NO EVIDENCE OF NEURONAL INJURY AFTER SWITCHING TO DOLUTEGRAVIR/LAMIVUDINE FROM A THREE-DRUG REGIMEN

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NO SIGNIFICANT CHANGES IN CEREBROSPINAL FLUID LEVELS OF THE AXONAL BIOMARKER NEUROFILAMENT LIGHT (NFL) WERE OBSERVED AFTER SWITCHING TO DTG/3TC

Background

Dual-drug therapy with dolutegravir/lamivudine (DTG/3TC) is effective in achieving viral suppression in the blood, but its impact on HIV infection in the central nervous system (CNS) remains insufficiently explored. In this study, we aimed to investigate its effect in the CNS through assessment of cerebrospinal fluid (CSF) in individuals switching to DTG/3TC from a three-drug regimen.

Methods

The Gothenburg HIV CSF Study Cohort comprises a longitudinal study investigating HIV infection in the CNS. From this cohort, we retrospectively included all adult individuals on suppressive antiretroviral therapy who switched to DTG/3TC and had undergone lumbar punctures at baseline , up to one year before the switch, and up to two years after. CSF NfL levels were measured by ELISA, HIV RNA quantitative PCR was performed using Cobas 6800. ß2-microglobulin was measured using nephelometry, IgG using immunoturbidimetry. Other analyses were performed using standard laboratory methods.

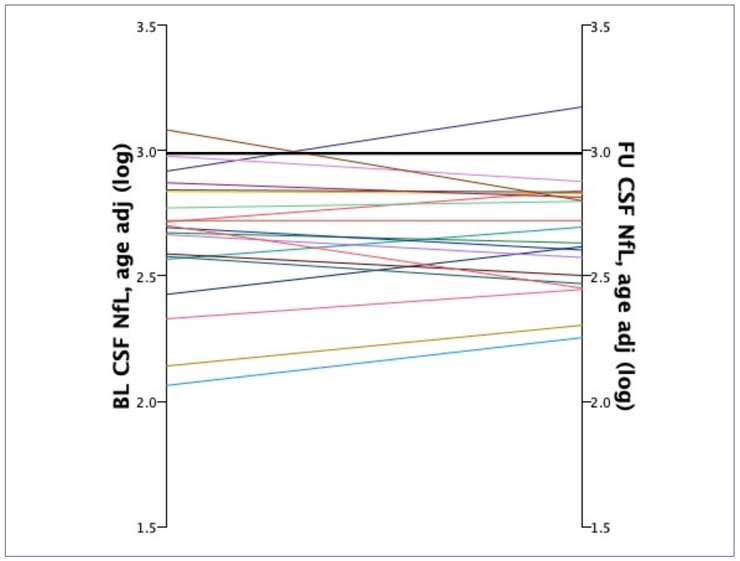


Figure 1. Parallel line plot of Cerebrospinal fluid (CSF) neurofilament light protein (NfL) at baseline (BL) and follow-up (FU). Each line represents an individual. Black line marks upper reference limit (967 ng/L, 2.98 log).

Results

Lumbar punctures were performed in 20 of the 119 individuals with HIV who switched to DTG/3TC between 2017 and 2023. All were virally suppressed (< 50 HIV RNA copies/mL) in blood and CSF at the time of switch. Fifteen were on a regimen containing an integrase inhibitor at baseline. Seven participants were female. Median age at switch was 55 years. All participants remained suppressed in blood throughout the follow-up period, mean 384 days, while one patient had an asymptomatic minor increase of CSF HIV RNA to 70 copies/ml without elevation of CSF white blood cell count or NfL. Mean age-adjusted NfL (50 years) levels were 528 ng/L at baseline and 520 ng/L at follow-up (not significant). Neither were any significant differences observed in albumin ratio, IgG index, CSF ß2-microglobulin, CSF white blood cell count between baseline and follow-up. *Figure 1 and Table 1*

Conclusion

In this study, we observed no evidence of neuronal injury, as measured by NfL, or any change in markers of CNS inflammation following the switch to DTG/3TC. The results will be further explored by investigating additional inflammatory biomarkers in CSF, as well as NfL and other CNS markers in plasma, in the entire cohort who switched to DTG/3TC.

Table 1. Baseline and follow-up data of all participants

	Baseline	Follow-up
	Mean (SD)	Mean (SD)
CSF HIV RNA (copies)	<50 (<50)	<50 (<50)
CSF NfL (ng/L)	611 (348)	613 (340)
CSF NfL (50 y) (ng/L)	528 (272)	520 (291)
P HIV RNA (copies)	<50 (<50)	<50 (<50)
B CD4+ cell count (cells/mm^3)	677 (150)	691 (206)
P ß2-microglobulin (mg/L)	2.0 (0.49)	1.8 (0.42)
CSF ß2-microglobulin (mg/L)	1.4 (0.44)	1.3 (0.31)
Albumin ratio (CSF/S)	4.9 (1.9)	4.7 (1.7)
IgG index (CSF/S)	0.53 (0.16)	0.53 (0.10)
Weight (kg)	81 (15)	80 (16)
Creatinine (umol/L)	87 (12)	88 (18)

CSF: cerebrospinal fluid. P: Plasma. B: Blood. S: Serum
NfL: Neurofilament Light protein. 50 y: Adjusted to 50 years

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