A 48-year-old man with AIDS and chronic hepatitis B was treated with zidovudine (600 mg/day), lamivudine (300 mg/day), indinavir (2400 mg/day) and trimethoprim–sulfamethoxazole as a secondary prophylaxis. Five weeks after the beginning of this highly active antiretroviral treatment, the CD4 cell count had risen from 60 to 213 cells/μl and the plasmatic viral load had fallen from 834 000 to less than 200 RNA/ml. Hepatitis B DNA was undetectable by hydridation (instead of 180 pg/ml before lamivudine). His haemoglobin was 8.1 g/dl, mean corpuscular volume 101 μm^3. Treatment was continued. Five weeks later, haemoglobin was 4.7 g/dl, mean corpuscular volume 97 μm^3, leukocytes 2.7×10^9/l, with a normal differential count, platelets 355×10^9/l and reticulocytes 0%. A bone marrow aspiration consisted primarily of myeloid elements (granulopoiesis, 69%); erythroblasts were absent. The patient was treated without success with intravenous immunoglobulins (IVIG) (0.4 g/kg/day for 5 days). The serum tested positive for IgG and negative for IgM antibodies to parvovirus B19 and was negative for B19 DNA by polymerase chain reaction. The patient was transfused. At day 12 of IVIG treatment, haemoglobin was 4.7 g/dl and reticulocytes 0%. Zidovudine was stopped and replaced by stavudine (80 mg/day). Other treatments were continued. Seven days later, haemoglobin was 8.3 g/dl and the reticulocyte count was 100.8×10^9/l.

Drug-induced PRCA is rare. Only phenytoin, azathioprine, isoniazid, and, less frequently rifampicine, carbamazepin, sodium valproate or chloramphenicol have sufficient evidence of causality [2]. PRCA in HIV-infected patients is caused by persistent parvovirus B19 infection and is treatable with high-dose IVIG [1]. Three cases of reversible zidovudine-induced PRCA have been described but no reference to parvovirus B19 infection was made in the 10-year-old communication [3]. No further case has been reported in association with zidovudine or other antiretroviral treatment. Zidovudine has even been used with success to treat PRCA as the initial manifestation of HIV infection [4]. Our observation shows that zidovudine must be added to the list of drugs causing PRCA.

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Quality of life in asymptomatic patients with early HIV infection initiating antiretroviral therapy

Highly active antiretroviral therapy (HAART) induces beneficial changes in various immunological parameters even when it is initiated early during asymptomatic HIV infection with high CD4 cell counts [1]. Until now, however, the impact of an early initiation of HAART on the quality of life (QoL) in asymptomatic, treatment-naive, HIV-infected individuals has not been reported. Recently, ritonavir in combination with other antiretroviral medications has been shown to influence positively the functioning and well-being in patients with advanced disease [2].

Within the ongoing Early Antiretroviral Therapy (EARTH) study [3], 41 asymptomatic individuals with CD4 cell counts of over 400×10^6/l were randomly assigned to either double therapy (n = 19), consisting of zidovudine (300 mg twice a day) and lamivudine (150 mg twice a day), or triple therapy (n = 22), consisting of zidovudine (300 mg twice a day), lamivudine (150 mg twice a day) and ritonavir (600 mg twice a day).

We report here the treatment-induced changes in QoL by assessing the HIV Medical Outcome Study (HIV–MOS) [4] and the Karnofsky score at baseline and at weeks 12 and 24. The HIV–MOS is a well established generic instrument [5–7]. It is a self-administered questionnaire, consisting of 36 questions assessing 11 dimensions (overall health, physical-, role-, social- and cognitive function, pain, mental health, energy/fatigue, health distress, QoL as well as health transition) of health-related QoL. We assessed mean changes in 10 out of 11 dimensions of the HIV–MOS (data regarding overall health was not recorded in the MOS version used) and Karnofsky score.

At baseline, all 41 individuals reported well-being with a Karnofsky score of 100; there were no significant differences in QoL between the randomized groups. Both treatment groups scored lowest at week 12 in nearly all HIV–MOS dimensions, also exemplified by a significant decline in the Karnofsky score (Table 1,

Table 1. Intra-individual changes in quality of life scores (intent-to-treat analysis irrespective of treatment changes)

Dimension	Score at baseline (mean) double/triple therapy[a]	Intra-individual change in QoL scores				
		Week 0–12 All patients (n = 41)	Week 0–12 Double therapy (n = 19)	Week 0–12 Triple therapy (n = 22)	Week 0–24 Double therapy (n = 19)	Week 0–24 Triple therapy (n = 20)
Physical function	86.4/93.9	−2.2	1.3	−5.3	4.8	−4.2
Role function	81.6/97.2	−7.3	7.9	−20.5*	5.3	−2.5
Social function	92.6/93.6	−6.8*	−3.2	−10.0	−1.1	−6.0
Cognitive function	82.9/85.0	−4.3	−1.3	−6.8*	−2.9	−4.8
Pain	87.4/90.0	−11.7**	−7.4	−15.5*	1.1	−5.0
Mental health	69.1/75.1	−5.5	−4.0	−6.7	5.5	−5.8
Energy/fatigue	63.7/68.9	−6.8*	−3.2	−10.0**	0.5	−11.3*
Health distress	80.0/83.3	−1.1	4.6	−6.1	6.7*	−4.0
Quality of life	76.3/72.7	−9.1**	−2.6	−14.8**	5.3	−1.3
Health transition	60.5/64.8	−3.7	2.6	−9.1	5.3	1.3
Karnofsky score	100/100	−1.5*	−1.1	−1.8	−1.8	−0.5

*$P < 0.05$, **$P < 0.01$ (Wilcoxon rank-sum test, comparisons always against baseline = week 0). [a]Double therapy, zidovudine + lamivudine; triple therapy, zidovudine + lamivudine + ritonavir. The scores at baseline did not show significant differences between the two arms. QoL, Quality of life.

intent-to-treat analysis). All study participants taken together showed a significant decline in QoL at week 12 in social function, pain, energy/fatigue and QoL. However, these changes were solely explained by the decline in QoL of the group receiving triple therapy. In addition to the above-mentioned dimensions, role function scored significantly lower in the triple therapy arm at week 12. The decline in the various QoL scores in the triple therapy group correlated with the occurrence of adverse events to ritonavir: Between weeks 0 and 12, two patients receiving triple therapy stopped ritonavir and either continued on double nucleoside therapy or changed to another protease inhibitor, respectively. Between weeks 12 and 24, six additional patients receiving triple therapy changed regimens: two continued with a double therapy, two replaced ritonavir with another protease inhibitor and two dropped out. In view of these treatment modifications and the cessation of ritonavir-associated intolerance, the differences of each group to baseline were no longer statistically significant at week 24.

The comparison of changes between the two groups confirmed significant differences in the dimensions role function, health distress and QoL, which persisted up to week 24 (intent-to-treat analysis), in the presence of rising scores in both arms. An on-treatment analysis of our data did not reveal any new information (results not shown) due to the fact that the above-mentioned six patients scored higher after they discontinued ritonavir.

The only other description of the impact on QoL of HAART including ritonavir describes advanced symptomatic individuals with CD4 cell counts of less than 100×10^6/l, in whom treatment improved scores in various dimensions of the HIV–MOS [2]. A direct comparison of asymptomatic individuals with patients suffering from AIDS is difficult. For example, in a study [8] comparing three different regimens of combinations of nucleoside agents there was a difference between the AIDS and non-AIDS (CD4 cell count > 200/μl) groups in the mean change in scores from baseline. Therefore, it is important to distinguish between the impact of disease versus that of therapy on the QoL outcomes.

In conclusion, the early initiation of triple therapy in asymptomatic individuals caused a significant short-term impairment of QoL, mainly due to the known adverse effects of ritonavir, 600 mg twice a day [2]. However, the impairment was not severe and reversed towards baseline values at week 24 for the entire group, particularly after those patients with the strongest adverse events modified their treatment regimen. The double therapy with zidovudine and lamivudine was well tolerated and did not adversely affect the QoL, but its virological efficacy was inferior [3]. The divergent aspects of the desired full viral suppression, the immunological and clinical benefit of treatment, versus its effect on QoL are important considerations both for the physician and the patient, particularly if HAART is initiated in individuals who previously felt healthy.

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Treatment of painful distal sensory polyneuropathy in HIV-infected patients with a topical agent: results of an open-label trial of 5% lidocaine gel

Distal sensory polyneuropathy (DSP) is the most common neurological disorder in HIV-infected patients and can be diagnosed in over 30% of patients with AIDS, as defined by the Centers for Disease Control and Prevention [1]. Typical symptoms of DSP include pain and burning sensations, primarily in the soles and dorsum of the feet, often associated with numbness and paresthesias. DSP is generally progressive and the upper extremities may be affected later in the course of the disorder [2].

Although DSP is not in itself a cause of mortality, it seriously affects the quality of life of patients and is a probable source of psychiatric morbidity [3]. Often patients who would otherwise be capable of independent self-care or even gainful employment find that they need assistance with their living arrangements or must go on disability [4]. Furthermore, some medications used to treat HIV-related conditions (e.g. stavudine, didanosine, zalcitabine) are neurotoxic, complicating the medical management of HIV infection in patients with DSP [5].

No specific therapy exists to reverse HIV-associated DSP, and current management focuses on pain relief [6]. One promising approach is the use of topical anesthetic agents applied to painful sites. This approach is particularly attractive because relatively high doses can be applied locally with minimal systemic absorption, thereby reducing the risk of generalized complications. One such medication, lidocaine [acetamide, 2-(diethylamino)-*N*-(2,6-dimethylphenyl)] has been successful in treating peripheral neuropathy, such as post-herpetic neuralgia [7,8]. It has the further desirable property of a mechanism of action depending on the analgesic modulation of abnormally functioning sensory nerve fibers, without interfering with normal nerve function [9]. In the present study, we present preliminary data concerning the safety and effectiveness of topical lidocaine in treating HIV-associated painful DSP.

Thirty outpatients attending the Mount Sinai Neuro-AIDS Program with DSP received a supply of 5% Lidoderm gel (5% lidocaine in solution with propylene glycol and polysorbate 20; Hind Health Care, Sunnyvale, CA, USA) and were instructed in its use. DSP was diagnosed by the treating neurologist (A.K. or D.S.) by the following mininum criteria: (i) symptoms of pain, burning, or dysesthetic discomfort in both feet at least 2 h per day for at least 14 consecutive days before to the examination; (ii) diminished or absent ankle reflexes (relative to the knees) or distal diminution of vibration, pain, or temperature sensation in the legs.

Patients completed pain report and side-effect questionnaires at baseline and at their follow-up clinic visit, typically 2 weeks later. Patients rated average pain on a scale from 0 (no pain) to 10 (worst pain imaginable). Parallel questionnaires were completed at baseline and follow-up clinic visit by the treating neurologist indicating patients' pain level on a similar scale: 0 (no unpleasant sensation) to 10 (worst unpleasant sensation).*

Of the 27 patients completing the global pain relief item, three reported no relief, four some relief, nine moderate relief, 10 a lot of relief, and one complete relief. A total of 75% of the patients thus reported moderate relief or better. Mean global relief was 3.7 on a scale from 0 to 10, ($t = 5.21$, df = 26, $P < 0.001$). There was a 46% reduction in mean pain scores from 7.11 at baseline to 3.81 after treatment ($t = 7.05$, df = 26, $P < 0.001$). Physician ratings followed the same trend. For example on the global relief measure physician ratings were 2.87 ($t = 3.71$, df = 29, $P < 0.002$) and were highly correlated with patient ratings ($r = 0.88$). The only significant side-effects were dry skin (three patients) and blisters (one patient).

*Copies of the questionnaires can be obtained from the first author (D.D.).