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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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 control 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 baseline demographic characteristics of the HIV-1 immunogen-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 log₁₀ 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⁺ cell count from the baseline is displayed in Fig. 1A. Over the course of the study there was a statistically significant increase in the CD4⁺ 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

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TABLE 1. Baseline demographic characteristics

| Characteristic                  | Treatment Group              |
|--------------------------------|-------------------------------|
|                                | IFA                          | HIV-1 Immunogen               |
| Total sample size (no. of subjects) | 99                           | 198                           |
| Age (yr)                        |                               |                               |
| Minimum–maximum                 | 18–46                        | 18–43                         |
| Mean ± SD                       | 29.5 ± 7.1                   | 28.4 ± 6.1                    |
| Median                          | 29                           | 27                            |
| Sex                             |                               |                               |
| % Male                          | 31.3                         | 28.1                          |
| % Female                        | 68.7                         | 71.9                          |
| % Without childbearing potential| 10.1                         | 10.7                          |
| % Homosexual                    | 2.3                          | 3.4                           |
| % IDUa                          | 1.1                          | 0.0                           |
| % HIV-positive partner          | 96.0                         | 88.0                          |
| % Hemophiliac                   | 0.0                          | 0.6                           |
| % Transfusion recipient         | 0.0                          | 1.1                           |
| % Occupational exposure         | None                         | None                          |

* IDU, intravenous drug user.

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

| Group                  | CD4 | CD8 | % CD4/CD8 | Viral load | Body wt |
|------------------------|-----|-----|----------|------------|---------|
|                        | No. of cells/mm³ |       |          | copies/ml  | (kg)    |
| HIV-1 immunogen        | 552.21 | 1,213.54 | 22.42 | 48.95 | 0.487 | 3.66 (n = 82) | 53.70 |
| IFA                    | 545.05 | 1,201.26 | 22.26 | 48.72 | 0.493 | 3.53 (n = 42) | 56.21 |
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 bands for the HIV-1 immunogen-treated group compared to that for the IFA-treated group over the study period. There were no significant differences in laboratory findings, results of physical examinations (data not shown), or adverse events between the two treatment groups, as depicted in Table 6. The most common adverse event was transient local injection site reaction, and this occurrence was similar between the HIV-1 immunogen- and IFA-treated groups (P > 0.05). These reactions subsided without medication.

### 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 immunobased 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.

![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.](http://cvi.asm.org/)
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 superiority 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 assayed 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 (an average of 1 log from the baseline) have been observed in subjects treated with HIV-1 subtype in Thailand. AIDS 12:1521–1527.

TABLE 6. Adverse events at week 40

| Group          | No. of subjects | % Subjects with adverse event | % Subjects with adverse event that was: |
|---------------|----------------|------------------------------|---------------------------------------|
|               |                |                              | Mild        | Moderate                 |
| IFA           | 95             | 20.6                         | 20.6        |                          |
| HIV-1 immunogen | 194           | 16.6                         | 14.2        | 2.4                      |

*P = 0.548 by the Fisher exact test.

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

1. Anand, B., A. Virendra, T. S. Li, C. Blanche, D. Mathay, R. Tubiana, C. Katlama, P. Debre, and J. Leibowitch. 1997. Positive effects of combined antiretroviral therapy on CD4+ T cell homeostasis in advanced HIV disease. Science 277:112–116.

2. Baun, S. E., J. T. Morris, R. V. Gibbons, and R. Cooper. 1999. Reduction in human immunodeficiency virus patient hospitalizations and nontraumatic mortality after adoption of highly active antiretroviral therapy. Mil. Med. 164:609–612.

3. Boulware, D. P. Debre, and J. Leibowitch. 1997. Sequence note: HIV type 1 isolate Z321, the strain used to make a therapeutic HIV type 1 immunogen, is intersubtype recombinant. AIDS Res. Hum. Retroviruses 13:357–361.

4. Choi, D. J., S. Dube, T. P. Spicer, H. B. Slade, F. C. Jensen, and B. I. Poiesz. 1997. Sequence note: HIV type 1 isolate Z321, the strain used to make a therapeutic HIV type 1 immunogen, is intersubtype recombinant. AIDS Res. Hum. Retroviruses 13:357–361.

5. Deeks, S. G., S. W. Lagakos, R. T. Schooley, and P. A. Volberding. 1993. CD4+ lymphocytes are an incomplete surrogate marker for clinical progression in persons with asymptomatic HIV infection taking zidovudine. Ann. Intern. Med. 118:674–680.

6. Choudhuri, T. W., L. Carruth, D. Finzi, X. Shen, J. A. DiGiosepe, H. Taylor, M. Hermankova, K. Chadwick, J. Margolick, T. C. Quinn, T.-H. Kuo, R. Brookmeyer, M. A. Zelger, P. Barditch-Crovo, and R. F. Siliciano. 1997. Quantification of latent tissue reservoirs and total body viral load in HIV-1 infection. Nature 387:183–188.

7. Choudhuri, V. B. Moss, W. Sirawaraporn, B. Smitharaks, R. Suthent, F. C. Jensen, P. Vacharach, J. Grimes, G. Theofan, and D. J. Carlo. 1999. Effect of HIV-specific immune-based therapy in subjects infected with HIV-1 subtype E in Thailand. AIDS 12:1521–1527.

8. Deeks, S. G., M. H. Hecht, M. Swanson, T. Elbeik, R. Loftus, P. T. Cohen, and R. M. Grant. 1999. HIV RNA and CD4 cell count response to protease inhibitor therapy in an urban AIDS clinic: response to both initial and salvage therapy. AIDS 13:F35–F43.

9. Delwart, E. L., E. G. Shaper, J. Loawagie, F. E. McCutchan, M. Grez, H. Russumen-Wagmann, and J. I. Mullins. 1993. Genetic relationships determined by a DNA heteroduplex mobility assay: analysis of HIV-1 env genes. Science 262:1257–1261.

10. Eron, J. J., Jr., M. A. Ashby, M. F. Giordano, M. Chernow, W. M. Reiter, S. G. Deeks, J. P. Lavelle, M. A. Conant, B. G. Yangco, P. G. Pate, R. A. Torres, R. T. Mitsuya, and T. Waddell. 1996. Randomised trial of MNGer1 HIV-1 vaccine in symptomless HIV-1 infection. Lancet 348:1547–1551.

11. Garzino-Demo, A., B. R. Moss, J. B. Margolick, F. Cleghorn, A. Sill, W. A. Blattner, F. Cocchi, D. J. Caro, A. L. DeVico, and R. C. Gallo. 1999. Spontaneous and antigen-induced production of HIV-inhibitory β-chemokines are associated with AIDS-free status. Proc. Natl. Acad. Sci. USA 96:11986–11991.

12. Getchell, J. P., D. R. Hicks, A. Srinivasan, J. L. Heath, D. A. York, M. Mehta, D. N. Forthal, B. J. Mann, and J. B. McCormick. 1987. Human immunodeficiency virus isolated from a serum sample collected in 1976 in Central Africa. J. Infect. Dis. 156:833–837.

13. Getchell, J. P., D. R. Hicks, A. Srinivasan, J. L. Heath, D. A. York, M. Mehta, D. N. Forthal, B. J. Mann, and J. B. McCormick. 1987. Human immunodeficiency virus isolated from a serum sample collected in 1976 in Central Africa. J. Infect. Dis. 156:833–837.
14. Goebel, F. D., J. W., Mannhalter, R. B. Belshe, M. M. Eibel, P. J. Grob, V. de Groottula, P. D. Griffinfly, V. Erle, M. Kunshack, and W. Englund. 1999. Re-combinant gp160 as a therapeutic vaccine for HIV-infection: results of a large randomized, controlled trial. European Multinational IMMUNO AIDS Vaccine Study Group. AIDS 13:1461–1468.

15. Graham, N. M., S. Plantadoti, L. P. Park, J. P. Pifar, C. R. Rinaldo, and J. L. Fahey. 1993. CD4+ lymphocyte response to zidovudine as a predictor of AIDS clinical-free time and survival time. J. Acquir. Immun. Defic. Syndr. 6:1258–1266.

16. Kitchen, A. D., G. F. Mann, J. F. Harrison, and A. J. Zuckerman. 1989. Effect of gamma irradiation on the human immunodeficiency virus and human coagulation proteins. Vox Saf. 56:223–229.

17. Ledergerber, B., M. Egger, M. Opravil, A. Telenti, B. Hirschel, M. Battegay, and J. F. Harrison, and A. J. Zuckerman. 1989. Investigations of the use of beta-propiolactone in virus inactivation. Ann. N. Y. Acad. Sci. 578–594.

18. Levien, A. M., S. Groshen, J. F. Harrison, and A. J. Zuckerman. 1989. Vigorous HIV-1-specific CD4+ T cell responses associated with control of viremia. Science 278:764–774.

19. Mofenson, L. M., D. R. Harris, K. Rich, W. A. Meyer III, J. S. Read, J. Moye, Jr., R. P. Nugent, J. Korelitz, J. Bethel, and S. Palha. 1999. Serum HIV-1 p24 antibody, HIV-1 RNA copy number and CD4 lymphocyte percentage are independently associated with risk of mortality in HIV-1-infected children. National Institute of Child Health and Human Development Intravenous Immunoglobulin Clinical Trial Study Group. AIDS 13:31–39.

20. Monteforto, A., T. Valeria, F. Adorni, B. Castanello, T. Bini, L. Testa, G. Moscatelli, E. Chiesa, S. Ruscono, C. Abeli, S. Sollima, M. Musico, L. Meroni, G. Melli, and M. Moroni. 1999. CD4 cell counts at the third month of the era of combination antiretroviral therapy. AIDS 13:1609–1676.

21. Moore, R. D., and R. E. Chiasson. 1999. Natural history of HIV infection in the era of combination antiretroviral therapy. AIDS 13:1933–1942.

22. Moss, B. R., W. Giemskowska, P. Lanza, J. L. Turner, M. R. Wallace, F. C. Jensen, G. Theodan, S. P. Richieri, and D. J. Carlo. 1997. Cross-clade immune responses after immunization with a whole-killed gp120-depleted human immunodeficiency virus type-1 immune serum in HIV-infected children. J. Infect. Dis. 177:25–34.

23. Nelson, K. E., D. D. Celetanno, S. Emako, R. D. Hoover, C. Beyer, S. Suprasert, S. Kultobunla, and C. Khamboonrug. 1999. Changes in sexual behavior and a decline in HIV infection among young men in Thailand. N. Engl. J. Med. 343:297–303.

24. Nicholson, J., P. Kidd, I. F. Mandy, D. Livnat, J. Kagan. 1996. Three-color supplement to the NIAID guideline for flow cytometric immunophenotyping. Cytometry 26:227–230.

25. Ortil, G. M., D. F. Nom, A. Trkola, J. Binley, X. Jin, S. Bonhoeffer, P. J. Kuebler, S. M. Donohoe, M. A. Demotie, W. M. Kikimoto, T. Ketas, B. Clas, J. J. Heymann, L. Zhang, Y. Cao, A. Hurley, J. P. Moore, D. D. Ho, and M. Markowitz. 1999. HIV-1-specific immune responses in subjects who tempo-

rarily contain virus replication after discontinuation of highly active antiretroviral therapy. J. Clin. Invest. 104:R13–R18.

26. Patterson, B. K., D. J. Carlo, M. H. Kaplan, M. Marecki, S. Paresh, and R. B. Moss. 1999. Cell-associated HIV-1 p24 RNA and DNA in T-helper cell and monocytes in asymptomatic HIV-1-infected subjects on HAART plus an inactivated HIV-1 immunogen. AIDS 13:1607–1611.

27. Pau, C.-P., S. Lee-Thomas, W. Awanini, J. R. George, C. Y. Ou, B. S. Parekh, T. C. Gramale, D. L. Hohnin, and A. E. Daigle, et al. 1993. Highly specific V-3 peptide enzyme immunoassay for serotyping HIV-1 spec-

imens from Thailand. AIDS 7:337–340.

28. Pether, C. G., C. Quinett, D. M. Peterson, M. Connors, R. P. Koop, V. C. Maini, and L. Picker. 1998. Inactivated HIV-1-specific CD4+ T cells are detectable in most individuals with active HIV-1 infection, but decline with prolonged viral suppression. Nat. Med. 4:558–525.

29. Pomaranz, R. J., J. 1999. Primary HIV-1 resistance: a new phase in the epi-

demic? JAMA 282:1177–1179.

30. Pontellis, O., P. Carotenuto, S. R. Kerkhof-Garde, M. T. Roos, I. P. Keet, R. A. Coutinho, J. Goudsmit, and F. Miedema. 1999. Lymphoproliferative response to HIV type I p24 in long-term survivors of human immunodeficiency virus type 1 infection is predictive of persistent AIDS-free infection. AIDS Res. Hum. Retrovir. 15:43–58.

31. Pontellis, O., E. G. Guerra, A. Ammassari, C. Tomino, M. Carlesimo, A. Antinori, E. Tamburrini, A. Prozzo, A. C. Seber, S. Vella, L. Ortona, and F. Aiuti. 1998. Phase II controlled trial of post-exposure immunization with recombinant gp160 versus antiretroviral therapy in asymptomatic HIV-1-infected adults. VaxSyn Protocol Team. AIDS 12:473–480.

32. Prior, C. R., P. Gore, J. Harter, M. Berbaum, C. Duffy, F. Ferre, R. Hancock, P. Lowry, C. Vithig, J. T. Siglitz, D. J. Carlo, S. P. Richieri, and R. M. Zane. 1996. Inactivated HIV-1 immunogen induced CD4+ T cell responses associated with control of viremia. Science 278:1447–1450.

33. Surasengsup, S., S. Kiranandana, K. Wongboonsin, G. P. Garnett, R. M. Anderson, and G. J. van Griensv. 1999. Demographic impact of the HIV epidemic in Thailand. AIDS 13:775–784.

34. Trauger, R. J., F. Ferre, A. E. Daigle, F. C. Jensen, R. B. Moss, S. H. Mueller, S. P. Richieri, H. B. Slade, and D. J. Carlo. 1994. Effect of immunization with inactivated gp120-depleted human immunodeficiency virus type 1 (HIV-1) immunogen on HIV-1 immunity, viral DNA, and percentage of CD4 cells. J. Infect. Dis. 169:1256–1264.

35. Turner, J. L., R. J. Trauger, A. E. Daigle, and D. J. Carlo. 1994. HIV-1 immunogen induction of HIV-1-specific delayed-type hypersensitivity: results of a double-blind, adjuvant-controlled, dose-ranging trial. AIDS 8:1423–1435.

36. UNAIDS and World Health Organization. 1998. Report on the global HIV/ AIDS epidemic. World Health Organization, Geneva, Switzerland.

37. Wit, W. F. M. N., R. van Leeuwen, G. J. Weterling, S. Jurriaans, K. Nauta, R. Steingrover, J. Schuijtemaker, X. Eyssen, D. Fortuin, M. Weeda, F. de Wolf, P. Reiss, S. A. Danner, and J. M. A. Lange. 1999. Outcome and predictors of failure of highly active antiretroviral therapy: one year fol-

low-up of a cohort of human immunodeficiency virus type 1-infected per-

sons. J. Infect. Dis. 179:793–798.

38. Young, N. L., P. Ponglertnppakorn, N. Shaffer, C. Srisak, T. Chaowanachan, V., On-Thern, C. Kittinunvorakoon, A. Bunwattanakul, S. Suksaweang, V. Pobkeeree, J. Punnotok, and T. D. Mastro. 1999. Clinical field site evaluation of the FACSCount for absolute CD3+ CD4+ and CD3+ CD8+ cell count determinations in Thailand. Clin. Diagn. Lab. Immunol. 4:783–788.

39. Zhang, L., B. Ramratnam, K. Tenner-Racz, Y. He, M. Vesnalan, S. Lewis, A. Talal, P. Racz, A. S. Perelson, B. T. Korber, M. Markowitz, D. D. Ho, Y. Guo, M. Duran. A. Hurley, J. Tsai, Y. C. Huang, and C. C. Wang. 1999. Quan-

tifying residual HIV-1 replication in patients receiving combination antiret-

roviral therapy. N. Engl. J. Med. 340:1605–1613.

TREATMENT EFFECTS MONITORING SYSTEM
AUTHOR’S CORRECTION

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