

CBV/EFV arm at 48 weeks.³⁰ Concerns about ART and intrusiveness were also reported lower in those switched to the TDF/FTC/EFV arm. There were however no significant differences in necessity, beliefs, quality of life or viral loads between the randomized groups. A study of the psychosocial factors affecting medication adherence among HIV-1 infected adults receiving combination antiretroviral therapy in Botswana, though not describing the dosing types, found adults receiving HAART for the first 6 months to be least adherent.³¹

Pharmaceutical superiority

This is another confounding factor not catered for in this research. Some studies have comparatively shown superiority over the TDF/FTC/EFV arm against CBV/EFV in ART naïve patients through measurements of HIV RNA levels (VL) at 48 weeks.¹⁶

Natural course of HIV infection

The study results could be affected by several factors relating to the natural course of HIV infection. Several strains of HIV have been recorded in different parts of the world and although the most prevalent HIV strain in Botswana is HIV-1 subtype C, there may potentially be patients with different strains in Botswana. There are specific biological characteristics of HIV-1C including high genetic diversity which may potentiate the emergence of ARV drug resistant HIV strains.³² Evidence of greater rates of disease progression in globally prevalent C and D subtypes highlight the importance of expanding early HIV detection, and determining subtype profile at baseline with CD4 staging to optimize the quality of ART delivery and care in global settings³³. These facts have not been adjusted for in this study.

Study Limitations

The sampling method as already described was conveniently selected and not randomized as initially proposed. Although this was noted in the statistical analysis, it negatively impacts on the credibility of the results obtained as the likelihood of selection bias is introduced.

The study is limited to response to treatment in the initial 3 month period. The initial response does not necessarily translate to long term treatment outcome. Absolute CD4 cell counts were used as an endpoint but this variable has been found to fluctuate with individuals and with intercurrent illnesses.¹⁰

Conclusion

Treatment response at 3 months post initiation between once daily and twice daily HAART in Gaborone Botswana by use of virologic and immunologic response has been shown to be comparable. The use of one regimen over the other as first line as recommended by WHO and the subsequent adoption of the current first line regimen by the Botswana Ministry of Health may be justified. This study has therefore reinforced the applicability of previous findings in other settings of this recommendation. As part of the targeted audience and indeed as a partner in the care and management of HIV, the responsibility to ensure applicability of the recommendations set out for resource limited areas has been achieved through this study. However, bigger randomized trials in resource limited settings are needed to justify and accredit these findings as well as add to the evidence obtained in developed countries.

References

1. WHO, UNAIDS, UNICEF. Global HIV/AIDS Response-Epidemic update and health sector progress towards Universal Access-Progress Report; 2011. Available from: www.unaids.org (accessed 28/05/2012)
2. Ministry of Health. Botswana National HIV/AIDS Treatment Guidelines; December 2011. Chapter 5; HAART initiation and follow-up; p.48-52
3. National Institute of Health. Clinical trials. Last updated; October 2011. Available from: <http://www.clinicaltrials.gov> (accessed on 26/05/2012)
4. WHO: Adherence to long-term therapies. Evidence for action.[Online]. 2003. Available from: http://www.who.int/chp/knowledge/publications/adherence_report/en/index (accessed on 09/04/2010)
5. Eldred LJ et al. Adherence to antiretroviral and pneumocystis prophylaxis in HIV disease. *Journal of Acquired Immune Deficiency Syndromes* 1998; **18**:117-125.
6. Gallant JE, Rodriguez AE, Weinberg WG, Young B, Berger DS, Lim ML et al. Early Virologic response to Tenofovir, Abacavir and Lamivudine in HIV infected Antiretroviral –Naïve Subjects. *J Infect Dis* 1 Dec 2005; **192(11)**:1921-30.
7. Molina JM. Efficacy and safety of once daily regimens in the treatment of HIV infection. *Drugs* 2008; **68(5)**:567-78.
8. Steingrover R, Garcia EF, van Valkengoed IG, Bekker V, Bezemer D, Kroon FP et al. Transient lowering of the viral set point after temporary antiretroviral therapy for primary HIV type 1 infection. *AIDS Res Hum Retroviruses* 2010 Apr **26(4)**:379-87.
9. Crabtree-Ramirez B, Villasis-Keever A, Galindo-Fraga A, del Rio C, Sierra-Madero J. Effectiveness of highly active antiretroviral therapy (HAART) among HIV-infected patients in Mexico. *AIDS Res Hum Retroviruses* 2010 Apr **26(4)**:373-8.
10. WHO. Antiretroviral therapy for HIV infection in adults and adolescents; Recommendations for a public health approach. 2010 rev Available from www.who.int. (accessed 21/08/2012)
11. Miguel Goicechea & Brookie Best. Efavirenz/emtricitabine/tenofovir disoproxil fumarate fixed-dose combination: first line therapy for all? *Expert opin.Pharmacother.* 2007; **8(3)**:371-382.
12. Mathias A, Hinkle J, Menning M, Hui J, Kaul S, Kearney BP. Bioequivalence of efavirenz/emtricitabine/tenofovir disoproxil fumarate single-tablet regime. *J Acquir Immune Defic Syndr.* 1 Oct 2007; **46(2)**:167-73.

13. Campo R, Cohen C, Grimm K, Shangguan T, Maa J, Seekins D. Switch from protease inhibitor to efavirenz based antiretroviral therapy improves quality of life, treatment satisfaction and adherence with low rates of virological failure in virologically suppressed patients. *Int J STD AIDS* 2010 Mar **21(3)**:166-71.
14. Piliero PJ, Colagrecio JP. Simplified regimens for treating HIV infection and AIDS. *J AM Acad Nurse Pract.* 2003 July **15(7)**:307-12.
15. Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squier C et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann of Intern Med* 2000 Jul 4; **133**:21-30.
16. Gallant JE, Dejesus E, Arribas JR, Pozniak, Gazzard B, Campo RE et al. Tenofovir DF, emtricitabine and efavirenz versus zidovudine, lamivudine and efavirenz for HIV. *N Engl. J. Med.* 2006; **354**:251-60.
17. Molina JM, Andrade-Villanueva J, Echevarria J, Chetchotisakd P, Corral J, David N et al. Once daily atazanavir/ritonavir versus twice daily lopinavir/ritonavir, each in combination with tenofovir and emtricitabine, for management of antiretroviral-naïve HIV-1 infected patients:48 week efficacy and safety results of the CASTLE study. *Lancet.* 23 Aug 2008.**372(9639)**:646-55.
18. Elion R, Cohen C, Ward D, Ruane P, Ortiz R, Reddy YS et al. Evaluation of efficacy, safety, pharmacokinetics and adherence in HIV-1-infected antiretroviral-naïve patients treated with ritonavir-boosted atazanavir plus fixed dose tenofovir DF/emtricitabine given once daily. *HIV Clin Trials.* 2008 Jul-Aug; **9(4)**:213-24.
19. Fisher M, Moyle GJ, Shahmanesh M, Orkin C, Kingston M, Wilkins E et al. A randomized comparative trial of continued zidovudine/lamivudine or replacement with tenofovir disoproxil fumarate/emtricitabine in efavirenz-treated HIV-1 infected individuals. *J Acquir Immune Defic Syndr.* 2009 Aug 15;**51(5)**:562-8.
20. DeJesus E, Ruane P, McDonald C, Garcia F, Sharma S, Corales R. Impact of switching virologically suppressed HIV1-infected patients from twice-daily fixed dose zidovudine/lamivudine to once-daily fixed-dose tenofovir disoproxil fumarate/emtricitabine. *HIV Clin Trials.*2008 Mar-Apr;**9(2)**:103-14.
21. Arasteh K, Weitner L, Feneske S, Kuhlmann B, Freiwald M, Ebrahimi R. Switch from a ZDV/3TC-based regimen to a completely once daily (QD) regimen of emtricitabine/tenofovir DF fixed dose combination plus a third QD agent (SONETT). *Eur J Med Res.*2009 May 14;**14(5)**:195-9.
21. Cockroft-Gault formula:

$$eC_{Cr} = \frac{(140 - \text{Age}) \times \text{Mass (in kilograms)} \times \text{Constant}}{\text{Serum Creatinine (in } \mu\text{mol/L)}}$$

Where *Constant* is 1.23 for men and 1.04 for women.

Available from: <http://en.wikipedia.org> (accessed on 14/07/2010)

23. WHO.WHO initiative on HIV/AIDS and sexually Transmitted infections
WHO/HIS/2000.04
<http://www.who.int/hq/2000/WHO> (accessed on 24/06/2010)
24. Gafni RI, Hazra R, Reynolds JC, et al. Tenofovir disoproxil fumarate and an optimized background regimen of antiretroviral agents as salvage therapy: Impact on bone mineral density in HIV-infected children. *Pediatrics*. 2006;**118**(3):e711–e718.
[PubMed]
25. Republic of Botswana. Guidelines for Application for Research Permit. Gaborone.2004
<http://www.gov.bw> (accessed on 27/08/2012)
26. World Medical Association Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects
Available on <http://www.wma.net> (accessed on 14/07/2010)
27. Ford N, Calmy A, Mofenson et al. Safety of efavirenz in the first-trimester of pregnancy: an updated systematic review and meta-analysis. *AIDS* 2011. 25(18) : 2301-4.
28. Arribas JR, Pozniak AL, Gallant JE, Dejesus E, Gazzard B, Campo RE, et al. Tenofovir disoproxil fumarate, emtricitabine, and efavirenz compared with zidovudine/lamivudine and efavirenz in treatment-naïve patients: 144-week analysis. *J Acquir Immune Defic Syndr* 2008;**47**(1):74-8.
29. Pozniak A, Gallant J, DeJesus E, Arribas J, Gazzard B, Campo R et al. Tenofovir Disoproxil Fumarate, Emtricitabine and Efavirenz Versus Fixed-Dose Zidovudine/Lamivudine and Efavirenz in Antiretroviral-Naïve Patients: Virologic, Immunologic and Morphologic Changes-A 96 Week Analysis. *J Acquir Immune Defic Syndr*. 2006 Dec;**43**(5):535-540.
30. Cooper V, Moyle GJ et al. Beliefs about antiretroviral therapy, treatment adherence and quality of life in a 48 week randomized study of continuation of zidovudine/lamivudine or switch to tenofovir DF/emtricitabine, each with efavirenz. *AIDS care*. 2011;**23** (6):705-13.
31. Do NT, Phiri K, Bussmann H, Gaolathe T, Marlink RG, Wester CW. Psychosocial factors affecting medication adherence among HIV-1 infected adults receiving combination antiretroviral therapy (cART) in Botswana. *AIDS Res Hum Retroviruses*.2010 Jun;**26**(6):685-91.
32. Bussman H, Noritsky V, Wester W, Peter T, Masupu K, Gabaitiri L et al. HIV-1 subtype C drug-resistance background among ARV-naïve adults in Botswana. *Antivir Chem Chemother*.2005;**16**(2):103-15.
33. Pant Pai N, Shivkur S, Cajas JM. Does genetic diversity of HIV-1 non-B subtypes differentially impact disease progression in treatment naïve HIV-1 infected individuals? A systematic review of evidence:1996-2010. *J Acquir immune DeficSyndr*.2012 April;**59**(4):382-8.