

Biomarkers of neuronal injury and neuroinflammation after switching to dolutegravir/lamivudine in people with HIV

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Background:

Dual-drug therapy with dolutegravir/lamivudine (DTG/3TC) achieves reliable viral suppression in blood and may reduce long-term drug exposure. However, its effect on HIV infection in the central nervous system (CNS) remains insufficiently explored. We aimed to investigate CNS impact by measuring biomarkers of neuronal injury and neuroinflammation in cerebrospinal fluid (CSF) before and after switching to DTG/3TC.

Methods:

We retrospectively included all adults from the longitudinal Gothenburg HIV CSF Study Cohort who were virally suppressed on antiretroviral therapy and switched to DTG/3TC. Plasma and CSF and NfL levels were measured using ELISA and Simoa, respectively. In addition, 127 CSF biomarkers were analyzed using the novel nucleic acid linked immuno-sandwich assay (NULISA).

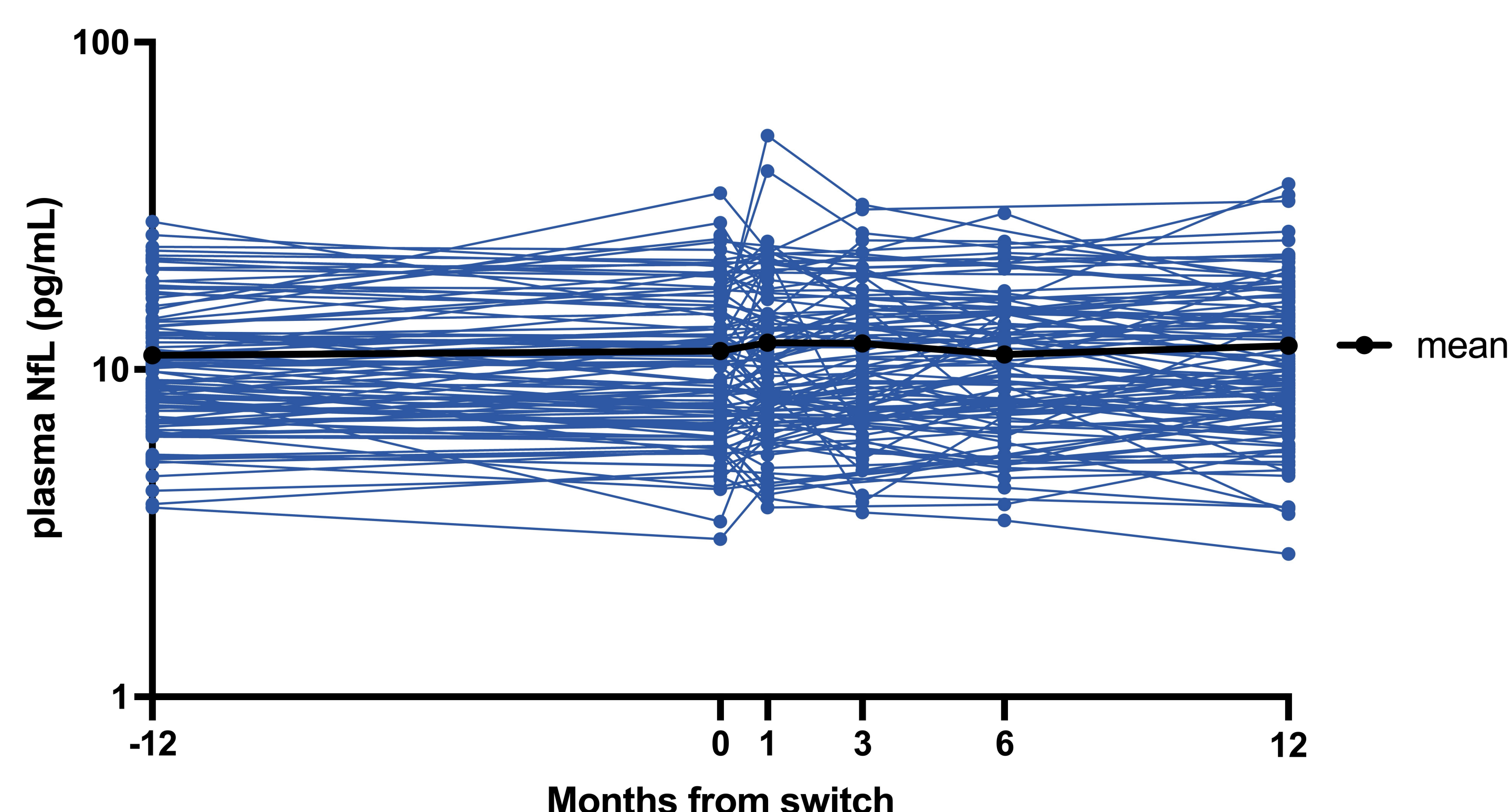


Figure 1. Parallel line plot of plasma neurofilament light protein (NfL) with sample occasions (-12, 0, 1, 3, 6 and 12 months from switch to DTG/3TC) marked by blue dots. Black line marks mean value.

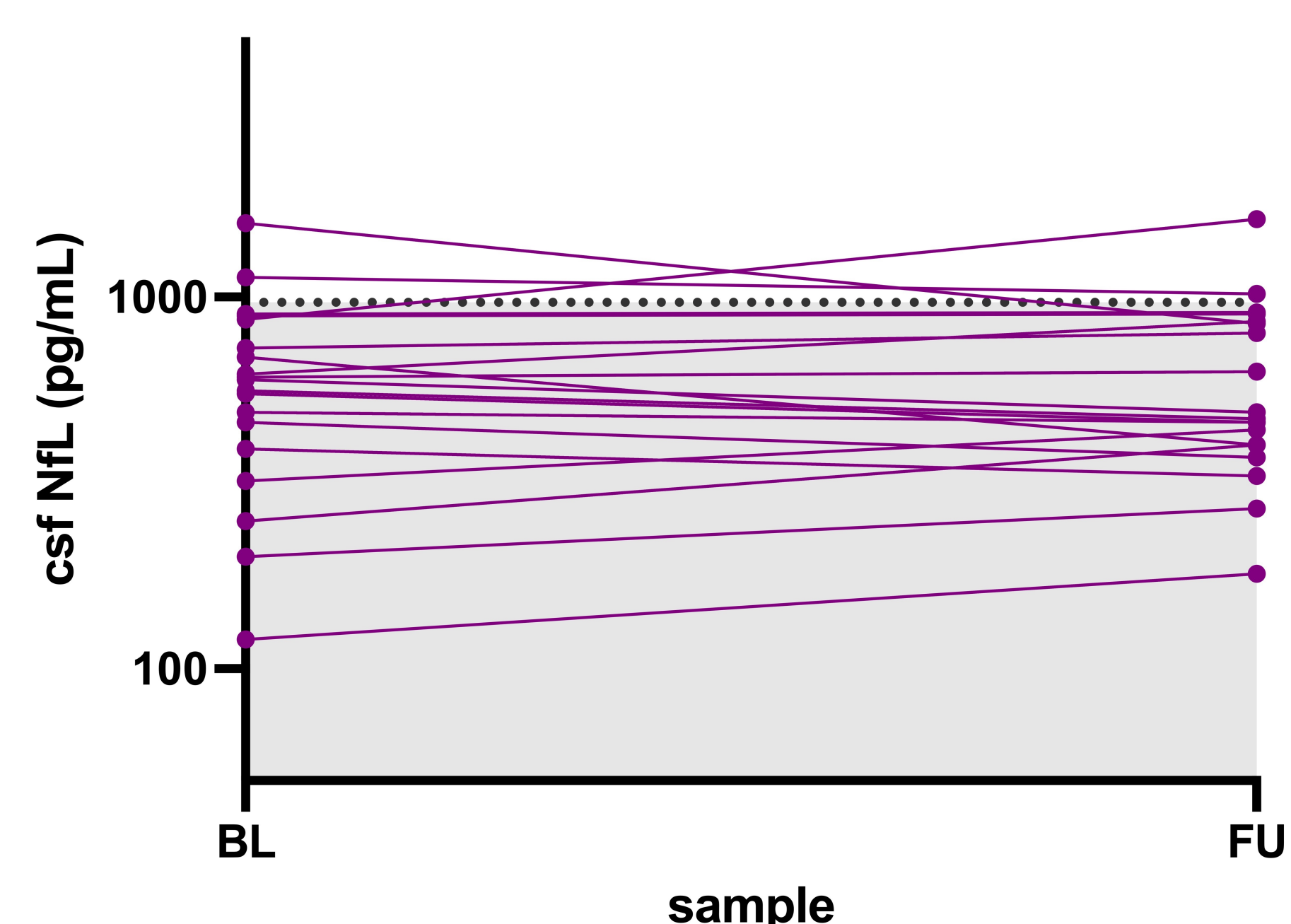


Figure 2. Parallel line plot of Cerebrospinal fluid (CSF) neurofilament light protein (NfL) at baseline (BL) and follow-up (FU), 12 months from switch to DTG/3TC. Each line represents an individual. Dotted line and grey shade marks upper reference limit 967 pg/mL.

Results:

Plasma samples from 113 participants were analyzed at baseline and after a median of 357 days. HIV RNA was <50 copies/mL at baseline and all but one at follow-up. Geometric mean of plasma NfL were 10.1 pg/mL at baseline and 10.3 pg/mL at 12 months, a non-significant difference of 2.8% (95% CI -3.5–9.5%, $p = 0.39$) (fig 1). Twenty participants underwent lumbar punctures before and up to two years after regimen switch (median 382 days). CSF HIV RNA was undetectable in all at baseline and measured 70 copies/mL in one participant at follow-up. Age adjusted CSF NfL (standardized to 50 years) remained unchanged (455 pg/mL vs 459 pg/mL) (fig 2). None of the 127 CNS related biomarkers analyzed using NULISA, showed significant change after correction for multiple comparisons (fig 3).

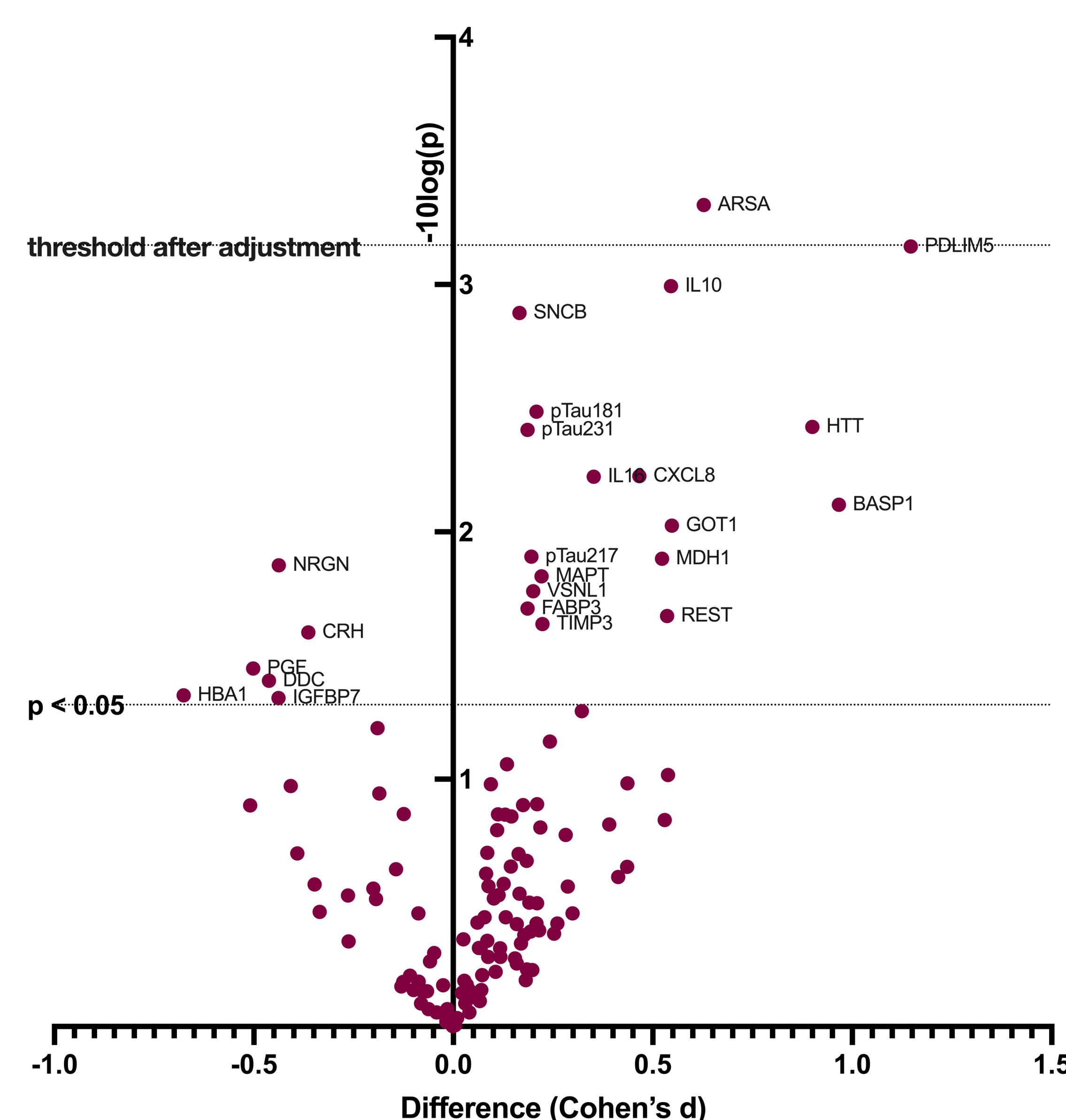


Figure 3. Volcano plot of all biomarkers analyzed by NULISA, with change calculated using Cohen's d on x axis, and significance on y axis. Dotted lines mark p value of 0.05 and the significance threshold adjusted to multiple comparisons using permutation test ($p < 0.00069$).

Conclusion:

Longitudinal plasma NfL measurements, CSF biomarker profiling, and CSF HIV RNA analyses showed no evidence of neuronal injury, increased neuroinflammation, or CNS viral breakthrough after switch to DTG/3TC. These findings support the CNS safety of DTG/3TC in virally suppressed individuals