

**Efficacy of Intermittent Subcutaneous Interleukin-2 (IL-2)  
in Antiviral-experienced HIV-infected Individuals with  
Detectable Viral Load. Three year extended follow-up.**

**G. Tambussi, G.P. Rizzardì, S. Nozza, L. Magenta, G. Poli, A. Lazzarin**

**San Raffaele Scientific Institute. Milano - Italy**

---

# **INTRODUCTION (i)**

---

**The highly active antiretroviral therapy (HAART) is the cornerstone of HIV-1 therapy, and it leads to a remarkable extent of both suppression of HIV-1 replication and immune restoration. However, recent advances in the pathogenesis of the infection, including the analysis of T cell dynamic changes induced by the virus and HIV-1 cellular reservoirs, emphasize the fact that HIV-1 eradication might occur only following a life-long use of HAART.**

**The inability of HAART to achieve eradication of HIV-1 along with the emerging issues of long-term toxicity associated with a life-long commitment to therapy, also calls for the development of alternative therapeutic strategies aimed at achieving the long-term control of the virus**

# **INTRODUCTION (ii)**

---

**We have previously shown in a randomized study (\*) that one year of either high (7.5 MIU BID) or low doses (3 MIU BID) of intermittent subcutaneous IL-2 therapy, induce a substantial expansion of CD4 T cells in patients with CD4 between 200 and 500 cells/ $\mu$ L treated with two nucleoside reverse transcriptase inhibitors plus saquinavir as protease inhibitor.**

**Here we describe the results of an open-label observational study, in which the long-term outcome of 43 patients, who completed the randomized phase of the study and accepted an extended follow-up, has been evaluated.**

\* G. Tambussi et al. JID 2001; 183: 1476–84

# **PATIENTS and METHODS**

---

**Thirty-seven subjects (21 men, 16 women) were followed after the completion of the randomized trial. At the end of the study period, all subjects were evaluated monthly as outpatients, for determination of peripheral CD4 T cell counts, and every 3 months for viremia levels.**

**Patients underwent new cycles of IL-2 (3 MIU twice a day for 5 days every 8 weeks) if the number of circulating CD4<sup>+</sup> T lymphocytes dropped below 70% of the level reached at the end of the study (see table 1), calculated as the mean of the last 2 determinations.**

# **RESULTS (i)**

---

**In table 1 the values of both CD4 and CD4/CD8 ratio reached after one year of administration of IL-2 are shown. During the follow-up, we analyzed the patients together, regardless of the dosages of IL-2 that were used during the above mentioned trial.**

**This analysis refers to 36 month of follow-up. During the observation, 37.8 % (14/37) of patients needed one to three cycles of IL-2 in order to maintain CD4<sup>+</sup> T cells above the 70% of the baseline levels (fig 1).**

## **RESULTS (ii)**

---

**No differences between patients who received new cycles of IL-2 and those who did not were found. The latter maintained a stable number of circulating CD4 (fig. 2) above the levels reached after stopping the main trial.**

**The number of patients with undetectable viremia as well as those with incomplete control of viral replication, was comparable in two groups as shown in figure 3.**

**No AIDS-related events occurred throughout the study.**

# **SUMMARY**

---

**1. We show here that a maintenance regimen with low doses (3 MIU BID) of IL-2, with reasonable toxicity, and well manageable for the patients, may lead to a sustained (over three year) increase in CD4 T cell counts, in those patients previously responding to IL-2.**

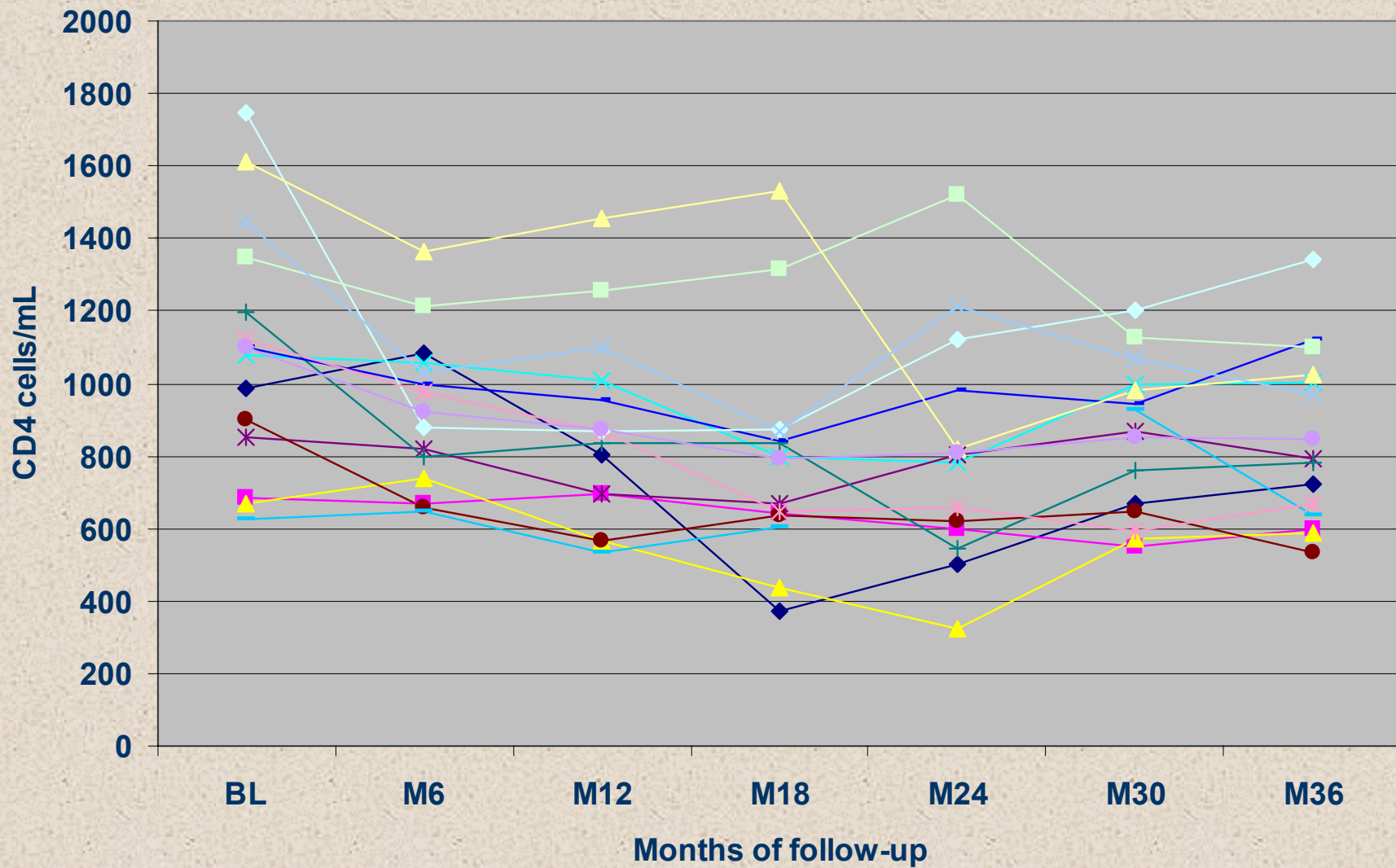
**2. This long term effect has been obtained in both subjects with undetectable viremia and in those with viral replication not fully controlled by antiviral treatment.**

**3. This therapy regimen may also spare the use of HAART.**

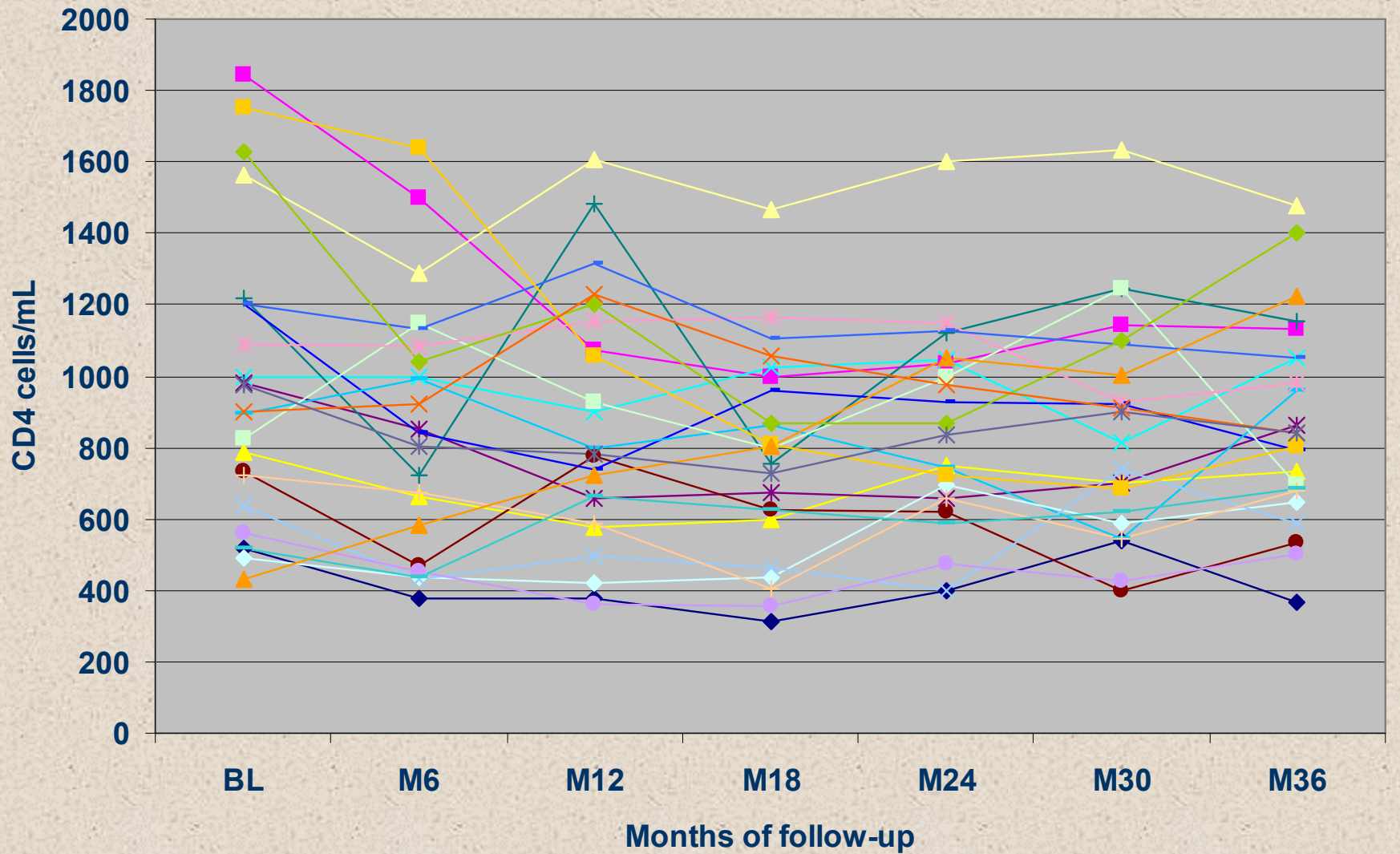
<b>Arm</b>	<b>N° pts</b>	<b>CD4 median (range)</b>	<b>CD4/CD8 median (range)</b>
<b>Civ/HD</b>	<b>14</b>	<b>947 (515-1500)</b>	<b>1.04 (0.43-2.87)</b>
<b>HD</b>	<b>15</b>	<b>825 (490-1280)</b>	<b>1.02 (0.34-1.69)</b>
<b>LD</b>	<b>14</b>	<b>926 (425-1320)</b>	<b>1.17 (0.67-3.10)</b>

---

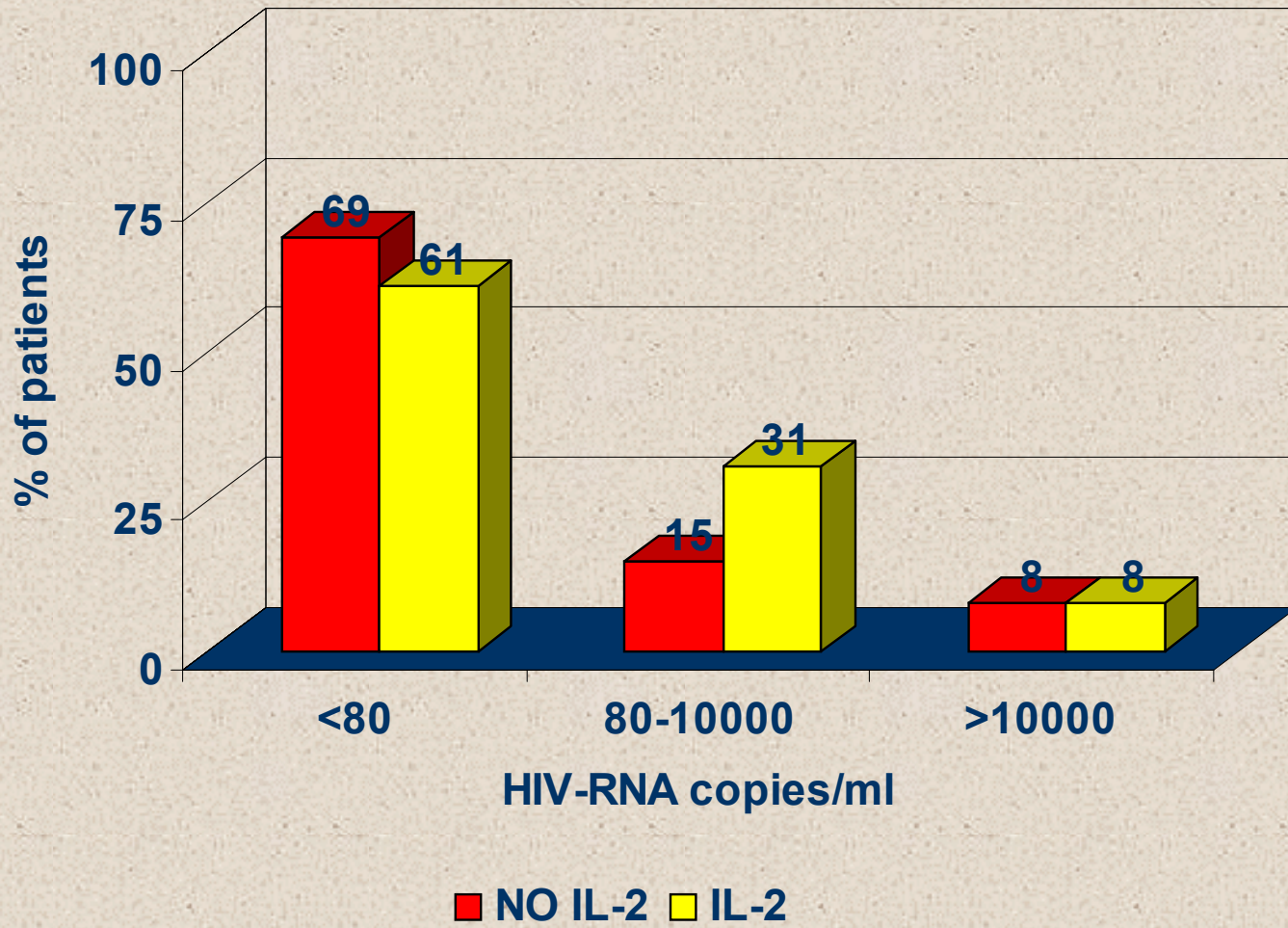
**Table 1.**



**Figure 1.**



**Figure 2.**



**Figure 3.**