A new biomarker in cART for HIV-infection: association of adverse events with ITPase activity

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Conclusions

Decreased Inosine 5'-triphosphate pyrophosphohydrolase (ITPase) activity seems to be protective against occurrence of adverse events (AEs) in tenofovir-containing combination anti-retroviral (cART) regimens, while it is associated with an increase in AEs in abacavir-containing regimens. This opposed effect in regimens containing tenofovir or abacavir may be due to the different chemical structures of these medications.

Introduction and purpose

The purine analogues tenofovir, abacavir and didanosine are precursors of potential substrates for the enzyme ITPase. Here, we determined whether ITPase activity and *ITPA* genotype are associated with the occurrence of AEs during cART for human immunodeficiency virus (HIV) infection.

Methods

In 393 adult HIV-seropositive patients, AEs were defined as events that led to stop of cART regimen. ITPase activity ≥4 mmol IMP/mmol Hb/hour was considered as normal. *ITPA* genotype was determined by testing two *ITPA* polymorphisms: c.94C>A (p.Pro32Thr, rs1127354) and c.124+21A>C (rs7270101). Logistic regression analysis was used to determine odds ratios (OR) for developing AEs in 1422 cART regimens.

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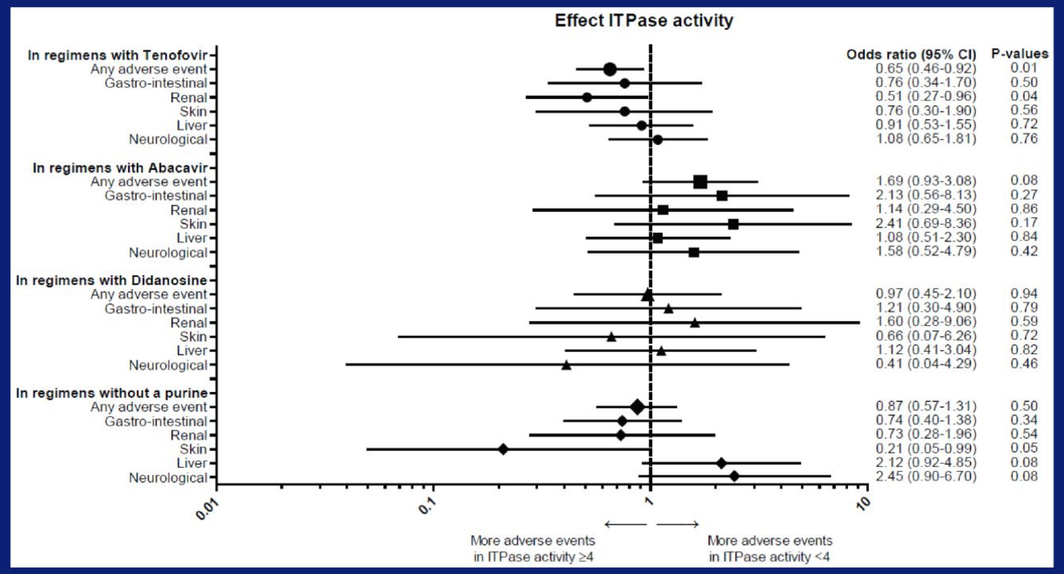
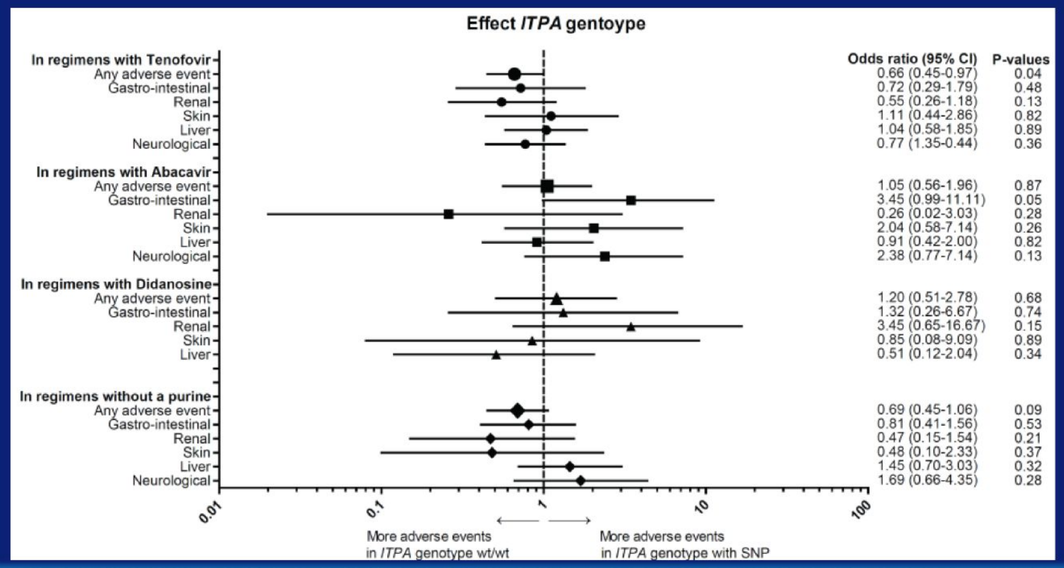
Results

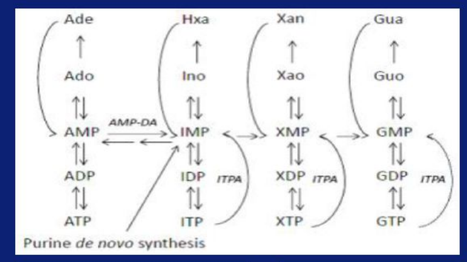
Decreased **ITPase activity:** *Less* AEs in regimens containing tenofovir and *more* AEs in regimens containing abacavir.

SNPs in ITPA **(non-wild type) genotype:** *Less* AEs in regimens containing tenofovir

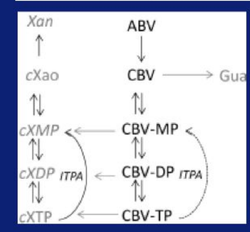




Metabolic pathways of purine nucleotides (A), abacavir (B) and Tenofovir (C)



A



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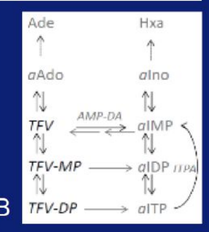

C

Ade = Adenine,Ado = adenosine, A = adenosine 5'-, MP = monophosphate, DP = diphosphate, TP = triphosphate, AMP-DA = AMP deaminase, Hxa = Hypoxanthine, Ino = inosine, I = Inosine 5'-, ITPA = Inosine 5'-triphosphate pyrophosphohydrolase, Xan = xanthine, Xao = xanthosine, X = Xanthosine 5'-, Gua = Guananine, Guo =guanosine , G = Guanosine 5'-, c = carbocyclic, ABV = abacavir, CBV = Carbovir, CBV, a = acyclic, TFV = Tenofovir.

Chemical structures: