National AIDS Treatment Advocacy Project

Nelfinavir: preliminary efficacy and safety data update 9/3/96

In Vancouver, at a satellite symposium to the Int'l. AIDS Conference in July '96, Agouron Pharmaceuticals presented updated data of their phase II trial # 510 which studies d4T in combination with nelfinavir (ViraceptTM, VCT); the new data is for a small number of study subjects and extends out to 5 months. Prior to this report, NATAP's most recent article about nelfinavir was written in June and reported 2 month's data; it may offer a fuller perspective of the development plans for nelfinavir. In Vancouver, Agouron reported new data indicating that nelfinavir's resistance profile was different than previously reported and may be unique from those of other protease inhibitors.

David Ho and Martin Markowitz of the Aaron Diamond AIDS Research Center are conducting an ongoing trial of nelfinavir in combination with AZT and 3TC in treatment-naive but chronically infected individuals; the preliminary data is available on the web-site in the article "Antiretroviral-Naive Subjects Chronically Infected With HIV-1: Triple therapy with nelfinavir in combination with AZT and 3TC."

Study #510
HIV+ study subjects are:

- d4T-naive
- protease inhibitor naive
- CD4 above 200
- plasma HIV RNA (viral load above 15,000 copies/ml)

Baseline characteristics:

	d4T	d4T+ 500 mg VCT	d4T+ 750 mg VCT	d4T+ 1000 mg VCT
mean RNA (copies/ml)	66,445	61,467	80,386	56,448
mean CD4 (cells/mm3)	390	367	334	310

As you can see, the study subjects are a relatively healthy group.

Thirty-six individuals were randomized to receive d4T monotherapy for 2 months (after 2 months nelfinavir was added to d4T for these individuals), or d4T in combination with nelfinavir at one of three doses--500 mg TID, 750 mg TID or 100 mg TID. Again, the following preliminary data are based upon a small number of study subjects. The larger phase III studies enrolled in the 1st QTR of '96 and are ongoing. Data from a smaller group of study subjects, as in this instance, can vary from the results of studies which include much larger numbers of participants. Therefore, the data that emerges from the phase III pre-accelerated approval studies should be more reliable. The FDA accelerated approval hearings are expected to be held in the 1st QTR of '97, where data will be presented from these larger studies. In the interim, whenever data may be made available from nelfinavir studies, NATAP will report it.

HIV RNA (viral load) reductions from baseline:
(n= the number of study subjects)

	2 months	5 months
d4T monotherapy (n=6)	-0.80 log	-
d4T+ added VCT tid (n=6)	-	-1.70 log
d4T+500 mg VCT tid	-1.70 (n=9)	-1.30 (n=6)
d4T+750 mg VCT tid	-2.20 (n=8)	-1.70 (n=6)
d4T+1000 mg VCT tid	-2.40 (n=8)	-1.90 (=6)

CD4 increases from baseline:

	2 months	5 months
d4T monotherapy	+70	-
d4T+ added VCT tid	+210	-
d4T+500 mg VCT tid	+100	+110
d4T+750 mg VCT tid	+140	+87
d4T+1000 mg VCT tid	+180	+110

Safety:

	d4T n=8	VCT 500 mg tid + d4T n=11	VCT 750 mg tid n=10 +d4T	VCT 1000 mg tid +d4T n=10
diarrhea	-	18%	30%	30%
asthenia	-	-	-	20%
headache	-	-	-	10%

rash	-	-	10%	-

* equal to or greater than grade 2 (moderate) severity, possibly related to nelfinavir

There was one report of increased CPK by one patient on d4T alone during the 60-day core study. After 60 days there was a grade 3 elevation in GGT during month 5.