Central nervous system toxicity of efavirenz in HIV-infected children in Tanzania

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Background: The World Health Organization recommends efavirenz as part of the first-line combination antiretroviral therapy (cART) for HIV-infected children. Awareness of central nervous system (CNS) side effects in adults is increasing. Reliable data on CNS toxicity in children, however, remain sparse. We compared neuropsychological symptoms, cognitive performance as well as adherence between long-term treated HIV-infected Tanzanian children on efavirenz vs. control regimens.

Methods: Cross-sectional observational study among HIV-infected children (6 to 12 years) on cART for ≥6 months and with viral loads ≤1000 copies/mL in Kilimanjaro, Tanzania. We used the Child Behavior Checklist (CBCL6-18) to evaluate behavioral and emotional problems. Cognitive performance was assessed using the Raven’s Colored Progressive Matrices and the Digit Span test. Non-adherence was defined as any reported missed doses over the previous three days or <100% adherence since the last clinical visit. Our study was powered to show a group difference of 0.5 SD in CBCL6-18 total problem scores. MANCOVA and logistic regression were used to assess differences between groups. Analyses were adjusted for age, sex, being treatment naïve, duration of cART, history of TB treatment, parental loss, and HIV disclosure.

Results: One-hundred-forty-one children were enrolled of whom 72 (51%) used efavirenz. Groups did not differ in age, sex, nadir CD4+ or general demographics. We found no differences in the CBCL6-18 behavioral and emotional problem scores (total/internalizing/externalizing), cognitive performance tests or adherence. Efavirenz-treated children had lower CBCL 6 to 18 competence scores (p = 0.025), which was mainly due to lower scores on school performance with mean (SD) 4.1 (1.4) and 4.7 (0.9) (p = 0.001) for efavirenz and controls respectively.

Conclusions: Overall, we did not see differences in emotional and behavioral problems, cognitive performance scores or adherence between efavirenz-treated children and controls, which is in contrast to earlier studies in adults. The lower school performance scores in efavirenz-treated children, however, warrant further study.

Outcomes of second-line antiretroviral therapy (ART) in HIV-infected children: a CIPHER cohort collaboration global analysis

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Background: There are limited data describing characteristics at second-line ART initiation and subsequent outcomes among children, particularly in resource-limited settings.

Methods: Data through 2015 on HIV-infected children aged <18 years initiating ART from 11 cohort networks were pooled. Characteristics at second-line ART initiation and immunological and clinical outcomes measured at one and two years after initiation were summarized by region: North America, Latin America (Caribbean, Central & South America), Europe, Asia, Southern Africa (South Africa & Botswana) and the rest of sub-Saharan Africa (SSA). Results were not adjusted for censoring due to loss to- or end of-follow-up.

Results: Of 85,389 children who started first-line ART, 3555 (4%) switched to second-line, primarily with protease inhibitors (92%). Median (interquartile range (IQR)) age at second-line ART initiation varied from 4.1 (1.9, 7.5) years in North America to 10.3 (6.7, 13.8) years in Latin America (Table 1). The lowest CD4 counts at second-line initiation were in SSA and Latin America (235 (81, 561) and 239 (63, 661) cells/mm3, respectively).

Conclusions: We found wide regional variations in age and CD4 count at second-line ART initiation among children. Immunological restoration was observed in all regions after switch to second-line. However, deaths continued to be observed in some regions through two years of follow-up.

Abstract WEAB0203-Table 1.