Risk of Progression to AIDS and Death in Women Infected With HIV-1 Initiating Highly Active Antiretroviral Treatment at Different Stages of Disease

Kathryn Anastos, MD; Yolanda Barrón, MS; Paolo Miotti, MD; Barbara Weiser, MD; Mary Young, MD; Nancy Hessol, MSPH; Ruth M. Greenblatt, MD; Mardge Cohen, MD; Michael Augenbraun, MD; Alexandra Levine, MD; Alvaro Muñoz, PhD; for the Women’s Interagency HIV Study Collaborative Study Group

Background: The optimal virologic and immunologic stage at which to initiate antiretroviral therapy in individuals infected with human immunodeficiency virus type 1 (HIV-1) is undefined.

Methods: Among 1054 HIV-1–infected women in a prospective cohort study, we determined the time from initiation of highly active antiretroviral treatment (HAART) to acquired immunodeficiency syndrome (AIDS) and death.

Results: Median follow-up was 3.4 years. Of 553 women without AIDS at HAART initiation, 62 (11%) developed AIDS. Compared with women with CD4+ cell counts greater than 350/µL at HAART initiation, women with cell counts of 200 to 350/µL and less than 200/µL had relative hazards (RHs) for progression to AIDS of 0.93 (95% confidence interval [CI], 0.46-1.86) and 2.48 (95% CI, 1.39-4.42), respectively. Compared with those with HIV-1 RNA values less than 5000 copies/mL, women with 5000 to 50000 copies/mL and greater than 50000 copies/mL had RHs of 1.39 (95% CI, 0.74-2.64) and 2.09 (95% CI, 1.09-3.99), respectively. Among women with AIDS at HAART initiation (n=501), RHs of death were 1.97 (95% CI, 0.84-4.66) and 3.35 (95% CI, 1.59-7.08) with CD4+ cell counts of 200 to 350/µL and less than 200/µL, respectively, relative to those with greater than 350/µL, and 1.90 (95% CI, 0.84-4.30) and 3.70 (95% CI, 1.81-7.54) for those with HIV-1 RNA values of 5000 to 50000 and greater than 50000 copies/mL, respectively, relative to those with less than 5000 copies/mL.

Conclusions: Progression to AIDS and death was predicted by pre-HAART values of less than 200/µL for CD4+ cells and greater than 50000 HIV-1 RNA copies/mL, indicating that deferral of HAART until the CD4+ cell count is between 350 and 200/µL is a valid strategy in the clinical management of HIV-1 infection.

tion of HAART is best guided by characterization of the treated course of HIV-1 infection. Cohort studies of HIV-1–infected individuals have characterized the risk of progression to AIDS while receiving HAART according to disease stage defined by CD4+ cell count and HIV-1 RNA. Such studies have identified the stages at which disease progression is low, making deferral of therapy an option. The significant toxicity associated with HAART also makes it imperative to determine the optimal time at which to initiate treatment. The primary objective of this report is to describe the factors associated with clinical progression after HAART initiation in a large cohort study conducted in 5 metropolitan areas of the United States.

Simple and direct comparisons of survival after HAART is initiated at different stages of disease do not suffice to allow conclusions regarding when to start: those who initiate treatment at a later stage had an unmeasured survival benefit before HAART was started. This lead time survival needs to be considered in analyses of data from cohort studies. If the survival is equal among those initiating HAART at different stages, deferral of treatment to a more advanced stage should be considered. This is because the addition of the lead time to the group treated later would result in survival at least equal to that among individuals receiving earlier treatment. On the other hand, if the survival of those initiating treatment at a later stage is worse, then adjustment for lead time (transition time between stages of disease) is necessary to ensure a valid comparison. To help guide strategic clinical decision making on when to initiate HAART, we provide herein data from a large cohort study of HIV-1–infected women followed up for more than 6 years. Our inferences are presented in the context of strengths and limitations (eg, lead time bias, for which we adjust) of observational studies.

STUDY POPULATION

The Women's Interagency HIV Study (WIHS) is a multicenter prospective study of the natural course of HIV-1 infection in women, conducted in 5 locations within the United States: New York, NY (2 sites); Washington, DC; Chicago, Ill; Southern California; and the San Francisco Bay area of California. The WIHS methods and baseline cohort characteristics have been described previously. Briefly, from October 1, 1994, through November 30, 1995, 2628 women (2039 HIV-1 seropositive and 569 seronegative) were enrolled. Informed consent was obtained from the participants in accordance with procedures and consent materials reviewed and approved by the committee on human experimentation at each of the collaborating institutions. Every 6 months, WIHS participants were interviewed by means of a structured questionnaire and underwent a physical examination. Multiple gynecologic and blood specimens were collected at each visit. Highly active antiretroviral treatment was defined to include the use of (1) 2 or more nucleoside analogue reverse transcriptase inhibitors (NRTIs) in combination with at least 1 protease inhibitor or nonnucleoside reverse transcriptase inhibitor (NNRTI); (2) 1 NRTI in combination with at least 1 protease inhibitor and at least 1 NNRTI; (3) a regimen containing ritonavir and saquinavir or saquinavir–me-
STATISTICAL METHODS

For individuals who initiated HAART while AIDS free and developed AIDS during the period of follow-up, we defined the time to AIDS as the years from HAART initiation to the midpoint between the last visit at which the individual did not report an AIDS-defining clinical condition and the first visit at which the individual did report one. For individuals who remained AIDS free, we right-censored the data at date of last follow-up. The AIDS-free survival time after HAART initiation was determined, and those not known to have died were censored at September 30, 2000.

Standard Kaplan-Meier methods were used to estimate the percentages of participants who were AIDS free and alive at different times after HAART initiation. All prognostic markers were categorized: the cutoff values for age, CD4+ cell count, and HIV-1 RNA were 35 and 45 years, 200 and 350/µL, and 5000 and 50000 HIV-1 RNA copies/mL, respectively. To achieve uniformity of direction of the effects of age and CD4+ cell count, we treated categories of both variables as dummy variables: the cutoff values for age, CD4+ cell count, and HIV-1 RNA were 35 and 45 years, 200 and 350/µL, and 5000 and 50000 HIV-1 RNA copies/mL, respectively. The multivariate proportional hazard regression models were used and included as covariates the indicator variables for the categories of the variable in the analysis.

The multivariate model for progression to AIDS included 4 indicator variables: 2 each for the 3 categories of both CD4+ and HIV-1 RNA, so that the baseline (reference) hazard corresponded to those with CD4+ cell count greater than 350/µL and HIV-1 RNA less than 5000 copies/mL. The multivariate model for progression to death included the same variables as well as an indicator variable for AIDS diagnosed before HAART initiation. To determine the appropriateness of the proportionality assumption in the regression models, we tested for interactions between the exposures of interest and time. All analyses were implemented by means of the options available in the PROC PHREG of the SAS statistical package.

RESULTS

Of the 2059 HIV-1 seropositive and 9 HIV-incident women in the cohort, 1163 (56.2%) initiated HAART before September 30, 2000. Of these, 1054 (90.6%) had initiated HAART on or after July 1, 1995, had a HAART initiation date known within 1 year, and were followed up after HAART initiation. The median follow-up was 3.2 years (interquartile range, 2.0-3.9 years). Only 53 (5.0%) of the 1054 included women were lost to follow-up.

Among 553 women without a clinical AIDS-defining event before HAART initiation, 62 (11.2%) developed AIDS. Of the 1054 included women who initiated HAART and before September 30, 2000, 1163 (56.2%) initiated HAART on or after July 1, 1995, had a HAART initiation date known within 1 year, and were followed up after HAART initiation. The median follow-up was 3.2 years (interquartile range, 2.0-3.9 years). Only 53 (5.0%) of the 1054 included women were lost to follow-up.

Of the 2059 HIV-1 seropositive and 9 HIV-incident women in the cohort, 1163 (56.2%) initiated HAART before September 30, 2000. Of these, 1054 (90.6%) had initiated HAART on or after July 1, 1995, had a HAART initiation date known within 1 year, and were followed up after HAART initiation. The median follow-up was 3.2 years (interquartile range, 2.0-3.9 years). Only 53 (5.0%) of the 1054 included women were lost to follow-up.

Among 553 women without a clinical AIDS-defining event before HAART initiation, 62 (11.2%) developed AIDS. Of the 1054 included women who initiated HAART, 102 (9.7%) died; of these, 77 (75.5%) had reported an AIDS-defining clinical event before HAART initiation. Of the 25 deaths in women without AIDS at HAART initiation, 14 (56.0%) were unrelated to AIDS, and 19 (76.0%) occurred in women who had not reported an AIDS-defining event before death.

The baseline demographic and clinical characteristics of the included women are shown in Table 1. The median pre-HAART CD4+ cell count was significantly lower in the 501 women who reported a clinical AIDS-defining event before initiation of HAART (median CD4+, 202/µL) than in the 553 reporting being AIDS free (319/µL) (Wilcoxon rank sum test, P<.001). Women who reported a history of a clinical AIDS-defining event before HAART initiation were more likely than women without such history to report previous injecting drug use (36.0% vs 24.7%; χ² test P<.001). Age, history of previous antiretroviral therapy, and race or ethnicity did not differ between AIDS-free
women and women with AIDS at time of HAART initiation \( (P < .05) \). Approximately 16% of the women initiating HAART reported no previous use of any antiretroviral therapy. HAART was initiated at a median HIV-1 RNA value of 23,000 and 9,200 copies/mL in the women reporting AIDS and those AIDS free, respectively, with a wide range in both groups \(< 80\text{ to } 690,000\text{ copies/mL}\).

**PROGRESSION TO AIDS**

**Figure 1** shows the Kaplan-Meier curves for AIDS according to CD4\(^+\) cell count and HIV-1 RNA in univariate analysis. Although progression to AIDS was significantly greater in women with CD4\(^+\) cell counts less than 200/\(\mu\)L at HAART initiation (RH, 2.48; 95% confidence interval [CI], 1.39-4.42), progression among women with CD4\(^+\) cell counts of 200 to 350/\(\mu\)L was similar to that in women with CD4\(^+\) cell counts greater than 350/\(\mu\)L (RH, 0.93; 95% CI, 0.46-1.86).

Compared with those with HIV-1 RNA values of less than 5000 copies/mL, the RHs of progression for women with values of 5000 to 50,000 copies/mL and more than 50,000 copies/mL were 1.39 (95% CI, 0.74-2.64) and 2.09 (95% CI, 1.09-3.99), respectively (Figure 1B). The Kaplan-Meier curves in Figure 1 demonstrate different patterns for the 2 markers: despite similar distribution of the cohort into 3 groups for each marker, analysis of HIV-1 RNA demonstrated divergence of the 3 groups, whereas there was almost complete overlap of the middle (200-350/\(\mu\)L) and the highest (>350/\(\mu\)L) CD4\(^+\) cell count categories. This divergence in pattern may indicate that there is a threshold effect for CD4\(^+\) cell counts, with a threshold value between 200 and 350/\(\mu\)L, but there does not seem to be such an effect for HIV-1 RNA.

There was no statistically significant association of age, history of previous use of antiretroviral treatment, ethnicity, or transmission category with disease progression.

**PROGRESSION TO DEATH**

In univariate analysis, death was strongly associated with having reported an AIDS-defining illness before HAART initiation (**Figure 2**). For women with AIDS at HAART initiation (**Figure 3A**), the RHs of death were 1.97 (95% CI, 0.84-4.66) and 3.35 (95% CI, 1.59-7.08) with CD4\(^+\) cell counts of 200 to 350/\(\mu\)L and less than 200/\(\mu\)L, respectively, relative to greater than 350/\(\mu\)L. Quantitative HIV-1 RNA values were strongly associated with death: RHs were 1.90 (95% CI, 0.84-4.30) and 3.70 (95% CI 1.81-7.54) with HIV-1 RNA values of 5000 to 50,000 copies/mL and greater than 50,000 copies/mL, respectively, relative to less than 5000 copies/mL, as demonstrated in Figure 3B.

Because there were only 25 deaths among the 553 women who were AIDS free at HAART initiation, comparisons for 3 categories of CD4\(^+\) cells and HIV-1 RNA could
not be made. Therefore, we simplified the CD4⁺ cell count and HIV-1 RNA categories to contain only 2 groups, with cutoff values of 200/µL and 50,000 copies/mL, respectively. CD4⁺ cell counts of less than 200/µL (RH, 3.06; 95% CI, 1.40-6.72) and HIV-1 RNA values greater than 50,000 copies/mL (RH, 3.78; 95% CI, 1.63-8.76) were strongly associated with death among these women.

A history of no exposure to antiretroviral treatment before HAART initiation was not significantly associated with death in the women who were AIDS free (RH, 0.78; 95% CI, 0.23-2.61) or who had AIDS (RH, 1.01; 95% CI, 0.53-1.91) at HAART initiation. Although it did not reach nominal levels of statistical significance, in women older than 45 years compared with those younger than 35 years the hazard of death was elevated (RH, 2.59, and 95% CI, 0.90-7.50 among AIDS-free women and RH, 1.60, and 95% CI, 0.89-2.88 among women with AIDS). Among those with AIDS at initiation, Latinas were less likely to die than African American or white women (RH, 0.56, and 95% CI, 0.30-1.03 for Latinas and RH, 0.92, and 95% CI, 0.52-1.66 for whites compared with African Americans, respectively). The HIV transmission category was not associated with death.

**MULTIVARIATE ANALYSIS FOR PROGRESSION TO AIDS AND DEATH**

Table 2 shows the RHs for the CD4⁺ cell count and HIV-1 RNA categories when both variables were simultaneously included in the regression analyses. As expected, because of the relationship between these 2 markers, the adjusted RHs all decreased when compared with the univariate RHs presented in Figure 1. Among women with similar HIV-1 RNA, those with CD4⁺ cell counts less than 200/µL had twice the hazard of developing AIDS of those with CD4⁺ cell count greater than 350 cells/µL, and it retained the statistical significance shown in the univariate analysis. Conversely, among women with similar CD4⁺ cell counts, as the HIV-1 RNA increased, the hazard of AIDS progression increased, and this was statistically significant in both the univariate and multivariate analyses.
Table 2. Multivariate Relative Hazards of AIDS Among AIDS-Free Women at HAART Initiation and Death After HAART Initiation*

<table>
<thead>
<tr>
<th>CD4+ cell count/µL at visit preceding initiation</th>
<th>AIDS After HAART (n = 509; AIDS, n = 57)†</th>
<th>Death After HAART (n = 959; Deaths, n = 89)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Subjects  AIDS, No.  RH (95% CI)</td>
<td>No. of Subjects  Deaths, No.  RH (95% CI)</td>
</tr>
<tr>
<td>&gt;350</td>
<td>232  20  1.00</td>
<td>355  14  1.00</td>
</tr>
<tr>
<td>200-350</td>
<td>155  13  0.80 (0.39-1.64)</td>
<td></td>
</tr>
<tr>
<td>&lt;200</td>
<td>122  24  2.00 (1.08-3.71)</td>
<td></td>
</tr>
<tr>
<td>HIV RNA at visit preceding initiation (copies/mL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5000</td>
<td>205  17  1.00</td>
<td>341  15  1.00</td>
</tr>
<tr>
<td>5000-50 000</td>
<td>187  20  1.18 (0.62-2.28)</td>
<td></td>
</tr>
<tr>
<td>&gt;50 000</td>
<td>117  20  1.80 (0.91-3.53)</td>
<td></td>
</tr>
<tr>
<td>Clinical AIDS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>NA  NA</td>
<td>509  22  1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>NA  NA</td>
<td>450  67  2.53 (1.53-4.17)</td>
</tr>
</tbody>
</table>

* AIDS indicates acquired immunodeficiency syndrome; HAART, highly active antiretroviral treatment; RH, relative hazard; CI, confidence interval; HIV, human immunodeficiency virus; and NA, not applicable.
† Forty-four women (5 with AIDS) had missing data on either CD4+ or HIV RNA.
‡ Ninety-five women (15 deceased) had missing data on either CD4+ or HIV RNA.

cell counts, those with HIV-1 RNA greater than 50000 copies/mL had nearly twice the hazard (RH, 1.8) of progression to AIDS of those with HIV-1 RNA less than 5000 copies/mL, but this was only marginally significant.

The multivariate analysis of time to death after HAART initiation included an indicator for AIDS at HAART initiation, and CD4+ and HIV-1 RNA values. The association of self-reported clinical AIDS with death persisted in multivariate analysis (RH, 2.53; 95% CI, 1.53-4.17). Both CD4+ cell count less than 200/µL and HIV-1 RNA greater than 50000 copies/mL were significantly associated with progression to death, with the latter showing a stronger (RH, 2.63) relationship than the former (RH, 2.09).

ADDITIONAL ANALYTICAL ISSUES

All the RH estimates were obtained under regression models assuming that the hazards between groups fulfilled the assumption of proportionality. To test whether this assumption was appropriate, we extended the regression models by allowing the RHs in different categories of a marker to vary linearly with time. In all instances, such interactions were not statistically significant (P > .15).

To adjust for possible temporal or secular trends (ie, changing practices in the indications for antiretroviral therapy), we adjusted all the univariate analyses presented in Figures 1 to 3 by adding an indicator variable for whether or not an individual had initiated HAART before 1997 (the approximate overall median). In all instances the estimates and CIs of the RHs presented in the figures were practically identical.

To adjust for potential differences across sites, we extended our regression analysis by adding 5 indicator variables for the 6 sites to the regression models yielding the RHs presented in Figures 1 to 3. The site-adjusted RHs were practically unchanged.

COMMENT

This analysis of clinical outcomes in a large cohort study of HIV-1–infected women starting HAART at different stages of disease and followed up for a median of 3.2 years demonstrated similar clinical progression in women initiating HAART with CD4+ cell counts of greater than 350/µL and 200 to 350/µL, with uniformity of results across geographic sites. This suggests that it may not be necessary to start HAART until the CD4+ cell count falls below 350/µL. The equality of prognosis in these 2 CD4+ categories is a solid inference because if the lead time (time in which the participants progressed from CD4+ cell count >350/µL to CD4+ cell count between 200 and 350/µL) were added to the lower category, the inference would be even stronger: delay of treatment until the CD4+ cell count falls below 350/µL appears to have clinical benefit at least equal to that conferred by earlier initiation of therapy.

On the other hand, women who initiated HAART with CD4+ cell count less than 200/µL had significantly more rapid progression. In this instance it is essential to adjust for the possible lead-time bias. To accomplish this, we used the observed distribution of times that occurred in the pre-HAART era to transition from the middle to the lowest CD4+ category. Sampling (at random) from this distribution, we added a lead time to each of the 135 women who started with less than 200 CD4+ cells per microliter (Figure 1). The comparison of these times with those observed among the 162 women who initiated HAART at CD4+ cell counts between 200 and 350/µL does not suffice, because it is also necessary to add to the analysis individuals who developed AIDS while treatment was being “deferred.” To accomplish this, we used extended Kaplan-Meier methods so that the lead times of the more advanced group are considered as late (staggered) entries. After adjustment for the lead time, the RH of those starting at CD4+ cell count less than 200/µL was 2.89 (95% CI, 1.46-5.70), providing evidence that it is detrimental to defer therapy until the CD4+ cell count is less than 200/µL. Thus, therapy may be deferred until the CD4+ cell count reaches 350/µL, but the optimal point at which to start therapy within the CD4+ cell count category between 200 and 350/µL remains to be defined. Further follow-up in this and other studies is necessary to elucidate more precisely a CD4+ cell count “threshold” defining the optimal time to initiate HAART.

Consonant with our results herein are those of a recent analysis that showed a significantly higher rate of AIDS...
counts less than 200/µL (8.3 vs 1.8 per 100 person-years; \(P<.001\)), but not at CD4+ cell counts of 200 to 349/µL (2.3 and 1.8 per 100 person-years; \(P=.32\)), compared with those with CD4+ cell counts of 350/µL or more. There was also a lower likelihood (RH, 0.80; \(P<.001\)) of obtaining an undetectable (<500 copies/mL) plasma HIV-1 RNA value among those who initiated HAART at a CD4+ lymphocyte count less than 200/µL; the association was obscured and diluted (\(P=.20\)) when the presence of AIDS and HIV-1 RNA, which are strongly related to low CD4+ cell count, were included in a multivariate model. As in the natural course setting, the prognostic information of HIV-1 RNA may not be the same for different categories of CD4+ cell count. Indeed, a recent analysis\(^2\) showed that for individuals who started HAART at CD4+ lymphocyte count greater than 200/µL and who had an HIV-1 RNA value greater than 100,000 copies/mL, there was a borderline significant trend (\(P=.07\)) toward an elevated risk of death, but such a trend was not significant (\(P=.21\)) for CD4+ lymphocyte count between 51 and 199/µL, and it was practically nonexistent for CD4+ cell counts less than 50/µL.

Women with an AIDS-defining clinical condition before HAART initiation had a higher risk of death than women who initiated HAART before development of clinical disease, even after adjustment for CD4+ cell count and HIV-1 RNA (Table 2), suggesting that therapy should not be delayed until the development of AIDS. Because it is not possible to predict a priori which HIV-1–infected patients will develop AIDS before initiation of therapy at a given CD4+ cell count, the prudent course may be to recommend initiation of HAART at a CD4+ cell count of 350/µL, pending further data. Fortunately, even women with self-reported AIDS before HAART initiation experienced a substantially better survival rate when compared with the short survival after AIDS in the absence of therapy reported in previous studies.\(^2\)\(^\text{23}\) This suggests that therapy carried clinical benefit for women who had already experienced an AIDS-defining illness and supports current treatment recommendations to offer HAART to all individuals with HIV-related clinical disease.

There is no consensus on the additional information that the HIV-1 RNA value provides beyond that of the CD4+ cell count. Recently, Sterling et al\(^2\)\(^\text{24}\) suggested that the CD4+ cell count at time of treatment initiation is a more important prognostic factor than the HIV-1 RNA value. Data in Table 2 do show that, although the strength of the prognostic values for CD4+ cell count less than 200/µL and HIV-1 RNA less than 50,000 copies/mL is similar (RH, 2.0 and 1.8, respectively), the relationship for CD4+ is strongly significant (\(P=.03\)) but that for HIV-1 RNA is only marginally significant (\(P=.09\)). To define the relative value of these markers, and to determine whether the similarity persists between women with CD4+ cell counts greater than 350/µL and those with CD4+ cell counts of 200 to 350/µL, longer follow-up will be useful. In this study, the median follow-up among women who were AIDS free at HAART initiation was 3.4 years (maximum, 5.1 years), and in none of the groups analyzed had more than 35% of the cohort died by the end of the follow-up period. Longer follow-up will also be key to assessing the statistical significance of the middle categories of CD4+ cell count and HIV-1 RNA values for time to death among women with AIDS at HAART initiation. Our data had power of 38% and 37% to detect the RH for the middle categories of CD4+ cell count and HIV-1 RNA, respectively, shown in Figure 3.

Clinically significant complications have developed in individuals using HAART, including fat redistribution syndromes,\(^2\)\(^5\)\(^\text{26}\) (development of insulin resistance or frank diabetes mellitus,\(^2\)\(^7\)\(^\text{28}\) abnormal serum lipid levels,\(^2\)\(^6\)\(^\text{27}\) and osteoporosis.\(^2\)\(^8\) In providing treatment to prevent HIV-related illness, which progresses over years or decades, it is important to define at what point in the asymptomatic stage of disease the initiation of therapy confers optimal clinical benefit. This will allow us to minimize exposure to drugs with substantial toxicity.\(^1\)\(^0\)

Several reports have indicated that HIV-1 RNA levels may be lower in women than in men with comparable CD4+ cell counts.\(^2\)\(^9\)\(^\text{31}\) Treatment with HAART in the women in the WIHS is driven predominantly by CD4+ cell counts, with the median CD4+ cell count in women without AIDS before HAART at 319/µL, and a median HIV-1 RNA value of 9200 copies/mL, a value lower than that recommended in the current guidelines for treatment.\(^4\) The public health implications of these data are important: women are receiving antiretroviral therapy even with viral loads that fall below the values at which initiation of treatment is recommended. However, Sterling et al,\(^2\)\(^3\) in a seroincident cohort, recently demonstrated that although quantitative HIV-1 RNA predicts progression to AIDS equally well in women and men, the development of AIDS occurs in women at lower viral load levels. This finding suggests the need for caution in extrapolating our data and inferences to treatment guidelines for men.

A limitation of our study was that clinical AIDS was based on self-report and may have been inaccurate. However, a recent study of a subset of women in the WIHS that assessed the validity of self-report compared the self-reported occurrence of AIDS-related conditions with AIDS diagnoses documented by local county AIDS surveillance registries; overall self-reporting of any AIDS-related condition was accurate, although there was variability in the accuracy of specific conditions.\(^3\)\(^3\)

In summary, this study of HIV-1–infected women was able to take advantage of the fact that HAART was introduced during a short time in a large population of HIV-1–infected individuals who initiated therapy at widely differing clinical, immunologic, and virologic stages of disease. Our results document the benefits of initiating treatment in individuals manifesting clinical disease or who have CD4+ cell counts of less than 200/µL or HIV-1 RNA values greater than 50,000 copies/mL. Furthermore, our data indicate that deferral of HAART until the CD4+ cell count is less than 350/µL is a valid strategy in the clinical management of HIV-1–infected individuals.

Accepted for publication February 6, 2002.

From the Departments of Internal Medicine, Montefiore Medical Center and Lincoln Medical and Mental Health Center, Bronx, NY (Dr Anastos); Department of Epidemiology, Bloomberg School of Public Health, The Johns Hopkins University, Baltimore, Md (Ms Barron and Dr Muñoz); National Institute of Allergy and Infectious Dis-

(Reprinted) Arch Intern Med/Vol 162, Sep 23, 2002 WWW.ARCHINTERNMED.COM

©2002 American Medical Association. All rights reserved.
Women's Interagency HIV Study (WHIS) Collaborative Study Group

New York City/Br: Consortium, New York, NY: Kathryn Anastos, MD, principal investigator; Brooklyn, NY: Howard Monkoff, MD, principal investigator; Washington, DC, Metropolitan Consortium: Mary Young, MD, principal investigator; The Connie Wofsy Study Consortium, San Francisco, Calif: Ruth M. Greenblatt, MD, Herminia Palacio, MD, principal investigators; Los Angeles County/Southern California Consortium: Alexandra Levine, MD, principal investigator; Chicago Consortium, Chicago, Ill: Margde Cohen, MD, principal investigator; Data Coordinating Center, Baltimore, Md: Alvaro Muñoz, PhD, Stephen J. Gange, PhD, principal investigators.

©2002 American Medical Association. All rights reserved.


(REPRINTED) ARCH INTERN MED/VOL 162, SEP 23, 2002 1980 www.archinternmed.com