

National AIDS Treatment Advocacy Project

July 9 in Vancouver--Afternoon session

I just heard a presentation about the 3rd generation Upjohn protease inhibitor---U-140690. The 2nd generation had a problem with protein binding. Upjohn says this 3rd generation has improved potency and antiviral activity, and that there are only 6 steps in the chemical processing of this drug and it has two chiral centers. The drug seemed to have good plasma concentrations well above the EC-90 for 6 to 8 hours in animal models.

In vitro experiments seemed indicate little cross-resistance with ritonavir. And that was with both pre- and post- treatment with ritonavir. Upjohn promised to talk about mutation profile but in this oral presentation they did not talk about it, although they say their protease has a unique mutation profile.

Phase I trials are expected to begin before the end of 1996.

Integrase Inhibitors

An oral presentation was given this afternoon by Edward Robinson of the University of California-Irvine. He said that potent new small molecule candidates have been discovered that block HIV in tissue culture. These are natural products, some of which have been synthesized. One of them is from a Bolivian plant.

He said these compounds are non-toxic and seem to have potent antiviral activity. They appear to block the integrase process. Some of the candidates are more potent than others. However, there are some problems with developing an integrase inhibitor. One limitation may be that once a cell is infected, an integrase inhibitor may be ineffectual. The current crop of potential integrase inhibitors may not be specific enough to inhibit HIV.

I have to go now to attend some evening meetings which will run til 9 pm.