Abstracts of the HIV Drug Therapy Glasgow Congress 2014
Ramón Santos J et al. *Journal of the International AIDS Society* 2014, **17(Suppl 3)**:19550
http://www.jiasociety.org/index.php/jias/article/view/19550 | http://dx.doi.org/10.7448/IAS.17.4.19550

Randomized, crossover, double-blind, placebo-controlled trial to assess the lipid lowering effect of co-formulated TDF/FTC

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Introduction: Previous studies have described improvements on lipid parameters when switching from other antiretroviral drugs to tenofovir (TDF) and impairments in lipid profile when discontinuing TDF. [1–3] It is unknown, however, if TDF has an intrinsic lipid-lowering effect or such findings are due to the addition or removal of other offending agents or other reasons.
Materials and Methods: This was a randomized, crossover, double-blind, placebo-controlled clinical trial (NCT 01458977). Subjects with HIV-1 RNA <50 copies/mL during at least 6 months on stable DRV/r (800/100 mg QD) or LPV/r (400/100 mg BID) monotherapy, with confirmed fasting total cholesterol ≥ 200 or LDL-cholesterol ≥ 130 mg/dL and not taking lipid-lowering drugs were randomized to (A) adding TDF/FTCduring 12 weeks followed by 24 weeks without TDF/FTC, or (B) continuing without TDF/FTC for 12 weeks, adding TDF/FTC for 12 weeks and then withdrawing TDF/FTC for 12 additional weeks. Randomization was stratified by DRV/r or LPV/r use at study entry. All subjects received a specific dietary counselling. Primary endpoints were changes in median fasting total, LDL and HDL-cholesterol 12 weeks after TDF/FTC addition. Analyses were performed by ITT.
Results: 46 subjects with a median age of 43 (40–48) years were enrolled in the study: 70% were male, 56% received DRV/r and 44% LPV/r. One subject withdrew the study voluntarily at week 4 and another one interrupted due to diarrhoea at week 24. Treatment with TDF/FTC decreased total, LDL and HDL-cholesterol from 235.9 to 204.9 ($p<0.001$), 154.7 to 127.6 ($p<0.001$) and 50.3 to 44.5 mg/dL ($p<0.001$), respectively. In comparison, total, LDL and HDL-cholesterol levels remained stable during placebo exposure. Week 12 total cholesterol ($p<0.001$), LDL-cholesterol ($p<0.001$) and HDL-cholesterol ($p=0.011$) levels were significantly lower in TDF/FTC versus placebo. Treatment with TDF/FTC reduced the fraction of subjects with abnormal fasting total-cholesterol (≥ 200 mg/dL) from 86.7% to 56.8% ($p=0.001$) and LDL-cholesterol (≥ 130 mg/dL) from 87.8% to 43.9% ($p<0.001$), which was not observed with placebo. There were no virological failures, and CD4 and triglyceride levels remained stable regardless of exposure.
Conclusion: Coformulated TDF/FTC has an intrinsic lipid-lowering effect, likely attributable to TDF.

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Published 2 November 2014