

## **MILD HAND PERSISTS DESPITE VERY LOW LEVELS OF HIV RNA ACTIVITY IN PLASMA AND CEREBROSPINAL FLUID**

### **Authors:**

GATES T<sup>1,2</sup>, Cysique L<sup>1,2,3</sup>, Palmer S<sup>4</sup>, Morcilla V<sup>4</sup>, Fisher K<sup>4</sup>, & Brew B<sup>1,2</sup> for the CHIEF Group

<sup>1</sup>Departments of Neurology and HIV Medicine, St. Vincent's Hospital, Sydney NSW

<sup>2</sup>Peter Duncan Neurosciences Unit, St Vincent's Centre for Applied Medical Research, Sydney NSW

<sup>3</sup>Neuroscience Research Australia, Sydney NSW

<sup>4</sup>The Westmead Institute for Medical Research, University of Sydney, Westmead NSW

### **Background:**

HAND persists despite viral suppression at standard detection thresholds of plasma/CSF <20 cp/mL. There is however less evidence that it persists at zero level of viral suppression by SCA. It is also unclear if very low residual CSF compartmentalization is a greater risk for HAND than non-compartmentalized residual viral load or plasma-only residual viral load. In this pilot study we examined whether SCA HIV RNA levels were related to HAND status.

### **Methods:**

Plasma and CSF samples taken from 14 HIV+ participants were analysed using HIV RNA SCA with detection thresholds set at 0.2 and 0.3 cp/mL respectively. Plasma and CSF HIV RNA SCA were dichotomized according to <1 and ≥1 cp/mL cut-off and further split into 4 groups to reflect plasma/CSF HIV compartmentalization (plasma-/CSF- *n*=7; plasma-/CSF+ *n*=3; plasma+/CSF- *n*=2; plasma+/CSF+ *n*=2). Participants also completed a 7-domain neuropsychological test battery. Global Deficit Score (GDS) and self-reported functional decline were used to classify HAND (GDS ≥0.5). We found 43% mild HAND and 57% cognitively normal.

### **Results:**

Mild HAND was present in 3/4 compartmentalization groups, the exception being plasma+/CSF-. Plasma+/CSF+ showed elevated CSF protein and CSF albumin levels compared to the other groups (*p*<.05). HIV duration was an average of 18 years longer in this group. Lower CD4:CD8 ratio was associated with CSF HIV RNA ≥1cp/ml.

### **Conclusion:**

Our findings support that mild HAND can occur despite very low residual viremia in plasma or CSF. In a minority of cases, mild HAND seems to be driven by longer HIV duration and blood-brain barrier compromise. However, in other cases the underlying mechanisms remain to be fully elucidated. While indicative, the data suggest that very low residual HIV RNA activity in the periphery is not the predominant contributor to mild HAND.