Use and outcomes of antiretroviral monotherapy and treatment interruption in perinatally HIV-infected adolescents in Asia

Adam Bartlett | Kirby Institute, UNSW Sydney

Disclosures

- Gilead

Background

- Combination antiretroviral therapy (cART) in adolescents living with perinatally-acquired HIV infection (PHIVA) is complicated by the impact of chronic disease on physical and psychosocial health.

- Monotherapy or treatment interruption as alternate treatment strategies has been considered to limit disease progression and/or antiretroviral resistance during periods of inadequate adherence or those awaiting access to effective cART.

- Data regarding viability of monotherapy or treatment interruption in PHIVA are mixed, with prior studies incorporating adolescents into broader cohorts with children or young adults.

Aims

1. Describe characteristics of PHIVA who received monotherapy or had treatment interruption.

2. Report trends in CD4 count and HIV viral load during and after periods of monotherapy or treatment interruption.

3. Evaluate WHO stage III/IV event-free survival during periods of monotherapy or treatment interruption.

4. Determine factors associated with monotherapy and treatment interruption.

Methods

- Study population
  - Regional data from the TREAT Asia pediatric HIV Observational Database (TApHOD).
  - PHIVA (aged 10-19 years) who received care 2001-2016 who experienced at least two weeks of lamivudine/emtricitabine monotherapy or treatment interruption.
- Statistical analyses
  - Descriptive analyses for characteristics of study population and trends in CD4 count and HIV viral load.
  - Kaplan-Meier survival analyses for WHO stage III/IV (clinical and immunologic) event-free survival.
  - Poisson regression analysis for factors associated with monotherapy or treatment interruption.

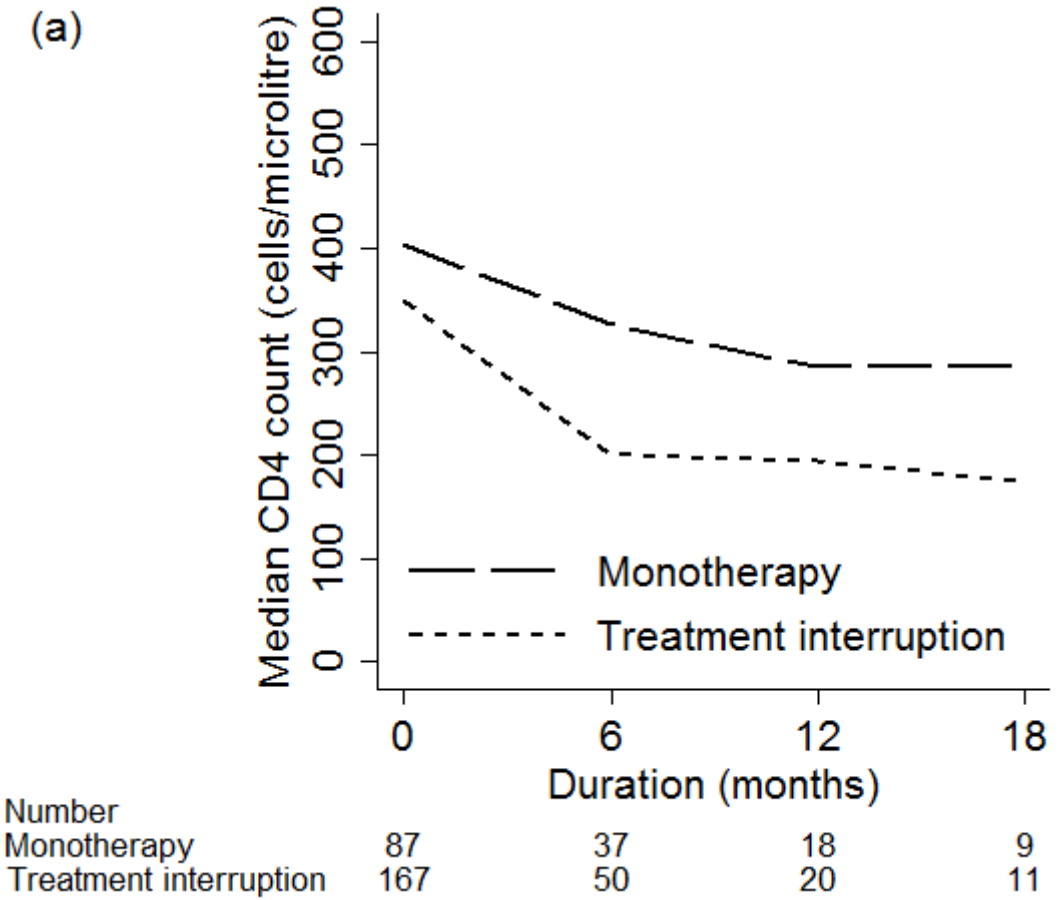
Results

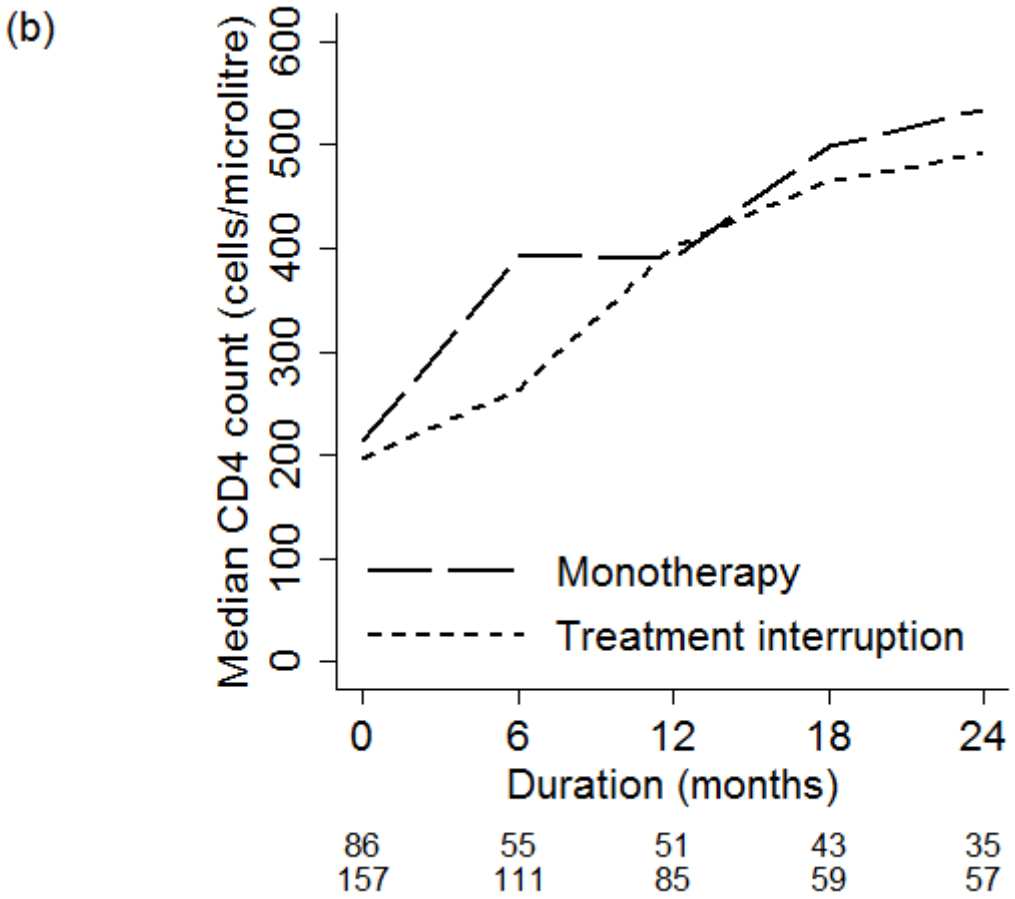
- Total 3,448 PHIVA
  - Median follow-up 4.7 years

- 84 (2.4%) received monotherapy
  - 94 episodes
  - Median age 15 [IQR 12.9, 16.5] years; median duration 198 [IQR 117, 365] days
  - Incidence rate 0.6 [95%CI 0.5, 0.7] per 100 person-years

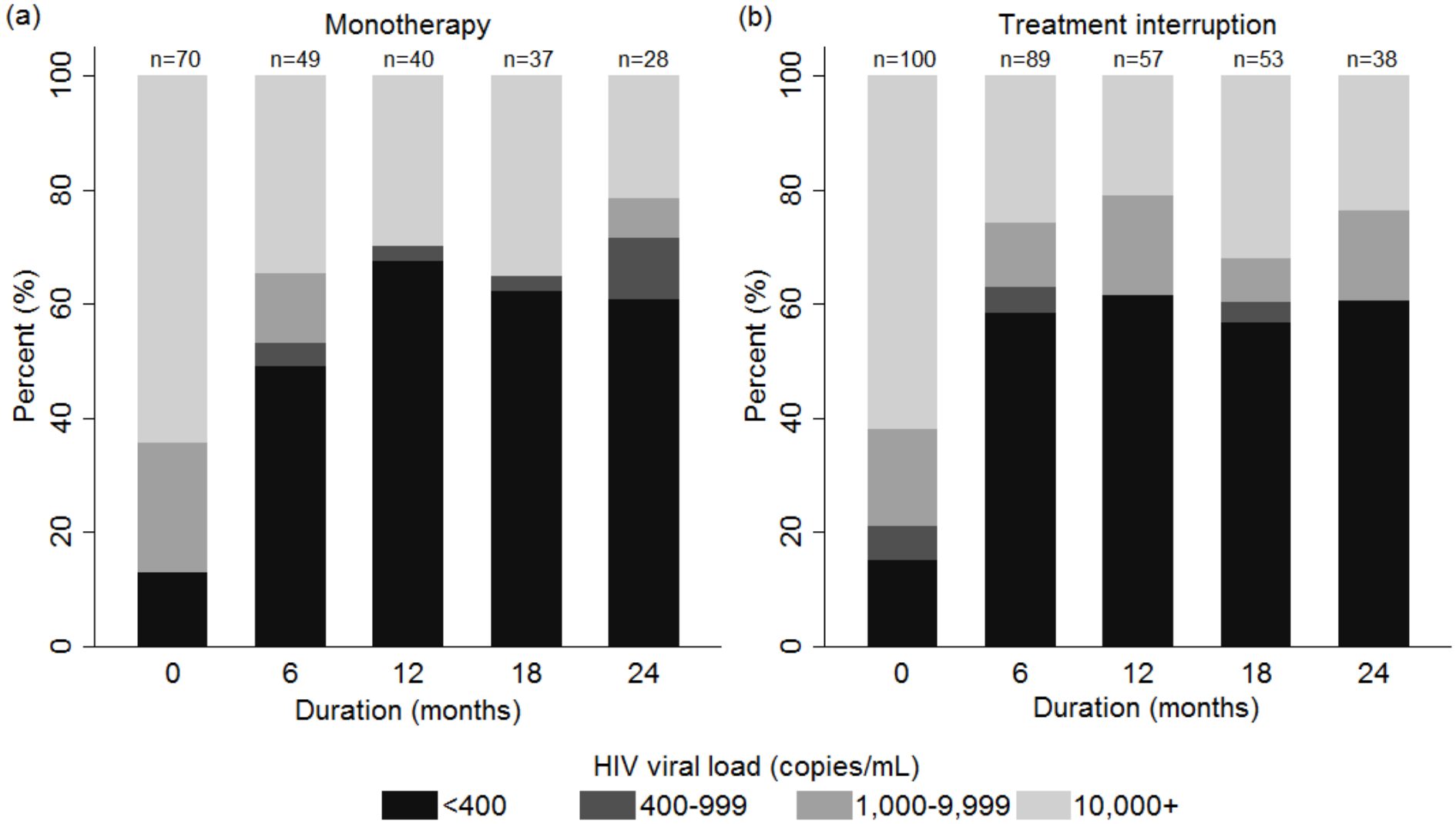
- 147 (4.3%) underwent a treatment interruption
  - 174 episodes
  - Median age 14.5 [IQR 12.5, 16.4] years; median duration 182 [IQR 65, 343] days
  - Incidence rate 1.1 [95%CI 0.9, 1.3] per 100 person-years

Median CD4 count trend (a) during monotherapy or treatment interruption and (b) with subsequent antiretroviral therapy

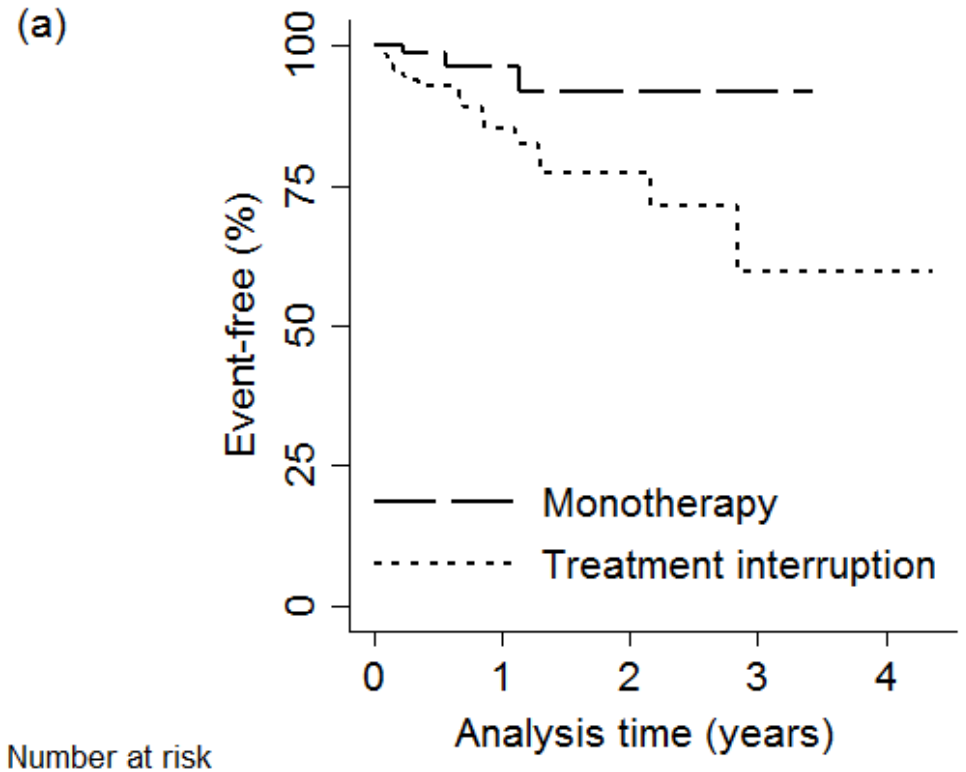




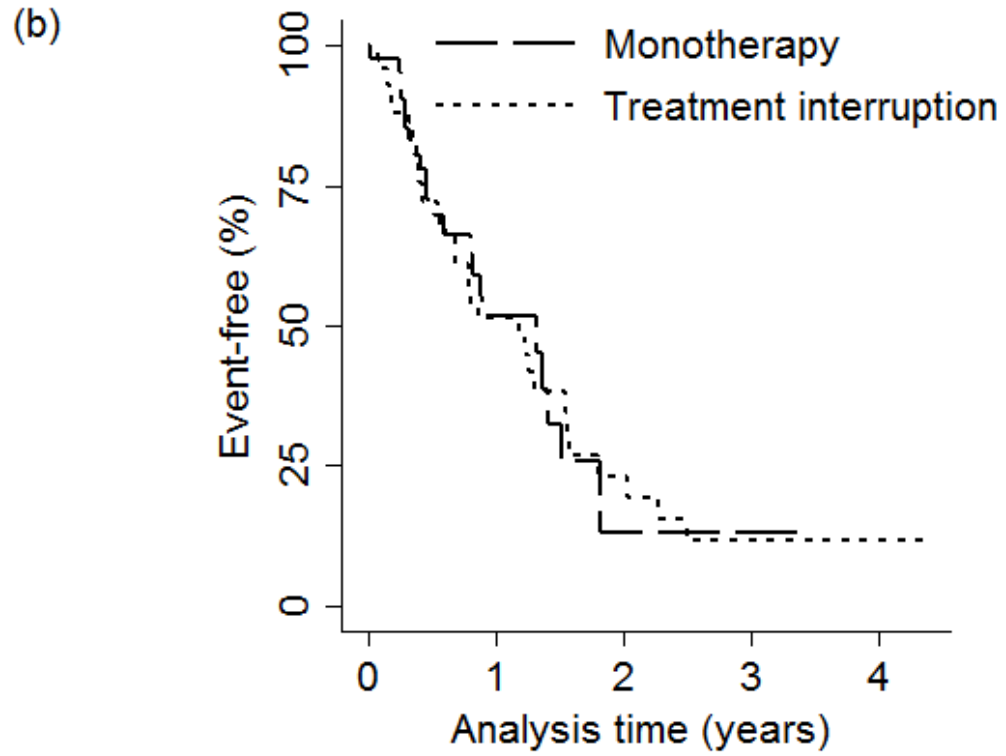
HIV viral load distribution with subsequent antiretroviral therapy following (a) monotherapy or (b) treatment interruption



(a) WHO clinical stage III/IV event-free survival and (b) WHO immunologic stage III/IV event-free survival during monotherapy or treatment interruption



Number at risk					
Monotherapy	84	23	4	4	0
Treatment interruption	147	36	14	4	1



	44	11	1	1	0
	81	16	6	3	1

Associated factors with monotherapy

aIRR = adjusted incidence ratio

- Older age
  - 15-19 years vs 10-14 years — aIRR 2.0 [95%CI 1.3, 3.1]
- Younger age at ART initiation
  - 5-9 years vs <3 years — aIRR 0.3 [95%CI 0.2, 0.6]
  - ≥10 years vs <3 years — aIRR 0.3 [95%CI 0.2, 0.6]
- More prior cART regimens
  - ≥2 regimens vs 1 regimen — aIRR 1.8 [95%CI 1.1, 3.0]
- Unsuppressed HIV viral loads
  - 400-999 copies/mL vs <400 copies/mL — aIRR 10.2 [95%CI 3.2, 32.5]
  - 1,000-9,999 copies/mL vs <400 copies/mL — aIRR 24.6 [95%CI 11.7, 51.7]
  - ≥10,000 copies/mL vs <400 copies/mL — aIRR 30.0 [95%CI 15.2, 59.1]
- NOT significant on multivariate analysis
  - Sex, WHO clinical stage, ART adverse event, prior monotherapy.

Associated factors with treatment interruption

aIRR = adjusted incidence ratio

- Older age at ART initiation
  - ≥10 years vs <3 years — aIRR 3.2 [95%CI 1.5, 6.6]
- Lower CD4 counts
  - 200-349 cells/μL vs ≥500 cells/μL — aIRR 2.3 [95%CI 1.5, 3.8]
  - <200 cells/μL vs ≥500 cells/μL — aIRR 2.9 [95%CI 1.8, 4.5]
- High HIV viral loads
  - 1,000-9,999 copies/mL vs <400 copies/mL — aIRR 3.8 [95%CI 2.2, 6.5]
  - ≥10,000 copies/mL vs <400 copies/mL — aIRR 3.4 [95%CI 2.0, 5.0]

- NOT significant on multivariate analysis
  - Age, sex, WHO clinical stage, prior combination ART regimens, prior treatment interruption.

Limitations

- Heterogenous PHIVA population with varying antiretroviral exposure and subsequent antiretroviral regimens.
- Insufficient data to evaluate treatment adherence.
- Unable to ascertain reported reasons for monotherapy or treatment interruption, including whether treatment interruptions were intentional or incidental.
- Incomplete ascertainment of treatment interruptions by excluding PHIVA that had stopped but not re-commenced antiretroviral therapy by the end of the study period.

Conclusions

- Monotherapy was observed in PHIVA with extensive antiretroviral exposure and poor virologic control, suggestive of treatment fatigue.
- Treatment interruption were encountered in PHIVA with poor immunologic and virologic control, suggesting issues with treatment adherence and engagement in care.
- Both monotherapy and treatment interruption render PHIVA immunologically vulnerable with poor virologic and immunologic responses following subsequent antiretroviral therapy.
- Enhanced treatment adherence support, lifting barriers to engagement in care, and increasing access to durable and tolerable suppressive cART regimens is of paramount importance.

Acknowledgements

Thanks to the patients and TApHOD study staff at our clinical research sites.

Funders: U.S. National Institutes of Health's National Institute of Allergy and Infectious Diseases, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Cancer Institute, National Institute of Mental Health, and National Institute on Drug Abuse as part of IeDEA (U01AI069907).

The Kirby Institute is funded by the Australian Government Department of Health and Ageing, and is affiliated with the Faculty of Medicine, UNSW Australia.

AWB received support from an Australian Government Research Training Program Scholarship.

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