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TITLE

Optimization of HIV and Tuberculosis co treatment in Africa: Pharmacokinetics and Pharmacogenetic Aspects of Interaction Between Efavirenz and Rifampicin

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Rifampicin, potent inducer of CYP enzymes reduces plasma level of EFV by 22–26% and the appropriate daily dosage of EFV (600 vs. 800mg/day) remains uncertain for use with rifampicin. We investigated pharmacogenetic and pharmacokinetic interaction between efavirenz and rifampicin with aim to identify whether there is a need for efavirenz dosage adjustment or not when given with rifampicin. >800 treatment naive HIV patients without tuberculosis (arm-1) and TB-HIV co-infected patients (arm-2) were enrolled and followed for up to one year in Addis Ababa, Ethiopia and Dar es Salaam Tanzania. Efavirenz kinetics, pharmacogenetic analysis and safety/efficacy (VL and CD4 count) were recorded over a year and data compared between the two arms and the two countries. A significant difference in genotype and efavirenz kinetics was found between patients from Ethiopia and Tanzania and its relevance for long-term clinical outcome will be presented. Both CYP2B6 genotype and duration therapy influences long-term efavirenz autoinduction in the absences of rifampicin. However in the presence of rifampicin, CYP2B6 genotype but not duration of efavirenz therapy is important. Effect of rifampicin on efavirenz kinetics is apparent during early therapy but has no significant effect in the long-term. Enzyme induction is pronounced mainly in patients with CYP2B6*1/*1 genotypes which may cause sub therapeutic efavirenz plasma concentration in long-term ART. We report for the first time CYP2B6 genotype dependent effect of rifampicin on long-term efavirenz autoinduction and disposition. The preliminary result indicates no need for efavirenz dosage adjustment during concomitant rifampicin based TB therapy in black Africans.

Biography

Dr Eleni Aklillu is Associate professor in pharmacology (2009) at the division of clinical pharmacology, Karolinska Institute, Stockholm, Sweden. She received her Ph.D. degree in molecular genetics (2003) from Karolinska Institutet, Stockholm Sweden. Her research area is focused on Pharmacogenetics, pharmacokinetics, PK/PD drug interaction and their effect on adverse events and treatment response with focus on HIV/AIDS, Tuberculosis, and psychiatry. Currently she is principal investigator of three multi-national capacity building clinical research projects financed by European and developing clinical trial partnership and SIDA Currently she is serving as senior research scientist at Karolinska Institutet and has published more than 40 original research papers in reputed journals.