

Frequency of lipodystrophy in a large cross-sectional study using either LPV/r or EFV in combination with contemporary nucleoside analogues

J. van Lunzen¹, R. Pauli², A. Trein³, A. Mutz⁴,
S. Hansen⁵, K. Fischer⁶

¹University Medical Center Hamburg-Eppendorf, Infectious Diseases Unit, Hamburg, Germany, ²Practice Pauli/Becker, Munich, Germany, ³HIV Center Practice Schnaitmann/Schaffert/Trein/Issler, Stuttgart, Germany, ⁴Klinikum Natruper Holz, Osnabrück, Germany, ⁵ICH (Infektionsmedizinisches Centrum Hamburg), Hamburg, Germany, ⁶Practice Fischer/Schranz, Berlin, Germany

Background

- HIV lipodystrophy is a disfiguring, socially stigmatizing disorder of fat metabolism that may increase the risk for cardiovascular disease.
- Though its pathogenesis is multifactorial, antiretroviral therapy (ART) plays a major role in it.
- There are several validated methods to assess body fat distribution, e.g. dual-energy X-ray absorptiometry (DEXA) or a lipodystrophy grading scale¹.

¹Carr et al., *J Acquir Immune Defic Syndr* 2003;33(5):571-6

Background

ACTG 5142 randomized clinical trial²:

- Used dual-energy X-ray absorptiometry (DEXA)
- *A priori* definition of lipatrophy: ≥ 20 % fat loss at 96 weeks
- Result: Higher rate of lipatrophy in a HAART regimen containing efavirenz (EFV) vs. a regime containing boosted lopinavir (LPV/r)
- The majority of patients received EFV or LPV/r in combination with more toxic nucleoside analogue (NA) backgrounds (e.g. d4T, ddI, AZT).
- Clinical observations with more contemporary NA were largely missing.

²Haubrich RH et al. , *AIDS* 2009;23(9):1109-18

Background

This trial:

- Used a modified lipodystrophy grading scale¹
- The patient's physical appearance was systematically rated by both physician and patient
- Analysis of the total population
- In addition: Subgroup analysis that differentiated between classical NA combinations and more modern regimen

¹Carr et al., *J Acquir Immune Defic Syndr* 2003;33(5):571-6

Background

Trial objective 1:

- To evaluate whether the use of a modified grading scale leads to results comparable to the DEXA method

Trial objective 2:

- To assess the rate of lipodystrophy
 - In patients receiving either LPV/r or EFV in combination with a nucleoside analogue
 - Further stratification according to the type of nucleoside analogue (NA) backbone (AZT + 3TC, TDF + FTC or 3TC vs. ABC + 3TC)

Methods

Study design:

- Retrospective, cross-sectional, multicenter survey
- Start in Q4 2007
- End in Q4 2008
- 28 HIV centers participating
- 332 patients

Inclusion criteria:

- Patients with a HIV infection treated with a standard first-line regimen containing either EFV or LPV/r and two NA
- Minimum of 2 years of unchanged therapy in advance of the survey
- Viral load < 400 copies during the past 6 months

Methods

Documented by patient

Lipodystrophy grading scale¹

Self-assessment of the satisfaction with the own body shape

Self-assessment of the disturbance in everyday life due to body shape

Assessment of adverse events

Self-assessment of compliance

Documented by physician

Lipodystrophy grading scale¹

Documentation of:

Age, gender, size, weight, waist-to-hip ratio, ethnical affiliation, CDC-stadium, concomitant disease, concomitant medication, CD4-cell count, viral load at beginning of therapy and actual lipid values

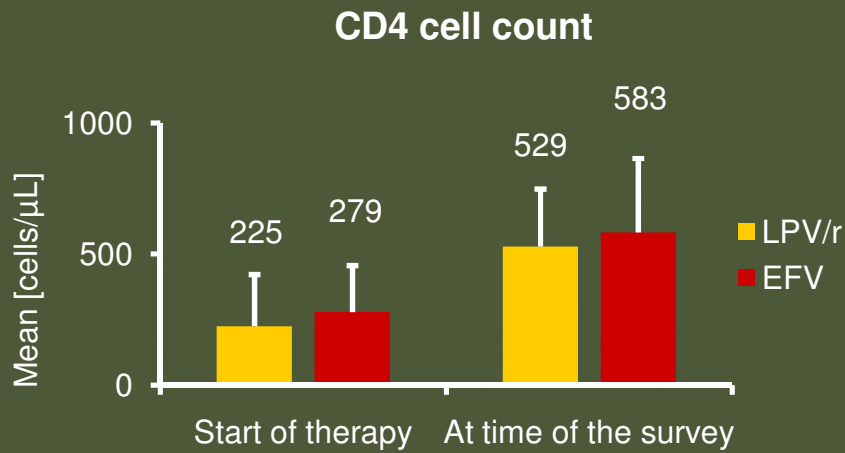
Results: Patient characteristics

- Out of 332 enrolled patients (165 EFV vs. 139 LPV/r) 28 patients were not eligible for analysis.
- Groups were well matched concerning characteristics at baseline and time of observation (VL, CD4, gender, ethnicity, NA backbone, concomitant diseases).
- Most of the patients had a white ethnicity (87 % LPV/r vs. 89 % EFV) and >70 % were male.
- Median duration of therapy was almost identical in the LPV/r and EFV groups (3.4 vs. 3.6 years).
- The mean self-reported compliance rate was very high (95 %) and similar in both groups.

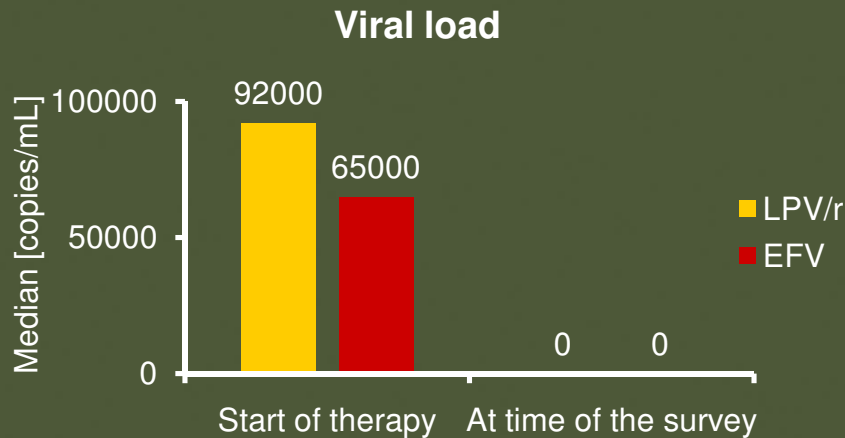
Results: Patient characteristics

	LPV/r group	EFV group
Number of patients	139	165
Mean age [years]	44.7	45.6
Mean duration of treatment [years]	3.4	3.6
Self-reported compliance [%]	> 95	> 95
CDC stage A [%]	14	25
CDC stage B [%]	31	28
CDC stage C [%]	34	24
Not known [%]	29	22

Results: Treatment efficacy

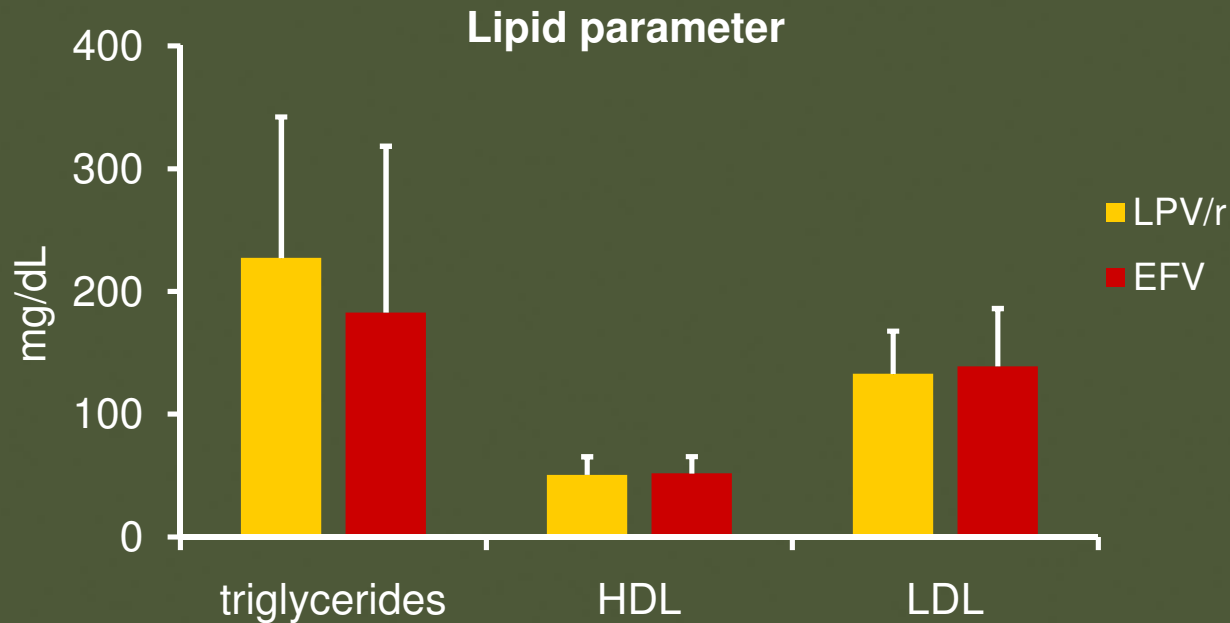


- CD4 count increase from baseline was identical (+ 304 cells/ μ L) in both groups.



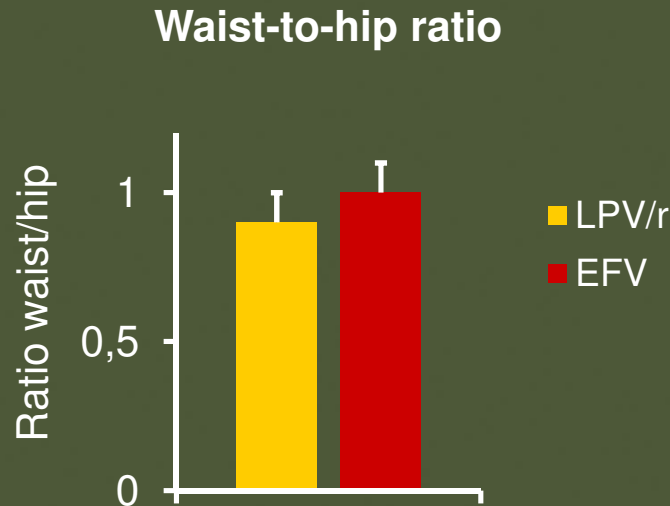
- Viral load was reduced below detection limit in both groups.

Results: Lipid parameters



- Median triglyceride levels were more pronounced in the LPV/r arm.
- HDL and LDL values were similar in both groups.
- The intake of lipid lowering agents was similar in both groups.

Results: Waist-to-hip ratio

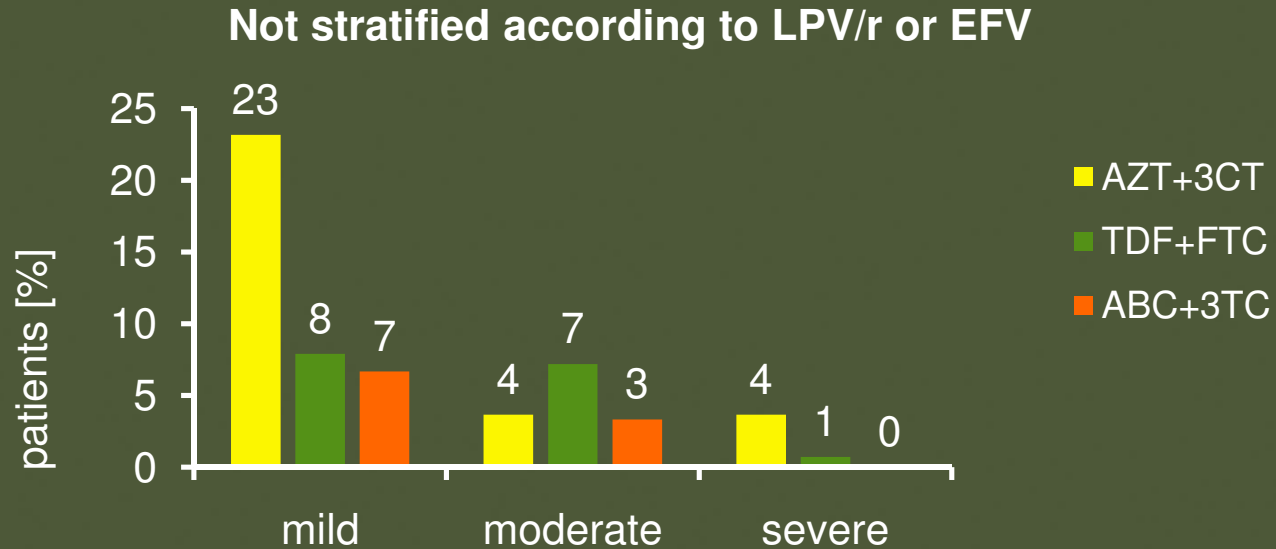


- Excessive trunk fat accumulation occurred only very rarely (<2 % of all cases, similar in both groups).
- Significant differences were observed in favor of LPV/r in waist and hip ratio ($p < 0.05$).

Results: Lipatrophy (overview)

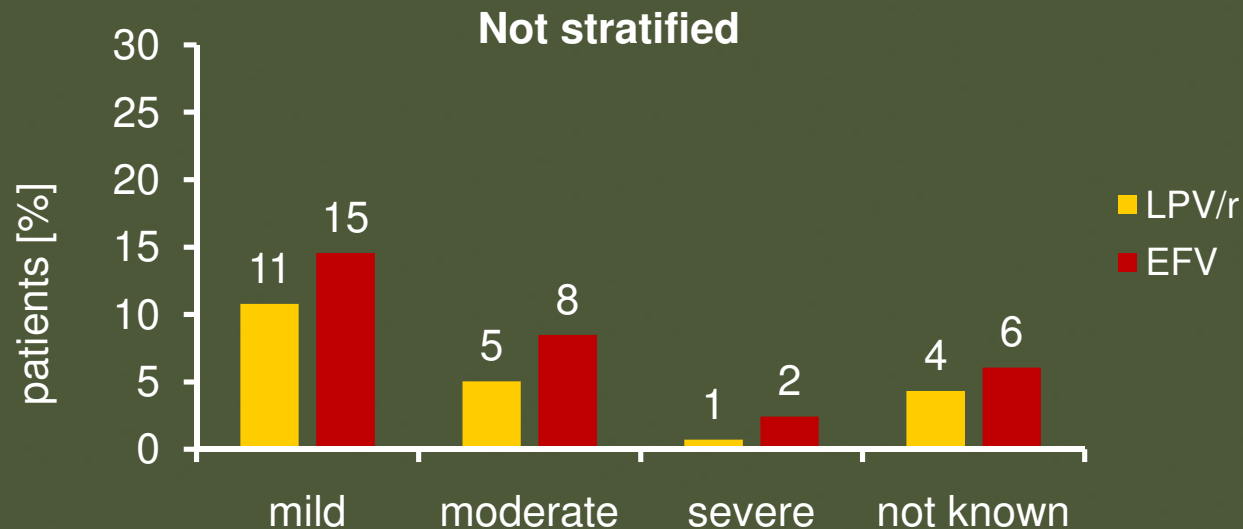
- Significant differences in lipodystrophy frequencies were found
 - in the limbs (leg lipatrophy).
 - in the breasts (lipaccumulation).
- A trend toward a more pronounced fat loss was also found
 - in the arms.
 - in the face.
 - in the buttocks.
- High concordance of physician and self-reported assessments.

Results: Patients with limb atrophy (legs)



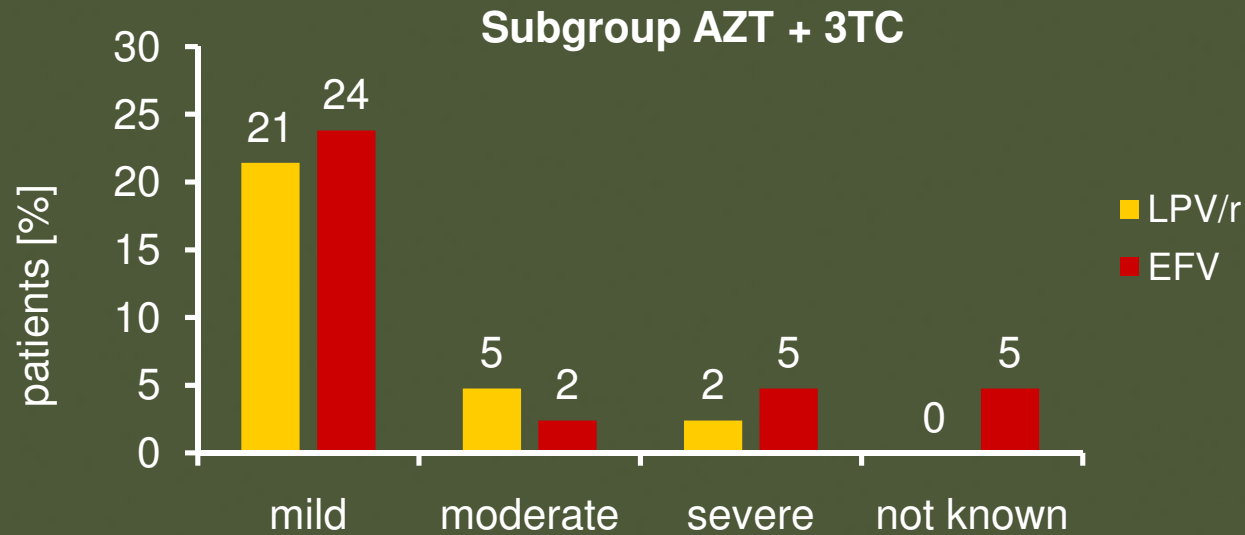
- TDF/FTC or 3TC was the most frequently used NA backbone (45 %), followed by AZT/3TC (28 %) and ABC/3TC (12 %).
- As expected, AZT/3TC most often caused lipatrophy of the legs, affecting a total 31 % of treated patients.
- Both TDF/FTC or 3TC and ABC/3TC had a significantly smaller effect on patients (16 % and 10 % of the patients, respectively) ($p < 0.05$).

Results: Loss of limb fat in the legs (1)



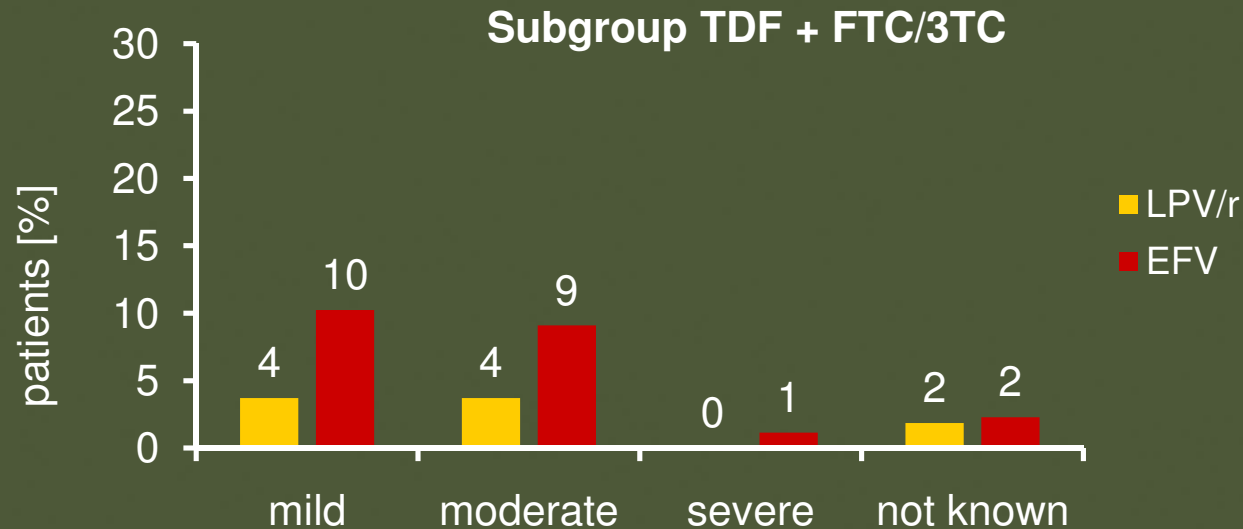
- There was less loss of limb fat in the LPV/r compared to the EFV group. 79% of patients treated with LPV/r had no signs of leg fat loss at all compared to 68 % in the EFV group ($p < 0,05$).
- A trend toward a more pronounced fat loss in the EFV group was found also in the arms, the face and the buttocks but did not reach statistical significance.

Results: Loss of limb fat in the legs (2)



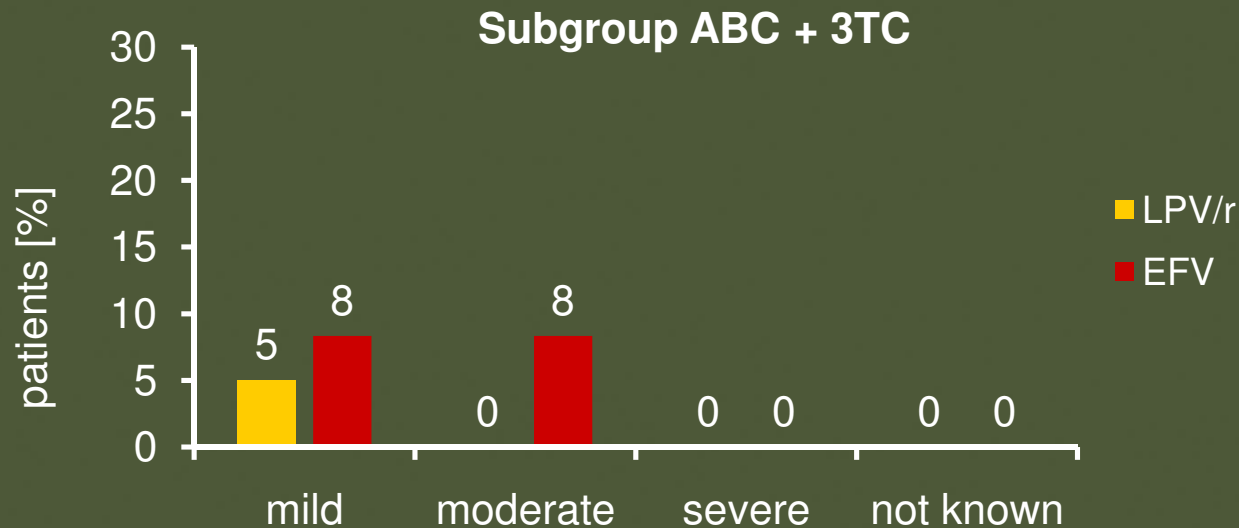
- As expected, in the AZT + 3TC subgroup, the frequency of lipatrophy was higher in both arms.
- The frequency of a lipatrophy of the legs was significantly decreased in the LPV/r arm than in the EFV arm.

Results: Loss of limb fat in the legs (3)



- In the TDF + FTC or 3TC subgroup, the frequency of lipatrophy was lower in both arms.
- The frequency of a lipatrophy of the legs was significantly decreased in the LPV/r arm than in the EFV arm.

Results: Loss of limb fat in the legs (4)



- In the ABC + 3TC subgroup, the frequency of lipatrophy was lowest compared to the other strata.
- The frequency of lipatrophy of the legs was significantly decreased in the LPV/r arm than in the EFV arm.

Results: Lipaccumulation in breasts and other regions

- There was also significantly less lipaccumulation in breasts as rated by patients receiving a regime containing LPV/r ($p < 0.05$) compared to EFV.
- 85 % of patients treated with LPV/r + nucleoside analogs documented no lipaccumulation in the breasts vs. 78 % of patients from the EFV group.

Conclusion (1)

- EFV and LPV/r containing regimens were equally effective in this observational cohort.
- Despite higher TG levels in the LPV/r group, significantly more leg fat loss was reported in the EFV group. This was the case both for a combination with classical and contemporary NA backbones.
- In every analyzed subgroup as well as in the non-stratified group, at least one fourth less cases of mild to severe lipatrophy were reported in regimen containing LPV/r- compared to EFV-containing regimen.
- A trend toward a more pronounced fat loss in the EFV group was found also in the arms, the face and the buttocks but did not reach statistical significance.
- There was significantly less lipaccumulation in the breasts in the LPV/r group as reported by patients. Trunk fat accumulation, however, was not different in the two groups.

Conclusion (2)

- Patient evaluation was similar to the physicians' assessment underlining the validity of the used questionnaire.
- This cross-sectional study is limited by relatively low patient numbers for each cohort that did not allow for statistical analysis in all subgroups.
- In conclusion, our study supports the ACTG 5142 trial results using a different tool for the assessment of body fat distribution. The lipodystrophy grading scale scored visible effects and thus provides new aspects of LA development during antiretroviral therapy of both EFV and LPV/r in combination with modern NA backbones.

Acknowledgments

- Dr. Arminia Carlebach, Frankfurt
- Dr. Jörg Claus, Berlin
- Dr. Olaf Degen, Hamburg
- Dr. Martin Dörler, Bochum
- Dr. Stefan Fenske, Hamburg
- Klaus Fischer, Berlin
- Dr. Friedrich Gläbel, München
- Dr. Dietrich Gorriahn, München
- Beatrice Gospodinov, Saarbrücken
- Dr. Peter Gute, Frankfurt
- Stefan Hansen, Hamburg
- Dr. Helmut Hartl, München
- Martin Hower, Dortmund
- Siegfried Köppe, Berlin
- Dr. Freidhelm Kwirant, Duisburg
- Leo Locher, Frankfurt
- PD Dr. Jan van Lunzen, Hamburg
- Dr. Thomas Lutz, Frankfurt
- Dr. Christoph Mayr, Berlin
- Dr. Markus Müller, Stuttgart
- Dr. Antonius Mutz, Osnabrück
- Dr. Clemens Scheidegger, München
- PD Dr. Wolfgang Schmidt, Berlin
- Dietmar Schranz, Berlin
- Dr. Christoph Schuler, Berlin
- Dr. Jan Michael Siehl, Berlin
- Dr. Andreas Trein, Stuttgart
- Dr. Ramona Volkert, München

Special thanks to all participating patients

This study was sponsored by Abbott Virology Germany