



# Neurofilament Light Chain in A HIV Cure Study Utilising A Kick-And-Kill Approach

Muhammad Shoab\*

Department of neurology, COMSATS University Islamabad, Attock Campus, Attock 43600, Pakistan

## Description

Kick-and-kill HIV remission techniques may cause viral transcription and immunological activation in the central nervous system, resulting in neuronal damage. We looked examined how kick-and-kill affected plasma neurofilament light (NFL), a measure of neuro-axonal injury, in RIVER trial participants who started antiretroviral therapy (ART) during primary infection and were randomly assigned to either ART-alone or kick-and-kill (ART + vaccine + vorinostat).

At randomisation (after 22 weeks of ART), week 12 (on the final intervention day in ART + V + V), and week 18 post-randomisation, plasma NFL, plasma HIV-1 RNA, and total HIV-1 DNA were quantified in peripheral CD4+ T-cells using a quantitative polymerase chain reaction. At randomization and week 12, HIV-specific T-cells were counted using intracellular cytokine labelling. Mixed models and the Student's t-test were used to examine differences in plasma NFL over time and by study arm. Linear regression and rank statistics were used to analyse the associations with plasma NFL [1,2].

During kick-and-kill, careful monitoring of the CNS is necessary but difficult; frequent brain biopsies are impractical, and MRI is expensive. NFL (neurofilament light protein) is a confirmed, sensitive, and dynamic biomarker of CNS neuroaxonal damage found in the CSF, and is a sensitive neural biomarker for HIV infection across the board. Neurofilaments are a heteropolymer family of intermediate filaments found in neurons that help maintain axon structural and functional integrity. Neurofilament proteins are important structural components of axons, and their expression is especially high in big myelinated axons, where they affect conduction speed. Neurofilaments make up roughly 85% of cytoskeleton proteins and are made up of four main subunits with varying molecular weights: light neurofilament (68 kDa), medium neurofilament.

Neurofilament proteins can be employed as a biomarker of axonal injury in cases of cortical neuronal injury. Following an injury, neurofilament proteins from injured neuro-axonal units are released into interstitial fluid and enter the cerebrospinal fluid, where they may be quantified. The most abundant and soluble protein is neurofilament (NFL). However, due to the intrusive nature of CSF collection, it is impossible to quantify CSF NFL on a regular basis. A new Simoa assay has recently been developed that can consistently measure blood NFL (which is typically 50–100 times lower than CSF NFL), 38 reducing the hurdles to CSF sampling and allowing more frequent assessments because blood samples are easier to obtain. According to preliminary evidence, plasma and serum NFL are moderately to highly correlated with CSF NFL in a range of neurological illnesses, including HIV disease [3-5].

Our findings are consistent with previous research that found no evidence of CNS side effects after treatment with panobinostat, a histone deacetylase inhibitor, as measured by CSF biomarkers. Our findings support previous research that has found a link between plasma NFL and age. While age-related reference ranges for CSF NFL have been established, plasma NFL reference ranges have yet to be established. The discovery that a greater CD8+ cell count is associated

with higher plasma NFL is novel, and it could mean that higher CD8+ T-cell counts (connected to continued immunological activation and poorer immune reconstitution) are linked to ongoing inflammation, which can cause neuronal injury. The fact that a lower BMI is related with increased plasma NFL has been seen previously, possibly indicating a link between the two.

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## Conflicts of Interest

The author has no known conflicts of interested associated with this paper.

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\*Corresponding author: Muhammad Shoab, Department of neurology, COMSATS University Islamabad, Attock Campus, Attock 43600, Pakistan, E-mail: dr.shoib@cuatk.edu.pk

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