SITTING TO ETV IN ETV-BASED REGIMENS: CSF PHARMACOKINETICS AND ANTIVIRAL ACTIVITY

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Introduction

Tenofovir alafenamide (TAF) co-formulated with emtricitabine (EVG), cobicistat and disoproxil fumarate (CBI) has become a recommended regimen, replacing E/C/F/TDF due to improved renal and bone safety. Limited data are available on TAF/EVG in CSF in conjunction with E/C/F/TDF. This study assesses to measure TAF, tenofovir (TFV), and emtricitabine (CBI) concentrations in CSF and compare them to HIV RNA in CSF and CSF/neurocognitive (NC) performance.

Methods

This was a single-arm, open-label, single-center study in 14 participants. After an initial assessment, 9 participants switched from E/C/F/TDF to E/C/TAF and were followed for 24 weeks. At week 0 and visits 2, 4, 6 and other times, plasma and CSF samples were collected. Plasma and CSF concentrations were measured by LC/MS/MS. Clinical and laboratory abnormalities were monitored. Adherence was determined by pill counts.

Results

Mean plasma concentrations of TFV and CBI were stable for 24 weeks (Table 1). Median EVG concentrations in CSF were lower than in plasma, but an increase in CPR was observed post-switch. In CSF, TFV concentrations were expected to be stable, whereas EVG concentrations in CSF were lower compared to plasma. In CSF, more than 50% of EVG was observed, with a score <26 indicating impairment. No clinically significant trends in NC or post-dose abnormalities were observed.

Conclusions

Comparison of TFV and EVG concentrations between CSF and plasma in patients who switched from E/C/F/TDF to E/C/TAF for up to 24 weeks confirmed the predicted pharmacokinetic profile. An increase in CPR was detected, with a score <26 indicating impairment. No clinically significant trends in NC or post-dose abnormalities were observed. More than 50% of EVG was observed in CSF.

References


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Figure 1. Study Design

Figure 2. Tenofovir and CPR

The brain barrier permeability remained unchanged.

The mean CSF serum albumin ratio was 3.84 before switching and 3.84 at week 24 for clinically significant trends in NC or post-dose observations.

The switch was associated with reductions in TFV concentrations in CSF, but an increase in CPR was detected.