A Double-Blind, Adjuvant-Controlled Trial of Human Immunodeficiency Virus Type 1 (HIV-1) Immunogen (Remune) Monotherapy in Asymptomatic, HIV-1-Infected Thai Subjects with CD4-Cell Counts of >300

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Received 25 April 2000/Returned for modification 16 June 2000/Accepted 27 June 2000

We examined the effect of a human immunodeficiency virus (HIV)-specific immune-based therapy in Thailand, where access to antiviral drug therapy is limited. A 40-week trial was conducted with 297 asymptomatic, HIV-infected Thai subjects with CD4-cell counts greater than 300 µl/mm³. Subjects were randomized to receive either HIV type 1 (HIV-1) immunogen (Remune; inactivated HIV-1 from which gp120 is depleted in incomplete Freund’s adjuvant or adjuvant control at 0, 12, 24, and 36 weeks at five different clinical sites in Thailand. Neither group received antiviral drug therapy. The a priori primary endpoint for the trial was changes in CD4-cell counts with secondary parameters of percent changes in CD8-cell counts (percent CD4, CD8, and CD4/CD8) and body weight. Subsets of subjects were also examined for changes in plasma HIV-1 RNA levels, Western blot immunoreactivity, and HIV-1 delayed-type hypersensitivity (DTH) skin test reactivity. There was a significant difference in changes in CD4-cell counts that favored the HIV-1 immunogen-treated group compared to those for the adjuvant-treated control group (P < 0.05). On average, for HIV-1 immunogen-treated subjects CD4-cell counts increased by 84 cells by week 40, whereas the increase for the control group was 38 cells by week 40. This increase in CD4-cell count was associated with increased HIV-specific immunogenicity, as shown by Western blotting and enhanced HIV-1 DTH skin reactivity. No significant differences in adverse events were observed between the groups. The results of this trial suggest that HIV-1 immunogen is safe and significantly increases CD4-cell counts and HIV-specific immunity compared to those achieved with the adjuvant in asymptomatic HIV-1-infected subjects not taking antiviral drugs.

Recent advances in human immunodeficiency virus (HIV) type 1 (HIV-1) antiviral drug therapy have had a significant impact on AIDS morbidity and mortality in industrialized countries (2, 25; R. A. Torres and M. Barr, Letter, N. Engl. J. Med. 336:1531–1532, 1997). In North America and Europe, antiviral drug “cocktails” (antiretroviral therapies [ARTs]) which include a protease inhibitor have become the standard of care, but their access is greatly limited in the countries where more than 90% of the individuals with HIV-1 infection live (4, 40).

In Thailand, despite aggressive public health measures and a possible slowing of the epidemic, an estimated 1 million deaths will occur from AIDS by the year 2014 (27, 37). Thus, cost-effective strategies including preventive and therapeutic approaches to further slow progression of the disease are urgently needed. Recently, there has been increased interest in the relationship between strong HIV-1-specific immune function, improved clinical outcomes, and the potential to use immune-based therapies to stimulate similar immune responses (12, 28, 31, 33). Previous studies with HIV-1 immunogen as a monotherapy (inactivated HIV-1 from which gp120 is depleted in incomplete Freund’s adjuvant [IFA]; Remune) had shown activity in the slower increase in the number of proviral DNA copies and increased the percentage of CD4 cells, body weight, and HIV-1-specific immune function in asymptomatic subjects prior to the advent of potent antiviral drug therapy (38, 39). Furthermore, phase I trials of the HIV-1 immunogen as a monotherapy with 30 asymptomatic Thai subjects not taking ARTs confirmed the safety and immunogenicity of this approach (8, 20). We therefore hypothesized that use of this HIV-1-specific immune-based approach as monotherapy might improve clinical outcomes as measured by CD4-cell counts in Thai subjects who have little access to antiviral drug therapy. We conducted a phase II double-blind, adjuvant-controlled, multisite clinical trial to examine the effects of the HIV-1 immunogen in an asymptomatic Thai cohort not taking ARTs.

MATERIALS AND METHODS

Approval for the study described here was obtained from the Technical Subcommittee on AIDS Vaccines under the Ministry of Public Health, Bangkok, Thailand, and from the Ethical Review Committee for Research in Human Subjects of the National AIDS Committee. Informed consent was obtained from 297 HIV-infected, asymptomatic Thai subjects with CD4-cell counts >300 µl/mm³. HIV-1-infected individuals were positive by Western blotting and enzyme-linked immunosorbent assay (ELISA) and were randomized to receive either HIV-1 immunogen or IFA adjuvant, with the subjects and the investigators blinded to the treatment codes. Five different clinical sites in Thailand participated in this protocol, and 33 patients were enrolled at each site (allowing a 10% dropout rate). The subjects were randomized to be treated at a 2:1 ratio with an intramuscular injection into the triceps muscle of HIV-1 immunogen or IFA.
The a priori primary endpoint of the study was a change in CD4
0.45
by ultrafiltration and ion-exchange chromatography (35) from filtered (pore size,
U of p24 antigen in IFA. HIV-1 from which gp120 is depleted is highly purified
inactivated HIV-1 from which gp120 was depleted and was used at a dose of 10
control on day 1 and at weeks 12, 24, and 36. HIV-1 immunogen consisted of
% IVDU
% Homosexual
% Occupational exposure
% Transfusion recipient
% With childbearing potential
% Without childbearing potential
% Male
% Female
% % HIV-positive partner
% Hemophilic
% IVDU
% HIV-infected partner
% Without childbearing potential
% With childbearing potential
% Sex
Total sample size (no. of subjects)
Age (yr)
Minimum–maximum
Mean ± SD
Median
The baseline demographic characteristics of the HIV-1 imm-
unogen-treated (n = 198) and the IFA-treated (n = 99) groups are shown in Table 1. Both groups are comparable in terms of baseline percent CD4 and CD8 cells, age and gender. The baseline mean CD4 count for the HIV-1 immunogen-treated group was 545.05 cells/mm³, whereas it was 552.21 cells/mm³ for the IFA-treated group, as shown in Table 2. Baseline mean body weights were also similar for the HIV-1 immunogen-treated and IFA-treated groups (56.21 compared to 53.70 kg, respectively). For the subset of subjects for whom plasma RNA levels were determined, the HIV-1 immunogen-treated group (n = 82) and the IFA-treated group (n = 42) likewise had similar levels at the baseline (3.53 and 3.66 \log_{10} copies/ml, respectively). None of the subjects was on antiviral drug therapy at the baseline or during the trial. The predominant subtype of HIV-1 in this cohort was determined to be E, which occurred in 94% of the subjects, and the rest of the subjects (6%) were infected with subtype B. By week 40, data were available for 289 of the 297 subjects.

The mean change in the CD4
0.45
cell count from the baseline
was used to measure the antibody responses to the HIV-1 immunogen in seven cohorts (8). Plasma HIV RNA level determination was done by the NU-
CLEISENS method with a subset of four cohorts (n = 124). Viral subtyping was performed by the Department of Microbiology, Faculty of Medicine, Siriraj Hospital, Bangkok, Thailand, by a peptide ELISA (30) and heteroduplex mo-
bility assay (10). The 14 amino acids specific for subtype E (env subtype E; T S
I T I G P G Q V F Y R T) and subtype B (env subtype B; K S I H L G P G Q A
W Y T) were used with the ELISA for this study. The primers ED 3/14 and ED
5/12 were used in the heteroduplex mobility assay, and their PCR products were compared in 5% polyacrylamide gels. Blood chemistry studies for assess-
ment of safety and toxicities were done with samples from all cohorts, as were complete physical examinations by the site physician.

Study data were recorded on case report forms and were entered into a database, which was verified by the Biostatistics Department, Faculty of Public Health, Mahidol University, prior to unblinding.

HIV-1 immunogen (Remune) is obtained by concentration and purification from the supernatant of HIV-1 HZ321-infected Hut-78 cells (13). HZ321 is a Za-irian isolate classified as a clade envelope A and clade G gag (5). Antigen preparations were inactivated through a sequential application of \beta-propiolactone (21) and 60Co irradiation (16). HIV-1 immunogen was prepared by com-
bining equal volumes of inactivated HIV-1 antigen containing 10 U of p24 in isotonic saline and IFA. IFA is formulated by adding one part of the surfactant Montanide
80 (mannide monoleate; Seppic, Paris, France) to nine parts of Drakeol 6 VR light mineral oil (Penreco, Karnes City, Pa.). Subjects were monitored at each visit during the trial for adverse events, and the body weight was also recorded. Safety laboratory investigations included liver function tests (aspartate aminotransferase, alanine aminotransferase) and renal function (blood urea nitrogen, creatinine). For the primary statistical analysis, the Wil-
coxon rank, Fisher's exact, and chi-square tests were used. All P values are two tailed.

TABLE 1. Baseline demographic characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Treatment Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IFA</td>
</tr>
<tr>
<td>Total sample size (no. of subjects)</td>
<td>99</td>
</tr>
<tr>
<td>Age (yr)</td>
<td></td>
</tr>
<tr>
<td>Minimum–maximum</td>
<td>18–46</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>29.5 ± 7.1</td>
</tr>
<tr>
<td>Median</td>
<td>29</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>% Male</td>
<td>31.3</td>
</tr>
<tr>
<td>% Female</td>
<td>68.7</td>
</tr>
<tr>
<td>% Without childbearing potential</td>
<td>10.1</td>
</tr>
<tr>
<td>% With childbearing potential</td>
<td>58.6</td>
</tr>
<tr>
<td>% Homosexual</td>
<td>2.3</td>
</tr>
<tr>
<td>% % IVDU</td>
<td>1.1</td>
</tr>
<tr>
<td>% HIV-positive partner</td>
<td>96.0</td>
</tr>
<tr>
<td>% Hemophiliac</td>
<td>0.0</td>
</tr>
<tr>
<td>% Transfusion recipient</td>
<td>0.0</td>
</tr>
<tr>
<td>% Occupational exposure</td>
<td>None</td>
</tr>
</tbody>
</table>

* IVDU, intravenous drug user.

control on day 1 and at weeks 12, 24, and 36. HIV-1 immunogen consisted of
inactivated HIV-1 from which gp120 was depleted and was used at a dose of 10
U of p24 antigen in IFA. HIV-1 from which gp120 is depleted is highly purified
by ultrafiltration and ion-exchange chromatography (35) from filtered (pore size,
0.45 µm) extracellular supernatant of HIV-1 HZ321-infected Hut-78 cells (5). The a priori primary endpoint of the study was a change in CD4
0.45-cell counts, and these were evaluated at day 1 and weeks 12, 24, 36, and 40. Secondary parameters were percent CD4, CD8 CD4/CD8 cells, body weight, plasma HIV-1 RNA levels, and HIV-1-specific immune function markers.

Lymphocyte phenotyping analysis for the counting of CD4
0.45 and CD8
0.45 cells was done at the BioService Unit, Mahidol University (BSU), and at the Armed Forces Research Institute of Medical Sciences with fresh cells by the same validated methodology (42) at both locations. Enumeration of the CD4
0.45 and CD8
0.45 cells in blood samples of HIV-infected patients was determined by three-
color immunofluorescence (e.g., CD3/CD4/CD45 and CD3/CD8/CD45 [27a]) and the use of a TRUECOUNT Absolute Tube with known amounts of fluo-
rescent dye beads to allow calculation of the absolute counts of the leukocytes using the equation recommended by the reagent supplier: number of events in the upper right quadrant containing cell population/number of events as ob-
tained from absolute count bead region × total number of beads/blood volume (in microliters).

The absolute cell numbers were calculated by using the average value for the values from both reactions. The percentage of CD4 and CD8 cells was obtained directly from the percentages of the gated lymphocyte population. Monitoring of CD4 and CD8 levels from blood samples drawn from HIV-infected patients was performed upon receipt of HIV-1 immunogen and IFA (control) on day 1 and at weeks 12, 24, 36, and 40.

The two laboratories calculated absolute cell numbers by using the average value of the number of standard bead events.

Secondary analyses included an HIV-1 antigen delayed-type hypersensitivity (DTH) skin test performed with one cohort to assess functional HIV-specific cell-mediated immunity as described elsewhere (39). Western blot analysis was

TABLE 2. Mean baseline CD4 and CD8 counts, percent CD4/CD8 cells, viral load, and body weight

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of cells/mm³</th>
<th>% Cells</th>
<th>Viral load (log_{10} no. of copies/ml)</th>
<th>Body wt (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CD4</td>
<td>CD8</td>
<td>CD4 CD8 CD4/CD8</td>
<td></td>
</tr>
<tr>
<td>IFA</td>
<td>552.21</td>
<td>1,213.54</td>
<td>22.42    48.95 0.487</td>
<td>53.70</td>
</tr>
<tr>
<td>HIV-1 immunogen</td>
<td>545.05</td>
<td>1,201.26</td>
<td>22.26    48.72 0.493</td>
<td>56.21</td>
</tr>
</tbody>
</table>

The baseline demographic characteristics of the HIV-1 imm-
unogen-treated (n = 198) and the IFA-treated (n = 99) groups are shown in Table 1. Both groups are comparable in terms of baseline percent CD4 and CD8 cells, age and gender. The baseline mean CD4 count for the HIV-1 immunogen-treated group was 545.05 cells/mm³, whereas it was 552.21 cells/mm³ for the IFA-treated group, as shown in Table 2. Baseline mean body weights were also similar for the HIV-1 immunogen-treated and IFA-treated groups (56.21 compared to 53.70 kg, respectively). For the subset of subjects for whom plasma RNA levels were determined, the HIV-1 immunogen-treated group (n = 82) and the IFA-treated group (n = 42) likewise had similar levels at the baseline (3.53 and 3.66 \log_{10} copies/ml, respectively). None of the subjects was on antiviral drug therapy at the baseline or during the trial. The predomin-
ante subtype of HIV-1 in this cohort was determined to be E, which occurred in 94% of the subjects, and the rest of the subjects (6%) were infected with subtype B. By week 40, data were available for 289 of the 297 subjects.

The mean change in the CD4
0.45 cell count from the baseline
was displayed in Fig. 1A. Over the course of the study there was a statistically significant increase in the CD4
0.45-cell count (the primary endpoint) in the HIV-1 immunogen-treated group compared to that in the IFA-treated group by area-under-the-
curve-minus-baseline analysis, as shown in Fig. 1B (P < 0.05). By week 40, after four treatments, the counts in the subjects in the HIV-1 immunogen-treated group increased by 84 cells, on average, from the baseline count, and the counts in the IFA-
treated group increased by 38 cells, on average, as shown in
Table 3. Similarly, trends in the values for the other cytologic parameters favoring the HIV-1 immunogen-treated group, as shown in Table 3. Stable viral loads were found for subsets of patients in both treatment groups (Table 3). There was no reactivity to HIV-1 as measured by DTH skin test reactivity at the baseline. The reactivity to HIV-1 antigens in vivo as measured by DTH skin test reactivity in the HIV-1 immunogen-treated group compared to that in the IFA-treated control group increased by week 40 (Table 4). Furthermore, as shown in Table 5 and Fig. 2, there was increased HIV-1-specific antibody immunoreactivity on Western blots in terms of the increased generation of new bands and less of an attenuation of antibody immunoreactivity on Western blots compared to baseline for the HIV-1 Immunogen and IFA groups, respectively—a twofold difference favoring active immunization. Changes in CD4 counts, independent of changes in viral loads, have been examined extensively with respect to their ability to predict clinical outcomes for patients with HIV-1 infection. For example, in one study, an increase in CD4 count of approximately 100 cell/mm³ after 6 months of zidovudine therapy was associated with improved survival of 78% after adjusting for baseline covariates (15). More recently, CD4 counts obtained at the 3rd month of potent antiviral drug therapy have been demonstrated to be a reliable independent predictor of long-term clinical outcome (24). It should be noted, though, that both CD4-cell counts and viral load are imperfect in their ability to completely explain a clinical treatment effect (3, 6). Nevertheless, these two markers are clinically useful and are the only two accepted, validated clinical markers for HIV-1 infection (22). Interestingly, the results of a recent AIDS cohort study suggested that the CD4-cell count increases in response to potent antiviral drug therapy can be quite variable in a clinical setting (9). Factors such as drug resistance, toxicity, and noncompliance are the main factors associated with poor clinical responses to antiviral drug therapy (32). Such factors may be less important for an immune-based therapy, which is administered infrequently and which has low levels of toxicity, such as the HIV-1 immunogen, for which in this study an extremely low rate of discontinuation was demonstrated (<5%).

The results presented in this report confirmed the results of previous studies with the HIV-1 immunogen in terms of its ability to augment CD4-cell numbers and HIV-1-specific immune function in asymptomatic subjects not taking antiviral drug therapy (19, 38, 39). Furthermore, the augmentation of absolute CD4-cell numbers observed in this study is in contrast to the lack of beneficial effects observed with gp160 or gp120 therapeutic vaccines

Table 4. Distribution of DTH skin test reactivities at Week 40

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of subjects</th>
<th>% (no.) of subjects with induration (mm) of:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>IFA</td>
<td>10</td>
<td>40.0 (4)</td>
</tr>
<tr>
<td>HIV-1 immunogen</td>
<td>18</td>
<td>17.0 (3)</td>
</tr>
</tbody>
</table>

*P = 0.042 (Fisher exact test).

DISCUSSION

This is the first report of a phase II double-blind, placebo-controlled trial of an HIV-specific immunotherapeutic agent in Thailand. In this study, asymptomatic HIV-infected Thai subjects not taking antiviral drug therapy were randomized to receive an HIV-1 immunogen or the adjuvant control (IFA). Subjects received four treatments of the HIV-1 immunogen, and their absolute CD4⁺ cell counts increased significantly without any associated significant toxicity. The changes in CD4 counts represented increases of approximately 15 and 7% relative to baseline for the HIV-1 Immunogen and IFA groups, respectively—a twofold difference favoring active immunization. Changes in CD4 counts, independent of changes in viral loads, have been examined extensively with respect to their ability to predict clinical outcomes for patients with HIV-1 infection. For example, in one study, an increase in CD4 count of approximately 100 cell/mm³ after 6 months of zidovudine therapy was associated with improved survival of 78% after adjusting for baseline covariates (15). More recently, CD4 counts obtained at the 3rd month of potent antiviral drug therapy have been demonstrated to be a reliable independent predictor of long-term clinical outcome (24). It should be noted, though, that both CD4-cell counts and viral load are imperfect in their ability to completely explain a clinical treatment effect (3, 6). Nevertheless, these two markers are clinically useful and are the only two accepted, validated clinical markers for HIV-1 infection (22). Interestingly, the results of a recent AIDS cohort study suggested that the CD4-cell count increases in response to potent antiviral drug therapy can be quite variable in a clinical setting (9). Factors such as drug resistance, toxicity, and noncompliance are the main factors associated with poor clinical responses to antiviral drug therapy (32). Such factors may be less important for an immune-based therapy, which is administered infrequently and which has low levels of toxicity, such as the HIV-1 immunogen, for which in this study an extremely low rate of discontinuation and loss to follow-up was demonstrated (<5%).

The results presented in this report confirmed the results of previous studies with the HIV-1 immunogen in terms of its ability to augment CD4-cell numbers and HIV-1-specific immune function in asymptomatic subjects not taking antiviral drug therapy (19, 38, 39). Furthermore, the augmentation of absolute CD4-cell numbers observed in this study is in contrast to the lack of beneficial effects observed with gp160 or gp120 therapeutic vaccines.
It is tempting to speculate that immune responses (both cell-mediated and antibody responses) against core proteins but not the more variable envelope proteins may be more pivotal for the induction of a clinically relevant effect (23, 36).

This increase in absolute CD4⁺ cell numbers in the HIV-1 immunogen-treated group was also associated with enhanced HIV-specific immunogenicity, as determined by DTH skin test reactivities and Western blotting. These data suggest that this treatment increased both humoral and cell-mediated immune responses to core proteins of the virus. Clearly, the effects on virus-specific immune function also differentiate this approach from antiviral drug therapy, which potently suppresses viral replication but which has yet to demonstrate an effect on HIV-1-specific immunity, with the exception of when treatment is administered very early during primary infection (1, 18, 36). Thus, it is likely that the magnitude of increase in absolute CD4⁺ cell numbers as observed in this study is related to the induction of HIV-specific memory T-helper clones, which represent a small subpopulation of total CD4 T cells.

**TABLE 5. Distribution of Western blot results at week 40**

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of subjects</th>
<th>% (no.) of subjects with the following change in Western blot immunoreactivity:</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Decrease</td>
<td>No change</td>
<td>Increase</td>
</tr>
<tr>
<td>IFA</td>
<td>71</td>
<td>18.3 (13)</td>
<td>38.0 (27)</td>
<td>43.8 (31)</td>
</tr>
<tr>
<td>HIV-1 immunogen</td>
<td>147</td>
<td>9.5 (14)</td>
<td>21.1 (31)</td>
<td>69.4 (102)</td>
</tr>
</tbody>
</table>

*P = 0.001* by the chi-square test.

(11, 14, 34). It is tempting to speculate that immune responses (both cell-mediated and antibody responses) against core proteins but not the more variable envelope proteins may be more pivotal for the induction of a clinically relevant effect (23, 36).

**FIG. 2.** Western blots for three subjects each at day 1 and weeks 24 and 40. Subjects A and B are representative responders in terms of increased breadth and intensity of bands with immunization. Subject C is a nonresponder.
Recently, persistent reservoirs of virus have been demonstrated in subjects on long-term, potent antiviral drug therapy (7, 43). This may in part explain some recent reports that have suggested the occurrence of virologic failure in approximately 20 to 40% of patients after 2 years of potent antiviral drug therapy (17, 41). Thus, additional treatment modalities are warranted to limit viral reservoirs in subjects on even the most potent antiviral drug therapies. Therefore, the effect of treatment with the HIV-1 immunogen in combination with potent antiviral drug therapy on virologic failure in various reservoirs is now being examined in other studies (29).

Interestingly, both absolute CD4-cell counts and HIV-1-specific immune function were enhanced from those at the baseline in the IFA treatment group in this study. This could be potentially explained by the improved care that subjects received by participating in a clinical trial. Alternatively, these findings could be explained by a direct immunostimulatory activity of IFA, as observed in infected subjects in other clinical trials who express HIV-1-specific memory CD4 T-cell clones at a low frequency in the presence of ongoing viral replication (38, 39). Nevertheless, this trial and others have noted the superior efficacy of HIV-1 in IFA compared to IFA alone on CD4-cell counts and HIV-1 functional immunity. No effect on viral load was demonstrated in the subset of patients for whom this was assessed during the 40 weeks of this trial. Interestingly, the viral loads remained stable in both treatment groups for the duration of this study. This result is consistent with those of previous studies in which the effects on viral load were observed after only three treatments (38). Longer follow-up of the subjects treated with HIV-1 immunogen in an open-label extension has observed decreases or stabilization of the viral loads for approximately 90% of subjects at week 88 of the trial. Viral load decreases in the absence of antiviral drug therapy may require the induction of specific anti-HIV immune responses that was:

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of subjects</th>
<th>% Subjects with adverse event</th>
<th>% Subjects with adverse event that was:</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFA</td>
<td>95</td>
<td>20.6</td>
<td>20.6</td>
</tr>
<tr>
<td>HIV-1 immunogen</td>
<td>194</td>
<td>16.6</td>
<td>14.2</td>
</tr>
</tbody>
</table>

* P = 0.548 by the Fisher exact test.

where different clades of HIV-1 exist (26). In fact, the predominant HIV-1 subtype among the subjects in this trial and Thailand in general is E. This is in contrast to the predominant subtype in the United States and Europe, which is subtype B.

In summary, the results of this trial demonstrate that HIV-1 immunogen (Remune) is safe and significantly increased CD4-cell counts and HIV-specific immunity compared to those achieved with the adjuvant control in HIV-1 infected Thai subjects. While significant gains in the treatment of HIV-1 infection with more potent antiviral therapies have been made in industrialized countries, only prevention or cost-effective therapies may affect the global AIDS epidemic. This study further suggests that this HIV-1-specific immune-based therapy may be an important treatment alternative in countries where access to antiviral drugs is limited. Longer-term studies are under way to further optimize the use of this immune-based therapy and also to combine this intervention with cost-effective antiviral drugs or other biologic approaches in developing countries.

REFERENCES


