Assessing efficacy of different nucleos(t)ide backbones in NNRTI-containing regimens in the Swiss HIV Cohort Study

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BACKGROUND
The most recommended NRTI combinations as first-line antiretroviral treatment for HIV-1 infection in resource-rich settings are tenofovir/emtricitabine, abacavir/lamivudine, tenofovir/lamivudine and zidovudine/lamivudine. Efficacy studies of these combinations also considering pill numbers, dosing frequencies and ethnicities are rare.

METHODS
We included patients starting first-line combination ART (cART) with or switching from first-line cART without treatment failure to tenofovir/emtricitabine, abacavir/lamivudine, tenofovir/lamivudine and zidovudine/lamivudine plus efavirenz or nevirapine. Cox proportional hazards regression was used to investigate the effect of the different NRTI combinations on two primary outcomes: virological failure (VF) and emergence of NRTI resistance. Additionally, we performed a pill burden analysis and adjusted the model for pill number and dosing frequency.

RESULTS
Failure events per treated patient for the four NRTI combinations were as follows: 19/1858 (tenofovir/emtricitabine), 9/387 (abacavir/lamivudine), 11/344 (tenofovir/lamivudine) and 45/1244 (zidovudine/lamivudine). Compared with tenofovir/emtricitabine, abacavir/lamivudine had an adjusted HR for having VF of 2.01 (95% CI 0.86-4.55), tenofovir/lamivudine 2.89 (1.22-6.88) and zidovudine/lamivudine 2.28 (1.01-5.14), whereas for the emergence of NRTI resistance abacavir/lamivudine had an HR of 1.17 (0.11-12.2), tenofovir/lamivudine 11.3 (2.34-55.3) and zidovudine/lamivudine 4.02 (0.78-20.7). Differences among regimens disappeared when models were additionally adjusted for pill burden. However, non-white patients compared with white patients and higher pill number per day were associated with increased risks of VF and emergence of NRTI resistance: HR of non-white
ethnicity for VF was 2.85 (1.64-4.96) and for NRTI resistance 3.54 (1.20-10.4); HR of pill burden for VF was 1.41 (1.01-1.96) and for NRTI resistance 1.72 (0.97-3.02).

CONCLUSIONS
Although VF and emergence of resistance was very low in the population studied, tenofovir/emtricitabine appears to be superior to abacavir/lamivudine, tenofovir/lamivudine and zidovudine/lamivudine. However, it is unclear whether these differences are due to the substances as such or to an association of tenofovir/emtricitabine regimens with lower pill burden.