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## Introduction:

The central nervous system (CNS) may be at risk for persistent HIV replication despite HIV suppression in plasma because of poorer drug penetration into CNS. We assessed HIV-1 viral load in CSF from patients on suppressive HAART undergoing a lumbar puncture as baseline investigation for an ongoing treatment simplification study (MOST).

## Methods:

**Patients had to be on triple-combination HAART for >6 months with plasma HIV-1 RNA <50 c./ml for ≥3 months and without prior history of any virologic treatment failure.** So far, 45 CSFs were examined. The HIV-1 viral load in the CSF was quantified by COBAS Ampliprep/ COBAS Taqman HIV-1, Roche. Additionally we measured white cell count, protein and glucose in CSF. The CNS penetration-effectiveness rank (CPE) for each antiretroviral regimen was calculated by summing the penetration rank of 0 (low), 0.5 (intermediate) or 1 (high) for each drug taken at the time of lumbar puncture; a higher CPE rank indicates better CNS penetration (Tab 1).

Tab 1. CNS Penetration Effectiveness Rank

ARV class	0	0.5	1
<b>NRTIs</b>	Tenofovir Didanosine Zalcitabine	Stavudine Lamivudine Emtricitabine	Zidovudine Abacavir
<b>NNRTIs</b>		Efavirenz	Delavirdine Nevirapine
<b>PIs</b>	Nelfinavir Saquinavir/r Ritonavir Tipranavir/r	Amprenavir Fosamprenavir Indinavir Atazanavir Atazanavir/r	Amprenavir/r Fosamprenavir/r Lopinavir/r
<b>Entry inhibitors</b>	Enfuvirtide		

Reference: S. Letendre, 9<sup>th</sup> International Workshop on Clinical Pharmacology of HIV-Therapy, New Orleans, USA, 9<sup>th</sup> April 2008

## Results:

Table 2. Participant Characteristics

Total, No	45
Gender No (%)	Female: 14 (31%) Male: 31 (69%)
Median Age, years	43 ( IQR 38-49)
Way of Transmission, No (%)	Heterosexual: 26 (58) Homosexual: 16 (36) Unknown: 2(4) Unknown: 1 (2)
CDC-Stage, No (%)	Stage A: 23 (51) Stage B: 10 (22) Stage C: 12 (27)
Median CD4 Nadir	160 (IQR 62- 225)
Median Current CD4	532 (IQR 363- 667)
Median Time of HIV-1 Suppression, months	40 (IQR 21-63)
Type of ARV Regimen, No (%)	PI: 32 (71) NNRTI: 12 (27) NRTI: 1 (2)

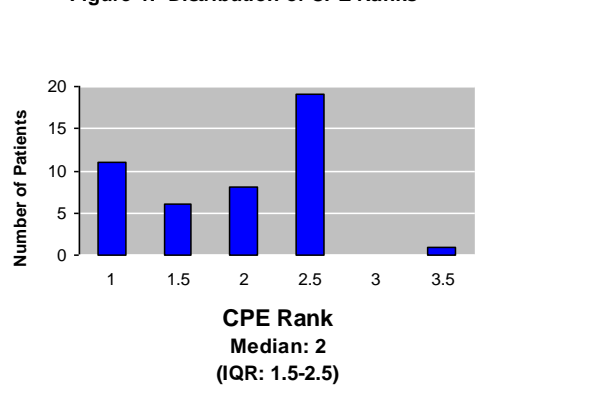
## Results:

Table 3. Features of Cerebrospinal Fluid

HIV-1 viral load in CSF	in 44 patients: not detectable in 1 patient: 82c/ml
median white cell count (cell/ul)	1 (IQR 1-2)
median protein (g/l)	0.4 (IQR 0.4-0.5)
median glucose (mmol/l)	3.1 (IQR 3.0-3.5)

In 44 (97.7%) subjects, viral load in CSF was undetectable (<40 c./ml). **One** subject had a viral load of 82 c./ml in CSF; viral load in plasma of this patient had been suppressed by an NNRTI based regimen with a CPE rank of 1 for 37 months. The other measured markers like white cell count, protein and glucose in all 45 CSFs were normal.

Figure 1. Distribution of CPE Ranks



## Conclusions:

Successful long-term HAART, defined as HIV-1 RNA in plasma <50 c./ml during at least 3 months, achieved complete suppression of HIV replication in CSF in all but one of 45 patients, even if not all of the drugs taken had an ideal CNS penetration. The remaining standard CSF laboratory markers were normal in all patients, consistent with a lack of CNS inflammation in patients on HAART.

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