## Crixivan + DDI and D4T

In September '97 at the IDSA meeting (Infectious Disease Society of America), R Petrak and others reported the preliminary results of a small open-label study evaluating the triple regimen of indinavir + ddI/d4T in nucleoside experienced and protease naive individuals.

Fifty persons were enrolled; an interim analysis was performed after 27 participants reached 6 months. The analysis was based on the 22 compliant participants. Their median baseline viral load and CD4 count was 25,090 copies/ml and 95 cells. The range of viral load at baseline was <500 to 175,000 copies/ml and the mean was >100,000; two or three individuals had <500 copies at baseline. Nine out of 27 persons had >3 months AZT/3TC experience, however, five of those individuals were eliminated from the analysis because of non-compliance with taking the study drugs.

Participants received indinavir 800 mg every 8 hours, d4T 40 mg every 12 hours, and ddI 400 mg once daily. Study investigators reported a 400 mg dose of ddI taken once daily was well tolerated and resulted in no serious adverse events. Preliminary data from several studies indicate that dosing ddI once a day at 400 mg may be as equally effective as the previously used standard regimen of 200 mg twice daily, as measured by CD4 increases and viral load reductions. In these studies of ddI once daily dosing, ddI was used in a multi-drug regimen. Its use once a day has not been explored using ddI as monotherapy and cannot because of ethical considerations.

To ensure adequate gastric buffering, all once daily doses of ddI were dispensed in 20 mls of a double strength antacid such as Mylanta. Patients were instructed to take indinavir and d4T first, wait one hour, and then take ddI. After taking all medications, the patients were to allow one half-hour before eating. 48% of participants were Caucasion and 44% were African-American.

**Results.** After 6 months the median reduction in viral load from baseline was 1.70 log. Fifty-six percent of participants with prior AZT/3TC experience became undetectable (<500 copies/ml). By one month, 55% of participants reached undetectable and at 6 months, 94% were undetectable. CD4 counts increased from 95 to 245 cells.

Six participants (22%) had an increase in viral load and received nucleoside and protease gentotypic testing. One person showed resistance at positions M184V, T215Y, and L74V; a second person showed resistance at V82A and T215Y/F; a third person had a wild-type virus (no resistance mutations). The results for the other three persons were not available ( ed note - at this point in its development, genotypic testing results may be of questionable utility in treatment decision making).

**Adverse events and opportunistic infections**. No serious adverse events were reported. Two individuals developed peripheral neuropathy which resolved after being taken off the study; Two individuals complained of abdominal pains which resolved without therapy and three people experienced opportunistic infections while on study meds. All three had the following infections prior to enrolling in study: 2, Herpes Zoster; 1, Herpes Simplex Virus.