

Implementation of an antiretroviral access program for HIV-1 infected individuals in resource-limited settings. Clinical results from four African countries

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Background

Data on the effectiveness and safety of highly-active antiretroviral treatment (HAART) in resource-limited settings is limited. Here we describe the final results of the CARE-initiative, a treatment program that provides access to HIV-1 screening, therapy, counseling, monitoring and training & education free of charge in four urban clinics in four low-income African countries.

Methods

This open-label cohort program recruited 206 HAART naïve HIV-1 infected patients in 4 urban clinics in Senegal (Dakar), Ivory Coast (Abidjan), Uganda (Kampala) and Kenya (Nairobi). Treatment was a regimen of SQV/RTV (1,600/100mg QD), 3TC (150mg BID) and ZDV (300mg BID). Primary outcome was a plasma HIV-1 RNA viral load (pVL) < 400 copies/mL at week 96. Secondary analyses included the change in CD4 cells between baseline and week 96 and the occurrence of serious adverse events (SAEs).

Results

Baseline characteristics and patient disposition are presented in table 1 and figure 1 respectively. High overall patient attendance was observed, 166 of 206 patients (81%) were still receiving HAART after 96 weeks.

Table 1. Baseline characteristics of all patients that started HAART

	Abidjan n=57	Dakar n=50	Kampala n=49	Nairobi n=50	All patients n=206
Age, years, median (qtr)	33.0 (29.0 – 40.0)	37.0 (29.0 – 42.0)	38.0 (34.0 – 43.0)	36.0 (30.0 – 40.0)	36.0 (30.0 – 41.0)
Sex, % male	31.6	40.0	40.8	40.0	37.9
BMI, kg/m ² , median (qtr)*	21.0 (19.4 – 23.4)	18.1 (16.5 – 20.5)	22.9 (20.3 – 26.7)	24.1 (20.2 – 26.5)	21.0 (18.6 – 24.7)
CDC-class, %*					
A	12.3	4.0	26.5	46.0	21.8
B	47.4	60.0	42.9	24.0	43.7
C	40.4	36.0	30.6	30.0	34.5
CD4 cells, cells/mm ³ , median (qtr)*	132 (82 – 215)	113 (35 – 214)	94 (36 – 207)	189 (83 – 262)	119 (70 – 225)
< 50, %	14.8	32.0	28.9	11.6	21.9
≥ 50, %	85.2	68.0	71.1	88.4	78.1
HIV-1 RNA, log ₁₀ copies/mL, median (qtr)*	5.5 (5.3 – 5.9)	5.3 (4.9 – 5.8)	5.7 (5.2 – 5.9)	5.2 (4.1 – 5.7)	5.5 (4.9 – 5.8)
< 100,000, %	13.0	39.0	18.0	46.0	27.5
≥ 100,000, %	87.0	61.0	82.0	54.0	72.5
Hepatitis B co-infection, %**	14.0	24.0	10.2	2.0	12.6
Hepatitis C co-infection, % †	10.5	12.0	0.0	2.0	6.3
HIV-2 co-infection, %	7.0	2.0	2.4	0.0	3.0
Initial antiretroviral regimen					
AZT, 3TC, ritonavir, saquinavir (Fortovase®), %	68.4	100.0	98.0	72.0	84.0
Other, %	31.6	0.0	0.0	28.0	15.5
AZT, 3TC, ritonavir, saquinavir (favirase®), %	0.0	0.0	2.0	0.0	0.5

On-Treatment (OT) results are based on the number of evaluable patients per time-point still on treatment and the Intent-To-Treat (ITT) results on the number of enrolled patients.

At week 96 65%/52% (OT/ITT) of the patients had a pVL < 400 copies/mL. These proportions were statistically significant different between the sites (p=0.0131/0.0217, OT/ITT). Results over time are presented in figures 2A and 2B.

Figure 1. Patient disposition

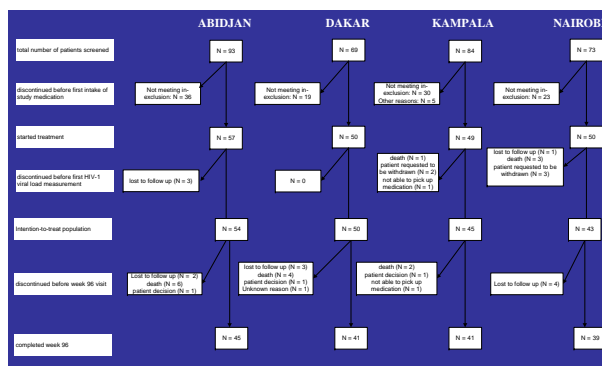


Figure 2A.
% pVL < 400 c/ml (OT)

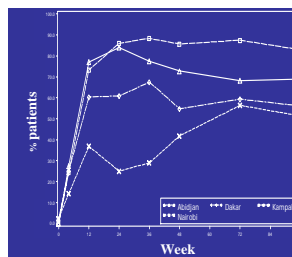


Figure 2B.
% pVL < 400 c/ml (ITT)

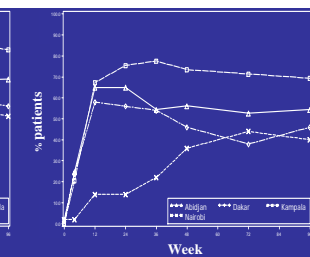


Figure 3A.
% pVL < 50 c/ml (OT)

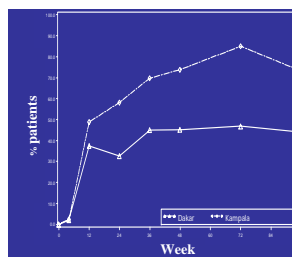
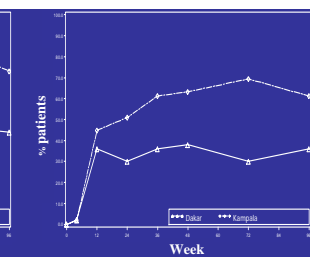


Figure 3B.
% pVL < 50 c/ml (ITT)



In the first year there were laboratory issues that may explain the lower percentage of patients with a pVL < 400 copies/ml in Nairobi. In two of the sites Dakar and Kampala the ultrasense test with a detection limit of 50 copies/ml could be performed.

Limiting the analysis to those two sites showed that, overall, 59%/48% (48/82 or 48/99) had a pVL of less than 50 copies/mL at week 96 (OT/ITT). There was a statistically significant difference between the two clinics at scheduled week 96 (p = 0.0071/0.0120, OT/ITT). These results are presented in figures 3A and 3B. Median increase from baseline in CD4 cell count was 198 cells/μl (IQR 86-319), ranging from 191 to 292 cells/μl between the sites. However, no statistically significant differences were observed between the sites with respect to these numbers (p=0.4312). Results are presented in figures 4 and 5.

Between 8 and 96 weeks follow-up 14 patients (6.8%) died and 18 (9%) developed a CDC-C HIV-event. Non-HIV related SAEs were reported in 55 patients (26.7%). Anaemia and neutropenia were the most frequently reported SAEs (13 and 7 patients respectively). Also, 35 patients (17%) changed treatment for toxicity reasons.

Figure 4.
Median change in CD4 count

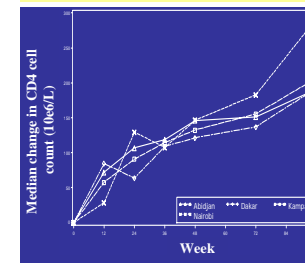
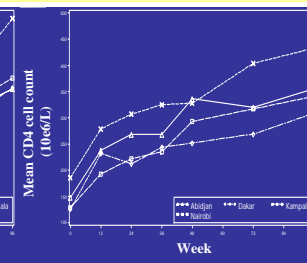


Figure 5.
Mean CD4 count



Conclusions

The virologic and immunologic response to HAART in resource-limited African settings can be as good as in western settings. Although a statistical significant difference between the sites with respect to virologic success was observed.

We experienced some difficulties (a.o. laboratory, logistics, proper training) during the early phase of the program. On the one hand patients need the most proper medical care in this phase, because then they are most vulnerable. On the other hand most of these difficulties may occur in this early phase. Therefore, provision of adequate medical care and proper instruction and education of patients and medical staff during the entire study is warranted in such programs, but with special alertness in the early phase.

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