

Effectiveness of cotrimoxazole (CTX) prophylaxis on survival and in program retention in sub-Saharan African HAART treated adults with baseline CD4 > 200/mm³

Charlotte Lewden^{1,2}, Eric Balestre^{1,2}, Rodolphe Thiébaud^{2,3} ..., François Dabis^{1,2}, Catherine Seyler^{1,2} for the ART-LINC Collaboration of IeDEA.

¹INSERM, U593, Bordeaux, France ; ²Université de Bordeaux 2, ISPED, Bordeaux, France ; ³INSERM, U875, Bordeaux, France

Background. In Sub-Saharan Africa, 2006 WHO guidelines recommended CTX prophylaxis prescription in HIV-infected adults in case of symptomatic HIV disease or CD4 cell counts <350 cells/mm³. Nevertheless, these recommendations have not been fully implemented. In settings where tuberculosis, bacterial infections and malaria are a predominant cause of HIV-associated morbidity and mortality, evaluation of additional impact of CTX prophylaxis after initiation of highly active antiretroviral therapy (HAART) is scarce. We aimed at estimating survival and program retention after HAART initiation according to CTX use in patients without AIDS or without CD4 cell counts <200/mm³ at baseline.

Methods. The Antiretroviral Therapy in Low-Income Countries Collaboration (ART-LINC of IEDEA) is an international network of cohorts of patients starting HAART. Among cohorts from Sub-Saharan Africa who collected information on CTX prophylaxis, we selected antiretroviral naïve patients who initiated HAART with WHO stage 1 or 2 and CD4 cell count above 200 cells /mm³ or unknown, and with at least one day of follow-up after HAART initiation. CTX use was considered in intention to continue treatment. The outcomes were (1) death and (2) death or loss-to-follow-up (LFU). Patients were considered as LFU if they had at least one year of potential follow-up after their last visit. Follow-up was censored 2 years after initiation of HAART. We estimated Kaplan-Meier probabilities of survival and performed Weibull parametric survival model adjusted for following baseline characteristics: age, gender, HAART regimen, body mass index, haemoglobin, CD4 and with random effects controlling for cohort heterogeneity.

Results. Seven cohorts (from Senegal, Cote d'Ivoire, Rwanda, Kenya, Zimbabwe and South Africa) provided data on 16,565 adults, of whom 2,710 had inclusion criteria for this analysis. Median age was 33 years (interquartile range 28-39), 79% were women and 62% received CTX prophylaxis in addition to HAART. The probability of death did not differ according to CTX use. Cumulated probabilities of death or LFU at 12 months were 5.0% and 8.9% in patients with and without CTX use, respectively. At 24 months, these figures were 8.9% and 9.8%, respectively. In multivariate analysis, the hazard ratio for death or LFU was 0.46 (95% confidence interval 0.30-0.73, p=0.001) for CTX + HAART versus HAART alone. Moreover, male gender and baseline low haemoglobin tend to be associated with death or LFU.

Conclusion. In Sub-Saharan Africa, CTX prophylaxis in addition to HAART had a positive effect on program retention in asymptomatic HIV-infected adults with CD4>200/mm³. National HIV Programs and funders should more specifically focus on cotrimoxazole prophylaxis forecasting and delivery in order to reduce lost to follow-up rates in sub-Saharan HIV programs.