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SWITCHING TO FTC/TAF FROM ABC/3TC OR FTC/TDF DOES NOT AFFECT CENTRAL NERVOUS SYSTEM HIV-1 INFECTION

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Background

Despite suppressive antiretroviral therapy (ART), many HIV-infected individuals have low-level persistent immune activation in the central nervous system (CNS). There have been concerns regarding the CNS efficacy of tenofovir alafenamide fumarate (TAF) because of its low cerebrospinal fluid (CSF) concentrations and because it is a substrate of the active efflux transporter P-glycoprotein. Our aim was to investigate whether switching from emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF) or abacavir (ABC)/lamivudine (3TC) to FTC/ (tenofovir alafenamide fumarate (TAF) would lead to changes in residual intrathecal immune activation, viral load, or neurocognitive function.

Methods

In this prospective study we included 20 HIV-infected neuro-asymptomatic adults (11 on ABC/3TC and 9 on FTC/TDF) who for backward comparison recently had undergone a previous lumbar puncture within a research protocol when on treatment with the baseline regimen. At the baseline visit all participants changed their nucleoside analogues to FTC/TAF without any other changes to the ongoing ART regimen. We performed lumbar punctures, venepunctures, and neurocognitive testing at baseline and after three and 12 months. We analysed CSF and plasma HIV RNA, CSF neopterin, CSF β2-microglobulin, IgG index, albumin ratio, and CSF neurofilament light chain protein (NFL) at the pre-study visit, baseline, and follow-up. Cognitive function was assessed by CogState.

Results

At baseline, there were no significant differences between the groups (Figure 1). After three and 12 months of follow-up, there were no significant changes in CSF and plasma HIV RNA, CSF neopterin, CSF β2-microglobulin, IgG index, albumin ratio, CSF NFL, or neurocognitive function in any of the groups (Figures 2 and 3).

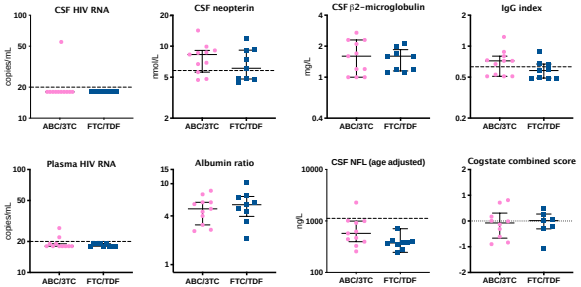


Figure 1. Baseline concentrations of CSF neopterin, CSF ß2-microglobulin, IgG index, albumin ratio, CSF NFL, and results from the neuropsychological testing with CogState for participants on ABC/3TC and FTC/TDF. Bars indicate median and IQR. The dashed lines indicate upper normal reference values for CSF neopterin, CSF ß2-microglobulin, IgG index, CSF NFL, and for CSF and plasma HIV RNA levels it indicates 20 copies/mL. There were no significant changes between the groups.

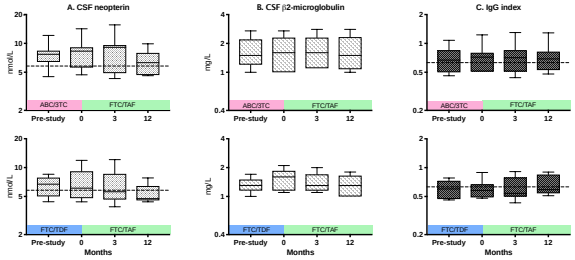


Figure 2. Longitudinal follow-up of CSF biomarkers of immune activation. The upper panel shows the results of all four lumbar punctures, from pre-study to 12 months of follow up, for participants switching from ABC/3TC to FTC/TAF and the bottom panel for participants switching from FTC/TDF to FTC/TAF. On the left (A) is CSF neopterin, in the middle (B) CSF ß2-microglobulin, and on the right (C) IgG index. Boxes depict median and interquartile range and whiskers the minimum and maximum values. The dashed lines indicate upper normal reference values. There were no significant changes after 3 and 12 months of follow-up.

Table 1: Characteristics of participants.

	ABC/3TC	FTC/TDF	Total
Number	11	9	20
Sex (male:female)	8:3	8:1	16:4
Age in years	50 (30–69)	55 (27–67)	54 (27–69)
CD4 nadir (cells/mm^3)	190 (40–357)	80 (10–780)	170 (10–780)
CD4 baseline (cells/mm^3)	630 (170–1100)	610 (330–1000)	620 (170–1100)
Years since HIV-diagnosis	15 (3–21)	12 (5–27)	14 (3–27)
Treatment duration (years)	11 (3–20)	6 (2–20)	11 (2–20)
Additional antiretroviral drugs			
- Protease inhibitor (number)	5	3	8
- NNRTI (number)	4	4	8
- Integrase inhibitor (number)	2	4	6

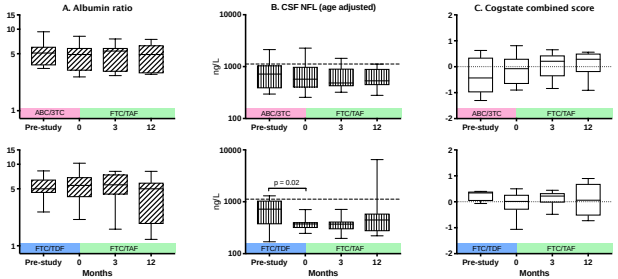


Figure 3. Longitudinal follow-up of CSF NFL, albumin ratio, and neuropsychological testing. The upper panel shows the results of all four lumbar punctures, from pre-study to 12 months of follow up, for participants switching from ABC/3TC to FTC/TAF and the bottom panel for participants switching from FTC/TDF to FTC/TAF. On the left (A) is albumin ratio, in the middle (B) age adjusted CSF NFL, and on the right (C) results from the neuropsychological testing with CogState. Boxes depict median and interquartile range and whiskers the minimum and maximum values. The dashed line for CSF NFL indicates the upper normal reference value and the dotted line for CogState results indicates zero standard deviations. There were no significant changes after 3 and 12 months of follow-up.

CONCLUSIONS

SWITCHING TO FTC/TAF FROM ABC/3TC OR FTC/TDF HAS NEITHER A POSITIVE, NOR A NEGATIVE EFFECT ON CSF BIOMARKERS OF THE CNS HIV INFECTION AFTER 12 MONTHS OF FOLLOW-UP.

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