Poster R-105

IMPROVEMENT in LIPOATROPHY ASSOCIATED with HIGHLY ACTIVE ANTIRETROVIRAL THERAPY in HIV-INFECTED CHILDREN SWITCHED from STAVUDINE to TENOFOVIR

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BACKGROUND

A number of cohort studies in HIV-infected adults have suggested that long-term exposure to thymidine-analogues, particularly dT4, results in peripheral lipoatrophy.

Recent studies have demonstrated improvements in peripheral fat mass a nd a partial reversion of lipoatrophy when HIV-infected adults are switched from stavudine to abacavir or tenofovir

A recent paediatric study exploring risk factors for lipodystrophy has identified stavudine exposure as an independent risk factor for peripheral lipoatrophy.

(European Paediatric Lipodystrophy Group, AIDS 2004, 18 1443-1451)

Another paediatric study has shown that annual peripheral fat accrual is impaired in HIV-infected children treated with 3TC+d4T+ 1 PI.

Annual increments (g) of fat masses in HIV+ males and females compared with HC

Boys	Regions	HC	HIV+	p
Fat	Arms	50.9	-138.2	0.001
	Legs	131.9	-184.5	0.064
Girls	**Regions**	**HC**	**HIV+**	**p**
Fat	Arms	100.3	-21.6	0.035
	Legs	644.0	325.8	0.009

A Viganò, JAIDS 2003,32:482

AIMS

To assess the impact on body composition of switching stavudine to tenofovir and replacing protease inhibitor with efavirenz in HIV-infected children and adolescents.

To assess the immunological and virological outcomes of this new antiretroviral regimen.

PATIENTS AND METHODS

Type of study: 96 weeks prospective, open-label study.

Study population: Twenty-four HIV-infected children and adolescents (age range: 5-20 years) receiving antiretroviral therapy containing d4T+3TC+1 PI with a plasma HIV RNA < 50 copies/ml for at least 48 weeks prior to enrolment in the study.

Treatment switch: HIV infected children and adolescents were maintained on 3TC and were switched from d4T to TDF and from PI to EFV. TDF was administrated once daily at body surface area-dependent doses: 150 mg for 0.5-0.84 m^2; 225 mg for 0.84-1.29 m^2; 300 mg for $\geq$ 1.3 m^2.

Assessment of body composition changes: Whole-body composition was assessed with a DXA scanner (Lunar DPX-L, Lunar Radiation Corporation, Madison, WI) equipped with specific paediatric software (version 1.5h). The entire body of each subject was scanned, beginning at the top of the head. Body fat and lean mass were expressed in kilograms, and three-compartment analyses were performed in the arms, trunk and legs.

DXA measurements were made at baseline and at week 96 in HIV-infected children and adolescents. As a control group (HC) for DXA data, we studied once 143 consecutive Caucasian healthy volunteers (age range: 4.9-20 years). None had a history of endocrine, nutritional, growth or renal problems.

Efficacy assessment: **Plasma HIV-RNA levels were measured at baseline and at weeks 24, 48, 72 and 96 using the Quantiplex (bDNA) Assay version 3.0 with a l ower limit detection of 50 copies/ml (Bayer Diagnostics, Norwood, Massachusetts, USA).**

$CD4^+$ ce ll count and percentage were measured by flow cytometry at baseline and at weeks 24, 48, 72 and 96.

STATISTICAL ANALYSIS

Descriptive statistics were calculated for all variables, and data are expressed as mean (SD) unless otherwise stated.

Expected body composition variables were computed from the data gathered from HC, by r egression analyses. Briefly, body composition variables were plotted against age separately for boys and girls; polynomial regression lines were used to calculate the expected values. The differences between observed and expected values were evaluated by unpaired t-tests.

Body variables accrual during the study period were calculated for both observed and expected data sets.

Demographic and antropometric characteristics in HIV + before and 96 weeks after switching from 3TC+d4T+1 PI to 3TC+TDF+EFV.

	Baseline	96 weeks
Male/female	12/12	12/12
Age, years	12.4 (3.9) 12.9 (5.0-17.9)	14.5 (3.9) 15.1 (7.0-20.0)
Weight, Kg	43.2 (17.1) 46.1 (20.0-77.5)	48.3 (15.7) 50.7 (28.0-84.6)
Height, cm	148.8 (20.6) 154.0 (114.5-176.8)	155.8 (16.2) 157.7 (126.9-179.5)
BMI, Kg/m^2	18.6 (3.1) 17.8 (14.2-25.3)	19.3 (3.0) 19.0 (14.6-26.0)
Tanner stage	I = 10 II = 0 III = 1 IV = 5 V = 8	I = 5 II = 2 III = 2 IV = 0 V = 15

Clinical and therapeutic characteristics in HIV+ before switching from 3TC+d4T+1 PI to 3TC+TDF+EFV.

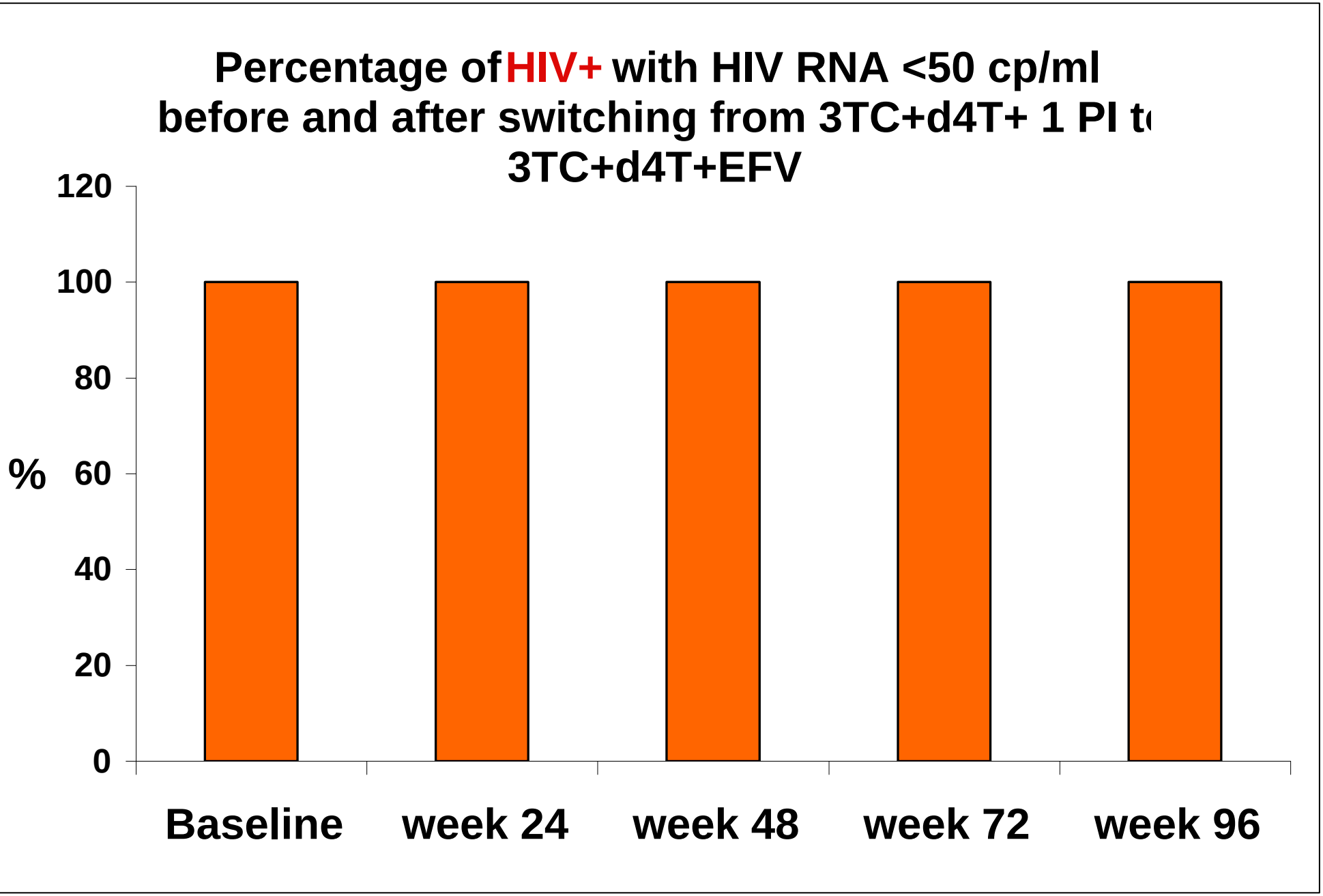
No of children with HIV RNA < 50 cp/ml	24
Previous HAART regimens (No of children)	3TC-AZT-RTV (1) 3TC-d4T-IDV (8) 3TC-d4T-NFV (6) 3TC-d4T-RTV (8) d4T-RTV-NFV (1)
Duration of previous HAART (mos)	
mean (SD)	70.7 (7.1)
median (range)	72.5 (53-81)

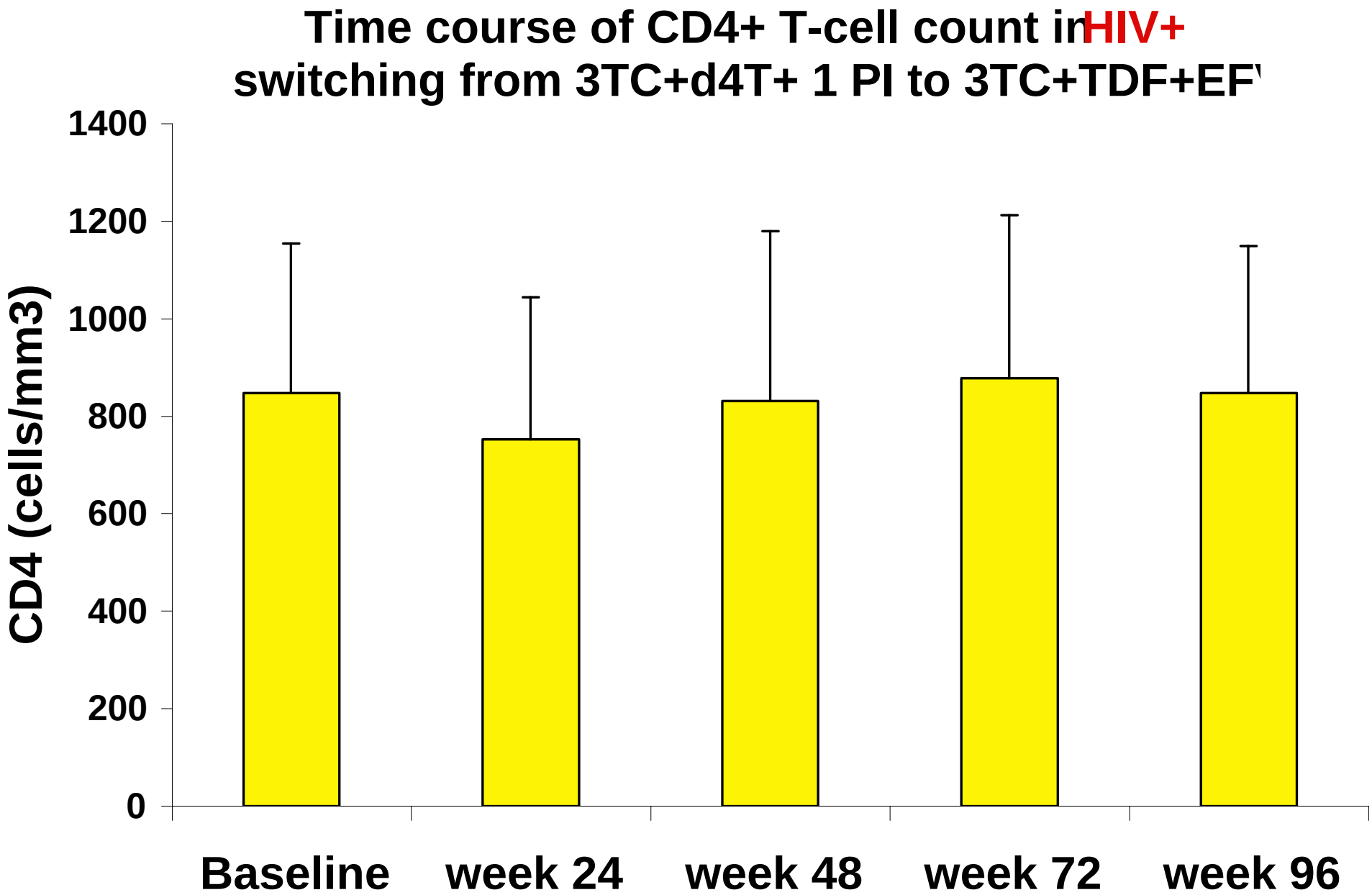
Data presented as mean (SD) and median (range).

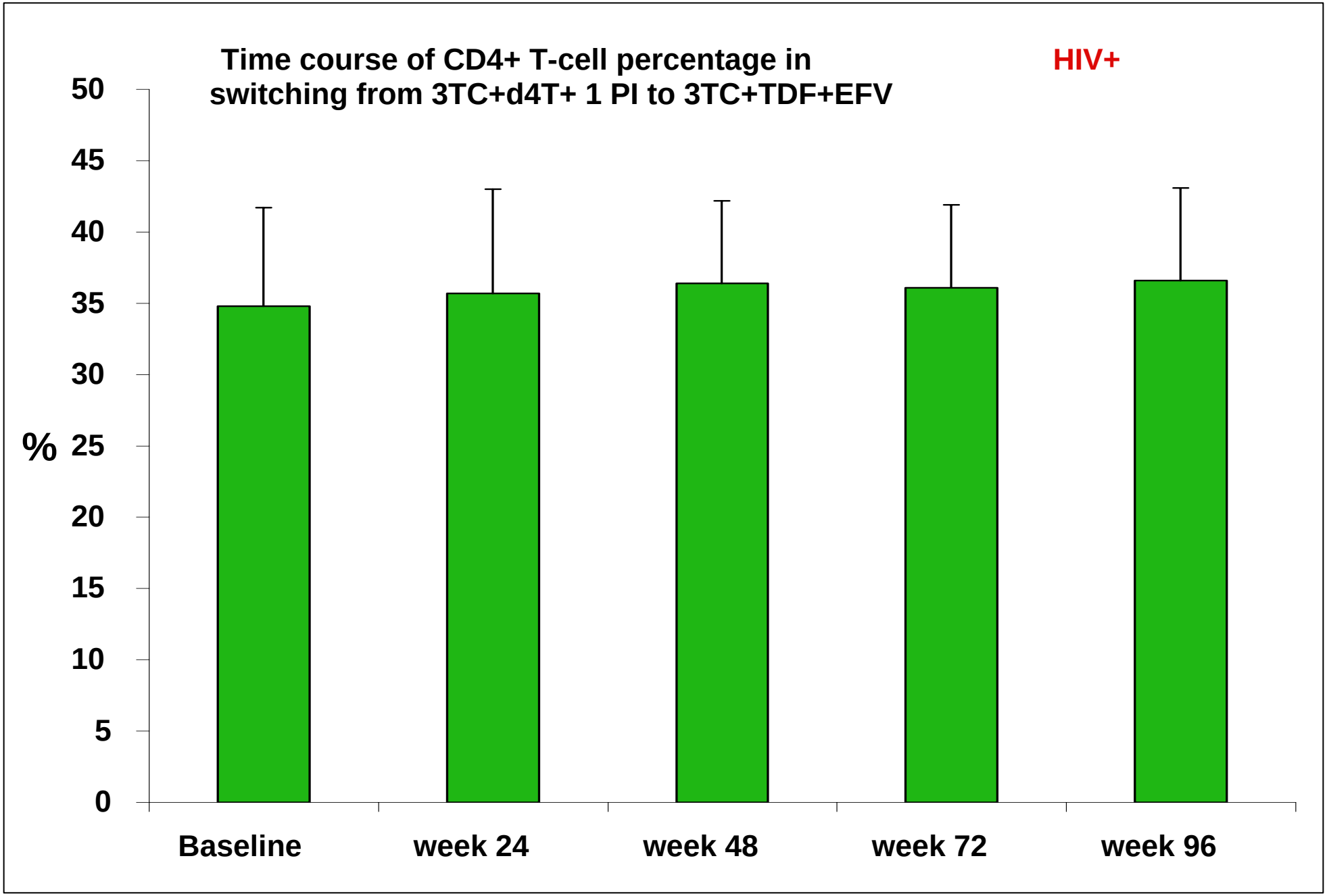
Demographic and antropometric characteristics of healthy controls (HC).

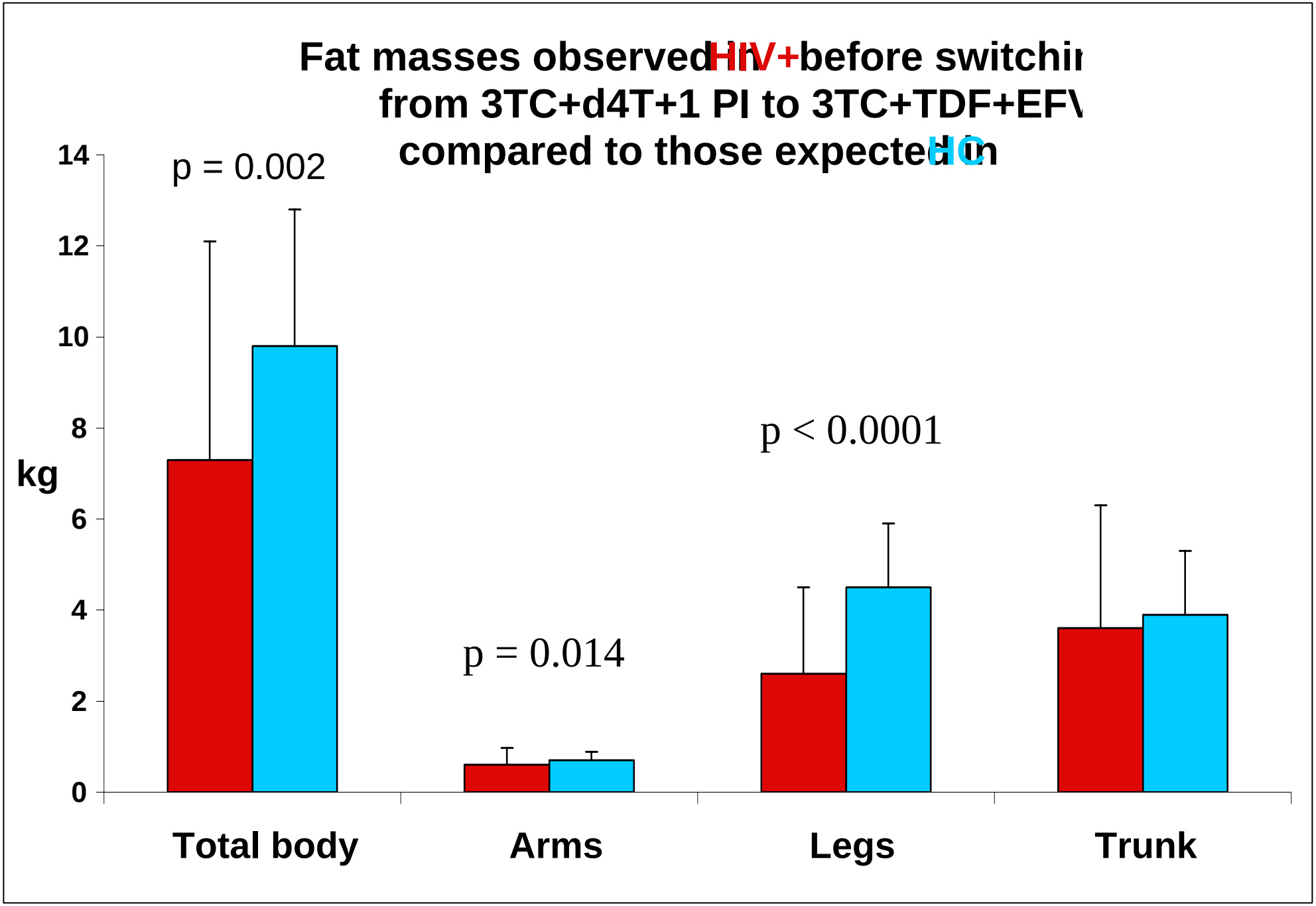
No of children	143
Male/female	76/67
Age, years	12.3 (4.4) 12.4 (4.9-20.0)
Weight, kg	42.4 (17.1) 42.0 (17.5-100.0)
Height, cm	146.6 (20.5) 148.7 (109.4-185.7)
BMI, kg/m^2	18.8 (3.0) 18.7 (12.4-29.3)

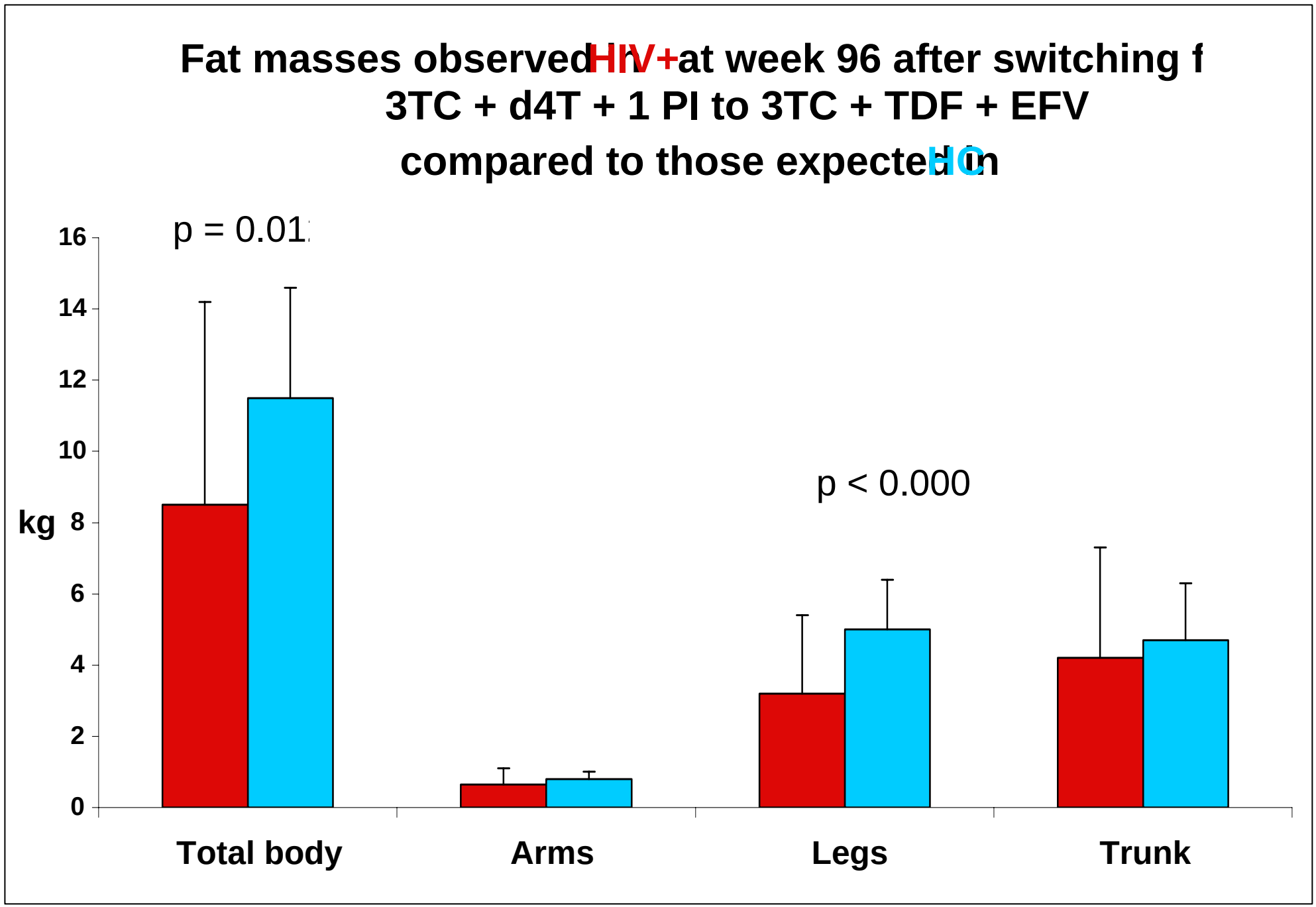
Data presented as mean (SD) and median (range).


Percentage of HIV+ with HIV RNA <50 cp/ml
before and after switching from 3TC+d4T+ 1 PI t
3TC+d4T+EFV
120
100
80
60
40
20
0
%
Baseline
week 24
week 48
week 72
week 96

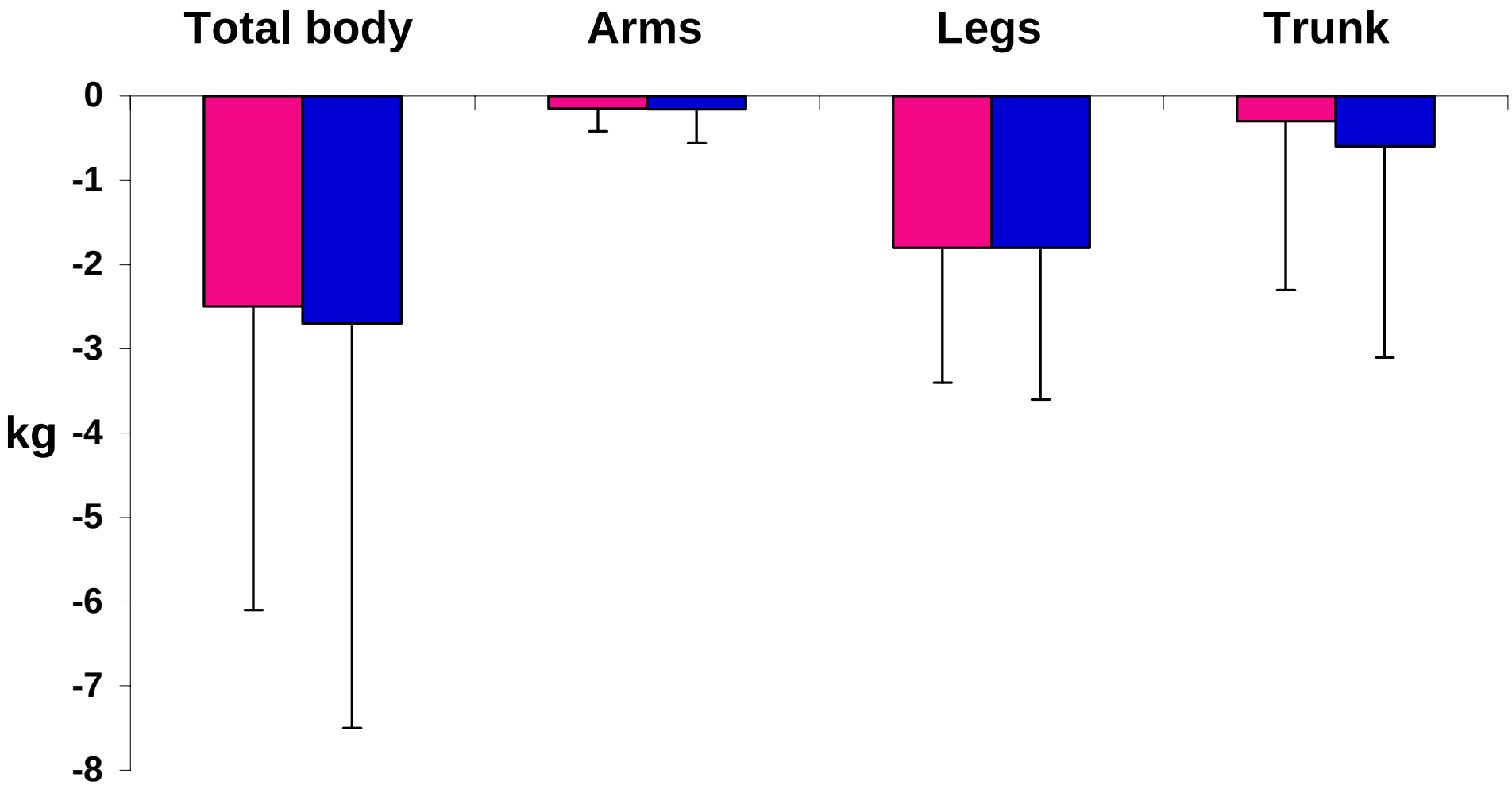

Time course of CD4+ T-cell count in HIV+
switching from 3TC+d4T+ 1 PI to 3TC+TDF+EF
CD4 (cells/mm3)
1400
1200
1000
800
600
400
200
0
Baseline
week 24
week 48
week 72
week 96

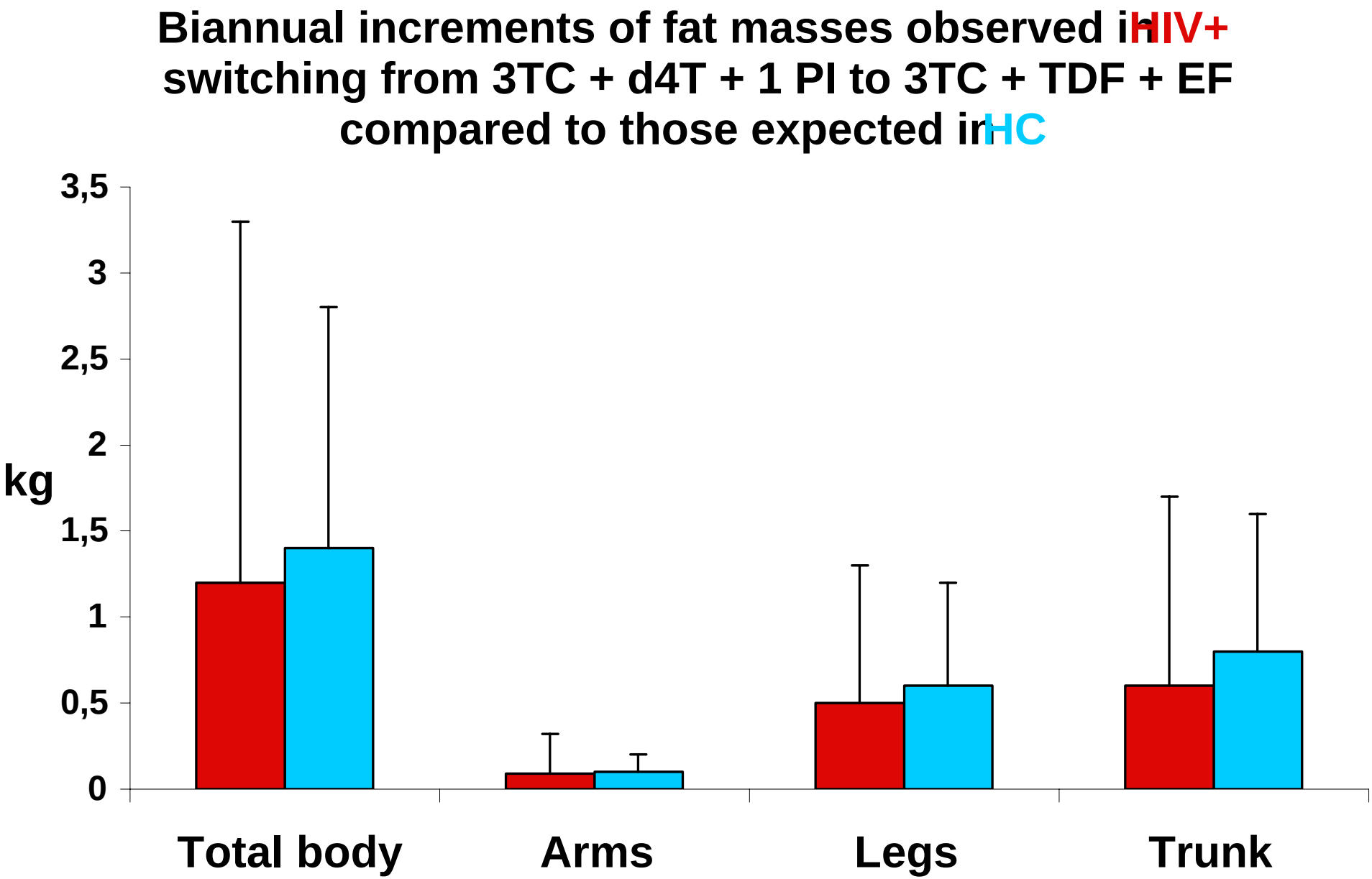

Time course of CD4+ T-cell percentage in switching from 3TC+d4T+ 1 PI to 3TC+TDF+EFV
HIV+
%
50
45
40
35
30
25
20
15
10
5
0
Baseline
week 24
week 48
week 72
week 96

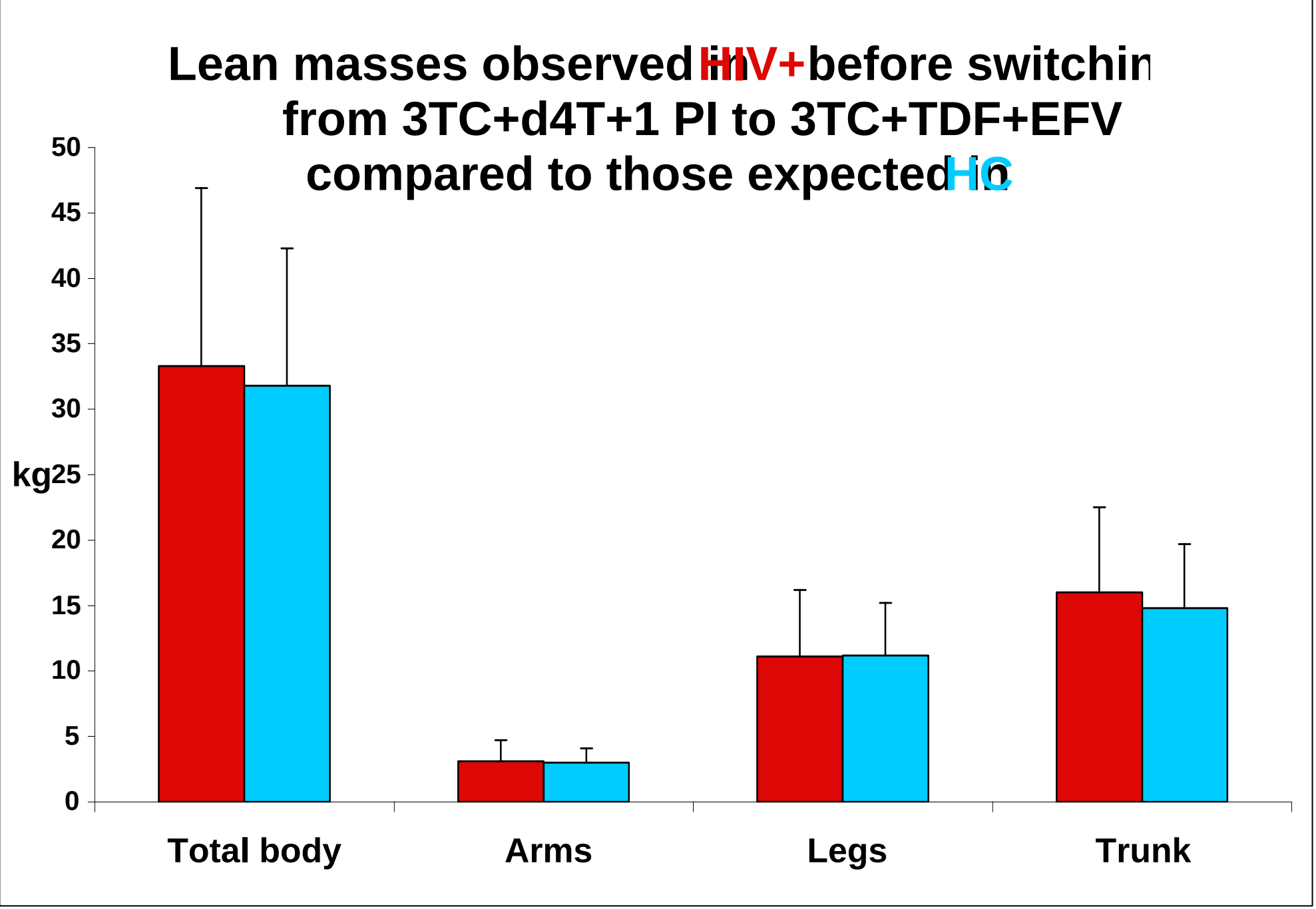

Fat masses observed in HIV+ before switchi
from 3TC+d4T+1 PI to 3TC+TDF+EF\
compared to those expected in HC
kg
14
12
10
8
6
4
2
0
p = 0.002
p = 0.014
p < 0.0001
Total body
Arms
Legs
Trunk


Fat masses observed in HIV+ at week 96 after switching f
3TC + d4T + 1 PI to 3TC + TDF + EFV
compared to those expected in HC
p = 0.01
p < 0.000
kg
16
14
12
10
8
6
4
2
0
Total body
Arms
Legs
Trunk

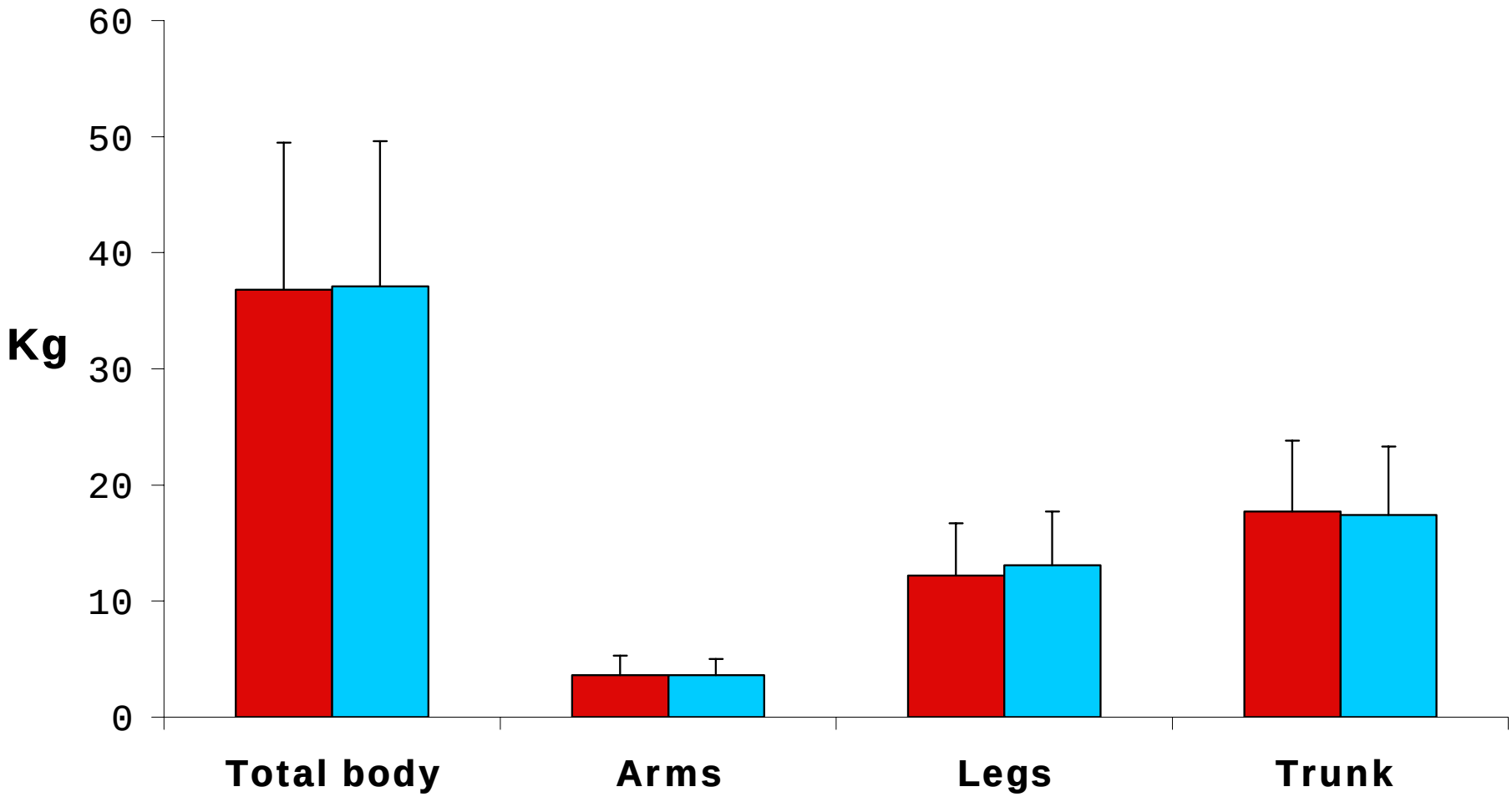
Differences between observed and expected fat masses in HIV+ before and 96 weeks after switching from 3TC+d4T+1 PI to 3TC+TDF+EFV




Biannual increments of fat masses observed in HIV+
switching from 3TC + d4T + 1 PI to 3TC + TDF + EF
compared to those expected in HC
kg
3,5
3
2,5
2
1,5
1
0,5
0
Total body
Arms
Legs
Trunk


Lean masses observed in HIV+ before switchin
from 3TC+d4T+1 PI to 3TC+TDF+EFV
compared to those expected in HC
50
45
40
35
30
kg 25
20
15
10
5
0
Total body
Arms
Legs
Trunk

Lean masses observed in HIV+ at week 96 after switching from 3TC + d4T + 1 PI to 3TC + TDF + EFV compared to those expected in HC



CONCLUSIONS

This study on lipoatrophic HIV-infected children and adolescents, switching from d4T to TDF for 96 weeks, shows the following:

1. **lipoatrophy does not change or worsen**
2. **biannual fat accrual is comparable to physiologically expected**
3. **lean mass is comparable to physiologically expected both at baseline and at week 96**
4. **HIV suppression is maintained**
5. **$CD4^+$ cell count and percentage remain stable**