

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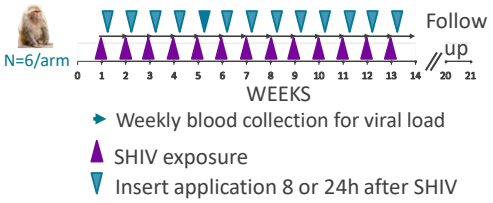
BACKGROUND

On-demand HIV prevention modalities used before or after vaginal sex may be a desirable alternative to daily oral pre-exposure prophylaxis (PrEP) for women with infrequent or clustered sexual activity. CONRAD has developed inserts containing tenofovir alafenamide fumarate (TAF) and elvitegravir (EVG) that were safe, well accepted, and showed good pharmacokinetics and pharmacodynamics in a clinical trial (CONRAD A18-146) after vaginal administration. We recently showed that TAF/EVG inserts fully protected macaques against repeated SHIV vaginal exposures when administered as post-exposure prophylaxis (PEP) 4h after virus exposure. Here, we sought to define the window of PEP activity by applying inserts 8 or 24 hours after SHIV exposure.

METHODS

Cycling pigtailed macaques were challenged with low-dose SHIV162p3 and dosed 8 or 24h later with a TAF/EVG (20 mg/16 mg) insert (n=6 per group) or placebo insert (n=9). Animals were challenged once weekly for 13 weeks. Infection was monitored by plasma virus load using RT-qPCR. Due to the small sample size, efficacy and 95% confidence intervals were calculated with Fisher's exact test. Survival analysis was conducted to compare time to infection in 8h and 24h treated arms relative to 9 placebo controls (n=2 for 8 and 24h, n=5 historical controls) using the Log-Rank test (LRT) in SAS Proc Lifetest (SAS 9.4).

STUDY DESIGN



ACKNOWLEDGMENTS
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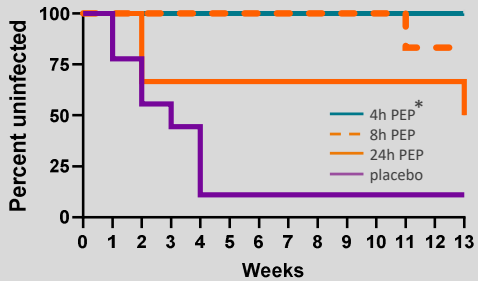
- In a previous study, we showed that TAF/EVG inserts applied vaginally 4h after SHIV exposure conferred 100% protection against repeated SHIV challenges (Dobard et al., eBioMedicine 2022).
- In this study, we show that TAF/EVG inserts applied 8h post-exposure maintain a high efficacy (94.4%) against vaginal SHIV infection.
- Insert application 24h post-exposure maintained a 77% efficacy against vaginal SHIV infection
- These results inform the timing of insert application and support clinical development of TAF/EVG inserts for on-demand PEP against HIV.

RESULTS

At 8h PEP, only 1/6 treated animals became infected (at exposure 11), resulting in high calculated efficacy of 94.41% (95% exact CI =57.03%, 99.27%) and a significant difference in the time to infection compared to placebo controls (p=0.0063, LRT). Extending the window of PEP to 24h resulted in 3/6 animals becoming infected at exposures 2, 2, and 13, thus decreasing the efficacy to 77.23% (95% exact CI =20.00%, 93.52%) and leading to the loss of significance in time to infection (p=0.1154, LRT) when compared to the controls. The median time to infection for the control group was 3 challenges.

VAGINAL EFFICACY OF TAF/EVG INSERTS 8 OR 24 HOURS AFTER SHIV EXPOSURE



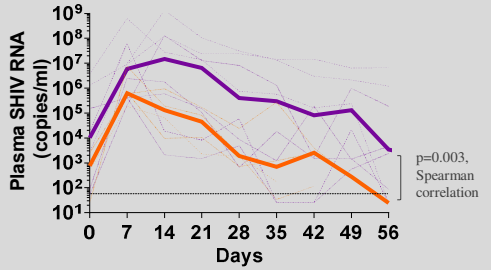
* - Dobard et al, eBioMedicine 2022;86; 104361

CALCULATED PEP EFFICACY

PEP time (h)	Efficacy
4	100% (95% CI = undefined)*
8	94.41% (95% exact CI =57.03%, 99.27%)
24	77.23% (95% exact CI =20.00%, 93.52%)

* - Dobard et al, eBioMedicine 2022;86; 104361

PLASMA VIRAL LOAD



CONCLUSIONS

These data extend the window of high post-exposure protection by a single TAF/EVG insert to 8h and define a reduction in efficacy at 24h post-exposure. The study supports the clinical development of the TAF/EVG insert as an on-demand PEP option for women and informs its dosing modality.

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