



Baseline Data from ACTG 5199: The International Neurological Study

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ABSTRACT

Background and Objective.

ACTG 5199: the International Neurological Study, aims to document the prevalence and incidence of neurological disease in HIV-infected patients in resource limited settings, and the impact of antiretroviral treatment on neurocognitive function. We present the baseline study data.

Methods.

ACTG 5199 sites included: Rio de Janeiro, Porto Alegre, Brazil; Chennai, Pune, India; Blantyre, Lilongwe, Malawi; Lima, Peru; Johannesburg, Durban, South Africa; Chiang Mai, Thailand; and Harare, Zimbabwe. Sites administered a standardized neurological exam and a brief motor-based neuropsychological exam (timed gait, grooved pegboard, fingertapping, semantic verbal fluency) at baseline prior to antiretroviral initiation. Staff were trained to standardize test administration.

Baseline Results

860 subjects enrolled: 53% were female, 49% were black, median age was 34, median (Q1, Q3) CD4 of 172 (97, 232) and plasma viral load of 5.0 (4.5, 5.5) logs. Overall 219 (25%) had an abnormal neurologic examination. Examinations revealed a low prevalence of AIDS dementia and minor cognitive motor disorder. However, 18% subjects were identified as having some evidence of peripheral neuropathy. As expected, there were significant differences across countries (p < .001) on the neuropsychological tests after adjusting for CD4 and viral load.

Conclusions

In this first large global neurological study of antiretroviral treatment in resource limited settings, there was a low prevalence of AIDS Dementia and MCMD, while peripheral neuropathy was more common. In addition, there was significant variation in neurocognitive test performance across countries. These differences may reflect differences in populations, cultures, HIV subtypes, or variation in test administration. Longitudinal follow-up on antiretroviral treatment is under way.

METHODS

Design

Subjects

- Antiretroviral naïve
- CD4+ cells < 300
- 860 subjects enrolled

Treatment Regimens

Step 1: Initial Regimen

- Arm 1 - 3TC/ZDV/EFV
- Arm 2 - FTC/ATV/DDIEC
- Arm 3 - FTC/TDF/EFV

Step 2: Failure Regimen

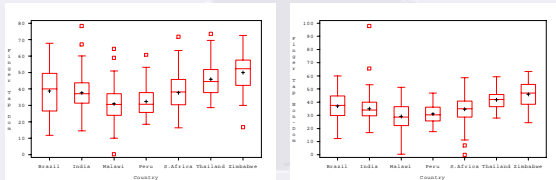
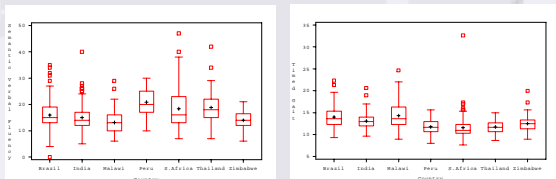
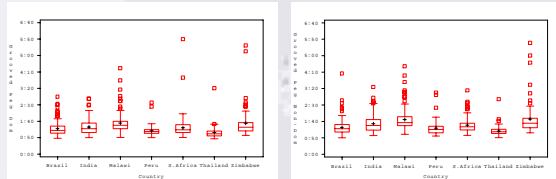
- Arm 1 – 2 NRTI + PI
- Arm 2 – 2 NRTI + EFV
- Arm 3 – 2 NRTI + PI

Neuropsychological evaluation

- Timed Gait
- Grooved Pegboard
- Finger Tapping
- Semantic Verbal Fluency

Neurological evaluation

- History, Symptoms, Exam:
 - Cognitive, Motor, Sensory, Reflex
- Neurologic Formulation:
 - Summary of Severity, Duration, Course
- AIDS Dementia



Step	Frequency	Percent
On Step 1	777	90.35
Dropped out on Step 1	48	5.58
On Step 2	33	3.84
Dropped out on Step 2	2	0.23

BASELINE RESULTS

Accrual n=860

- Brazil - 161
- Peru - 62
- India - 184
- Thailand - 73
- South Africa - 167
- Malawi - 133
- Zimbabwe - 80

Demographics

- Gender
 - Male 408 (47%)
 - Female 452 (53%)
- IV Drug use 13/860 (1.5%)
- Age
 - Median 34 yrs
- Education
 - Median 10 yrs, Q1=7, Q3=12

Diagnoses

- Abnormal neurologic exam 25%
- MCMD 4%
- Dementia 0.5%
- Peripheral neuropathy 18%

Neuropsychological evaluations

- Timed Gait
 - Mean 12.9 (2.4), Median 12.7
 - Q1 = 11.3, Q3 = 14
- Grooved Pegboard dominant
 - Mean 81.9 (28.1), Median 75
 - Q1 = 66, Q3 = 90
- Grooved Pegboard nondominant
 - Mean 90.5 (29.6), Median 84
 - Q1 = 72, Q3 = 99
- Semantic Verbal Fluency
 - Mean 16.2 (5.9), Median 15
 - Q1 = 12, Q3 = 19
- Finger Tapping dominant
 - Mean 38.3 (11.9), Median 37.8
 - Q1 = 29.6, Q3 = 46.8
- Finger Tapping nondominant
 - Mean 35.7 (10.4), Median 35.4
 - Q1 = 28.6, Q3 = 42.6

		Country							
		Total	Brazil	India	Malawi	Peru	South Africa	Thailand	Zimbabwe
CD4 count	Median	172.5	183	198	178	167	157	125	170.5
	Q1, Q3	97.5, 232.0	75, 257	136, 236	122, 232	88, 234	100, 216	37, 177	98.5, 217.5
	Median	5.0	5.2	5.1	4.8	4.8	5.2	5.0	5.2
Plasma HIV-1 RNA	Q1, Q3	4.5, 5.5	4.7, 5.6	4.5, 5.5	4.4, 5.2	4.2, 5.1	4.6, 5.7	4.6, 5.3	4.6, 5.6
		219 (25%)	52 (32%)	27 (15%)	29 (22%)	5 (4%)	15 (9%)	54 (74%)	37 (46%)
Abnormal neurological assessment		159 (18%)	41 (25%)	2 (1%)	22 (17%)	3 (5%)	9 (5%)	51 (70%)	31 (39%)
	Neuropathy	Equiv/Subclinical	159 (18%)	41 (25%)	2 (1%)	22 (17%)	3 (5%)	9 (5%)	51 (70%)
	Mild	6 (1%)	5 (3%)	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Moderate	1 (0%)	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
MCMD		36 (4%)	6 (4%)	5 (3%)	10 (8%)	1 (2%)	2 (1%)	0 (0%)	12 (15%)
ADC		4 (0%)	1 (1%)	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (3%)

INTRODUCTION

Little is known about neurological disease in international resource limited settings where the vast majority of HIV infection occurs. We report the baseline data from the ACTG A5199: The International Neurological Study.

Hypotheses

- Cognitive impairment and dementia due to HIV will be seen in at least 15% of subjects enrolled in this study.
- Neurological opportunistic infections will be seen in at least 20% of subjects enrolled in this study.
- A higher prevalence of dementia and neurologic opportunistic infections will be seen in those with plasma HIV-1 RNA >100,000 copies/mL.

This study is supported by NIMH and NIAID.

CONCLUSIONS

- Site variation in neuropsychological tests
- Possible differences in:
 - populations, cultures, HIV subtypes, or variation in test administration
- Relatively few diagnoses of Dementia
 - Possible selection bias in enrollment?
 - Higher functioning patients enrolled
- High prevalence of Peripheral Neuropathy
- Future studies
 - Normative controls
 - needed for assessment of individual impairment
 - Subtype/Clade differences