

The Virologic Effect of High Dose Recombinant Soluble CD4 (rsCD4) in HIV+ Individuals. T. Schacker, R. Coombs, A. Collier, I. Fox, E. Eggert, K. Nelson, and L. Corey, Departments of Medicine and Laboratory Medicine, University of Washington, Seattle, WA, and Biogen, Inc., Cambridge, MA, USA.

To date, therapeutic effectiveness of recombinant soluble CD4 (rsCD4) has been disappointing, perhaps because inhibition of clinical HIV-1 isolates requires a hundred-fold higher concentration of rsCD4 than laboratory strains. We tested the concept that high dose, IV bolus rsCD4 would demonstrate *in vivo* inhibition of HIV-1 in patients with HIV-1 plasma viremia. Four patients with advanced HIV infection (mean CD4 count 18, range 0-36) with HIV-1 plasma titers  $\geq 350$  TCID<sub>50</sub> were given IV boluses of rsCD4 at 2, 4, 6, 8 and 10 mg/kg at least two days apart. Antiviral effect was determined by serial quantitative plasma cultures at 0, 30, 45, 120 and 240 min. The drug was tolerated well; there were no serious adverse effects. All patients demonstrated reduced plasma virus titers that were dose dependent. Mean logs of TCID<sub>50</sub> at time 0, 30, 45, 120 and 240 min at 2 mg/kg were 3.02, 1.07, 2.14, 2.05 and 2.76 respectively, and at 10 mg/kg were 2.58, .45, .53, .71 and .71 respectively. Three of the patients cleared plasma virus at 30-45 min at doses  $\geq 6$  mg/kg. The percent mean log reduction of virus was:

	<u>2 mg/kg</u>	<u>6 mg/kg</u>	<u>10 mg/kg</u>
30 min	-75.2%	- 71.0%	-85.7%
45 min	+ 4.5%	-100.0%	-83.0%
120 min	- 3.7%	- 71.0%	-77.7%
240 min	+ 3.7%	- 39.0%	-77.7%

The average peak concentration of rsCD4 in Ug/Ml was:

	<u>30 min</u>	<u>2 hours</u>	<u>4 hours</u>
2 mg/kg	32	9	2
4 mg/kg	57	16	5
6 mg/kg	99	26	9
8 mg/kg	163	37	12
10 mg/kg	195	52	14

These data indicate that high dose rsCD4 binds to and clears HIV-1 from plasma of patients with advanced HIV infection with an effect that is dose dependent. Studies of the potential clinical effectiveness of prolonged high dose rsCD4 are warranted.