BACKGROUND

Nucleoside reverse transcriptase inhibitors (NRTIs) can induce hepatocyte damage through reduced cell proliferation, mitochondrial toxicity and mitochondrial DNA (mtDNA)-loss. Whilst liver abnormalities are observed in people living with HIV (PLWH) on antiretroviral therapy (ART), correlations of NRTI plasma exposure with markers of liver damage are ill-defined.

AIM: To investigate the associations of tenofovir (TFV), emtricitabine (FTC), abacavir (ABC) and lamivudine (3TC) pharmacokinetics (PK) with alanine aminotransferase (ALT) as part of a large cohort of PLWH.

METHODS

POPPLY is a multicentre, prospective, observational study to examine the effects of ageing on the clinical outcomes of people living with HIV (PLWH) in UK and Ireland (Figure 1). In this current study, we included a selection of patients who were on NRTIs.

RESULTS

BASELINE CHARACTERISTICS

- Most participants were white (90.2%) and male (87.6%) with a median age of 52 (range 23-82) years.
- Of the 488, 452, 92 and 122 participants with PK samples measured for TFV, FTC, ABC and 3TC, median (range) ALT was 30 (6-99), 30 (6-99), 27 (8-92) and 27 (7-89) U/L, respectively.

A greater proportion of those receiving ABC and FTC were female compared to those on TFV and FTC. More participants on ABC and 3TC were on boosted PIs compared to those on TFV and FTC. More participants on TFV and FTC were also on efavirenz compared to those on ABC and 3TC, whereas, fewer participants on TFV and FTC were on nevirapine compared to those on ABC and 3TC.

The remaining characteristics (Table 1) were similarly distributed among participants on each NRTI drug.

ASSOCIATION BETWEEN NRTI EXPOSURE AND ALT CONCENTRATION

- In univariate analysis, ALT values inversely correlated with TFV AUC(0-24h) (p<0.001), Cmax (p<0.001), and C24h (p<0.001). These associations were substantially attenuated after adjustment for confounders (Figure 3).
- Post-hoc analysis suggested that adjustment for BMI explained most of the attenuation.
- A weaker association between FTC PK parameters and ALT could be explained by co-administration of TFV in the regimen. Associations with FTC PK parameters were similar, regardless of whether TFV was or was not included in the regimen (Figure 4).

No associations were observed between ALT and either ABC or 3TC PK parameters.

CONCLUSIONS

We have observed a correlation between higher TFV plasma exposure and lower ALT concentrations, but no association between exposure of the other NRTIs and ALT concentration. These observations, however, were strongly attenuated by BMI.