

# Extended Regimen of Combination Recombinant Human Growth Hormone (rhGH), IL-2 and GM-CSF for Immune Reconstruction in Patients with HIV

MJ Scolaro\*, JA Nitahara, B Al-Farouk, T Speights and J Magpayo. \*Let There Be Hope Medical Foundation, Beverly Hills, CA (USA) and The University of Southern California School of Medicine, Los Angeles, CA (USA).

PRESENTED AT THE INTERNATIONAL SYMPOSIUM ON GROWTH HORMONE IN IMMUNE RECONSTITUTION: BASIC AND CLINICAL STUDIES. ST. PETERSBURG BEACH, FLORIDA, OCT. 7-10, 1999.

## ABSTRACT

**Background:** Immunotherapy (rhGH, IL-2, GM-CSF) used in conjunction with highly active anti-retroviral therapy (HAART) provides added benefit towards immune reconstruction in patients with HIV. A standard course of IL-2 consists of 6 one month cycles (one cycle: IL-2 7.5 million IU SC BID pulsed for five days of each month). We report our experience with three patients who exhibited sustained responses in their CD4 profiles during treatment with rhGH (Serostim 6mg SC QD), IL-2, GM-CSF (250-300 mcg SC BID either pulsed monthly with IL-2 or given continuously four times per week) and HAART (>2 nRTI's and >1PI) and thus elected to extend their regimens for a duration of at least 12 cycles (range 12-21 cycles). Complications included mild, self limited flu-like symptoms and minimal localized irritation, none of which prompted discontinuation of treatment. No patients were hospitalized and no opportunistic infections or AIDS related malignancies developed. A clear trend towards increased CD4 percentages and absolute counts is seen which has not waned at 12 to 21 months of therapy (See Table). Our data may indicate that patients require continuous treatment to maintain T-Cell immunity. Significantly, all of the patients maintained HIV viral RNA less than 1000 throughout the study and two of the three patients were transiently negative for DNA (at month six and 12) during the course of treatment.

**Table: Mean CD4 Percentages and Absolute Counts (averaged for 3 month intervals during each of the treatment phases)**

	A	B	C (0-3 mos.)	C (3-6 mos.)	C (6-9 mos.)	C (12-15 mos.)
1.	12%/148	13/364	15/471	18/500	18/407	17/458
2.	18%/438	21/652	23/725	27/640	32.8/866	33/961
3.	25%/430	25/493	26/600	29/629	30/626	31/951

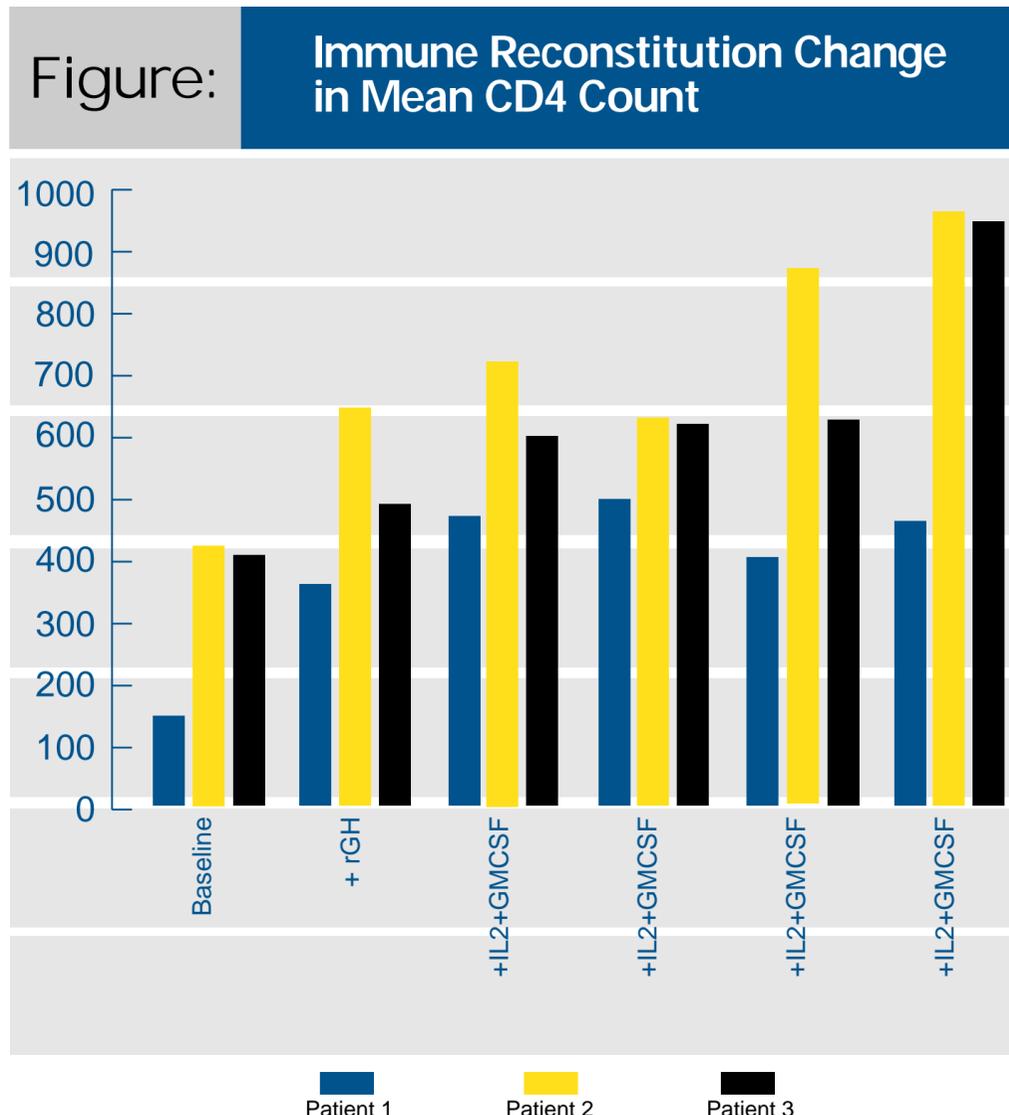
A. before admittance (baseline)  
 B. during treatment with rhGH and HAART  
 C. during combination therapy with HAART, rhGH, IL-2 and GM-CSF

## BACKGROUND

Highly active antiretroviral therapy combined with recombinant human growth hormone (rhGH), GM-CSF, and IL-2 for a period of 6 months (range 5-8 months) provided sustained increases of CD4 percentages and counts during the treatment period as well as during the follow-up after discontinuation of IL-2/GM-CSF.(1) Long term therapy (up to 30 months) with IL-2 and HAART alone has been previously investigated but has yet to be compared with long-term combination immunotherapy.(2) Here we report the laboratory and clinical courses of three HIV positive patients who underwent therapy with combined HAART, rhGH, IL-2 and GM-CSF after having been on antiretroviral therapy alone. The patients were treated with this immunogenic cocktail for a period of 12 to 21 months.

## METHODS

We reviewed three patients who had previously received anti-retroviral therapy and subsequently received HAART, rhGH, and monthly cycles of IL-2 and GM-CSF, who had favorable responses to the therapy and had elected to remain on the IL-2/GM-CSF regimen for a total treatment course of 12 to 21 months. Patients were monitored monthly for viral RNA, CD4 percentages and absolute counts, drug side effects, opportunistic infections or AIDS related malignancies. Baseline lab values while on



\* Each point on the x-axis represents the three-month average CD4 count while on that particular regimen.

anti-retroviral therapy were obtained as the three month average just prior to starting rhGH. Values on HAART/rhGH were taken as a three month average just prior to starting IL-2/GM-CSF. Subsequently, lab values covering a three month period averaged while on the HAART /rhGH/IL-2/GM-CSF combination therapy.

## RESULTS

Three patients were treated for 12 to 21 cycles. Side effects from the therapy were limited to mild flu like symptoms and local irritation from the IL-2/GM-CSF injections. None of the patients developed opportunistic infections or AIDS related malignancies and none were hospitalized. None of the patients discontinued treatment or had treatment discontinued by a physician. All patients remain in treatment. Durable increases in CD4 percentages and absolute counts are depicted (see table in abstract and figure), with dramatic rises in CD4 absolute counts of greater than 100 percent from mean baseline counts. Two of the three patients were observed to have transiently undetectable HIV DNA by PCR.

## CONCLUSIONS

- Extended courses of IL-2 and GM-CSF in our combined immunogenic regimen have produced promising results with sustained increases seen in CD4 counts and percentages.
- Continuous activation of T-Cells may be necessary to maintain elevated CD4 counts.
- Patients tolerated this regimen without mortality or significant morbidity. Viral RNA levels have remained stable throughout and no opportunistic infections or AIDS related malignancies developed.
- Two of three patients became transiently negative for DNA during the treatment. Whether or not this signifies a trend to be found in long-term immunogenic cocktail treatment needs to be studied in a larger population.
- Prospective studies to determine the role of maintenance therapy in immunologic reconstruction therapies utilizing HAART, rhGH, IL-2 and GM-CSF should be undertaken.

## REFERENCES

- Scolaro MJ, et al. Combined recombinant human growth hormone, IL-2 and GM-CSF for immune reconstruction in patients with HIV. In: Abstracts of The Sero Growth Hormone and Immune Reconstruction Symposium, St. Petersburg, FL, October 7-10, 1999.
- Kovacs JA, et al. Controlled trial of IL-2 infusions in patients infected with the human immunodeficiency virus. N Engl J Med 1996; 335:1350.