ITPase expression is decreased in leukocytes of HIV-infected patients using cART

N. Chantal Peltenburg[1], Mathie P.G. Leers[2], Jaap A. Bakker[3], Selwyn H. Lowe[4], Wim H.M. Vroemen[2], Aimée D.C. Paulussen[5], Bianca J.C. van den Bosch[5], Jörgen Bierau[5], Annelies Verbon[1,6]

[1]Dept. Internal Medicine, Div. Infectous Diseases, Erasmus MC, Rotterdam, [2]Dept. Clinical Chemistry and Hematology, Zuyderland MC, Heerlen, [3]Dept. Clinical Chemistry and Laboratory Medicine, LUMC, Leiden, [4]Dept. Medical Microbiology and Dept. Internal Medicine, Div. Infectious Diseases, MUMC+, Maastricht, [5]Dept. Clinical Genetics, MUMC+, Maastricht, [6]Dept. Medical Microbiology and Infectious Diseases, Erasmus MC, Rotterdam

Conclusions

HIV-infection interferes with the purine metabolism in leukocytes by decreasing Inosine triphosphatase (ITPase) expression and activity, independently of *ITPA* genotype. The backbone of most combination anti-retroviral therapy (cART) regimens includes one of the purine analogues abacavir and tenofovir. Given that the active metabolites of these purine analogues are potential substrates for ITPase, these results warrant further research to the effects of decreased ITPase activity in the effectiveness and adverse events during treatment of HIV, towards tailor-made therapy for every patient.

Introduction and purpose

Antiviral purine analogues are pivotal in the treatment of HIV-infection. A better understanding of ITPase expression in CD4+ lymphocytes may lead to novel insights to further elucidate the nucleotide metabolism and the (adverse) effects of combination cART in HIV treatment.

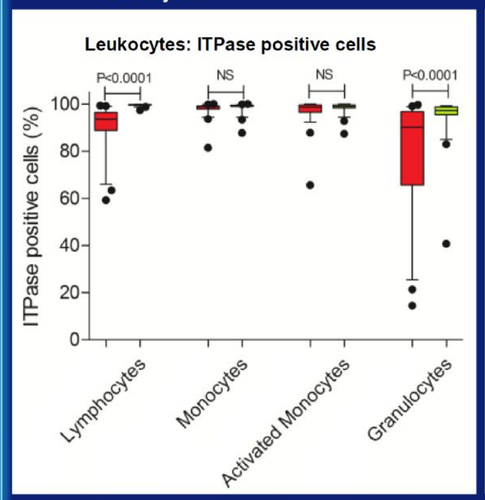
Methods

59 HIV-infected patients, visiting the outpatient clinic of a Dutch University Hospital, aged ≥18 years were included. The control population consisted of 50 hospital patients. All DNA samples were genotyped for the two functional *ITPA* SNPs; c.94C>A (rs1127354) and c.124+21A>C (rs7270101). ITPase expression was determined measuring the Median Fluorescent Intensity (MFI) in all leukocyte subsets.

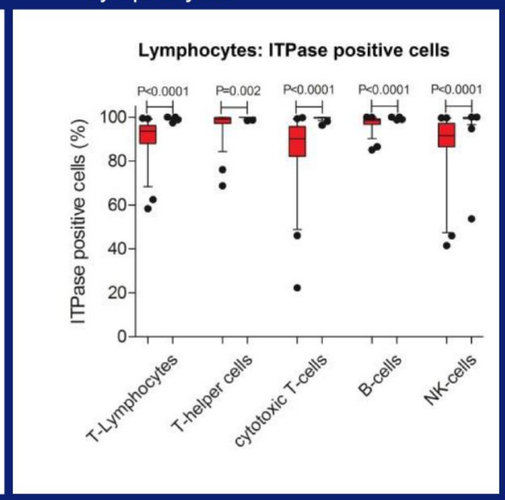
Correspondence: n.c.peltenburg@erasmusmc.nl; Disclosures: none to declare

Results

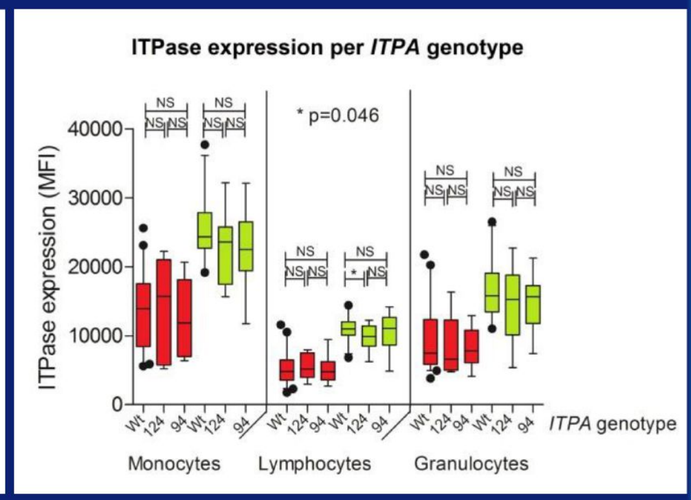
1. In HIV: percentage of ITPase positive cells decreased in leukocytes



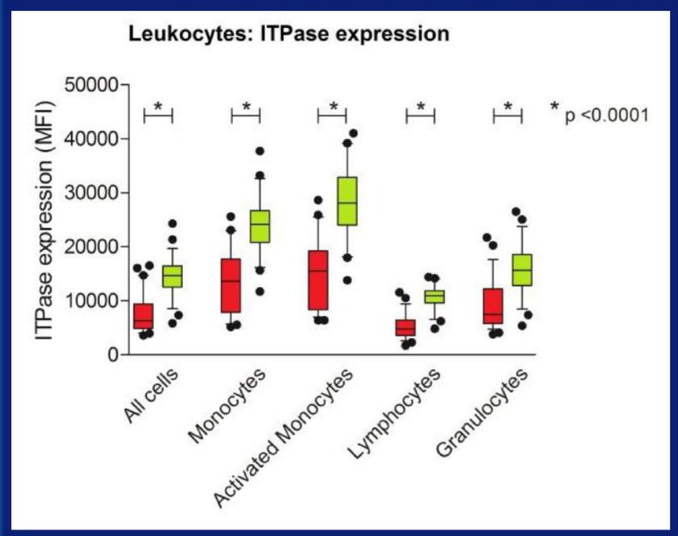
2. In HIV: percentage of ITPase positive cells decreased in lymphocytes

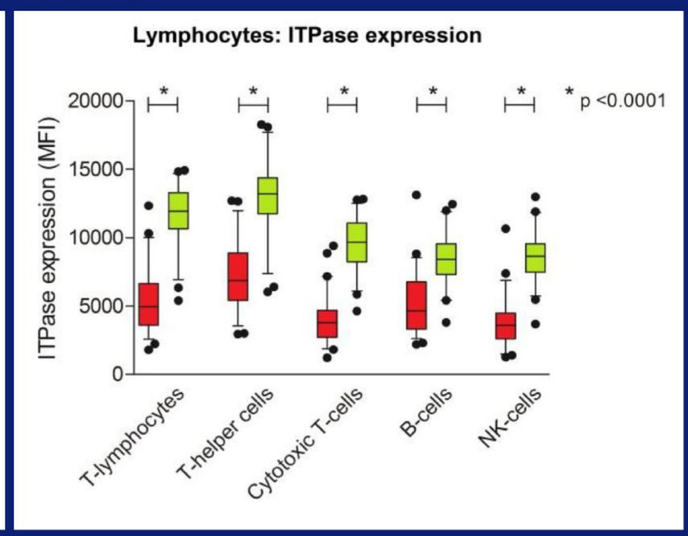


4. *ITPA* genotype: no association with ITPase expression.



3. In HIV: ITPase expression decreased in leukocytes and lymphocytes





HIV-patients
Controls