

# ZDV/3TC/LPV/r, But Not NVP/LPV/r, Is Associated With Limb Fat Loss And Relative Abdominal Fat Accumulation After 24 Months In Antiretroviral-naïve HIV-1-infected Men In a Randomized Clinical Trial (MEDICLAS).

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## ABSTRACT

- Background: Lipotrophy is associated with stavudine use, but less evidence exists whether this also applies to zidovudine. We prospectively evaluated body composition and metabolic changes in a randomized multicenter trial comparing zidovudine/lamivudine (ZDV/3TC)-containing and NRTI-sparing first-line ART.
- Methods: ART-naïve men were randomized to lopinavir/ritonavir (LPV/r, 400/100mg bid)+ZDV/3TC or LPV/r(533/133mg bid)+nevirapine (NVP). CT, DEXA and lipid profile were assessed before and after 3, 12, 24 and 36 months of ART. A mixed model repeated measures ITT final analysis correcting for baseline was performed as planned after 24 months.
- Results: Mean baseline age was 42±10 yrs, BMI 23.3±3.3 kg/m<sup>2</sup>. CD4 count 239±154 cells/ml, HIV-1 RNA 5±0.6 log<sub>10</sub> c/ml (comparable between arms). In the ZDV/3TC/LPV/r arm, after 3 months limb fat decreased progressively by 684±293 grams up to 24 months, whereas abdominal fat increased exclusively in the visceral compartment. In contrast, in the NVP/LPV/r arm, a generalized increase in fat mass was observed. After 24 months total and LDL cholesterol levels were higher in the NVP/LPV/r arm (6.1±0.2 vs 5.3±0.2 and 3.6±0.1 vs 2.8±0.1 mmol/l respectively) without significant differences in HDL and total/HDL ratio.

	ZDV/3TC/LPV/r (n=22)				NVP/LPV/r (n=26)			
	Mo 0	Mo 3	Mo 12	Mo 24	Mo 0	Mo 3	Mo 12	Mo 24
Weight (kg)	74.6±0.7	74.7±0.7	75.9±0.7	75.6±0.7	74.6±0.6	74.9±0.6	76.9±0.6	77.2±0.7*
Limb fat (kg)†	6.35±0.2	6.66±0.2	6.48±0.2	5.97±0.2*	6.34±0.2	6.27±0.2	7.01±0.2	7.20±0.2*
Trunk fat (kg)†	7.51±0.3	7.52±0.3	8.14±0.3	8.26±0.3*	7.48±0.3	6.97±0.2	8.23±0.2	8.42±0.2*
Total fat (kg)†	13.9±0.4	14.2±0.5	14.6±0.4	14.2±0.5*	13.8±0.4	13.2±0.4	15.2±0.4	15.6±0.4*
VAT (cm <sup>2</sup> )	100.2±6.1	92.4±6.7	102.1±6.9	122.2±6.7*	100.4±5.7	91.8±6.0	108.5±6.0	110.4±6.2
SAT (cm <sup>2</sup> )	118.5±5.4	116.3±6.0	124.5±6.0	122.5±6.0*	118.1±5.1	114.2±5.3	131.4±5.3	142.0±5.5*
VAT/SAT	0.89±0.05	0.84±0.05	0.89±0.05	1.06±0.05**	0.89±0.05	0.87±0.05	0.87±0.05	0.87±0.05
TAT (cm <sup>2</sup> )	218.4±9.8	208.4±10.8	226.9±10.9	244.4±10.8*	218.3±9.2	206.0±9.6	240.0±9.6	252.2±10.0*

Estimated means±sem. \*p<0.05 between arms at visit. †p<0.05 overall between arms. \*\*p<0.05 within arm 0-24 months. Conclusions: ZDV/3TC/LPV/r, but not NVP/LPV/r in ART-naïve patients, is associated with both lipotrophy and relative abdominal lipohypertrophy, suggesting that ZDV/3TC contributes to both these features of lipodystrophy. NVP/LPV/r is associated with a worse lipid profile. Other ZDV/3TC sparing initial treatment strategies are worth exploring.

## BACKGROUND

- Lipotrophy is known to be associated with stavudine as part of initial treatment for HIV infection, but less evidence exists whether the same applies to first-line zidovudine-containing treatment. We prospectively evaluated body composition and metabolic changes in a randomized multicenter trial comparing zidovudine/lamivudine (ZDV/3TC)-containing and ZDV/3TC-sparing first-line ART.

## METHODS

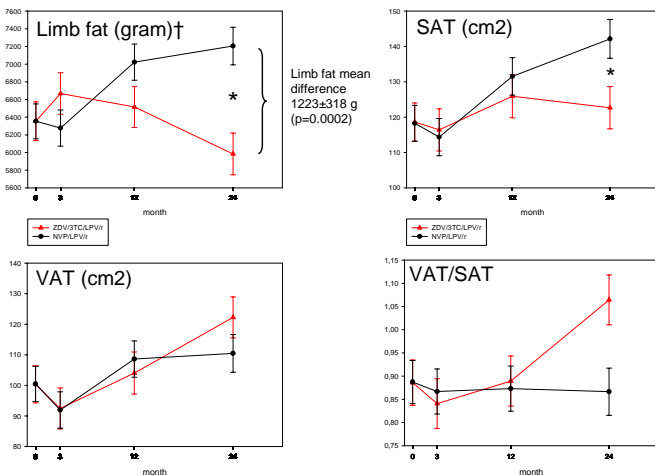
- HIV-1+, ART-naïve men were randomized to lopinavir/ritonavir(400/100mg bd)+ZDV/3TC or lopinavir/ritonavir(533/133mg bd)+nevirapine in a prospective, randomized, single blinded trial.
- Body composition (whole body DEXA and abdominal CT scan) and lipid profile were assessed before and after 3, 12 and 24 months of ART.

## RESULTS

Table 1 Baseline characteristics of the study population (median (IQR) or number (%))

	ZDV/3TC/LPV/r (n=22)	NVP/LPV/r (n=26)
Age (years)	38 (35-43)	43 (35-52)
Ethnic group		
Black	1 (4.5%)	2 (7.7%)
Caucasian	19 (86.4%)	20 (76.9%)
Hispanic	0 (0%)	2 (7.7%)
Other	2 (9.1%)	2 (7.7%)
CDC category		
A	14 (63.6%)	16 (61.5%)
B	3 (13.6%)	6 (23.1%)
C	5 (22.7%)	4 (15.4%)
CD4 cell count (10 <sup>6</sup> /l)	225 (170-280)	200 (120-360)
HIV-RNA (log 10 copies/ml)	5 (5-5)	5 (5-5)

## Body composition

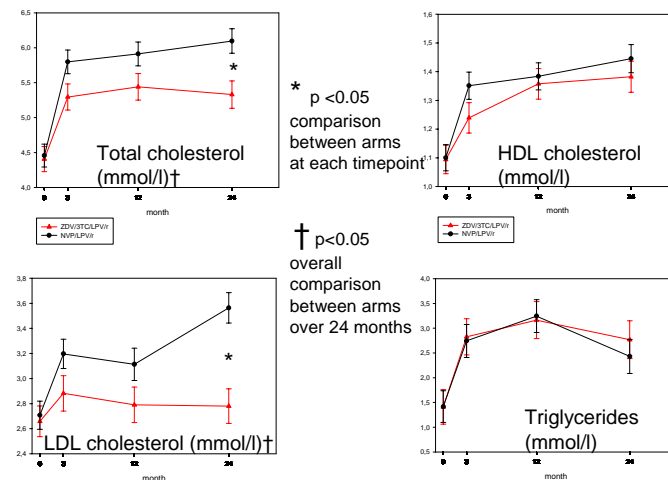


\* p <0.05 comparison between arms at each timepoint  
† p <0.05 overall comparison between arms over 24 months

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	ZDV/3TC/LPV/r				NVP/LPV/r			
	Mo 0	Mo 3	Mo 12	Mo 24	Mo 0	Mo 3	Mo 12	Mo 24
CD4 cell count (x 10 <sup>6</sup> /l)	220 (170-264)	344 (250-440)	428 (360-685)	502 (385-685)	200 (120-360)	315 (210-520)	370 (284-606)	485 (340-625)
HIV-RNA (log 10 copies/ml)	5.1 (5.0-5.3)	2.1 (1.7-2.5)	1.7 (1.7-1.7)	1.7 (1.7-1.7)	4.9 (4.6-5.3)	1.7 (1.7-2.3)	1.7 (1.7-1.7)	1.7 (1.7-1.7)

## Lipid profile



\* p <0.05 comparison between arms at each timepoint  
† p <0.05 overall comparison between arms over 24 months

## CONCLUSIONS

- ZDV/3TC/LPV/r, but not NVP/LPV/r in ART-naïve patients, is associated with both lipotrophy and relative intraabdominal lipohypertrophy. This suggests that ZDV/3TC may contribute to both these features of lipodystrophy.
- NVP/LPV/r however is associated with a worse lipid profile, with greater increases in total and LDL cholesterol.
- Other ZDV/3TC sparing initial treatment strategies expected to have less of an effect on serum lipids are worth exploring.

## Acknowledgement:

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