Neurocognitive Impairment in Diverse Resource Limited Settings:
The International Neuropsychological Study ACTG A5199 and The International Neurocognitive Normative Study ACTG A5271

ABSTRACT

While neurocognitive impairment in HIV remains prevalent despite potent antiretroviral therapy (ART), there is a lack of infrastructure conducting neurological research in resource limited settings (RLS), including normative data needed for clinical interpretation. ACTG 5271: the International Neurocognitive Normative Study provided training of clinical site personnel and collected normative comparison data on 2400 high risk HIV negatives from 10 VCT sites aligned with ACTG PEARLS (5175) in seven countries: Durban, South Africa, Zimbabwe, Blantyre, Malawi, Chennai, India, Porto, Portugal, Lima, Peru. We provided training for site personnel and collected normative comparison data on 2400 high risk HIV negatives from 10 VCT sites aligned with ACTG PEARLS (5175) in seven countries: Durban, South Africa, Zimbabwe, Blantyre, Malawi, Chennai, India, Porto, Portugal, Lima, Peru. We previously reported the first multinational neurological clinical trial of ART in RLS, ACTG 5199, the International Neuropsychological Study. Here we report the application of the normative data provided training of clinical site personnel and collected normative comparison data on 2400 high risk HIV negatives from 10 VCT sites aligned with ACTG PEARLS (5175) in seven countries: Durban, South Africa, Zimbabwe, Blantyre, Malawi, Chennai, India, Porto, Portugal, Lima, Peru.

INTRODUCTION

Neurocognitive Impairment over time
Baseline Prevalence
Neurocognitive Impairment
Baseline ART Naive
Improved with ART
- Reduced odds of NCI by 12% for every 24 weeks (p<.0001) on ART
- Normal improved from 54% to 72%
- No treatment differences

RESULTS

Baseline
Severe, 3%
Mild, 25%
Normal, 54%

Severe, 3%
Mild, 25%
Normal, 54%

Neuropsychological Exam S199
Timed Gait
Grooved Pegboard
 Finger Tapping
 Semantic Verbal Fluency
 S271 additions
Horns verbal learning
Color Trails 1 and 2
Digit Symbol

Impairment Ratings
Mild: 1 SD below mean on 2 tests, or 2 SDs on 1 test
Moderate: 1 SD on 3 to 4 tests, or 2 SDs on 2 tests
Severe: 1 SD on 5 or more tests, or 2 SDs on 3 tests or more

Neurocognitive Impairment over time
Baseline Naive and follow up on ART

CONCLUSIONS

- First multinational RLS study of NCI
  - This is the first multinational study addressing the prevalence of neurocognitive impairment in RLS. We found a substantial prevalence of neurocognitive impairment at baseline in HIV+ ART naïve participants in diverse RLS, consistent with US estimates.
  - NCI Prevalent
    - With ART initiation, there were significant overall reductions in neurocognitive impairment over time, especially in those with moderate and severe impairments. The observed changes after ART initiation may reflect improved learning effect.
    - ART improved NCI
      - ART in RLS led to reductions in neurocognitive impairment, and would likely lead to improved productivity and quality of life.
  - Normative Data Resource
    - A5271 provides a much needed resource for clinicians and researchers conducting neurological and neuropsychological assessments in diverse RLS.

Neurocognitive Impairment Ratings

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<th>Mild</th>
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Dysfunction Ratings:
- Normal: 1 SD below mean on 0 tests
- Mild: 1 SD below mean on 1 test
- Moderate: 1 SD below mean on 2 tests
- Severe: 1 SD below mean on 3 or more tests

Subjects
5199 HIV+ ART
- Antiretroviral naive
- CD4+ ≥ 300 cells/mm³
- 860 subjects enrolled

5271 HIV- Normative
- HIV- within 30 days
- Presenting to VCT
- 2400 subjects enrolled

Methods
Subjects
- HIV+ ART
  - Antiretroviral naive
  - CD4+ ≥ 300 cells/mm³
  - 860 subjects enrolled
- HIV- Normative
  - HIV- within 30 days
  - Presenting to VCT
  - 2400 subjects enrolled

- Stratified by:
  - Site, age (≥ 13, 35+)
  - Education (< 10, 10+)

Results

- Baseline prevalence of neurocognitive impairment in HIV+ ART naïve was 14% for every 24 weeks (p<.0001). At week 24, 62% were normal and at week 168, 72% were normal. Mild neurocognitive impairment was found in 25%, moderate in 17% and severe in 3%.
- With the initiation of ART, the odds of neurocognitive impairment reduced 12% (95% CI: 9%, 14%) for every 24 weeks (p<.0001). At week 24, 62% were normal and at week 168, 72% were normal. Mild impairment dropped slightly, and then remained at about 18% out to week 168. Analyses indicated that drop out did not account for improvement. There were no differences between treatment arms. There were differences between countries in overall neurocognitive performance as expected (p<.0001).

- CONCLUSIONS
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