P0033
Paper Poster Session
HIV biomarkers, resistance and diagnostics

A new biomarker in combination with anti-retroviral treatment for human immunodeficiency virus infection: association of adverse events with inosine triphosphate pyrophosphohydrolase activity

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Background: Predicting whether adverse events (AEs) will occur in combination anti-retroviral therapy (cART) for patients infected with the human immunodeficiency virus (HIV) would be a valuable tool in the choice of cART regimens. A biomarker predicting AEs in other diseases is the enzyme Inosine 5'-triphosphate pyrophosphohydrolase (ITPase). A decreased ITPase activity is associated with a reduced risk to develop anemia in patients treated for hepatitis C, but with an increased risk of AEs in patients treated with thiopurines. The purine analogues abacavir and tenofovir that are part of the backbone in most cART regimens, are a potential substrate for ITPase. The aim of this study was to determine whether ITPase activity may be used as biomarker for occurrence of AEs during tenofovir or abacavir use.

Material/methods: HIV-seropositive patients, visiting the outpatient clinic of a Dutch University Hospital, aged 18 years and older were included. Clinical and Demographic data were retrieved from the Dutch HIV monitoring foundation and if needed from the medical records. AEs that led to stop or change of cART regimen were used as definition for AEs. ITPase activity in erythrocytes was measured by formation of inosine monophosphate (IMP) from inosine triphosphate (ITP). ITPase activity ≥4 mmol IMP/mmol Hb/hour was considered as normal. Logistic regression analysis with

repeated statement and weighted by total duration of cART therapy and cumulative duration of purine analogue therapy was used to determine odds ratios (OR) for developing AEs.

Results: A total of 409 patients (1480 cART regimens) were included, of which 213 (52.1%) had an ITPase activity <4 mmol IMP/mmol Hb/hour. In patients with decreased ITPase activity using tenofovir we found a reduction in all AEs (p=0.01; OR 0.64), a longer mean regimen duration (p<0.0001) and significantly less often switching of medication secondary to AEs (p=0.018) compared to patients with normal ITPase activity. Moreover, of all the renal AEs that occurred in patients using tenofovir 63.6% occurred in the patients with normal ITPase activity (p=0.04). In contrast, in patients using abacavir having a decreased ITPase activity was associated with increased switching of medication due to AEs (p=0.022) and significantly more AEs occurred compared to patients with normal ITPase activity (p=0.008; OR 1.93; after correction p=0.06; OR 1.75). The OR for occurrence of a skin related AE for a patient with decreased ITPase activity using abacavir was 8.56 compared to patients not taking purine analogues (p=0.005).

Conclusions: Here, we show that ITPase activity is a biomarker for AEs in patients using tenofovir and abacavir in their cART regimen. ITPase enzyme activity <4 mmol IMP/mmol Hb/hour seems to be protective against occurrence of AEs in cART regimens containing tenofovir, while it leads to an increase in AEs in cART regimens containing abacavir.