

Anthropometric and immunological success of antiretroviral therapy and prediction of virological success in west African adults.

Eugène Messou, Delphine Gabillard, Raoul Moh, André Inwoley, Souleymane Sorho, Serge Eholié, François Rouet, Catherine Seyler, Christine Danel, Xavier Anglaret

► **To cite this version:**

Eugène Messou, Delphine Gabillard, Raoul Moh, André Inwoley, Souleymane Sorho, et al.. Anthropometric and immunological success of antiretroviral therapy and prediction of virological success in west African adults.: Predictors of virological success of ART in Abidjan. Bulletin of the World Health Organization, World Health Organization, 2008, 86 (6), pp.435-42. inserm-00266573

HAL Id: inserm-00266573

<https://www.hal.inserm.fr/inserm-00266573>

Submitted on 30 Jun 2008

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Early anthropometric and immunological success of antiretroviral therapy do not predict virological success in West African adults

Bull WHO in press

3204 words, 3 tables, 4 figures

Eugène Messou^{1,2}, Delphine Gabillard¹, Raoul Moh², André Inwoley^{2,3}, Souleymane Sorho², Serge Eholié^{2,4}, François Rouet^{2,3}, Catherine Seyler^{1, 2}, Christine Danel^{1, 2}, Xavier Anglaret^{1, 2}

¹ INSERM, U593, Bordeaux, France

² Programme PAC-CI, Abidjan, Côte d'Ivoire

³ Centre de Diagnostic et de Recherches sur le SIDA (CeDReS), CHU de Treichville, Abidjan

⁴ Service des Maladies Infectieuses et Tropicales, CHU de Treichville, Abidjan

Correspondence :

Xavier Anglaret, MD, PhD

INSERM, U593

Université Victor Segalen Bordeaux 2

33076 Bordeaux cedex

France

e-mail : Xavier.Anglaret@isped.u-bordeaux2.fr

This study was supported by the French Agence Nationale de Recherches sur le SIDA (ANRS) and the Ivoirian Ministry of Public Health within the collaborative Programme PAC-CI.

Running head: Predictors of virological success of ART in Abidjan

Abstract (247 words)

Background: The 6-month assessment of the response to antiretroviral therapy (ART) is a critical step. In sub-Saharan Africa, few people have access to plasma viral load (VL) measurement. We assessed the gain or loss in BMI (Δ BMI), alone or in combination with the gain or loss in CD4 (Δ CD4), as a tool for predicting the response to ART at 6 months.

Methods: In a cohort of 622 adults in Abidjan, we calculated the sensitivity, specificity and predictive values of Δ BMI and Δ CD4 for treatment success, with VL undetectability (<300 copies/ml) as gold standard.

Results: After 6 months of ART, the median Δ BMI was +1.0 kg/m² (interquartile range [IQR] +0.0; +2.1), the median Δ CD4 was +148/mm³ (IQR +54; +230) and 84% of patients reached VL undetectability. The distribution of Δ BMI was similar among patients who reached VL undetectability and those who did not (median +1.06 vs. +0.99 kg/m², p=0.51). With increasing Δ BMI, the specificity of Δ BMI for treatment success increased but its sensitivity decreased and its positive predictive value remained stable around 85%. All results remained similar when combining Δ BMI with Δ CD4 and when stratifying by groups of baseline BMI or CD4.

Discussion: In settings where VL measurement is not available, a high BMI gain should not be interpreted as reflecting virological success, even when combined with a high CD4 gain. In our population, most patients with detectable VL were probably sufficiently adherent to reach significant BMI and CD4 gain but insufficiently adherent to reach VL suppression.

Keywords: sub-Saharan Africa; HAART; body mass index; CD4 count; virological success; adults; predictive value

Introduction

The primary goal of antiretroviral therapy (ART) is to suppress human immunodeficiency virus (HIV) replication. This is considered to be achieved when the virus can no longer be detected in plasma. International guidelines recommend that plasma viral load undetectability should be reached within the first six months of ART¹. In patients with plasma viral load still detectable at month-6, the most frequent cause of virological failure is a poor adherence. At this point, reinforcing adherence is a key condition for improving long-term outcomes.

In sub-Saharan Africa, few people have access to viral load measurement. For the millions of African patients who will start ART within the next few years, treatment will have to be monitored using other tools, including clinical examination and CD4+ T-cell (CD4) count². Given the importance that viral suppression should be reached shortly after ART initiation, it seemed interesting to assess whether clinical and immunological indicators could predict viral load undetectability at 6 months, or if they should only be seen as variables independently associated with ART initiation but unable to predict virological suppression.

Previous studies already reported that the CD4 count evolution at month-6 poorly predicted viral load undetectability^{3,4}. To our knowledge, no study has assessed the predictive value for virological success of a gain in body mass index (BMI) in sub-Saharan adults starting ART. BMI is widely measurable, contrary to viral load, CD4 count, and also to WHO clinical staging which is largely based on etiological diagnosis often requiring laboratory investigations. BMI has been repeatedly associated with the prognosis of HIV disease either in patients on or off ART⁵⁻¹⁰. Before the ART era, BMI has also been shown to increase in African patients starting cotrimoxazole prophylaxis even though cotrimoxazole had no effect on CD4 count evolution¹¹. This suggests that BMI could be of use not only as a predictor for prognosis but also as a marker for HIV treatment efficacy.

We assessed the gain or loss in BMI, alone or in combination with a gain or loss in CD4, between ART initiation and the 6-month visit following ART initiation as a tool for predicting virological success or virological failure at month-6 in HIV-infected adults followed in a prospective cohort study in Abidjan, Côte d'Ivoire.

Methods

Patients

In December 2002, a multicentre randomised trial (Trivacan ANRS 1269 trial) was launched in five outpatients clinics of Abidjan¹². The main objective of this trial was to assess various Structured Treatment Interruptions (STI) strategies of ART. The trial was designed in two phases. Patients were included in the first phase (“pre-randomisation phase”) if they met the following criteria: age ≥ 18 years, naïve to curative antiretroviral therapy, CD4 count between 150 and 350/mm³ or CD4 percentage between 12.5% and 20%, absence of pregnancy, absence of severe renal or hepatic failure and written informed consent. In this pre-randomisation phase, all patients received continuous ART. After at least six months in the ART initiation phase, patients with undetectable plasma HIV-1 RNA and CD4 count $> 350/\text{mm}^3$ were randomised into the “ART interruptions strategies” phase.

Here we present data on BMI, CD4 count and viral load evolution during the first six months of continuous ART within the ART initiation phase of the Trivacan trial. All HIV-1 infected patients included in the ART initiation phase of the Trivacan trial were eligible for the present study if they had a pre-ART BMI $< 25 \text{ kg/m}^2$, a pre-ART CD4 count $< 500/\text{mm}^3$, if plasma viral load was detectable before ART initiation, and if they were still alive and followed-up at month-6. Eligible patients were excluded from the analysis if they had at least one missing value for BMI, CD4 and/or viral load at baseline and/or at month-6.

The protocol of the Trivacan trial was approved by the ethics committee of the Ivorian Ministry of Health and the Institutional Review Board of the ANRS.

Follow-up

The procedures of the ART initiation phase have been previously described^{13,14}. In summary, at enrolment, patients started zidovudine-lamivudine in combination with (i), preferably efavirenz, for HIV-1 infected or HIV-1+2 dually-infected men and women with effective contraception and no history of nevirapine prophylactic treatment; (ii) indinavir-ritonavir (800/100 mg twice daily), for HIV-2 infected patients and women not desiring contraception or with a history of nevirapine prophylaxis. Cotrimoxazole prophylaxis was systematically given to all patients, in accordance with WHO 2006 guidelines on cotrimoxazole prophylaxis¹⁵. After inclusion, participants were asked to return monthly to their study clinic. At enrollment and at each monthly visit, a standardized questionnaire was used to record clinical characteristics, including height, weight and self-reported adherence to treatment during the previous four days. Weight was measured at each visit using the same scales. Between these scheduled visits, patients had free access to the study clinics.

The CD4 count (True Count[®] technique on FACScan[®], Becton Dickinson) and plasma HIV-1 RNA load (real-time PCR on Taq Man technology Abi Prism 7000, Applied Biosystems,

quantification limit 300 copies/ml) were measured every three months¹⁶. In case of VL > 300 copies/ml, resistance genotype was performed by automated population full-sequence analysis (ABI system) using the ANRS consensus technique. French resistance algorithm 2006 was used for interpretation (www.hivfrenchresistance.org).

All care was free-of-charge.

Statistical analyses

Baseline was the date of enrolment in the pre-randomisation phase. The end of study date was the month-6 visit. In the main set of analysis, virological success at month-6 was defined as a plasma viral load below the threshold of detectability (300 copies/mL). In a second set of analysis, virological success was defined as a plasma viral load below 3 log₁₀ copies/ml.

First, at each scheduled visit, we described the distribution of CD4 count, BMI, and of the difference between the current CD4 and BMI values and their baseline values (Δ CD4 and Δ BMI). The mean Δ CD4 and mean Δ BMI at each point were compared between groups of baseline CD4 and or of baseline BMI values by means of the Kruskal-Wallis Test.

Secondly, we estimated the sensitivity, specificity, positive and negative predictive value for virological success or failure of the Δ CD4, the Δ BMI, or both, using different thresholds of Δ BMI and Δ CD4 and using successively the month-3 and month-6 values of Δ BMI and Δ CD4.

Thirdly, the distributions of Δ BMI and Δ CD4 at month-3 and month-6 were compared between patients who reached virological success at month-6 and those who did not by means of the Kruskal-Wallis test.

Finally, the association between adherence and virological success at month-6 was analysed using a multivariate logistic regression model, adjusted on baseline CD4 count, WHO clinical stage, plasma HIV-1 viral load and care center. Non-adherence was defined as self-reporting at least one ARV drug dose missed. We successively analysed the role of non-adherence during the overall follow-up (ie reporting at least one ARV drug dose missed at any of the six visits) and the role of early non-adherence (ie reporting at least one ARV drug dose missed at the first month visit

All analyses were made using SAS 8.2 software.

Results

Patients

Of the 840 patients included in the pre-randomisation phase of the Trivacan trial, 622 were included in the present study, 32 were eligible but were excluded from the analyses because they had at least one missing value for baseline or month-6 CD4, BMI or viral load, and 186 were non eligible for at least one of the following reasons: they had a baseline BMI $> 25/\text{m}^2$ (n=138, 16%), they were infected with HIV-2 only (n=16, 2%), they had a baseline CD4 count $> 500/\text{mm}^3$ (n=20, 2%), they had an undetectable viral load at baseline (n=25, 3%), they died before month-6 (n=10, 1%) and/or they were lost to follow-up before month-6 (n=9, 1%). As shown in table 1, the 622 patients included in the study were predominantly female. Their median CD4 count, BMI and plasma HIV-1 viral load were $250/\text{mm}^3$, $20.8 \text{ kg}/\text{m}^2$ and $5.0 \log_{10}/\text{ml}$, respectively.

Virological success at month-6

At month-6, 523 patients (84%) had undetectable plasma viral load. Of the remaining 99 patients with detectable viral load, 20 had a viral load $< 3 \log_{10}$ copies/ml, 36 had $3 \log_{10}$ copies/ml \leq viral load $< 4 \log_{10}$ copies/ml and 43 had a viral load $\geq 4 \log_{10}$ copies/ml. Of these 99 patients, 88 had available results for genotype resistance tests, showing no resistance to any antiretroviral drugs in 62 (70%) and at least one resistance mutation in 26 (30%). In the latter, the mutations were K103N alone (n=14), M184V alone (n=6), K103N and M184V (n=5) and M41L (n=1).

Body mass index and CD4 count evolution from baseline to month-6

At month-6, the median ΔBMI was $+1.0 \text{ kg}/\text{m}^2$ (IQR $+0.0$; $+2.1$) and the median ΔCD4 was $+148/\text{mm}^3$ (IQR $+54$; $+230$).

Figure 1 shows the mean ΔBMI at each monthly visit, by groups of baseline BMI. There was a significant difference between groups in terms of mean ΔBMI at month-6, which ranged from $+0.7 \text{ kg}/\text{m}^2$ in patients with baseline BMI at $22.5\text{-}25 \text{ kg}/\text{m}^2$ to $+2.2 \text{ kg}/\text{m}^2$ in patients with baseline BMI $< 18.5 \text{ kg}/\text{m}^2$ ($p < 0.001$).

Figure 2 shows the mean ΔCD4 at month-3 and month-6, by groups of baseline CD4. ΔCD4 at month-6 was significantly different between groups, ranging from $+131/\text{mm}^3$ in patients with baseline CD4 at $350\text{-}500/\text{mm}^3$ to $+176/\text{mm}^3$ in patients with baseline CD4 $< 150/\text{mm}^3$ ($p=0.02$).

Figure 3 and 4 show the distribution of Δ BMI (figure 3) and Δ CD4 (figure 4) at month-3 and month-6 in patients who reached virological success at month-6 and in those who did not. Patients reaching viral load undetectability had comparable distributions of Δ BMI at month-6 than those who did not. By contrast, patients reaching viral load undetectability had significantly but slightly higher CD4 count at month-6 than those who did not.

Morbidity from baseline to month-6

During the first six months, 26 (4.2%) of the 622 participants had at least one new WHO stage 3 or 4-defining morbidity episode not present at baseline (total number of new episodes 29, median time between last episode and month-6 82 days, IQR 50-133). This included 22 (4.2%) of the 523 patients with undetectable plasma viral load at month-6 (total number of episodes 24) and 4 (4.0%) of the 99 patients with detectable viral load at month-6 (total number of episodes 5). Patients with at least one severe morbidity episode had a significantly lower Δ BMI at month-6 than those who did not experience severe morbidity (median +0.3 [IQR -1.5;+1.7] *versus* +1.1 [IQR 0.0;+2.1], respectively). The 29 episodes of severe morbidity were episodes of tuberculosis (n=14), invasive bacterial diseases (n=11, including four pneumonias, two isolated bacteraemias, one sinusitis, one deep abscess, one meningitis and one pyelonephritis), isosporiasis (n=1), cryptosporidiosis (n=1), chronic genital herpes simplex virus infection (n=1) and unexplained diarrhea > days (n=1).

Predictors for viral load at month-6

Table 2 and 3 show the sensitivity, specificity and predictive values for virological success (table 2) or virological failure (table 3) of Δ BMI and/or Δ CD4 at month-6. The specificity of a gain in BMI for virological success rapidly increased with increasing gain, but it almost never rose above 90%. Meanwhile, its sensitivity rapidly fell with increasing gain, and its positive predictive value remained stable around 85%, ie close to the percentage of patients reaching virological success in the overall population. This remained true even for the highest gains, and even when combining gain in BMI with a gain in CD4 cells.

These results remained similar when virological success was defined as a viral load < 3 log₁₀ copies/ml, when stratifying analyses by groups of baseline BMI values or by groups of baseline CD4 values, and when using Δ BMI and Δ CD4 at month-3 to predict virological success at month-6 (data not shown).

Adherence

The percentage of patients self-reporting at least one missed dose for at least one ARV drug during the preceding four days was 11%, 12%, 11%, 9%, 10% and 8% at months 1, 2 and 3, 4, 5 and 6, respectively. The percentage of patients self-reporting at least one missed dose at any of the six visits was 39%. There was no association between missing at least one dose at any of the 6 visits and virological failure at month 6 (univariate analysis, $p=0.14$). However, self-reporting at least one missed dose at month-1 was significantly associated with virological failure at month-6 both in the univariate ($p=0.03$) and multivariate analysis ($p=0.04$). Adjusted on baseline CD4 count, WHO clinical staging, plasma viral load and care center, the odds ratio of virological failure at month-6 was 1.87 in patients declaring at least one missed dose during the preceding four days at month-1 compared with patients declaring no missed dose (95%CI 1.03-3.41).

Discussion

We reported BMI, CD4 count and viral load evolution between ART initiation and month-6 in 622 adults who started ART with a BMI < 25 kg/m² in Côte d'Ivoire. At month-6, we found that the overall rate of patients reaching undetectable viral load was 84%. Patients reaching undetectable viral load had comparable distributions of Δ BMI at month-3 and 6 with those who had detectable viral load. The percentage of patients who succeeded in suppressing their plasma viral load remained comparable among patients reaching anthropometric and/or immunological markers of success – ie high BMI and/or CD4 gain – and among those reaching markers of failure – high BMI and/or CD4 loss. The gain or loss in BMI and CD4, alone or in combination, was not useful in predicting virological success or failure at month-6, even when considering the highest gains or losses.

In countries where plasma viral load can be routinely measured, a detectable viral load at month-6 leads to subsequent investigation of the reason for insufficient suppression. Among these reasons, the most frequent is incomplete adherence¹⁷. At this stage, improving adherence in patients is crucial to avoid the emergence of resistance mutations and therefore to ensure long-term success of ART¹⁸. In our study, most patients with detectable viral load were probably insufficiently adherent to reach complete viral load suppression but sufficiently adherent to reach significant BMI and CD4 gains. Conversely, most patients who presented a loss in BMI and/or CD4 cells probably were adherent to treatment, as 87% of patients who lost at least 1 kg/m² and 79% of patients who lost at least 50 CD4/mm³ between baseline and month-6 had undetectable viral load at month-6. These findings have two consequences: firstly, they plead for making plasma viral load quantification routinely available in low resource settings; secondly, in settings where viral load measurement is not available yet, clinicians should be aware that a high CD4 gain – as previously shown^{3,4} – but also a high BMI gain, alone or in combination with a high CD4 gain – as shown in our study –, should not be seen as reflecting optimal adherence to treatment. Similarly, a BMI loss, alone or in combination with a CD4 loss, should not lead to the conclusion that a patient is not adherent. Thus, in these settings, direct markers for adherence should be even more closely monitored than in high resource settings.

In three large cohorts from low resource settings, the median gain in weight after 6 months on ART was estimated at +3 Kg (IQR 1 - 6), +5.0 kg (IQR 1.5 – 9.6) and + 4.0 kg (IQR : 0.9-7.7) in patients with a median pre-ART CD4 count at 48/mm³, 43/mm³ and 131/mm³, respectively¹⁹⁻²¹. To our knowledge, the gain in BMI on ART has never been reported in sub-Saharan Africa. It is important to point out that our study only focused on the 6-month response to ART. It cannot be inferred from our data that BMI evolution over longer follow-up, e.g. a break in the BMI evolution curve in a patient who previously reached criteria for treatment success, could not be useful for predicting later treatment failure. This should be

assessed in studies with BMI being systematically recorded over longer periods of follow-up. As BMI change could be independently associated with non-antiretroviral treatments, e.g. cotrimoxazole prophylaxis or antituberculous treatments ⁽¹¹⁾, further studies should include homogeneous populations with regards to non-ART drugs received by the patients, or have sufficient power to adjust for co-treatments.

Our study had some limitations.

First, our population was not representative of the overall population of adults receiving ART in sub-Saharan Africa. Participants started ART with less advanced immunosuppression, compared with most adults starting ART in sub-Saharan Africa ^{5,7,8}. They were followed under cohort conditions, with low rates of loss-to-follow-up and high rates of virological success. Because patients received care free of charge, including ART, they were under optimal conditions regarding adherence to treatment. In patients at a more advanced stage of immunosuppression and lower BMI at baseline, or in patients followed in program conditions with lower rates of success at month-6, the association between BMI gain and virological success might differ from our population. However, as our results remained similar when stratifying analyses by groups of baseline BMI and CD4 values, repeating our analyses in populations starting ART at a more advanced stage would be likely to give similar results.

Secondly, we did not perform resistance testing at baseline, and therefore were unable to distinguish patients with ART failure because of primary drug resistance from those with ART failure of other causes, including poor adherence. However, primary resistance to antiretroviral drugs is still rare in Côte d'Ivoire (5.6%) ^{22,23}. Furthermore, at month-6, only 30% of patients with detectable viral load had resistance to at least one drug. Therefore, the assumption that most patients with detectable viral load could have been imperfectly adherent patients may be reasonable.

Thirdly, we measured plasma HIV-1 RNA viral load by means of the automated TaqMan real-time reverse transcription-PCR assay, with a detection threshold of 300 copies/ml. Though it is impossible to rule out that using an assay with lower detection threshold might have had consequences on our findings, it is very unlikely that the BMI and CD4 gain would be more strongly predictive of virological success when defining success at a lower detection threshold. Of note, our results did not vary in the sensitivity analysis using 1000 copies/ml as the threshold for defining success.

In conclusion, the 6-months assessment of the response to ART is a critical step. At this stage, markers for unsatisfactory response to ART even though not useful for decisions regarding therapeutic switch could help elucidate responsible factors for early therapeutic failure. In low-resource settings, plasma viral load quantification has now become much more affordable due to the generalization of real-time PCR ¹⁴. Making viral load measurement widely available at month-6 would have two benefits. On the one hand, it would allow identifying

patients with virological failure among those who show markers of clinical and immunological success. These patients with discordant responses have been shown to have impaired prognosis compared to those with concordant responses^{17,24} and may benefit from being supported to become highly adherent. On the other hand, it would also be useful for patients with loss of CD4 and/or BMI. In these patients, finding that viral load is undetectable would help to actively search for intercurrent condition and not focus on adherence issues only. When viral load is not available, clinical and immunological markers cannot predict virological success. In settings where viral load cannot be measured yet, it is crucial that direct markers for adherence should be closely monitored.

Acknowledgements

We would like to thank Joanna Orne-Gliemann and Besigin Towne-Gold (INSERM U593) for her grammatical and editing contributions.

References

1. WHO. Antiretroviral therapy for HIV infection in adults and adolescents in resource-limited settings: towards universal access. Recommendations for a public health approach. 2006 revision.
<http://www.who.int/hiv/pub/guidelines/WHO%20Adult%20ART%20Guidelines.pdf>.
2. Gilks CF, Crowley S, Ekpini R, Gove S, Perriens J, Souteyrand Y, et al. The WHO public-health approach to antiretroviral treatment against HIV in resource-limited settings. *Lancet* 2006;**368**:505-10.
3. Moore DM, Mermin J, Awor A, Yip B, Hogg RS, Montaner JS. Performance of immunologic responses in predicting viral load suppression: implications for monitoring patients in resource-limited settings. *J Acquir Immune Defic Syndr* 2006;**43**:436-9.
4. Bisson GP, Gross R, Strom JB, Rollins C, Bellamy S, Weinstein R, et al. Diagnostic accuracy of CD4 cell count increase for virologic response after initiating highly active antiretroviral therapy. *AIDS* 2006;**20**:1613-9.
5. Stringer JS, Zulu I, Levy J, Stringer EM, Mwango A, Chi BH, et al. Rapid scale-up of antiretroviral therapy at primary care sites in Zambia: feasibility and early outcomes. *Jama* 2006;**296**:782-93.
6. Castetbon K, Anglaret X, Touré S, Chêne G, Ouassa T, Attia A, et al. Prognostic value of cross-sectional anthropometric indices on short-term risk of mortality in HIV-infected adults in Abidjan, Côte d'Ivoire. *Am J Epidemiol* 2001;**154**:75-84.
7. Zachariah R, Fitzgerald M, Massaquoi M, Pasulani O, Arnould L, Makombe S, et al. Risk factors for high early mortality in patients on antiretroviral treatment in a rural district of Malawi. *AIDS* 2006;**20**:2355-60.
8. Ferradini L, Jeannin A, Pinoges L, Izopet J, Odhiambo D, Mankhambo L, et al. Scaling up of highly active antiretroviral therapy in a rural district of Malawi: an effectiveness assessment. *Lancet* 2006;**367**:1335-42.
9. Etard JF, Ndiaye I, Thierry-Mieg M, Gueye NF, Gueye PM, Laniece I, et al. Mortality and causes of death in adults receiving highly active antiretroviral therapy in Senegal: a 7-year cohort study. *AIDS* 2006;**20**:1181-9.
10. van der Sande MA, Schim van der Loeff MF, Aveika AA, Sabally S, Togun T, Sarge-Njie R, et al. Body mass index at time of HIV diagnosis: a strong and independent predictor of survival. *J Acquir Immune Defic Syndr* 2004;**37**:1288-94.

11. Castetbon K, Anglaret X, Attia A, Toure S, Dakoury-Dogbo N, Messou E, et al. Effect of early chemoprophylaxis with cotrimoxazole on nutritional status evolution in HIV-1 infected adults in Abidjan, Côte d'Ivoire. *AIDS* 2001;**15**:869-876.
12. Danel C, Moh R, Minga A, Anzian A, Ba-Gomis O, Kanga C, et al. CD4-guided structured antiretroviral treatment interruption strategy in HIV-infected adults in west Africa (Trivacan ANRS 1269 trial): a randomised trial. *Lancet* 2006;**367**:1981-1989.
13. Danel C, Moh R, Anzian A, Abo Y, Chenal H, Guehi C, et al. Tolerance and acceptability of an efavirenz-based regimen in 740 adults (Predominantly women) in West Africa. *J Acquir Immune Defic Syndr* 2006;**42**:29-35.
14. Danel C, Moh R, Peytavin G, Anzian A, Minga A, Ba Gomis O, et al. Lack of indinavir-associated nephrological complications in HIV-infected adults (predominantly women) with high indinavir plasma concentration in Abidjan, Côte d'Ivoire. *AIDS Res Hum Retroviruses* 2007;**23**:62-66.
15. WHO. WHO Expert Consultation on Cotrimoxazole Prophylaxis in HIV Infection. WHO technical report series. Reference number: WHO/HIV/2006.01. <http://www.who.int/hiv/pub/meetingreports/ctx/en>.
16. Rouet F, Ekouevi DK, Chaix ML, Burgard M, Inwoley A, Tony TD, et al. Transfer and Evaluation of an Automated, Low-Cost Real-Time Reverse Transcription-PCR Test for Diagnosis and Monitoring of Human Immunodeficiency Virus Type 1 Infection in a West African Resource-Limited Setting. *J Clin Microbiol* 2005;**43**:2709-2717.
17. Moore DM, Hogg RS, Yip B, Wood E, Tyndall M, Braitstein P, et al. Discordant immunologic and virologic responses to highly active antiretroviral therapy are associated with increased mortality and poor adherence to therapy. *J Acquir Immune Defic Syndr* 2005;**40**:288-93.
18. Kantor R, Shafer RW, Follansbee S, Taylor J, Shilane D, Hurley L, et al. Evolution of resistance to drugs in HIV-1-infected patients failing antiretroviral therapy. *AIDS* 2004;**18**:1503-11.
19. Tassie JM, Szumilin E, Calmy A, Goemaere E. Highly active antiretroviral therapy in resource-poor settings: the experience of Medecins Sans Frontieres. *AIDS* 2003;**17**:1995-7.
20. Coetzee D, Hildebrand K, Boule A, Maartens G, Louis F, Labatala V, et al. Outcomes after two years of providing antiretroviral treatment in Khayelitsha, South Africa. *AIDS* 2004;**18**:887-95.
21. Severe P, Leger P, Charles M, Noel F, Bonhomme G, Bois G, et al. Antiretroviral therapy in a thousand patients with AIDS in Haiti. *N Engl J Med* 2005;**353**:2325-34.
22. Toni T, Masquelier B, Bonard D, Faure M, Huet C, Caumont A, et al. Primary HIV-1 drug resistance in Abidjan (Cote d'Ivoire): a genotypic and phenotypic study. *AIDS* 2002;**16**:488-91.
23. Toni TD, Recordon-Pinson P, Minga A, Ekouevi D, Bonard D, Bequet L, et al. Presence of key drug resistance mutations in isolates from untreated patients of Abidjan, Cote d'Ivoire: ANRS 1257 study. *AIDS Res Hum Retroviruses* 2003;**19**:713-7.
24. Schechter M, Tuboi SH. Discordant immunological and virological responses to antiretroviral therapy. *J Antimicrob Chemother* 2006;**58**:506-10.

Table 1: Patients baseline characteristics (n=622)

Women, number (%)	471	(76%)
Age in years, median (IQR)	34	(29-39)
Schooling, number (%)		
Illiterate	126	(20%)
Primary school level	180	(29%)
≥ Secondary school level	312	(51%)
Monthly family income in \$ US Dollars, number (%)		
None, number (%)	238	(38%)
< 90 \$US, number (%)	262	(42%)
≥ 90 \$US, number (%)	122	(20%)
Body mass index in kg/m ² , median (IQR)	20.8	(19.1-22.6)
WHO clinical stage, number (%)		
1	111	(18%)
2	256	(41%)
3	208	(33%)
4	47	(8%)
CD4/mm ³ , median (IQR)	250	(185-315)
Plasma HIV-1 RNA log10/ml, median (IQR)	5.0	(4.5-5.5)
Haemoglobin level in g/L, median (IQR)		
Men	12.6	(11.4-13 .6)
Women	10.9	(10-11.8)
Positive plasma HBs antigen, number (%)	86	(14%)

Footnotes for table 1:

IQR: interquartile range

Table 2: Sensitivity, specificity and predictive values of a gain in BMI, a gain in CD4 cells, or both, for predicting virological success at month-6

		Number of patients N	Number with virological success n	Se	Sp	PPV	NPV
Gain in BMI	$\geq 0 \text{ Kg/m}^2$	482	406	78	23	84	16
	$\geq +1 \text{ Kg/m}^2$	318	269	51	50	85	16
	$\geq +2 \text{ Kg/m}^2$	160	139	27	79	87	17
	$\geq +3 \text{ Kg/m}^2$	78	67	13	89	86	16
	$\geq +4 \text{ Kg/m}^2$	38	32	6	94	84	16
Gain in CD4	$\geq 0 /\text{mm}^3$	555	474	91	18	85	27
	$\geq +50 /\text{mm}^3$	474	407	78	32	86	22
	$\geq +100 /\text{mm}^3$	393	341	65	46	87	20
	$\geq +150 /\text{mm}^3$	302	263	51	61	87	19
	$\geq +200 /\text{mm}^3$	205	172	33	67	84	16
	$\geq +250 /\text{mm}^3$	127	105	20	78	83	16
	$\geq +300 /\text{mm}^3$	81	70	14	89	87	16
Combined gains	$\geq 0 \text{ Kg/m}^2$ and $\geq 0/\text{mm}^3$	440	373	71	32	85	18
	$\geq +1 \text{ Kg/m}^2$ and $\geq +50/\text{mm}^3$	256	219	42	63	86	17
	$\geq +1 \text{ Kg/m}^2$ and $\geq +100/\text{mm}^3$	209	181	35	72	87	17
	$\geq +1 \text{ Kg/m}^2$ and $\geq +200/\text{mm}^3$	114	94	18	80	82	16
	$\geq +2 \text{ Kg/m}^2$ and $\geq +50/\text{mm}^3$	135	116	22	81	86	16
	$\geq +2 \text{ Kg/m}^2$ and $\geq +100/\text{mm}^3$	113	98	19	85	87	16
	$\geq +2 \text{ Kg/m}^2$ and $\geq +200/\text{mm}^3$	65	55	10	90	85	16

Footnotes for table 2:

N: Number of patients in whom the gain in BMI and/or the gain in CD4 is higher than the corresponding threshold at month-6

n: number of patients with undetectable viral load at month-6

Se: sensitivity; Sp: specificity

NPV: negative predictive value; PPV: positive predictive value

Table 3: Sensitivity, specificity and predictive values of a loss in BMI, a gain in CD4 or both, in predicting virological failure at month-6

		Number of patients N	Number with Virological failure n	Se	Sp	PPV	NPV
Loss in BMI	< -4 Kg/m ²	2	0	0	99	0	84
	< -3 Kg/m ²	6	1	1	99	17	84
	< -2 Kg/m ²	23	4	4	96	17	84
	< -1 Kg/m ²	61	8	8	90	13	84
	< 0 Kg/m ²	140	23	23	78	16	84
Loss in CD4	< -150/mm ³	2	0	0	99	0	84
	< -100/mm ³	6	1	1	99	17	84
	< -50/mm ³	29	6	6	96	21	84
	< 0/mm ³	67	18	18	90	27	85
Combined losses	< -1 Kg/m ² and < -50/mm ³	8	1	1	99	13	84
	< 0 Kg/m ² and < 0/mm ³	25	9	9	97	36	85

Footnotes for table 3:

N: Number of patients with a loss in BMI and/or in CD4 higher than the corresponding thresholds at month-6

n: number of patients with detectable viral load at month-6

Se: sensitivity; Sp: specificity

NPV: negative predictive value; PPV: positive predictive value

List of figures

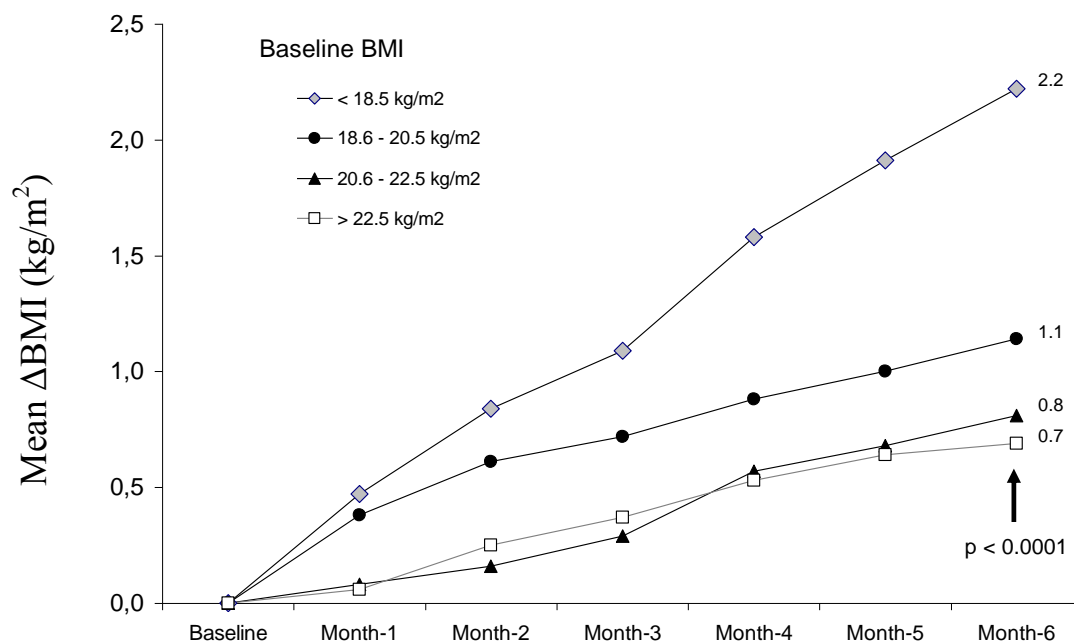
Figure 1: Mean Δ BMI at months 1 to 6, according to baseline BMI

Figure 2: Mean Δ CD4 count at months 3 and 6, according to baseline CD4 count

Figure 3: Median (IQR) Δ BMI at months 3 and 6, according to virological success at month-6

Figure 4: Median (IQR) Δ CD4 count at months 3 and 6, according to virological success at month-6

Figure 1: Mean Δ BMI at months 1 to 6, according to baseline BMI



Footnotes for figure 1:

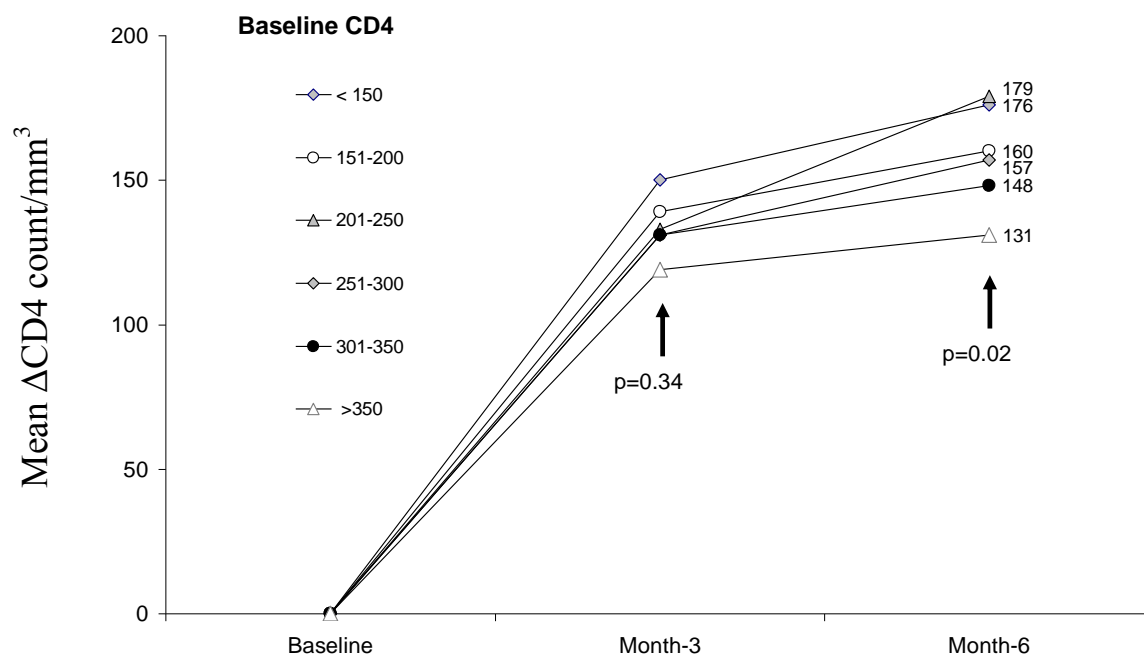
BMI: body mass index

Δ BMI: difference between baseline BMI and month-1 to 6 BMI

The number of patients in each sub-group was: <18.5 kg/m² (n=115), 18.6-20.5kg/m² (n=165), 20.6-22.5kg/m² (n=181), >22.5kg/m² (n=161)

p-value: Kruskal-Wallis test

Figure 2: Mean Δ CD4 count at months 3 and 6, according to baseline CD4 count



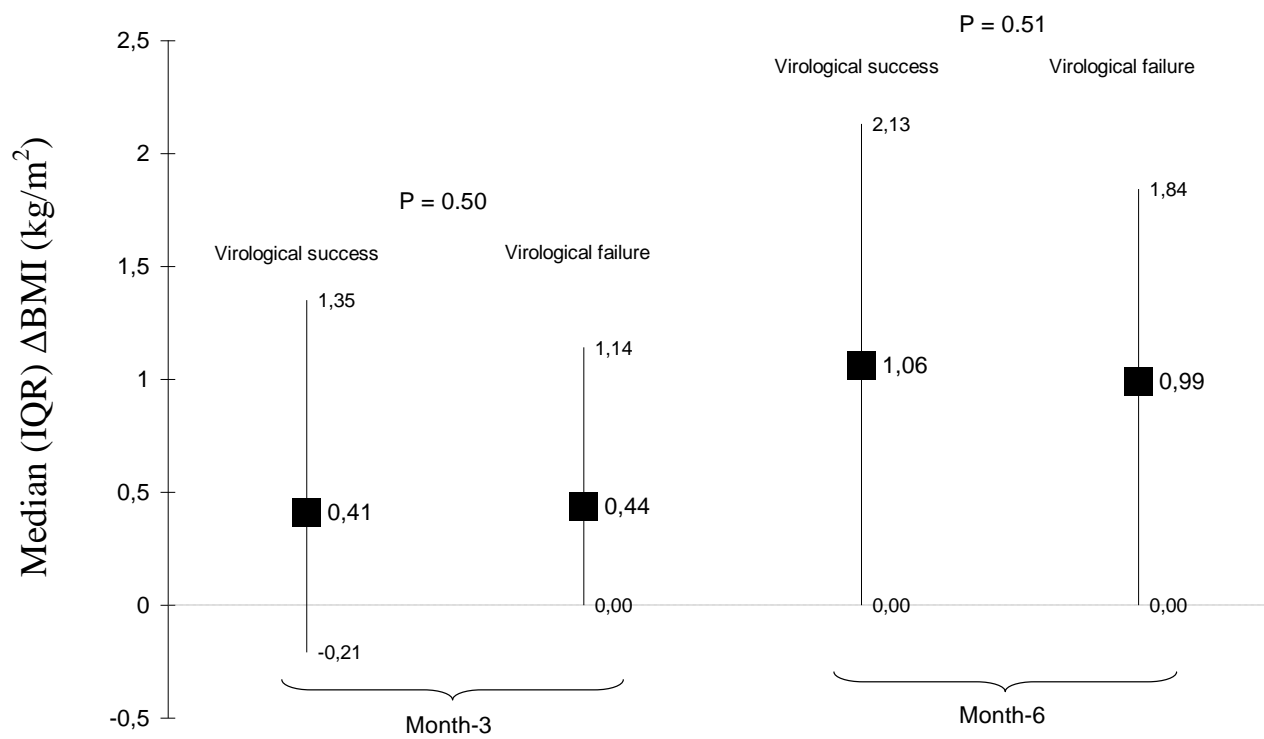
Footnotes for figure 2:

Δ CD4 count: difference between baseline CD4 count and month-3 or month-6 CD4 count

The number of patients in each sub-group was: <150/mm³ (n=75), 151-200/mm³ (n=114), 201-250/mm³ (n=124), 251-300/mm³ (n=120), 301-350/mm³ (n=91), >350/mm³ (n=98)

p-values: Kruskal-Wallis test

Figure 3: Median (IQR) Δ BMI at months 3 and 6, according to virological success at month-6



Footnotes for figure 3:

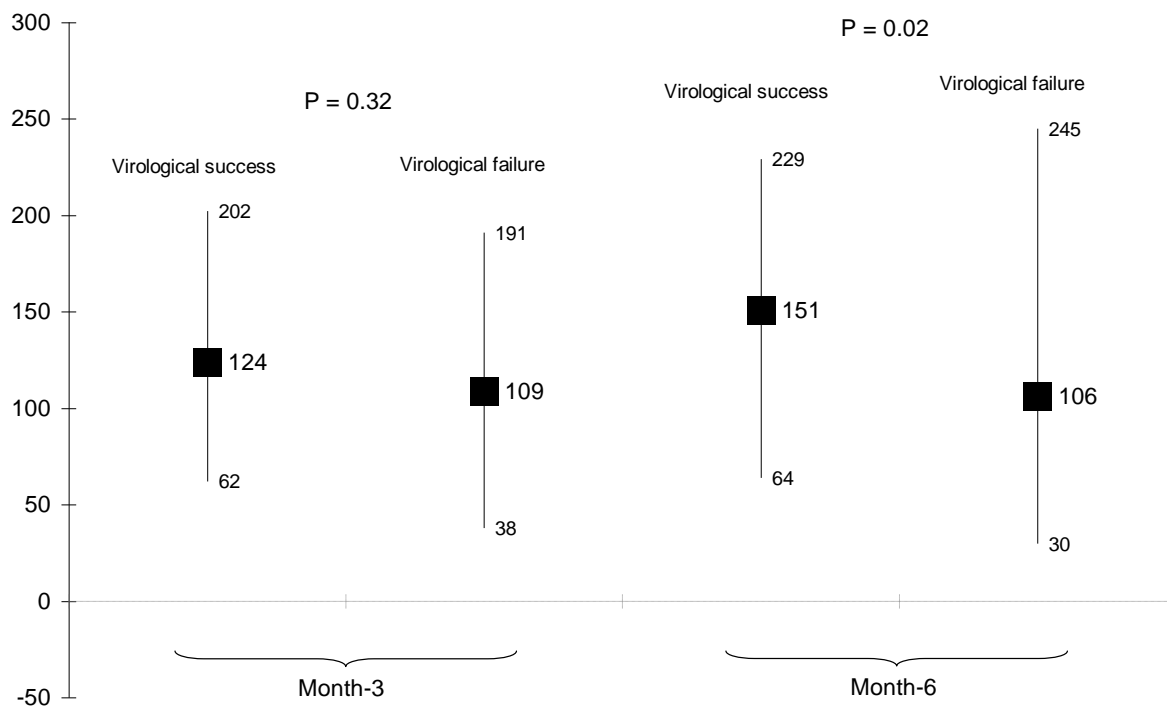
BMI: body mass index

IQR: interquartile range

Δ BMI: difference between baseline BMI and month-1 or month-6 BMI

p-values: Kruskal-Wallis test

Figure 4: Median (IQR) Δ CD4 count at months 3 and 6, according to virological success at month-6



Footnotes for figure 4:

IQR: interquartile range

Δ CD4 count: difference between baseline CD4 count and month-3 or month-6 CD4 count

p-values: Kruskal-Wallis test