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CSF VIREMIA AND INFLAMMATORY MARKERS IN PTS WITH NCI ON TDF/FTC/EFV AND AFTER SWITCHING TO ABC/3TC/MVC

Tiraboschi JM[1],Muñoz-Moreno JA[2], Puertas MC[3], Alonso C[4], Prats C[2], Ferrer E[1], Rozas N[1], Maso M[1], Martinez-Picado J[3,5], Podzamczer D[1].

Hospitals [1]Universitari de Bellvitge, [2]Germans Trias i Pujol, [3]Institut de Recerca de la SIDA IrsiCaixa, [4]Complex Sanitari Santa Tecla, URV, [5] ICREA, UAB . Barcelona, Spain

CORRESPONDENCE TO:
Dr. Juan Manuel Tiraboschi
HIV Unit, Infectious diseases department.
Hospital Universitari de Bellvitge
L'Hospitalet del Llobregat. 08907
Barcelona. SPAIN
Fax: 0034-932607669
jmtiraboschi@bellvitgehospital.cat

BACKGROUND

A low-level viremia in cerebrospinal fluid (CSF) while on cART may promote local immune activation, and inflammatory responses.

OBJECTIVE

To evaluate HIV-1 viral load (VL) and inflammatory markers in CSF, as well as the impact on neurocognitive performance in patients with neurocognitive impairment (NCI) while receiving TDF/FTC/EFV and after switching to a regimen with enhanced CNS penetrability, including Maraviroc a drug with potential immunomodulatory effects.

PATIENTS AND METHODS

Setting: Hospital Universitari de Bellvitge (Barcelona, Spain), University Teaching Centre, 1000 beds.
Patients: 70 pts receiving TDF/FTC/EFV were screened, 12 of them had documented NCI, CCR5 tropic virus determined from proviral HIV-1 DNA, and lacked the HLA-B*57:01 haplotype.
Variables: Age, sex, risk practice, prior AIDS, nadir CD4 count, hepatitis C, number of previous antiretroviral (ARV) regimen, time with undetectable plasma HIV VL and time on TDF/FTC/EFV at baseline.
Statistical analysis: Descriptive statistics were expressed as median (minimum and maximum) for quantitative variables and as frequencies and percentages for qualitative variables.
Methods: Cross sectional and longitudinal study. HIV+ virologically suppressed pts on TDF/FTC/EFV with documented NCI were included and switched to ABC/3TC/MVC. Pts with NCI due to a cause other than HIV were excluded. A trained neuropsychologist performed a 7-domain neurocognitive assessment at baseline and week 48. CSF and blood samples were taken at BL and week 24-36. HIV-1 RNA in plasma (LOD 40 c/ml) and CSF (LOD 2.5 c/ml) were determined by real-time PCR. Inflammatory markers in CSF were measured by ELISA. Baseline inflammatory markers were compared with already published data of healthy subjects.

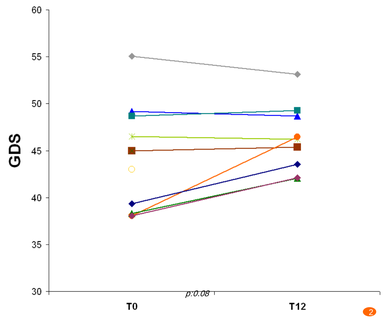
RESULTS

BASELINE CHARACTERISTICS

N (%)		12 (100%)
Age, median(range)		54 (33-65)
Gender, n (%)	Male	11 (91.67)
	Female	1 (8.33)
Risk practice, n (%)	Drug users	3 (25)
	Homosexuals	6 (50)
	Heterosexuals	3 (25)
	Others	-
Hepatitis C, n (%)	Yes	3 (25)
	No	9(75)
CD4 count (cells/uL), median (range)		529(483-576)
Nadir CD4 T cells/µl		178(15-482)
AIDS, n (%)	Yes	1 (8.33)
	No	11 (91.67)
Median time on TDF/FTC/EFV		42.5 (15-86)
Time with undetectable VL		78 (24-144) months

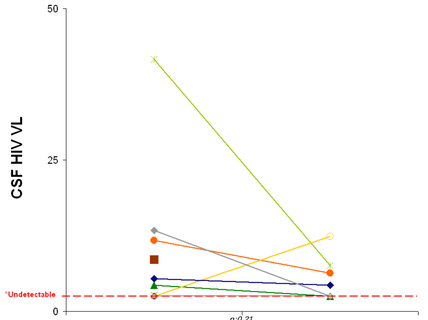
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GLOBAL DEFICIT SCORE



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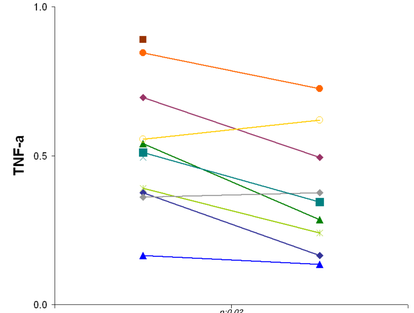
CSF-HIV VIRAL LOAD



* 5 patients presented undetectable Viral Load (<2.5) at baseline

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TNF-a



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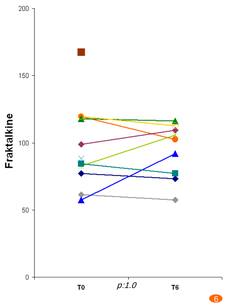
BL RESULTS AND CHANGES IN INFLAMMATORY MARKERS, CSF VIRAL LOAD AND NEUROPSYCHOLOGICAL TESTS

	Baseline visit		Follow-up visit		
	N	Median (Min-Max)	N	Median (Min-Max)	p-value
Neopterin (nM)	12	82.82 (36.64 - 155.16)	9	74.83 (43.85 - 160.28)	*0.91*
Fractalkine (pg/mL)	12	93.55 (57.47 - 167.42)	9	102.43 (57.47 - 116.17)	*1*
MCP-1 (ng/mL)	12	0.88 (0.66 - 1.66)	9	1.24 (0.48 - 1.58)	*0.477*
TNFa (pg/mL)	12	0.51 (0.17 - 0.89)	9	0.35 (0.14 - 0.73)	*0.027*
Tau (pg/ml)	12	265.68 (125.60 - 399.61)	9	287.84 (85.51 - 458.09)	*0.129*
IL-6 (pg/ml)	12	1.02 (0.23 - 3.79)	9	1.25 (0.40 - 4.71)	*0.82*
CSF HIV-1 RNA (c/mL)	12	3.49 (0.00 - 41.62)	9	0.00 (0.00 - 12.36)	*0.219*
Neurocognitive Tests					
Global Deficit Score (GDS)	12	0.55 (0.00 - 1.33)	9	0.40 (0.00 - 0.86)	*0.085*

* * At follow-up visit, 3 pts continued with detectable VL, 3 with undetectable VL, 2 switched from detectable to undetectable VL and 1 from undetectable to detectable VL. #Wilcoxon exact test.

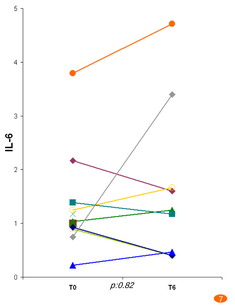
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FRAKTALKINE



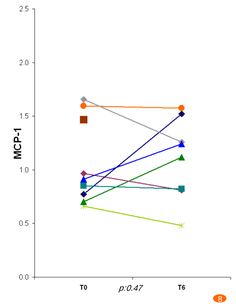
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IL-6



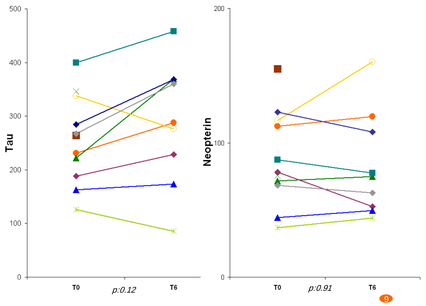
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MCP-1



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TAU AND NEOPTERIN



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CONCLUSIONS

- Most pts with NCI while receiving TDF/FTC/EFV had low-level viremia in CSF and/or increased inflammatory markers.
- After switching to a regimen with better CNS penetration and including Maraviroc, an improvement in neuropsychological tests was observed, as well as a significant reduction in TNF-a concentration in CSF, despite viral suppression in only 2 pts.
- Larger studies are needed to confirm if there may be a benefit from switching from TDF/FTC/EFV to ABC/3TC/MVC and to elucidate if this improvement is related to either a reduction in toxicity or to a better antiviral and immunomodulatory activities in CNS, or all.

Generalitat de Catalunya Departament de Salut
Institut Català de la Salut Gerència Territorial Metropolitana Sud
Bellvitge Hospital Universitari
IDIBELL Institut d'Investigació Biomèdica de Bellvitge
Universitat de Barcelona