Background
The World Health Organisation (WHO) recommends that in resource limited settings (RLS), initial treatment includes a thymidine analogue (e.g. zidovudine or stavudine) and lamivudine. In patients experiencing immunological/clinical failure to these regimens, which subsequent nucleos(t)ide analogue is associated with the best virological response remains poorly defined. This question cannot be answered in populations receiving treatment in RLS because there is no virological monitoring in place. In HIV-infected people in industrialized countries, the time to virological failure on lamivudine and detection of drug mutation (d4T) has been argued that the NRTI-pair tenofovir/lamivudine should be avoided as, when used in PI-spared regimens, it is associated with several adverse outcomes including increased rates of virological failure, reduced CD4 count responses and occurrence of drug-specific toxicities (i.e. pancreatitis and renal insufficiency) [Negredo E et al, Maitland D et al, van Lunzen J et al].

Methods
After the inclusion of one NTE, a patient could re-enter the analysis if he/she started tenofovir/lamivudine and had a viral load ≤400 copies/mL at 4 months; the 4 months viral load was defined as the closest measure to 4 months among those falling in the 3 month window from the date of the NTE, logistic regression was used, excluding patients with a missing month 4 VL and ignoring treatment switches.

Results
1,228 patients contributed 1,441 NTE. Patients' basic characteristics are described in Table 1. Overall, 1,182 patients (84%) who had a 4-month viral load measure were included in the analysis. Of these patients, 87% had been extensively pre-treated with nucleos(t)ide treatment episodes (NTE) that occurred after this date of failure on thymidine analogues. NTE had to include at least 3 drugs. The estimated median KM time to virological failure was 25 months (95% CI: 19-30).

Conclusion
Although subject to bias due to confounding and limited statistical power, these results suggest that patients who previously had virological failure on thymidine analogues experienced a virological response to a number of nucleos(t)ide backbones that was comparable to that achieved with ABC/ddI. We have no evidence to confirm that particularly undesirable virological outcomes may be observed if the tenofovir/lamivudine is used. Ideally, a world-wide collaboration including several cohort studies in Europe and USA should be set up in order to increase the power of this analysis.