364. Association of Maternal ARV Use with Microcephaly in HIV-Exposed Uninfected Children

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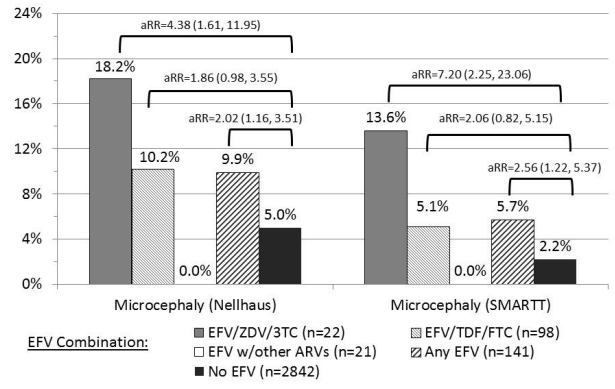
Background. Perinatal HIV transmission has dramatically decreased with combination antiretroviral (ARV) regimens, but complications among HIV-exposed uninfected (HEU) children, such as microcephaly, warrant ongoing surveillance.

Methods. We evaluated HEU children enrolled in the Surveillance Monitoring for ART Toxicities (SMARTT) study, a prospective cohort study conducted by the PHACS network at 22 US sites. Microcephaly was defined using 2000 CDC Growth z-scores for head circumference (HC) measured at 6–36 months of age (z-score <−2) and using Nellhaus standards (<2nd percentile) after age 3 ("SMARTT" criteria), or using Nellhaus standards across all ages. Modified Poisson regression models were fit to obtain relative risks (RRs) for associations between *in utero* ARV exposure and microcephaly status, adjusted for potential confounders. Sensitivity analyses were conducted. Neurodevelopmental functioning was compared between HEU children with vs. without microcephaly.

Results. Among 3055 SMARTT participants enrolled as of April 2017 with a HC measurement over 5.1 years median follow-up (IQR = 3.0, 7.2), 159 (5.2%, 95% CI: 4.4–6.1%) had microcephaly identified by Nellhaus criteria and 70 (2.3%, 95% CI: 1.8–2.9%) by SMARTT criteria. In adjusted models, *in utero* exposure to efavirenz (4.7% exposed) was associated with increased risk of microcephaly by both Nellhaus standards (aRR=2.02, 95% CI: 1.16, 3.51) and SMARTT criteria (adjusted RR = 2.56, 95% CI: 1.22, 5.37). These associations were more pronounced among children exposed to combination regimens of efavirenz which included zidovudine+lamivudine than those including tenofovir+emtricitabine (Figure 1). Associations of microcephaly with efavirenz persisted in several sensitivity analyses (Figure 2). Protective associations were observed for darunavir exposure (aRR = 0.50; 95% CI: 0.24, 1.00). HEU children with microcephaly had lower mean scores on neurodevelopmental assessments at ages 1 and 5 years and higher prevalence of impairment than those without microcephaly.

Conclusion. Efavirenz exposure during pregnancy was associated with a higher risk of microcephaly in infancy and childhood. These findings may support identification of alternatives to efavirenz as part of first-line ARV therapy.

Figure 1. Percent of HEU Infants with Microcephaly by EFV-containing Maternal ARV Regimen, with adjusted risk ratios (aRRs) and 95% CIs



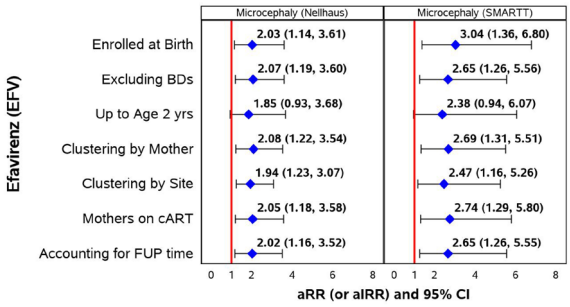


Figure 2. Sensitivity analyses evaluating association of *in utero* efavirenz exposure with microcephaly status by Nellhaus and SMARTT criteria

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365. Neurocognitive Function Change after Switching from Efavirenz to Rilpivirine in HIV-Infected Adults: A Randomized Control Trial

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Background. HIV-associated neurocognitive disorders (HAND) remain problematic even in the antiretroviral therapy (ART) era. Efavirenz (EFV) is well known for neuropsychiatric side effects and has been associated with worsening neurocognitive performance (NC). We hypothesized that switching from an ART regimen with EFV to one with rilpivirine (RPV) would improve NC.

Methods. This single-center, open-label, superiority, randomized controlled trial was conducted at Maharaj Nakorn Chiang Mai Hospital June 2018 to March 2019. HIV- infected adults (≥18 years), virologically suppressed on an EFV-containing regimen for at least 12 months, who met Frascati's criteria of asymptomatic neurocognitive impairment (ANI), were randomized to a switching arm (RPV-containing regimen) vs. a control arm (EFV-containing regimen). The primary objective was to compare the improvement of NC at month 6 (M6) after switching. Secondary outcomes were individual NC domains, tolerability, and safety after switching regimens.

Results. 20 ANI participants (10 per group) completed the study. 11 participants showed NC improvement at M6: 6 in the switching arm and 5 in the control arm. Global neuro deficit scores (GDS), figure learning, and figure memory at M6 significantly improved in both arms ($P < 0.05$). Verbal memory and speed of information processing improved over time in the switching arm only (0.6 (0.1–1.0); $P = 0.02$, and 0.7 (0.1–1.2); $P = 0.03$, respectively). However, no significant differences between the two groups were observed. Male gender, age < 50 and initiation of ART within 5 years after diagnosis all trended toward an association with improved NC. No tolerability issues or clinical significant adverse events were reported.

Conclusion. Despite some positive trends, switching from an EFV-containing regimen did not significantly improve NC. This finding was consistent with previous reports. A larger study with longer follow-up may be warranted.

Table 1 Baseline Patient Characteristics

	Switched to RPV n=10 (%)	Continue on EFV n=10 (%)	*p-value*
Age (Mean ±SD)	52.0 ±8.1	54.0±6.2	0.54
Male Sex	4(40)	3(30)	0.6
Years education	9.7(5.4)	8.9(4.306326)	0.72
Education			
- Primary school(PS) or lower	3(30)	4(40)	0.14
- Secondary school(SC)	1(10)	4(40)	
- High school (HS) or higher	6(60)	2(20)	
Occupation			
- Unemployed	1(10)	2(20)	0.660
- Employed	9(90)	8(80)	
Route of infection			
- Heterosexual	10(100)	9(99)	0.30
- Homosexual	0(0)	1(1)	
- CD4 Nadir (cells/uL) (Mean ±SD)	200.1(±171.2)	223.7(±201.4)	0.78
CDC Category			
- A	6(60)	8(80)	0.47
- B	1(10)	0(0)	
- C	3(30)	2(20)	
CD4 current (cells/uL) (Mean ±SD)			
- CD4 current (cells/uL)	647.6(±169.8)	733.9(±284.6)	0.42
- CD4 current (%)	30.7(±7.8)	30.2(±7.4)	0.89
Time since HIV diagnosis (yrs) (Mean ±SD)	14.8(±5.5)	12.1(±6.4)	0.32
Time on cART (yrs) (Mean ±SD)	13.3(±5)	9.6(±4.8)	0.11
Time on EFV (yrs) (Mean ±SD)	5.30(±5)	5.80(±4.8)	0.82
Concurrent medications, items			
- 0-1	9(90)	7(70)	0.26
- ≥ 2	1(10)	3(30)	
Previous cART regimens			
- 0	1(10)	1(10)	1
- 1	3(30)	3(30)	
- ≥ 2	6(60)	6(60)	

Table 2 Global deficit scores and domain Z-score at baseline

	Z-score Mean (±SD)		*p-value*
Parameters	RPV	EFV	
Global Deficit score	-1.3(1.3)	-0.9(1.3)	0.42
1. Verbal and language	-0.6(1.1)	-0.1(0.8)	0.26
2. Attention and working memory	-0.6(0.6)	-0.1(1.0)	0.23
3. Abstraction and executive function	-0.8(0.6)	-0.7(1.2)	0.83
4. Verbal Memory	-1.0(0.9)	-1.2(1.1)	0.63
5. Figural learning	-1.0(1.2)	-1.3(1.3)	0.63
6. Figural memory	-0.7(1.0)	-0.8(0.6)	0.87
7. Speed of information processing	-0.5(0.6)	-0.5(1.3)	0.89
8. Motor Skills/Complex Perceptual	-1.0(0.8)	-0.8(1.6)	0.74
9. Gross Motor	-1.3(1.3)	-0.9(1.3)	0.42