Duration of Highly Active Antiretroviral Therapy Regimens

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The median duration of highly active antiretroviral therapy (HAART) regimens was reported to be 11.8 months in one US study, but that study included both treatment-experienced and treatment-naive patients. The duration of initial HAART regimens for treatment-naive patients alone has not been reported. We selected 405 antiretroviral-naive patients who were seen at the University of Alabama at Birmingham HIV Outpatient Clinic from 1 January 1996 through 9 October 2001, and we assessed the duration of initial and successive HAART regimens in this group. Any antiretroviral medication change, excluding dosage changes, that lasted ⩾14 days was considered to indicate the start of a new regimen. The median duration of regimens was determined by Kaplan-Meier analysis, and proportional hazards regression was used to identify factors associated with shorter duration of initial regimen. The median duration of initial regimens was 1.6 years, and medication toxicity–associated events were the cause of one-half of discontinuations. Only a history of opportunistic infection and injection drug use were significantly associated with shorter regimen duration.

The availability of HAART has had a dramatic impact on the natural progression of disease caused by HIV [1–4]. Patients who adhere to HAART regimens and do not experience significant adverse effects may have almost normal life spans [5]. Despite this, it is difficult to adhere consistently to many HAART regimens because of pill burden and side effects [6–8], and drug resistance is increasingly a problem [9, 10]. Because of these factors, patients commonly switch to alternative regimens in an attempt to maintain virologic control without experiencing treatment-limiting side effects.

The importance of maintaining virologic control is based on the current understanding of HIV pathogenesis, in which continuous HAART is needed to suppress viral replication and prevent disease progression [11–15]. Several studies have evaluated HAART regimens on the basis of the duration of viral suppression [16, 17]. Patients for whom HAART fails and who develop detectable virus loads often switch to a new regimen. However, the level of viremia that mandates a change in therapy is not well defined, and, in clinical practice, patients with low but detectable virus loads may continue to receive their current regimens, as long as immunologic success is maintained. Other patients with undetectable virus loads may switch to a new regimen because of medication toxicity. Thus, the duration of a HAART regimen, when duration is defined by the presence of an undetectable virus load, is very different from the duration of the same regimen as defined in clinical practice.

The "real life" duration of HAART in clinical practice

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has been examined by Palella et al. [18] in the HIV Outpatient Study cohort. In that study, the median duration of initial HAART regimens was 11.8 months, and the second and third regimens were much shorter (7.4 and 7.2 months, respectively). The duration of the initial regimen was noted to be longer among antiretroviral-naive patients. Therefore, we analyzed the actual duration of initial HAART regimens in clinical practice among HIV-infected outpatients who were previously naive to antiretroviral therapy (ART).

METHODS

The University of Alabama at Birmingham (UAB) Outpatient HIV Clinic is a university-based clinic that includes ~10 physicians, 2 nurse practitioners, and 970–1040 active patients at any given time. The clinic began prospectively collecting information on all patients in a longitudinal, observational database in January 1994. Trained medical records personnel abstract clinical and treatment data from medical records daily. Laboratory data are downloaded from the hospital laboratory system directly into the database. All outside laboratory values are entered into the database manually. The UAB Institutional Review Board approved the database protocol.

The inclusion criteria were (1) patient attended the clinic, (2) patient began HAART after 1 January 1996, and (3) patient was naive to ART before that point. "HAART" was defined as any combination of ⩾3 antiretroviral drugs. Patients were followed up until 9 October 2001, at which point data collection was halted for purposes of analysis. Any change in ART, excluding dosage changes, that lasted ⩾14 days was considered to indicate the start of a new regimen, with 1 exception: in 1996, the regimens of some patients were intentionally escalated to 3 drugs over a period of weeks. These patients were considered to be still receiving their first regimen. Data from all patients with ongoing regimens, including those who were lost to follow-up, were censored on the date of the patients' last contact with the clinic. Baseline laboratory values were determined at the time of initiation of the first regimen for each patient (range, −120 to +14 days). Laboratory values at regimen discontinuation were determined using the same window around the discontinuation date. A manual review of medical charts was performed for all patients who were included in the analysis to confirm that they were antiretroviral naive before the initial regimen and to identify the reason for discontinuation of the initial regimen. Patients for whom poor adherence or virologic failure was identified as the reason for regimen discontinuation were included in a single group because of the difficulty in differentiating between these 2 reasons.

Statistical analyses were performed using SAS software, version 8.2 (SAS Institute). Demographic characteristics are presented using descriptive statistics. Kaplan-Meier survival analyses of duration of regimens were performed, and the median duration of each regimen was presented using product limit estimates. Univariate proportional hazards regression analyses were performed to identify factors associated with a shorter initial regimen, and multivariable proportional hazards regression analyses were performed that included all factors for which the results of univariate analysis were statistically significant ($P > .05$). The variables examined included demographic characteristics, baseline laboratory values, history of opportunistic infection (OI) before initiation of HAART, and the number of times that the patient cancelled clinic appointments or did not attend a scheduled appointment ("no show"). Duration of initial regimen was additionally dichotomized into ⩽90 days and >90 days. Patients with an initial regimen duration of ⩽90 days were compared with the rest of the cohort; the χ^2 test was used for dichotomous variables, and Student's t test was used for continuous variables to identify factors associated with an initial regimen duration of ⩽90 days.

RESULTS

Of 1206 patients who began HAART in January 1996 or later, 405 patients were naive to ART. The demographic characteristics of this cohort are listed in table 1. Most patients had advanced HIV disease before therapy; the median baseline CD4 cell count was 197 cells/μL, and the median baseline virus load was 70,146 copies/mL. Of note, baseline CD4 cell count and virus load data were missing for 87 (21.5%) and 101 (24.9%) of the 405 patients, respectively. These patients were already receiving HAART when they presented at the clinic but were able to provide accurate regimen initiation dates. Of all patients, 18% had a history of OI before initiation of HAART, and 65% had an initial HAART regimen that was protease inhibitor based. For 240 (59.3%) of the 405 patients, the initial regimen was discontinued. Data from patients who were still receiving the initial regimen ($n = 140$) or who were lost to follow-up ($n = 25$) at the end of the analysis were censored on the date of the patients' last contact with the clinic. The results of Kaplan-Meier analysis of the duration in days of the initial regimens are shown in figure 1. The median durations of initial and successive regimens are shown in table 2; the median duration of the initial regimen was 1.6 years (581 days). No difference in regimen duration among years of initiation was seen. Successive regimens were considerably shorter, and the longer a patient received HAART, the more likely he/she was to have received multiple regimens (figure 2). Despite this, a minority of patients successfully continued their initial regimens for much longer than 1.6 years. After 4 years, 11 (24.4%) of 45 patients for whom follow-up data were available were still receiving the initial regimen.

The results of univariate proportional hazards regression

Table 1. Baseline characteristics of 405 patients included in a study of the duration of HAART regimens.

Characteristic	Value
Age, median years (range)	36 (18–66)
Male sex	308 (76.1)
Race	
White	198 (48.9)
African American	198 (48.9)
Man who has sex with men	247 (61.0)
Injection drug use	32 (7.9)
Baseline CD4 cell count, median cells/μL (range)[a]	197 (2–1211)
Baseline virus load, median copies/mL (range)[b]	70,146 (53–7.7 $\times$ 10^6)
Previous opportunistic infection	74 (18.3)
Duration of follow-up, median days (range)	642 (14–2051)
Initial regimen[c]	
Triple NRTI	35 (8.9)
NNRTI based	97 (24.7)
PI based	255 (65.1)
NNRTI and PI based	5 (1.3)
Patient data censored[d]	165 (40.7)

NOTE. Data are no. (%) of patients, unless otherwise indicated. NNRTI, nonnucleoside reverse-transcriptase inhibitor; NRTI, nucleoside reverse-transcriptase inhibitor; PI, protease inhibitor.

[a] Data were available for 318 patients.

[b] Data were available for 304 patients.

[c] Excludes 13 patients enrolled in AIDS Clinical Trials Group Protocol 384, a double-blind study of PIs vs. NNRTIs.

[d] Data from patients who were still receiving the initial regimen at the time of the analysis were censored on the date of the patient's last contact with the clinic.

analyses to identify factors associated with a shorter duration of the initial regimen are shown in table 3. The only statistically significant factors were previous OI and a history of injection drug use (IDU). All other factors examined, including demographic characteristics, baseline CD4 cell count, baseline virus load, and composition of initial regimen by drug class, were not significant. In the multivariable analysis, both factors remained significant, although IDU was more significant than previous OI ($P = .0003$ vs. $P = .0278$, respectively). The median duration of initial regimen among patients with a history of IDU ($n = 32$) or OI ($n = 74$) (5 patients had a history of both) was 308 days. This was significantly shorter than the median duration of initial regimen for patients without IDU or OI (625 days; $P = .002$). In examining individual antiretroviral drugs (table 4), only the saquinavir soft gel capsule (SGC) formulation was associated with a significantly shorter initial regimen.

The reasons for initial regimen discontinuation were identified through a manual review of medical charts (table 5). Overall, almost one-half of discontinuations were due to ART toxicity–related effects, predominantly nausea or vomiting. The effect of toxicity, especially nausea and vomiting, was more pronounced in the group of patients who discontinued after ≤90 days of HAART (62.5%). Peripheral neuropathy and lipodystrophy were not reported during the first 90 days of treatment; rash was not observed after the first 90 days. Poor adherence and/or virologic failure were the next most common causes of regimen discontinuation. Almost 25% of patients overall and 14.3% of patients who discontinued HAART after ≤90 days discontinued the initial regimen for these 2 reasons. No other reason accounted for >5% of the total reasons for discontinuation. Among the 240 patients for whom the initial regimen was discontinued, the median CD4 cell count was 343 cells/μL (range, 1–1930 cells/μL; data from 37 patients were missing), and the median virus load was 303 copies/mL (range, 49–1 $\times$ 10^6 copies/mL; data from 41 patients were missing) at the time of treatment discontinuation. Both of these values were dramatically improved from the median values at baseline (197 cells/μL and 70,146 copies/mL, respectively).

Of the patients who discontinued the initial regimen, a disproportionate number discontinued within the first few months after therapy initiation. We considered the possibility that a threshold effect existed, beyond which patients had a significantly increased duration of initial regimen. On the basis of a

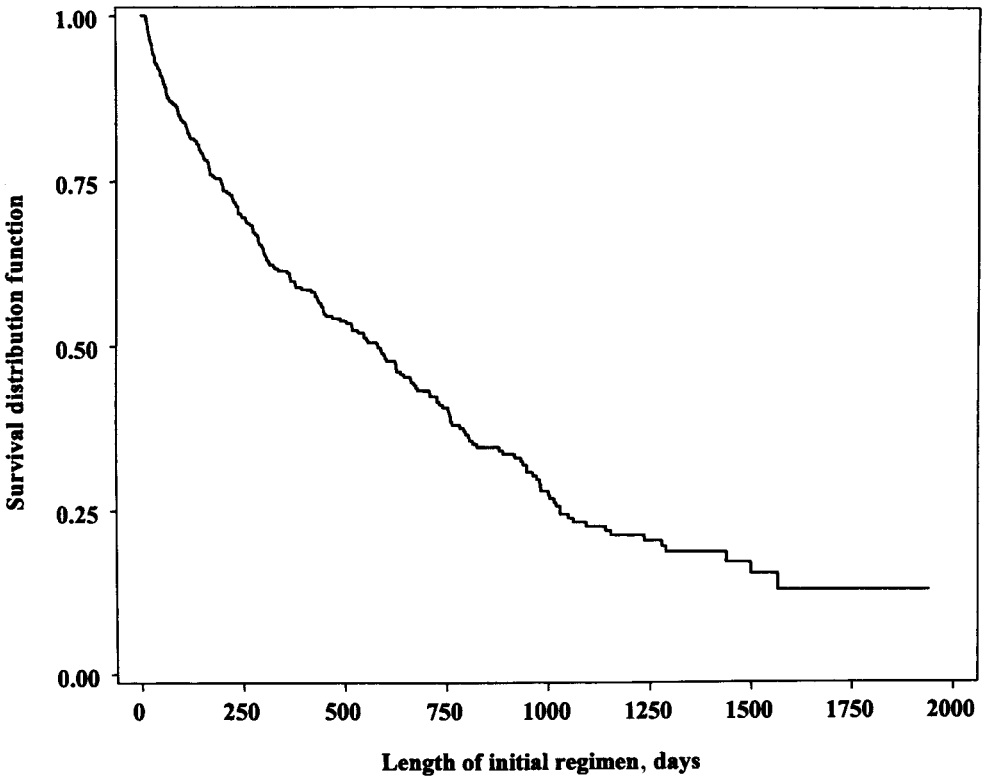

Figure 1. Kaplan-Meier analysis of the relationship between survival and duration of initial HAART regimens, based on data from 405 previously antiretroviral-naive patients.

histogram of the duration of initial regimens for noncensored patients, we found that therapy was discontinued for 25% of patients within the first 90 days. A subanalysis was performed using data from patients with initial regimen durations >90 days (table 2), and in this analysis, the median duration of initial regimen in the cohort of patients for whom the initial regimen was >90 days was 4 months (126 days) longer. There was no significant impact on the duration of successive regimens, except for the fourth regimen. The longer duration of this regimen likely reflects aberrancy due to small numbers, because the median durations of the fifth and sixth regimens were 217 and 121 days, respectively.

The baseline characteristics of the patients for whom the initial regimen was discontinued at ≤90 days were then compared with those of the rest of the cohort. The only significant differences noted between the 2 groups were duration of follow-up and history of OI before initiation of HAART. The duration of follow-up was significantly shorter in the group for whom HAART was discontinued after ≤90 days than in the group for whom HAART lasted >90 days (414 vs. 758 days, respectively; $P < .0001$). Patients in the former group were also significantly more likely to have a history of OI before initiation of therapy than were those in the latter group (30.4% vs. 16.5%, respectively; $P = .0135$). There was no difference associated with age, race, sex, IDU, sexual preference, baseline CD4 cell count or virus load, or initial regimen composition.

DISCUSSION

This study of 405 previously antiretroviral-naive patients at the UAB HIV Outpatient Clinic examined the actual duration of initial HAART regimens. This "real life" duration takes into account patients who have virologic success yet change regimens because of toxicity, patients who have detectable virus loads despite continued immunologic success, and patients who change regimens for any other reason. Using this approach, we found that the median duration of initial HAART regimens was 1.6 years (table 2). The primary reason for discontinuation of the initial regimen was medication-related toxicity, predominantly nausea or vomiting, rather than virologic failure. The only factors significantly associated with a shorter initial regimen were having an OI before initiation of therapy and a history of IDU. Successive regimens were considerably shorter in duration, which supports the dictum that the "first shot is the best shot." The longer a person received HAART, the more likely he/she was to have been treated with multiple HAART regimens.

The 1.6-year duration of initial HAART regimens we de-

Table 2. Results of product limit estimate analysis of the median HAART regimen duration, by regimen number, of all patients and of patients whose initial regimens lasted >90 days.

Regimen no.	All patients			Patients whose initial regimens lasted >90 days		
	Total no.	No. (%) censored[a]	Duration, median days (95% CI)	Total no.	No. (%) censored[a]	Duration, median days (95% CI)
1	405	165 (40.7)	581 (447–662)	322	138 (42.9)	707 (598–781)
2	113	48 (42.5)	324 (231–524)	83	35 (42.2)	366 (236–572)
3	113	47 (41.6)	218 (161–406)	84	34 (40.5)	215 (147–415)
4	37	12 (32.4)	112 (72–520)	28	11 (39.3)	448 (98–614)

[a] Data from patients who were still receiving the initial regimen at the time of the analysis were censored on the date of the patient's last contact with the clinic.

scribe, although seemingly short, is longer than the duration of 11.8 months described elsewhere by Palella et al. [18], likely because our study was 2.5 years longer and because we only examined patients who were previously antiretroviral naive. Palella et al. [18] noted that durable treatment success was associated with being antiretroviral naive before initiation of a first HAART regimen; therefore, the duration of 11.8 months that they reported likely would have been longer had they examined only patients who were previously naive to therapy. Mocroft et al. [19] also examined regimen discontinuations but focused on reasons for discontinuation and did not precisely quantify the regimen duration. Nonetheless, even 1.6 years is dismal, given that successive regimens are even shorter and that HAART currently is lifelong therapy. Thus, the reasons for such short duration must be examined to determine whether any can be modified.

Of the 240 patients for whom the initial regimen was discontinued, in almost one-half of cases, discontinuation was due to antiretroviral medication–related toxicity, primarily nausea or vomiting. Virologic failure and/or poor adherence accounted for discontinuation in <25% of these patients. One other study also identified medication-related toxicity as the primary reason for

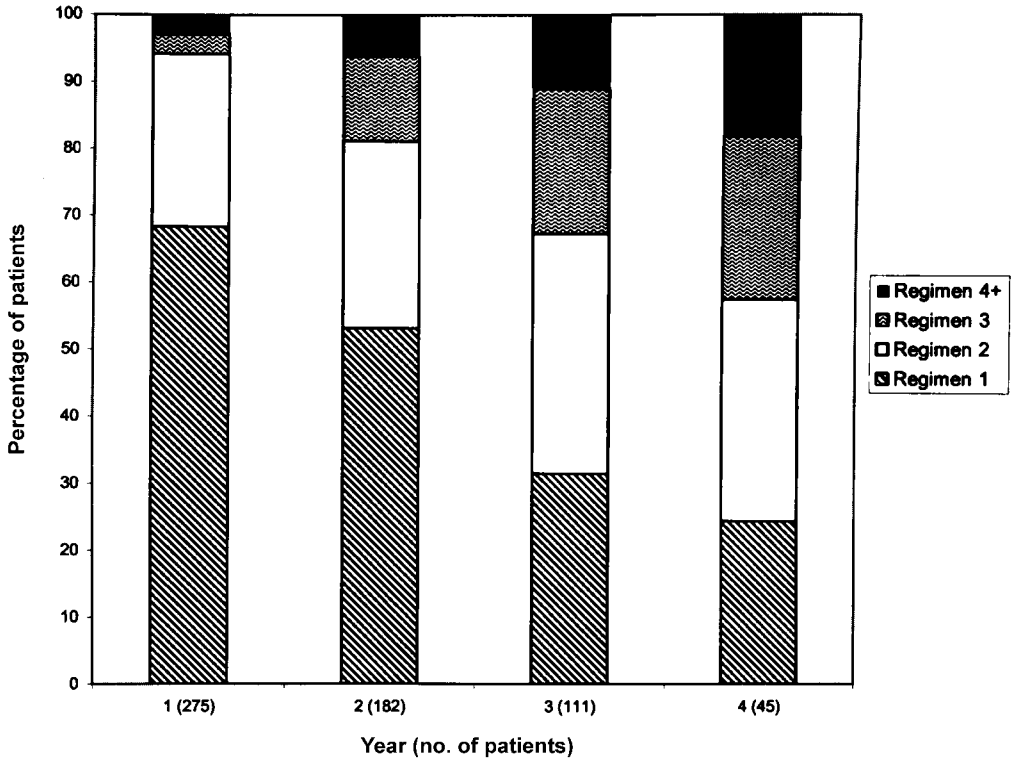

Figure 2. Percentage of patients receiving their first (regimen 1), second (regimen 2), third (regimen 3), or fourth or higher (regimen 4+) HAART regimen in the first 4 years of treatment.

Table 3. Results of univariate and multivariable proportional hazards analyses of risk of discontinuation of initial HAART regimens for the 405 patients.

Analysis, factor	Hazard ratio (95% CI)	*P*
Univariate		
Age	1.00 (0.98–1.01)	.84
Male sex	1.11 (0.82–1.50)	.50
White race	0.91 (0.71–1.18)	.48
Injection drug use	2.08 (1.37–3.16)	.0006
Previous opportunistic infection	1.37 (1.00–1.89)	.05
Man who has sex with men	0.93 (0.72–1.21)	.58
Caregiver was a nurse practitioner	1.10 (0.85–1.44)	.46
Individual attending physicians	…	.76[a]
Proportion of "no shows" to cancellations	1.35 (0.64–2.85)	.43
Baseline CD4 cell count[b]	1.00 (0.97–1.04)	.87
Baseline log virus load[c]	0.96 (0.81–1.13)	.63
Initial regimen with only NRTIs[d]	0.94 (0.55–1.63)	.83
Initial regimen is NNRTI based[d]	0.83 (0.59–1.16)	.28
Initial regimen is PI based[d]	1.21 (0.88–1.65)	.24
Twice-daily dosing[d]	0.90 (0.68–1.20)	.47
Multivariable		
Injection drug use	2.17 (1.42–3.29)	.0003
Previous opportunistic infection	1.43 (1.04–1.97)	.0278

NOTE. NNRTI, nonnucleoside reverse-transcriptase inhibitor; NRTI, nucleoside reverse-transcriptase inhibitor; PI, protease inhibitor.

[a] Calculated using the log-rank test, on the basis of data from 10 different attending physicians.

[b] Per 50 cells/μL; data were available for 318 patients.

[c] Data were available for 303 patients.

[d] Excludes 13 patients who were enrolled in AIDS Clinical Trials Group Protocol 384, a double-blind study of PIs vs. NNRTIs.

regimen discontinuation [20], whereas others have identified virologic failure [19, 21] and poor adherence [22] as the primary reasons. In reality, virologic failure and poor adherence are often intertwined and difficult to separate. A substantial proportion of patients with virologic failure likely had suboptimal adherence. Moreover, suboptimal adherence may be driven, at least in part, by low-grade toxicity-related events, such as intermittent headache, mild nausea, and chronic diarrhea, that often are not reported to clinicians. Some of the newer antiretroviral agents in development may have fewer side effects and improved overall tolerability. This factor, along with more-convenient dosing schedules, may help explain the higher degree of virologic success observed in more-recent clinical trials, in which 70%–80% of patients have been found on intent-to-treat analyses to have virus loads <50 copies/mL [23, 24].

Regardless of the reason for discontinuation, the initial HAART regimen for our patients was immunologically and virologically successful in most; the median CD4 cell count and the median virus load at initial regimen discontinuation were 343 cells/μL and 303 copies/mL, respectively. These values should be interpreted cautiously, however, because of the number of missing values. For a disproportionate number of patients, the initial regimen was discontinued within the first 90 days (often because of toxicity), and yet no significant threshold effect on initial regimen duration was seen. When patients whose initial regimens lasted $\leqslant$90 days were excluded from the analysis, the median duration of the initial regimen increased by only 4 months (table 2).

To determine patient factors that predict short initial regimens, proportional hazards regression models were run (table 3). The only statistically significant factors in the univariate analysis were a history of IDU and an OI before initiation of HAART. These 2 factors remained significantly associated with short initial regimens in the multivariable analysis. All other factors examined, including baseline CD4 cell count, baseline virus load, and the type of regimen used, were not significantly associated with shorter initial regimens. Although the missing baseline CD4 cell count and virus load data may bias this analysis if the referred patients were systematically different from our other subjects, the *P* values suggest no correlation whatsoever ($P = .87$ and $P = .63$ for baseline CD4 cell count and virus load, respectively).

Table 4. Frequency and results of univariate proportional hazards regression analyses of antiretroviral drug use in initial HAART regimens for 392 patients.

Drug	Frequency, no. of patients	Hazard ratio (95% CI)	*P*
Lamivudine	350	0.78 (0.54–1.13)	.19
Zidovudine	270	0.89 (0.66–1.12)	.26
Stavudine	122	1.14 (0.87–1.50)	.33
Didanosine	52	1.29 (0.92–1.81)	.15
Abacavir	23	0.57 (0.21–1.54)	.27
Zalcitabine	2	ND	
Efavirenz	80	0.73 (0.48–1.10)	.14
Nevirapine	18	0.91 (0.51–1.63)	.75
Delavirdine	4	ND	
Nelfinavir	132	0.85 0.65–1.11()	.23
Indinavir	129	1.19 (0.92–1.55)	.18
Saquinavir			
Hard gel capsule	11	1.35 (0.69–2.63)	.38
Soft gel capsule	10	2.68 (1.32–5.44)	.0065
Ritonavir			
High dose	2	ND	
Low dose	14	1.34 (0.63–2.84)	.45
Amprenavir	1	ND	

NOTE. Excludes 13 patients enrolled in AIDS Clinical Trials Group Protocol 384, a double-blind study comparing protease inhibitors with nonnucleoside reverse-transcriptase inhibitors. ND, not done.

The reasons that injection drug users and patients with a previous OI have a shorter duration of initial regimen are not clear. One possible explanation is that injection drug users present at more advanced stages of disease than do other patients. In our cohort, however, the median baseline CD4 cell count among injection drug users was 242 cells/μL, and the median baseline virus load was 66,721 copies/mL, both of which are better than the median values for the entire cohort. It is also possible that injection drug users are less likely to adhere to treatment regimens than are other patients, and thus discontinue the regimens sooner, or that individuals with a previous OI are sicker than are other patients, and thus experience more medication-related side effects. Again, this was not found to be true among our patients. The reasons for regimen discontinuation among patients with IDU or previous OIs were similar to those for the rest of the cohort. Of the 73 patients with IDU or previous OI who had discontinuation of the initial regimen, the regimen was discontinued in 45% because of medication toxicity and in 23% because of poor adherence/virologic failure, and 7% died. Another possible explanation is that patients with IDU or previous OI do not access care as quickly as others because of insurance status, socioeconomic status, or education level. Our database does not accurately capture this information well enough to assess this.

Nevertheless, because IDU is a poor prognostic factor, public health initiatives need to target this risk group to decrease HIV transmission and encourage HIV testing and diagnosis. Likewise, because the development of a previous OI is indicative of more-advanced disease, HAART should be initiated in such patients before their CD4 cell counts decrease to <200 cells/μL. The median CD4 cell count at initiation of HAART in our cohort was only 197 cells/μL, which demonstrates that one-half of our patients were already at risk of developing an OI at presentation. The cohort we described elsewhere [25] and other reports [26–29] have demonstrated decreased survival among patients who have CD4 cell counts <200 cells/μL when HAART is initiated. This may, in part, be due to the decreased duration of initial regimens. Initiation of HAART while CD4 cell counts are >200 cells/μL has a tremendous potential impact on survival, and, because many patients are still being diagnosed with advanced disease, public health campaigns to encourage earlier testing and diagnosis must continue.

Table 5. Reasons for discontinuation among 240 patients who discontinued the initial HAART regimen.

Reason for discontinuation	No. (%) of patients who discontinued therapy after indicated period: ⩽90 days (*n* = 56)	>90 days (*n* = 184)	Overall (*n* = 240)
Toxicity	35 (62.5)	82 (44.6)	117 (48.8)
Nausea/vomiting	14 (25.0)	17 (9.2)	31 (12.9)
Anemia	10 (17.9)	7 (3.8)	17 (7.1)
Peripheral neuropathy	0	17 (9.2)	17 (7.1)
Other gastrointestinal effects[a]	3 (5.4)	11 (6.0)	14 (5.8)
CNS-related effects[b]	5 (8.9)	6 (3.3)	11 (4.6)
Nephrolithiasis	1 (1.8)	8 (4.3)	9 (3.8)
Lipodystrophy	0	9 (4.9)	9 (3.8)
Rash	2 (3.6)	0	2 (0.8)
Lactic acidosis	0	1 (0.5)	1 (0.4)
Arthralgias	0	1 (0.5)	1 (0.4)
Unspecified toxicity	0	5 (2.7)	5 (2.1)
Poor adherence/virologic failure	8 (14.3)[c]	46 (25)	54 (22.5)
Financial reasons	2 (3.6)	11 (6.0)	13 (5.4)
Death	2 (3.6)	10 (5.4)	12 (5.0)
Unspecified in chart	2 (3.6)	10 (5.4)	12 (5.0)
Entered research study	1 (1.8)	7 (3.8)	8 (3.3)
Patient self-discontinued	2 (3.6)	4 (2.2)	6 (2.5)
Therapy intensification	2 (3.6)	4 (2.2)	6 (2.5)
Other[d]	2 (3.6)	10 (5.4)	12 (5.0)

[a] Hepatitis, diarrhea, pancreatitis, or reflux.
[b] Mania, headache, fatigue, or depression.
[c] All of these patients discontinued because of poor adherence.
[d] Hospitalized, trial period not receiving medications due to low baseline virus load, patient request, incorrect medication, pregnancy only, or change from saquinavir hard gel capsule–ritonavir combination to saquinavir soft gel capsule.

Additional univariate proportional hazards regression analyses of individual antiretroviral medications only found an association between saquinavir SGC and a significantly shorter initial regimen (table 4). Of the 10 patients who received saquinavir SGC, data from 2 were censored while the patients were still receiving this regimen. Nausea and vomiting were the reason for discontinuation in 5 of the remaining 8 patients. However, because only 10 patients were included in this univariate analysis, care must be taken not to over-interpret the results.

The present study has several potential limitations. First, missing laboratory values, as mentioned previously, may bias the results. Because the baseline median CD4 cell count and virus load were not found to closely correlate with regimen duration, however, this is less likely. Another limitation is that we do not capture variables such as insurance status, income level, and education level, all of which may be important factors. These missing laboratory and demographic data, however, do not affect the overall regimen duration estimate. Third, the reasons for regimen discontinuation were determined via a retrospective chart review. The actual reasons for discontinuation were not always clear, and some category mixing could have occurred (e.g., between toxicity and poor adherence). Finally, our clinic population may be different from those of other clinics, making our results less externally valid. Many urban clinics, for example, would serve more injection drug users.

In summary, our analysis shows that, with currently available medications, the median duration of initial HAART regimens in treatment-naive patients is only 1.6 years. The primary reason for regimen discontinuation is medication-related toxicity, rather than primary drug failure. Because successive regimens are significantly shorter, the likelihood that successful HAART will last a lifetime is poor. This bleak outlook is tempered by the fact that 25% of the patients for whom we have 4 years of follow-up are still receiving the initial regimen. In addition, new medications being developed have fewer side effects and may be better tolerated. The only factors significantly associated with shorter regimens were a history of IDU and of an OI before initiation of therapy. Thus, to increase the chances that HAART can be used to successfully treat HIV infection and AIDS, prevention and treatment programs for injection drug users must be emphasized, and people who are at risk for HIV infection must get tested and receive a diagnosis and treatment before they develop advanced disease.

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