

Oral presentation

O125 Impact of efavirenz and nevirapine on pharmacokinetics of lopinavir/ritonavir as tablets and capsules in African patients

C Kityo*¹, AS Walker², F Lutwana³, F Ssali⁴, R Nalumenya³, D Tumukunde⁴, J Kawiya⁵, P Munderi⁶, A Reid⁷, CF Gilks⁸, DM Gibb² and SH Khoo⁹

Address: ¹CRC, Uganda, Uganda, ²MRC Clinical Trials Unit, London, UK, ³Infectious Diseases Institute, Mulago, Uganda, ⁴Joint Clinical Trials Unit, London, UK, ⁵Joint Clinical Research Centre, Kampala, Uganda, ⁶MRC/UIVRI Research Unit on AIDS, Entebbe, Uganda, ⁷University of Zimbabwe, Harare, Zimbabwe, ⁸Imperial College, London, UK and ⁹Liverpool University, Liverpool, UK

* Corresponding author

from Ninth International Congress on Drug Therapy in HIV Infection
Glasgow, UK. 9–13 November 2008

Published: 10 November 2008

Journal of the International AIDS Society 2008, **11**(Suppl 1):O10 doi:10.1186/1758-2652-11-S1-O10

This abstract is available from: <http://www.jiasociety.org/content/11/S1/O10>

© 2008 Kityo et al; licensee BioMed Central Ltd.

Purpose of the study

With NNRTI, the recommended dose of lopinavir/r (LPV/r) is 4 capsules (533/133 mg) BD. With LPV/r tablets, the closest doses are 2 tablets (400/100 mg) BD or 3 tablets [tabs] (600/150 mg) BD. Improved bioavailability of the tablet suggests that 2 tabs BD should be sufficient, but PK data are few and generally from Caucasians.

Methods

We conducted a three-period crossover PK study in 40 patients receiving LPV/r tablets with NNRTIs (21 EFV, 19 NVP) second-line (first PI) in one Ugandan centre in the DART trial. Patients on 3 tabs BD underwent 6-point PK sampling (0, 2, 4, 6, 8 and 12 hours) after observed intake with a standardised breakfast. They then switched to 4 caps BD for 2 weeks before a second PK, then switched to 2 tabs BD for 2 weeks before a third PK, after which they returned to 3 tabs BD. Analysis excluded two patients with minimal LPV/r exposure on 4 caps BD.

Summary of results

6/20 EFV and 13/18 NVP patients included were female (reflecting contra-indication of EFV in women with child-bearing potential), with median age 41 and 35 years, and weight 60 and 64 kg, respectively. On EFV, mean (SD) LPV AUC was 104 (54), 70 (27) and 63 (33) ug.h/l on 3 tabs BD, 4 caps BD, and 2 tabs BD, respectively, with corresponding GMR vs. 4 caps BD 1.40 (90% CI 1.18–1.65, $p = 0.002$) and 0.82 (0.68–0.99, $p = 0.09$). On NVP, mean

(SD) LPV AUC was 118 (33), 77 (39) and 69 (34) ug.h/l, respectively, with corresponding GMR vs. 4 caps BD 1.66 (1.46–1.88, $p < 0.001$) and 0.90 (0.77–1.06, $p = 0.27$) for 3 and 2 tabs BD, respectively. On EFV, 15%/15%/40% had C12(trough) < 1 ug/ml ($p = 0.1$) with corresponding GMR vs. 4 caps BD 1.48 (1.09–2.02, $p = 0.04$) and 0.62 (0.39–0.98, $p = 0.08$) for 3 and 2 tabs BD, respectively. On NVP, 0%/22%/28% had C12 < 1 ug/ml ($p = 0.06$) with corresponding GMR vs. 4 caps BD 2.31 (1.64–3.24, $p < 0.001$) and 0.80 (0.57–1.12, $p = 0.26$) for 3 and 2 tabs BD, respectively. However, 40%/5%/15% EFV and 56%/28%/17% NVP patients had C12 > 5 ug/ml. There was no effect of sex, age, weight or BMI on AUC or C12.

Conclusion

When co-administered with NVP or EFV in African patients, LPV AUC and C12 are higher with 3 tablets BD and lower with 2 tablets BD compared to 4 capsules BD. Higher plasma levels on 3 tablets BD may lead to greater long-term toxicity, whereas low plasma C12 on 2 tablets BD may increase the risk of virological failure. However, AUC on 4 caps BD was lower than expected, and tablet AUC variability was higher than expected. Further PK sampling is therefore ongoing to estimate PK parameters in African patients taking 2 LPV/r tablets BD without NNRTIs.