Poster # 478

Ignacio Perez-Valero | Pº Castellana 261 | Madrid 28046, Spain | +347277099 | ignacio.perez@salud.madrid.org

# HIV-replication control rates needed to prevent Neurocognitive Performance (NP) decline.

**Ignacio Pérez-Valero[1, 2], Robert Heaton[2], Donald Franklin[2], Scott Letendre[2], Reena Deutsch[2], Benjamin Gelman[3], David Simpson[4], Ann Collier[5], Igor Grant[2], Justin McArthur[6], David Clifford, J. Allen McCutchan[2] and THE CHARTER GROUP.**

1. Hospital Universitario La PAZ, Madrid, SPAIN. 2. University of California, San Diego, San Diego, C., 3. University of Texas, Galveston, TX. 4. Mont Sinai Hospital, New York, NY. 5. University of Washington, Seattle, WA. 6. The Johns Hopkins University School of Medicine, Baltimore, MD. 7. Washington University School of Medicine, Saint Louis, MO.

CHARTER
CNS HIV Anti-Retroviral Therapy Effects Research
CNS HIV ANTI-RETROVIRAL THERAPY EFFECTS RESEARCH

## Objective

- To evaluate the impact of viral suppression rates in neurocognitive decline.
- To compare neurocognitive decline rates in aviremic patients treated with a NNRTI + 2NRTIs or with a PI + 2 NRTIs.

## Background

- The level of HIV-suppression needed to prevent neurocognitive decline has not been clearly established.
- The capacity of NNRTI and PI-based ART regimens to prevent neurocognitive decline in aviremic HIV patients is unexplored.

## Methods

- We selected HIV-infected (HIV+) volunteers enrolled in the CHARTER and non-HIV (HIV-) controls enrolled in the HNRP cohort with ≥2 years of neurocognitive follow up.
- We HIV+ volunteers in three categories according to their virological control:
  - ✓ HIV always suppressed: (HIV RNA <50 cop/mL during all the follow up).
  - ✓ HIV sometimes suppressed: (HIV RNA fluctuated between <50 & >50 during the follow up).
  - ✓ HIV always detectable: (HIV RNA was always >50 cop/mL during all the follow up).
- NP was assessed every 6 months according to Frascati Criteria (Neurology 2007;69: 1789-99). Neurocognitive decline was diagnosed using published regression-based norms for neurocognitive performance change that corrected for known factors that may influence test-retest differences in HIV- controls.
- We compared the rates of neurocognitive decline calculated for each of the 3 categories of virological control, using HIV- controls as reference.
- We also compared, in HIV+ aviremic volunteers, the rates of neurocognitive decline observed in patients that received a NNRTI + 2 NRTIs or a PI + 2 NRTIs.

## Conclusions

- Comparing to HIV- controls, we only detected higher rates of NP decline in the group of volunteers that always had detectable HIV viral load.
- The risk of neurocognitive decline in aviremic patients was higher when patients were treated with a NNRTI than with a PI (+ 2 NRTIs).

## Results

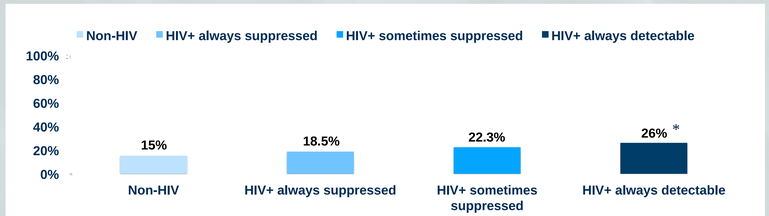
### BASELINE CHARACTERISTICS (HIV+ Vs. non-HIV)

| | Non-HIV controls (N=93) | HIV-infected volunteers (N=346) | p Value |
|---|---|---|---|
| Age, mean (SD) | 36.1 (10.3) | 43.8 (8.6) | p < 0.01 |
| Education, mean (SD) | 12.9 (2.2) | 12.9 (2.5) | p = 0.93 |
| Gender: Male, N (%) | 62 (66.7) | 279 (80.6) | p < 0.01 |
| Ethnicity: Caucasian, N (%) | 61 (65.6) | 155 (44.8) | p < 0.01 |
| NP evaluations, mean (SD) | 5.2 (0.8) | 6.7 (3.5) | p = 0.07 |

### BASELINE CHARACTERISTICS (by level of HIV-suppression)

| | HIV+ always suppressed (N=103) | HIV + sometimes suppressed (N=112) | HIV+ always detectable (N=131) | p Value |
|---|---|---|---|---|
| Age, mean (SD) | 46.4 (8.4) | 44.3 (8.1) | 41.4 (8.6) | p < 0.01 |
| Education, mean (SD) | 13.0 (2.3) | 12.8 (2.5) | 12.9 (2.8) | p = 0.94 |
| Gender: Male, N (%) | 83 (80.6) | 95 (84.8) | 101 (77.1) | p = 0.32 |
| Ethnicity: Caucasian, N (%) | 57 (55.3) | 42 (37.5) | 56 (42.8) | p = 0.03 |
| HCV condition: HCV Ab+, N (%) | 34 (33) | 28 (25) | 25 (19) | p = 0.05 |
| AIDS condition: CDC, N (%) | 75 (72.8) | 86 (76.8) | 40 (30.53) | p < 0.01 |
| Years known HIV+, median (IQR) | 12.4 (5.8-15.9) | 12 (5.9-15.9) | 8.1 (2.5-14.4) | p < 0.01 |
| Plasma | | | | |
| CD4 nadir, median (IQR) | 137 (20-232) | 108 (23-205) | 315 (199-500) | p < 0.01 |
| Current CD4, median (IQR) | 489 (360-679) | 410 (206-645) | 447 (289-620) | p = 0.01 |
| CSF | | | | |
| CSF Pleocytosis, N (%) | 12 (12.5) | 19 (18.4) | 52 (42.6) | p < 0.01 |
| CSF Proteins, mean (SD) | 41.4 (12.8) | 44.1 (17.4) | 48.9 (25.9) | p = 0.55 |
| Neurognitive performance | | | | p = 0.10 |
| Normal, N (%) | 53 (51.5) | 58 (51.8) | 83 (63.4) | |
| Impaired, N (%) | 50 (48.5) | 54 (48.2) | 48 (36.6) | |
| Comorbidities: Incidental, N (%) | 60 (58.3) | 65 (58) | 85 (64.9) | p = 0.45 |

### PROPORTION OF NEUROCOGNITIVE DECLINERS



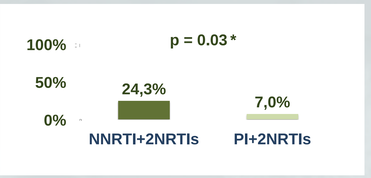

* p <0.05 (compared to non-HIV controls), after adjusting for significant cofactors (age, gender, ethnicity & NP evaluations).

### BASELINE CHARACTERISTICS (By ART type)

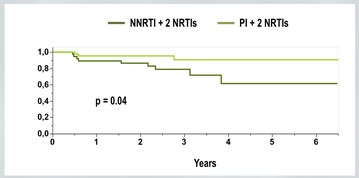
| HIV+ always suppressed * | NNRTI + 2 NRTIs (N=37) | PI + 2 NRTIs (N=43) | p Value |
|---|---|---|---|
| Age, mean (SD) | 46.4 (8.8) | 47 (8.3) | p 0 0.76 |
| Education, mean (SD) | 12.9 (2.2) | 13 (2.3) | p = 0.87 |
| Gender: Male, N (%) | 30 (81.1) | 34 (79) | p = 0.83 |
| Ethnicity: Caucasian, N (%) | 20 (54.1) | 21 (48.8) | p = 0.83 |
| HCV condition: HCV Ab+, N (%) | 11 (29.7) | 16 (37.2) | p = 0.48 |
| AIDS condition: CDC, N (%) | 25 (67.6) | 35 (81.4) | p = 0.15 |
| Years known HIV+, median (IQR) | 8.7 (4.4-15.1) | 13.8 (7.8-17.4) | p = 0.02 |
| Plasma | | | |
| CD4 nadir, median (IQR) | 180 (76-285) | 93 (10-206) | p = 0.04 |
| Current CD4, median (IQR) | 512 (391-716) | 428 (358-652) | p = 0.17 |
| CSF HIV RNA >50 cop/mL, N (%) | 0 (0) | 2 (4.9) | p = 0.19 |
| NP: impaired, N (%) | 20 (54.1) | 18 (41.9) | p = 0.28 |
| Comorbidities | | | p = 0.12 |
| Incidental, N (%) | 17 (46) | 29 (67.4) | |
| Contributing, N (%) | 15 (40.5) | 12 (27.9) | |
| Confounding, N (%) | 5 (13.5) | 2 (4.7) | |
| ART | | | |
| CPE Vs. 2.0 (2010), median (IQR) | 8 (7-9) | 7 (6-8) | p = 0.04 |
| Years on ART, median (IQR) | 4.7 (1.9-8.6) | 6.3 (3.3-8.3) | p =0.27 |
| ABC/3TC, N(%) | 8 (21.6) | 12 (27.9) | p = 0.43 |
| TDF/FTC, N(%) | 22 (59.5) | 23 (53.5) | p = 0.71 |
| AZT/3TC, N(%) | 7 (18.9) | 8 (18.6) | p = 0.55 |

* 23 HIV+ always suppressed receiving ART regimens different to NNRTI or a PI (+2 NRTI) were excluded.

### PROPORTION OF NEUROCOGNITIVE DECLINERS (by ART type)




### TIME TO NEUROCOGNITIVE DECLINE (By ART type)




* After adjusting for significant cofactors: (CPE Score, CD4 nadir and years being HIV+).

### RELATIVE RISK OF NEUROCOGNITIVE DECLINE (By ART type)

**NNRTI + 2 NRTIs: (PI + 2 NRTIs as reference) 3.41 (95% CI: 1.02 – 11.93)**

***Supported by NIH contract N01 MH22005 & HHSN271201000036C (CHARTER; PI: I. Grant).*** *Participating sites include: Johns Hopkins University (J. McArthur); Mt. Sinai School of Medicine (S. Morgello & D. Simpson); University of California, San Diego (J.A. McCutchan); University of Texas Medical Branch, Galveston (B. Gelman); University of Washington, Seattle (A. Collier & C. Marra); Washington University, St. Louis (D. Clifford)*