Changes in fat mitochondrial DNA and function in subjects randomized to abacavir-lamivudine or tenofovir DF-emtricitabine with atazanavir-ritonavir or efavirenz: AIDS Clinical Trials Group study A5224s, substudy of A5202.

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BACKGROUND: The effect of nonthymidine nucleoside reverse-transcriptase inhibitors (NRTIs) on fat mitochondrial DNA (mtDNA) content and function is unclear.

METHODS: A5202 randomized antiretroviral therapy-naive human immunodeficiency virus-infected subjects to abacavir-lamivudine (ABC/3TC) versus tenofovir DF-emtricitabine (TDF/FTC) with efavirenz (EFV) or atazanavir-ritonavir (ATV/r). A5224s, substudy of A5202, enrolled 269 subjects with fat measurements by dual-energy x-ray absorptiometry and computed tomography. A subset of subjects underwent fat biopsies at baseline and week 96 for mtDNA content (real-time polymerase chain reaction) and oxidative phosphorylation nicotinamide adenine dinucleotide (reduced) dehydrogenase (complex I) and cytochrome c oxidase (complex IV) activity levels (immunoassays). Intent-to-treat analyses were performed using analysis of variance and paired t tests.

RESULTS: Fifty-six subjects (87% male; median age, 39 years) were included; their median body mass index, CD4 cell count, and fat mtDNA level were 26 kg/m(2), 227 cells/μL, and 1197 copies/cell, respectively. Fat mtDNA content decreased within the ABC/3TC and TDF/FTC groups (combining EFV and ATV/r arms; median change, -341 [interquartile range, -848 to 190; P = .03] and -400 [-661 to -221; P < .001] copies/cell, respectively), but these changes did not differ significantly between the 2 groups (P = .57). Complex I and IV activity decreased significantly in the TDF/FTC group (median change, -12.45 [interquartile range, -24.70 to 2.90; P = .003] and -8.25 [-13.90 to -1.30; P < .001], optical density × 10(3)/µg, respectively) but not the ABC/3TC group. Differences between the ABC/3TC and TDF/FTC groups were significant for complex I (P = .03).

CONCLUSIONS: ABC/3TC and TDF/FTC significantly and similarly decreased fat mtDNA content, but only TDF/FTC decreased complex I and complex IV activity levels.

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