Research on compounds tested in new HIV eradication strategies should cover different critical safety levels, including the central nervous system (CNS). That necessity becomes more critical considering that reactivation of latent reservoir is aimed to be reached, and, additionally, that antiviral therapy cessation is a requirement of HIV eradication strategies currently.

Romidepsin (RMD) is a potent histone deacetylase inhibitor (HDACi) that has shown efficacy on latent HIV infection, as well as combination antiretroviral therapy (cART) resumption (9). Studies performed in early-treated HIV-infected patients show no differences when neuroimaging analyses applied whole-brain voxel-wise comparisons, either at Pre or Post assessment. All brain regions studied, including subcortical areas involving cortico-striato-cerebellar circuits (i.e., caudate nucleus, ventral striatum/accumbens, putamen, pallidum, and thalamus) and frontal cortex (i.e., dorsomedial, dorsolateral, cingulate, ventromedial, orbital/ventral, and lateral orbitalfrontal cortex), showed no statistically significant volumetric or structural discrepancies between the Intervention and Control groups at any of the study timepoints. Figure 5 represents a graphical summary of the main findings in the neuroimaging analyses.

Conclusions

No detrimental effects on cognitive status, functional outcomes, and neuroimaging parameters were observed after the use of 3 weeks infusions of RMD (5 mg/m2) in the setting of a kick-off eradication strategy of HIV.

After a short MAP with plasma viral load threshold of criteria of >2,000 cop/mL and 24 weeks follow-up of cART interruption, no negative contributing effects were observed in cognitive, functional, or neuroimaging outcomes.

The HIV cure investigated in this small trial, including the use of a MVA HIV vaccine, administration of RMD, cART interruption, and posterior 24-week therapy reinitiation, appears to be safe for the CNS.

Acknowledgements


### RESULTS (I)

#### Sample Characteristics

A total of 11 individuals from the main study sample accepted to participate. Ten patients were recruited as controls. Study participant 5 was not evaluable for therapeutic impact with RMD (95% CI: 0.3-5.3) weeks. Figure 2 shows the study flowchart in the Intervention group.

#### Functional Outcomes

Baseline cognitive functioning was comparable between groups, as well as functional outcomes. Cognitive change was significant for the Intervention group compared to both between-group and intra-group comparisons. Change in functional outcomes was not significant for any dimension for the Intervention group compared to both between-group and intra-group comparisons. Figure 3 shows the main cognitive and functional results from Pre to Post assessment.

#### Neuroimaging Outcomes

No differences were found between neuroimaging analyses applied whole-brain voxel-wise comparisons, either at Pre or Post assessment. All brain regions studied, including subcortical areas involving cortico-striato-cerebellar circuits (i.e., caudate nucleus, ventral striatum/accumbens, putamen, pallidum, and thalamus) and frontal cortex (i.e., dorsomedial, dorsolateral, cingulate, ventromedial, orbital, and lateral orbital frontal cortex), showed no statistically significant volumetric or structural discrepancies between the Intervention and Control groups at any of the study timepoints. Figure 5 represents a graphical summary of the main findings in the neuroimaging analyses.