BACKGROUND: Most resource-constrained countries reserve boosted PI (LPV/r) for second-line following WHO recommendations. Lipid profiles at first-line clinical immunological failure and following EM-based second-line have not been studied in Africa.

METHODS: DART is a randomized trial comparing HIV/AIDS management strategies in Uganda/Zimbabwe to determine the need to switch to LPV/r-containing second-line ART at clinical failure (WHO 4). In those randomized to laboratory monitoring, increased levels (ΔHDL±100mg/dL/mm) were noted. We evaluated lipid profiles at second-line initiation and 48 weeks subsequently in stored samples from patients in Zimbabwe measured with the WAAL-KALA database for ≥48 weeks. Lipid profiles were determined at first-line, and at switch to LPV/r containing second-line ART (WHO 5) or LPV/r containing third-line ART (WHO 6). Patients who died or were lost to follow-up before 48 weeks were included. Lipid profiles were measured at switch to first-line non-PI ART regimens and at >3 months post switch at second-line ART. Changes in TG levels during LPV/r second-line ART were not clinically significant.

RESULTS: 91 patients switched to second-line before 18 September 2006, of whom 66 (73%) had fasting samples at switch and 48 weeks, 14 (15%) died between switch and 48 weeks, 10 (11%) were lost to follow-up, and 15 (16%) had no lipid measures at switch. Of the 66 included patients (14 males), 57 (86%) received ZDV/d4T+3TC+TDF first-line, 6 (9%) ZDV+sAL+3TC+TDF, and 3 (5%) ZDV+sAL+3TC+TDF and with TDF at different times. Median lipid profiles at switch from first-line ART regimens (mostly with NNRTIs), and at 48 weeks were: serum TC 3.3 (2.9-4.2), LDL-C 1.8 (1.5-2.3), HDL-C 0.8 (0.7-1.1) respectively with triglycerides 0.7 (0.6-1.1) (Lipids were significantly increased after 48 weeks of Kaletra-containing second-line, by mean ±SE (95% CI): +2.0 (1.1, 2.9) for TC (P<0.0001), +1.8 (1.3, 2.4) for LDL-C (P<0.0001) and +0.5 (0.05, 1.0) for triglycerides also increased by +0.5 (0.05, 1.0) (P=0.016). At second-line initiation, 1 (2%) patient had grade 1 hypercholesterolaemia (LDL-C >3.4 mmol/L) and 1 (2%) grade 1 hypertriglyceridaemia (≥2mmol/L) and grade 2 LDL-C (<1.8mmol/L) and grade 2 cholesterol/HDL-C<5.47 (total cholesterol ≥5.7 mmol/L and grade 2 LDL-C ≥4.9mmol/L) no triglycerides were elevated but 39 (60%) had cholesterol/HDL-C ≥5, and 60% cholesterol/HDL-C ratio ≥3.5. At 48 weeks, the prevalence of grade 1/2 cholesterol/LDL was 29% (12/185) (3%) and 5% (9/185) (1%) respectively, but only 14% (23%) had HDL-C <0.9mmol/L and 2% (3%) had grade 2 triglycerides; 66% had cholesterol/HDL-C<5.47.

CONCLUSION: Lipid elevations were observed in African patients mostly on LPV/r ART regimens. This may have long term implications for total atherogenic risk assessment in patients on LPV/r regimens in Africa.

OBJECTIVE

The objective of this study was to evaluate lipid profiles in HIV-infected patients on lopinavir/ritonavir (LPV/r, Kaletra capsules) containing second-line ART regimens (mostly with NNRTIs) in the DART Zimbabwe centre.

METHODS

- Patients were switched to LPV/r-containing second-line ART at clinical failure (WHO 4) in those randomized to clinical monitoring only; or at clinical immunological failure if ≥48 weeks on first-line ART and those randomized to laboratory monitoring arm.
- Most patients received LPV/r with NNRTIs following tripterygium villosa first-line regimens.
- 91 patients in DART-Zimbabwe were switched to second-line ART before 18 September 2006, of whom 66 (73%) had fasting samples at switch and 48 weeks, 14 (15%) died between switch and 48 weeks, 10 (11%) were lost to follow-up, and 15 (16%) had no lipid measures at switch. Of the 66 included patients (14 males), 57 (86%) received ZDV/d4T+3TC+TDF first-line, 6 (9%) ZDV+sAL+3TC+TDF, and 3 (5%) ZDV+sAL+3TC+TDF and with TDF at different times. Median lipid profiles at switch from first-line ART regimens (mostly with NNRTIs), and at 48 weeks were: serum TC 3.3 (2.9-4.2), LDL-C 1.8 (1.5-2.3), HDL-C 0.8 (0.7-1.1) respectively with triglycerides 0.7 (0.6-1.1) (Lipids were significantly increased after 48 weeks of Kaletra-containing second-line, by mean ±SE (95% CI): +2.0 (1.1, 2.9) for TC (P<0.0001), +1.8 (1.3, 2.4) for LDL-C (P<0.0001) and +0.5 (0.05, 1.0) for triglycerides also increased by +0.5 (0.05, 1.0) (P=0.016). At second-line initiation, 1 (2%) patient had grade 1 hypercholesterolaemia (LDL-C >3.4 mmol/L) and 1 (2%) grade 1 hypertriglyceridaemia (≥2mmol/L) and grade 2 LDL-C (<1.8mmol/L) and grade 2 cholesterol/HDL-C<5.47 (total cholesterol ≥5.7 mmol/L and grade 2 LDL-C ≥4.9mmol/L) no triglycerides were elevated but 39 (60%) had cholesterol/HDL-C ≥5, and 60% cholesterol/HDL-C ratio ≥3.5. At 48 weeks, the prevalence of grade 1/2 cholesterol/LDL was 29% (12/185) (3%) and 5% (9/185) (1%) respectively, but only 14% (23%) had HDL-C <0.9mmol/L and 2% (3%) had grade 2 triglycerides; 66% had cholesterol/HDL-C<5.47.

CONCLUSION: Lipid elevations were observed in African patients mostly on LPV/r ART regimens. This may have long term implications for total atherogenic risk assessment in patients on LPV/r regimens in Africa.

RESULTS - Lipid profiles at switch to second-line ART in patients receiving LPV/r + Nelfinavir (NVP) or at switch to second-line ART in patients with high LDL-C at ≥48 weeks after switch to LPV/r compared to those who received TDF and NNRTIs only.

1. Serum lipid (TC, triglycerides, LDL-C, and HDL-C) levels were statistically significantly increased >28 weeks after switching to LPV/r containing second-line ART regimens (mostly with NNRTIs) (median (IQR) in Figure 1) in men, and (SD) in Table below.

2. In multivariable regression models adjusting for sex, age, BMI, second-line regimen and lipid levels at switch to second-line, 48 weeks after switch - women had greater increases in LDL-C than men - older patients had greater increases in TC, LDL-C and HDL-C - those with higher BMI had greater increases in TG, and smaller increases in HDL-C - patients taking LPV/r with NNRTIs appeared to have greater increases in TC, LDL-C and HDL-C than those taking LPV/r with NNRTIs (numbers were small) - those taking EFV appeared to have larger increases in LDL-C (than NRTI-based second-line)

3. Those taking NVP had more increases in LDL-C than those taking LPV/r with NNRTIs - those taking EFV had more increases in LDL-C than those taking LPV/r with NNRTIs (numbers were small). Modest lipid elevations were observed in African patients most likely on LPV/r ART regimens. This may have long term implications for total atherogenic risk assessment in patients on LPV/r regimens in Africa.

DISCUSSION

- Similarly to other studies, serum lipids (TC, TG, LDL-C, HDL-C) increased significantly following switch to boosted PI (LPV/r) containing second-line regimens.
- Most patients in our study were taking LPV/r with NNRTIs as a second-line regimen. Follow-up results from first-line ARTs were consistent with work from other first-line ARTs.
- Host patients were taking NVP with LPV/r; given the small numbers, caution is needed in interpreting comparisons with EFV or no NNRTIs.

CONCLUSION

- Lipid elevations were modest in African patients on second-line therapy with LPV/r (mostly with NNRTIs). Assessment and management of the total atherogenic risk of the increasing number of patients on LPV/r-based second-line therapy in Sub-Saharan Africa requires further study.