Antiretroviral therapy (ART) is associated with body composition changes. Thymidine analogue-nucleoside reverse transcriptase inhibitors (ta-NRTIs) [AZT/d4T] have been consistently associated with lipodystrophy; protease inhibitors have in some studies been associated with central visceral fat accumulation. Raltegravir (RAL) has not been associated with body composition changes.

NRTI-sparing ART may be attractive for second-line ART, particularly in low- and middle-income countries, if it offers non-inferior efficacy and reduced toxicity. The SECOND-line randomised trial compared LPV/r+400mg bid + 2NtRTIs versus LPV/r+400mg bid + RAL+400mg bid in 541 participants with virological failure of standard first-line NRTI+2NRTI ART over 96 weeks.

A subset of patients enrolled into the SECOND-line dual-energy x-ray absorptiometry (DXA) sub-study at 8 sites in South Africa (n=144), India (n=49), Thailand (n=48), Malaysia (n=13), and Argentina (n=7) from 2010-2011.

We hypothesised that participants randomised into the NRTI-sparing arm (RAL-arm) would demonstrate greater increases in limb fat over 96 weeks than those randomised into the N(t)RTI arm (LPV/r+2 NtRTIs).

Introduction

- Antiretroviral therapy (ART) is associated with body composition changes.
- Thymidine analogue-nucleoside reverse transcriptase inhibitors (ta-NRTIs) [AZT/d4T] have been consistently associated with lipodystrophy; protease inhibitors have in some studies been associated with central visceral fat accumulation. Raltegravir (RAL) has not been associated with body composition changes.
- NRTI-sparing ART may be attractive for second-line ART, particularly in low- and middle-income countries, if it offers non-inferior efficacy and reduced toxicity.

Methods

- DXA-scans of total body composition were performed at week 0, 48, and 96.
- Primary endpoint: percent change in total limb (arm+ leg) fat mass over 96 weeks.
- Complete case analyses included all participants who consented to the body composition sub-study, underwent randomisation, received at least one dose of study medication and completed DXA-scans at both week 0 and 96. No imputation for missing data or change from randomised therapy (ITT population).
- All analyses were adjusted for baseline differences between the 2 treatment groups for gender, body mass index (BMI), and smoking status.
- Linear regression was used to compare adjusted mean differences from baseline to week 96 for gender, BMI, smoking status, age and ethnicity were retained in the model used to determine risk factors for limb fat change at week 96.
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- The models were adjusted for missing data or change from randomised therapy (ITT population).

Conclusion

- The study affords novel insights into key predictive variables of peripheral fat changes after switch to 2nd line ART including sex, body mass index and patient population.
- NRTI-sparing in SECOND-line was associated with improved peripheral limb fat gain over 96 weeks, but the association was not retained upon multivariate analysis.
- In this study in which nearly all participants had been exposed to ta-NRTIs in 1st line ART, most gained peripheral fat but with less gain in the NtRTI-arm, most likely driven by those 128 of the 271 NRTI- arm participants receiving improved AZT or d4T.
- Current WHO guidelines recommend the use of TDF in first-line ART (preferably the EFV/TDF/3TC single tablet regimen). WHO recommended 2nd-line ART should include recognized 3TC plus ACTG regimen lead to peripheral fat loss and other negative effects. An NRTI-sparing second-line ART regimen may be preferable – non-inferior efficacy (Lanier 2013:381-2091), less BMD loss (JADA 2014:67-161) and no lipodystrophy.

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