

National AIDS Treatment Advocacy Project

141W94 Double Protease Inhibitor Study and Brief Protease Therapy Discussion

January 11, 1997

Today, Vertex Pharmaceuticals announced the start of a double-protease study combining 141W94 (protease inhibitor licensed to Glaxo Wellcome for development from Vertex). This is an important event for HIV treatment because of the potential for potent therapy using double protease regimens. In addition, pre-clinical in vitro data from Glaxo indicated that saquinavir may reverse 141W94 resistance and possibly be a promising combination.

48 HIV+ individuals will enroll in 24-week open-label phase II trial designed to test tolerability, pharmacokinetics and antiviral efficacy of 3 double-protease regimens: 141W94 plus either saquinavir, indinavir or nelfinavir. A 4th treatment group will use 141W94 + AZT/3TC as a comparison group. Entry criteria include above 200 CD4 and above 20,000 copies/ml viral load.

In 1997, a number of other double protease inhibitor studies will begin. This author, Jules Levin of NATAP, lobbied for protease-protease studies two years ago, but the research was delayed except for the saquinavir/ritonavir study. Unfortunately, research proceeds very slowly and at the dictate of the drug companies. My hope is that protease-protease containing regimens may be potent enough to suppress resistance that may have developed to a particular protease inhibitor. Many individuals are very discouraged because they've developed resistance already to a protease inhibitor. I think there is hope that a potent double protease regimen could address their needs.

Another important focus of research is to improve the dosing regimens of available drugs. Manufacturers will be trying to improve to bid dosing or possibly once a day dosing. DMP-266, the NNRTI from DuPont Merck promises to be once a day dosing.

One 4-drug study has already begun--ritonavir/saquinavir +AZT/3TC--and another should start soon if it hasn't already begun--141W94/1592U89/AZT/3TC. I expect that soon other 4-drug studies will begin. Four drug combinations are already in clinical use. Ritonavir/saquinavir with AZT/3TC or d4T/3TC are popular regimens. A main concern is the tolerability and compliance for such potent and complicated regimens.

We now know that initiation of a potent therapy should include at least two new drugs that have never before been used by the individual. Studies indicate that this is the best way to delay resistance, achieve maximal suppression of viral production and to prolong durability. Individuals are advised to be careful in selecting a regimen and in planning for future treatment. Proper strategies should be planned. In the past, we would add one new drug and its benefits would not last very long. In order to take maximal advantage of today's new more potent therapies, they should be properly used. Don't waste these

opportunities.