

**Risk of lipoatrophy in antiretroviral-naive  
HIV-infected adults:  
A prospective cohort study with objective  
measurements of limb fat**

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# BACKGROUND

- **The natural history of body composition changes and the risk for developing lipoatrophy in HIV-infected patients are poorly known.**
- **HIV-associated lipoatrophy has been assessed through subjective definitions in some prospective cohort studies.**
- **Objective measurements of body fat have been performed mainly in cross-sectional studies. Longitudinal studies with objective measurements of body fat have been few and usually including exclusively patients receiving antiretroviral therapy.**

# OBJECTIVES

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- **Longitudinal assessment of body composition with DEXA.**
- **Longitudinal assessment of laboratory parameters (glucose, triglycerides, total-HDL-LDL cholesterol, lactate, IL-2 and IL-6 receptors, insulin, DHEA, TNF- $\alpha$ , CD4 cells and HIV-1 RNA).**
- **Impact of antiretroviral therapy on body composition and laboratory parameters.**
- **Study of risk factors for limb fat loss.**

# METHODS

## PATIENTS

- Consecutive HIV-infected adults
- Clinically stable
- Antiretroviral-naïve
- Decisions regarding initiation of antiretroviral therapy and type of antiretrovirals included were in accordance with current recommendations and independent from the participation in this study
- Written informed consent

## DESIGN

- Prospective cohort study
- 2 HIV clinics in Barcelona, Spain
- 2-year follow up
- Body composition and metabolic parameters at baseline, 6, 12, and 24 months

# METHODS

## BODY COMPOSITION

- Whole body dual-energy X-ray absorptiometry (DEXA):
  - Lunar Prodigy absorptiometer
  - same technician in each participating center.

## LABORATORY PARAMETERS

- Glucose
- Triglycerides
- Total, HDL, and LDL cholesterol
- Insulin, and DHEA
- Lactate
- TNF-alpha, IL-2 receptor, and IL-6 receptor
- CD4 cells, and plasma HIV-1 RNA

# POPULATION

- From December 2001 until September 2003, 169 patients included:
  - 110 (65%) started antiretroviral therapy
  - 59 (35%) remained untreated
- 147 (87%) men and 22 (13%) women \*
- Median age 38 years; IQR: 32-41; range: 24-72 \*
- Median BMI 22.7 kg/m<sup>2</sup>; IQR: 20.9-24.7; range: 17.5-43.3 \*
- Antiretroviral drugs prescribed (within triple regimens):

AZT	25 (23%)	EFV	48 (44%)
d4T	25 (23%)	NVP	21 (19%)
TDV	50 (45%)		
3TC	67 (61%)	LPVr	17 (15%)
ddl	57 (52%)	NFV	6 (5%)
ABC	14 (13%)		

\* No significant differences between treated and untreated patients

## Risk of lipodystrophy in antiretroviral-naive HIV-infected adults

# BASELINE BODY COMPOSITION

<b>DEXA</b>	<b>Treated (n=110)</b>	<b>Untreated (n=59)</b>
Limb fat, mg	6394 ± 3925	6646 ± 4276
% of weight	8.8 ± 4.3	9.0 ± 4.7
Trunk fat, mg	8521 ± 5067	8655 ± 5423
% of weight	11.7 ± 5.3	12.2 ± 5.8
Total fat, mg	15534 ± 8986	15903 ± 8410
% of weight	21.4 ± 9.4	21.8 ± 9.1
Limb FFM, mg	23244 ± 4970	22699 ± 4733
% of weight	33.3 ± 4.9	33.6 ± 4.5
Trunk FFM, mg	24661 ± 4172	24147 ± 4391
% of weight	35.5 ± 4.2	35.4 ± 4.8
Total FFM, mg	52195 ± 9332	50854 ± 8912
% of weight	75.1 ± 9.2	74.6 ± 8.8
Total BMD, g/cm <sup>2</sup>	1.195 ± 0.096	1.197 ± 0.101

Data are mean ± SD.

P>0.05 for each comparison

## Risk of lipodystrophy in antiretroviral-naive HIV-infected adults

# BASELINE LABORATORY

	<u>Treated (n=110)</u>	<u>Untreated (n=59)</u>
Glucose, mg/dL	83 ± 10	80 ± 12
Triglycerides, mg/dL	107 ± 74	115 ± 80
Total cholesterol, mg/dL	168 ± 37	160 ± 43
HDL cholesterol, mg/dL	43 ± 11	41 ± 12
LDL cholesterol, mg/dL	106 ± 35	103 ± 32
Lactate, mg/dL	7.9 ± 2.8	9.1 ± 2.7
IL-2 receptor, pM	115 ± 70	110 ± 68
IL-6 receptor, ng/mL	100 ± 34	104 ± 38
Insulin, mU/L	11.5 ± 6.9	10.8 ± 6.3
DHEA, µg/mL	1.6 ± 0.9	1.8 ± 0.8
TNF-α, pg/mL	60.9 ± 28.1	63.4 ± 26.3
HIV-1 RNA, log copies/mL *	5.0 ± 0.8	4.2 ± 0.6
CD4 cells, /mm <sup>3</sup> *	230 ± 134	386 ± 92

Data are mean ± SD.

\* P<0.05

# BODY COMPOSITION: 1-YEAR CHANGE

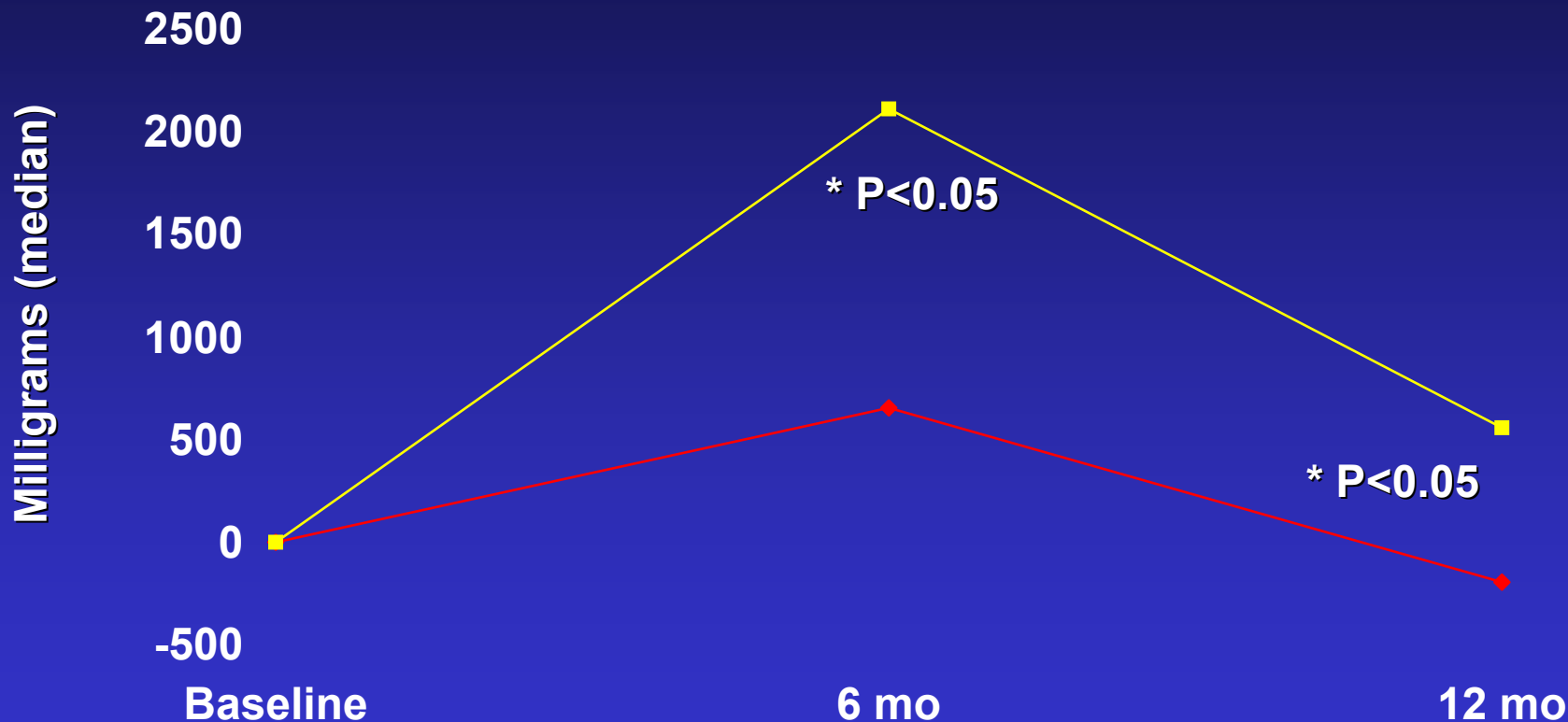
## Percentage of change from baseline

	<u>Treated (n=57)</u>	<u>Untreated (n=24)</u>
BMI	0 (-1.1, 5.9)	2.4 (-0.6, 6.7)
Limb fat *	10.7 (-4.3, 53.7)	29.5 (-18.3, 116.3)
Trunk fat *	7.2 (-9.3, 26.4)	28.5 (-5.9, 50.3)
Total fat *	8.3 (-7.9, 29.1)	25.5 (-11.3, 56.9)
Limb FFM	-0.7 (-3.3, 0.5)	-0.6 (-6.5, 1.9)
Trunk FFM	-1 (-2.7, 1.3)	-1.5 (-7.2, 0.4)
Total FFM	-0.2 (-2.5, 1.4)	-0.8 (-5.7, 1.7)
Total BMD	-1.1 (-1.3, 0.2)	-0.6 (-1.6, 0.1)

Risk of lipoatrophy in antiretroviral-naive HIV-infected adults

# LIMB FAT: 1-YEAR CHANGE

## Change from baseline



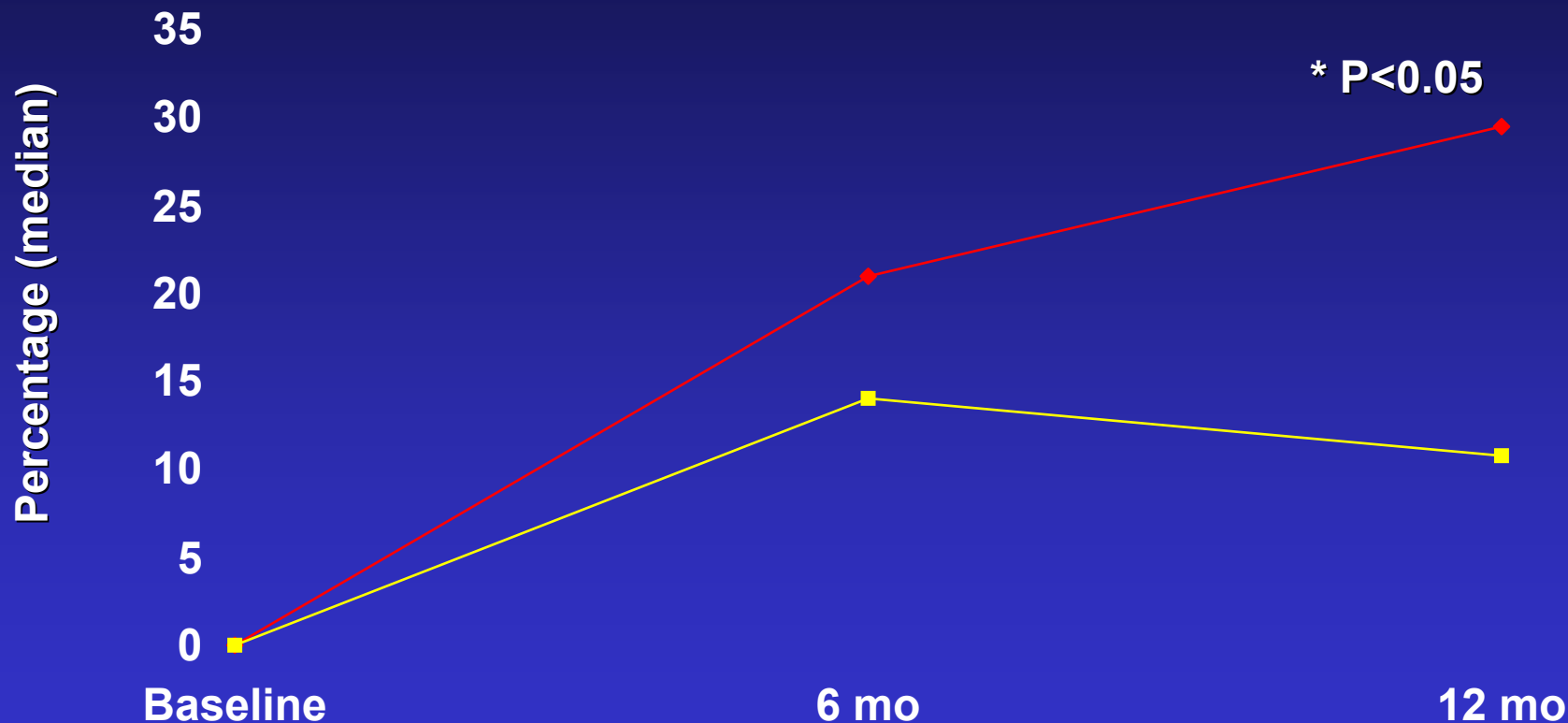
Patients at risk

Treated	110	89	57
Not treated	59	42	24

Risk of lipoatrophy in antiretroviral-naive HIV-infected adults

# LIMB FAT: 1-YEAR CHANGE

Percentage of change from baseline



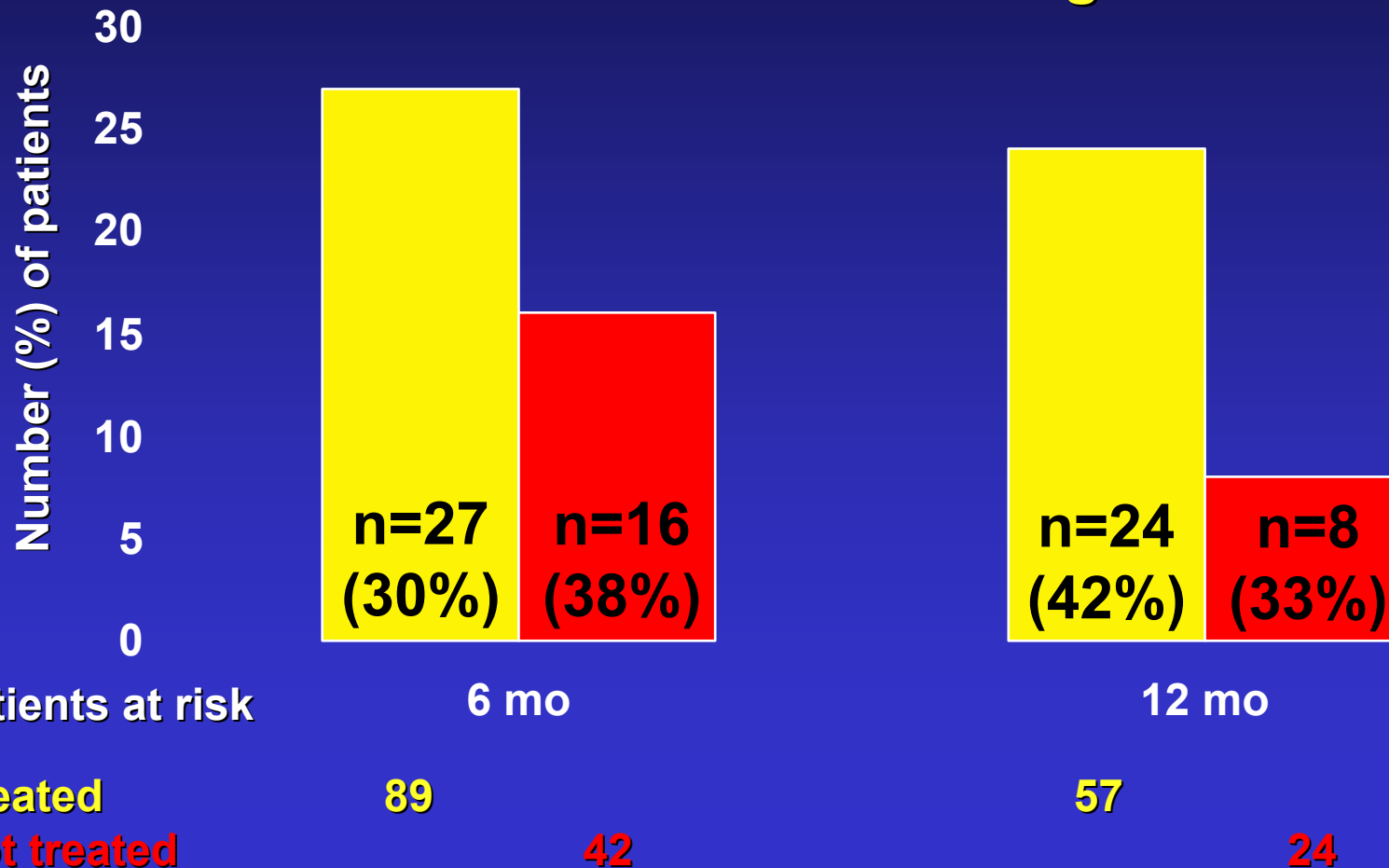
Patients at risk

Treated	110	89	57
Not treated	59	42	24

Risk of lipoatrophy in antiretroviral-naive HIV-infected adults

# LIMB FAT LOSS

Patients with limb fat at 6 and 12 months lower than at baseline according to treatment



## Risk of lipoatrophy in antiretroviral-naive HIV-infected adults

# LABORATORY: 1-YEAR CHANGE

	<u>Treated (n=57)</u>	<u>Untreated (n=24)</u>
Glucose, mg/dL	3.5 (-2, 10.5)	2.1 (-1.8, 5.2)
Triglycerides, mg/dL	15.5 (-7, 62.5)	1.4 (0.6, 4.5) #
Total cholesterol, mg/dL	32.5 (18, 59.5) *	3.0 (0.9, 6.3) #
HDL cholesterol, mg/dL	12 (6, 21.5) *	0.8 (0.4, 1.3) #
LDL cholesterol, mg/dL	15.5 (3.5, 30) *	2.5 (0.2, 4.7) #
Lactate, mg/dL	3 (0.2, 4) *	0.2 (-0.1, 0.3)
IL-2 receptor, pM	-32 (-70.3, -9.8) *	-3 (-10.4, 1.4) #
IL-6 receptor, ng/mL	-15 (-33, -1)	1 (0.3, 2.7) #
Insulin, mU/L	-0.3 (-2.9, 1.9)	-0.1 (-0.3, 0.5)
DHEA, µg/mL	0.21 (-0.16, 0.87) *	0.22 (0.04, 0.79)
TNF-α, pg/mL	-31.7 (-54.6, -18.5) *	3.6 (2.9, 5.3) #
HIV-1 RNA, log copies/mL	-3.0 (-3.4, -2.1) *	0.3 (-0.1, 0.5) #
CD4 cells, /mm <sup>3</sup>	220 (131, 299) *	-96 (-255, 84) #

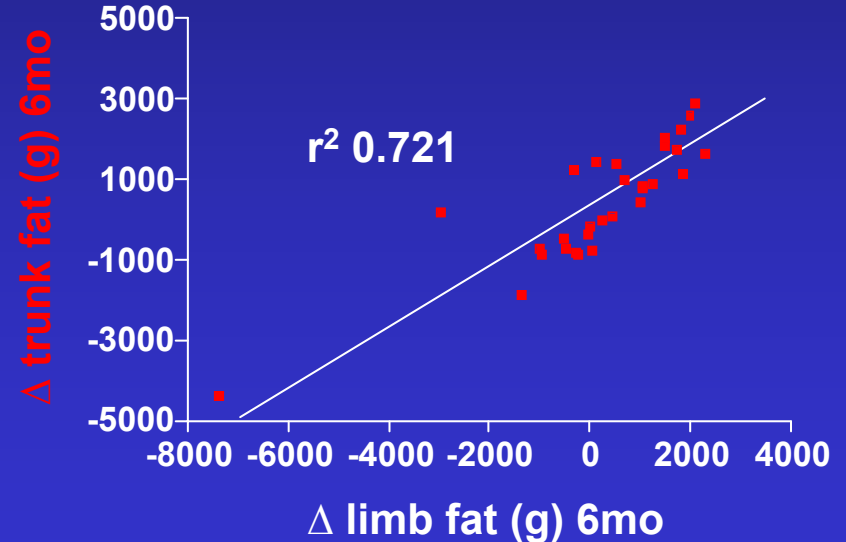
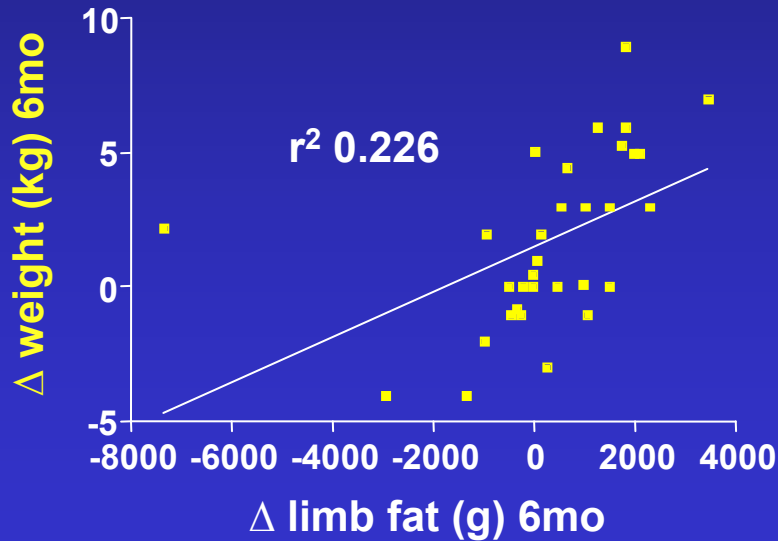
Data are median (IQR)

\* P <0.05 compared with baseline

# P <0.05 compared with treated

# LIMB FAT CHANGE: SIGNIFICANT ASSOCIATIONS

Limb fat change was positively associated with change in weight and trunk fat



# RISK OF LIMB FAT LOSS

- Considering the following baseline variables:

Gender	Limb fat (DEXA)	Glucose	IL-2 receptor
Age	Trunk fat (DEXA)	Triglycerides	IL-6 receptor
BMI	Total fat (DEXA)	Cholesterol	Insulin
	Limb FFM (DEXA)	HDL-chol	DHEA
	Trunk FFM (DEXA)	LDL-chol	TNF-alpha
	Total FFM (DEXA)	Lactate	CD4 cells
	Total BMD (DEXA)		HIV-1 RNA

- The decrease of limb fat (DEXA) at month 12 was significantly associated with:

	<u>NO (n=49, 60%)</u>	<u>YES (n=32, 40%)</u>	<u>P value</u>
• Baseline limb fat (g)	4533 ± 2424	7171 ± 4638	0.046
• Baseline insulin (mU/L)	12.6 ± 7.4	7.8 ± 2.8	0.040

# ROLE OF INDIVIDUAL DRUGS

Drug	n	Δ limb fat at 12 mo (g) (median, IQR)	Fat loss at 12 mo in treated patients *	
			WITH drug	vs WITHOUT drug
AZT	17	71 (-582, 1083)	40%	38%
3TC	42	562 (-844, 1220)	38%	40%
ddl	22	-380 (-682, 569)	43%	35%
d4T	22	-178 (-1084, 987)	29%	47%
ABC	10	-282 (-915, 902)	67%	32%
TDF	10	42 (-325, 769)	17%	44%
EFV	24	438 (-334, 987)	21%	53%
NVP	14	-51 (-982, 810)	56%	32%
NFV	4	-231 (-409, 202)	25%	41%
LPVr	6	27 (-356, 1717)	33%	39%

\* Not significant differences

# CONCLUSIONS

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- In naïve HIV-infected patients in whom the initiation of antiretroviral therapy was decided according to current recommendations, there was a trend towards an initial gain of fat at 6 months followed by a relative loss at 12 months.
- Patients on antiretroviral therapy had a higher negative impact on limb fat than untreated patients.
- Nevertheless, there was a high interindividual variability in the longitudinal assessment of limb fat.
- Limb fat change was positively correlated with changes in weight and trunk fat.
- A higher limb fat and a lower insulin at baseline were factors significantly associated with a decrease of limb fat at 12 months.
- We did not find any specific antiretroviral drug associated with a higher limb fat loss.