[National AIDS Treatment Advocacy Project]

Birmingham Update from NATAP: Nov 20

Nevirapine lymph node biopsy results--
Dr. Marianne Harris, of the University of British Columbia, reported the results of lymph node biopsies on a group of patients in the nevirapine study of nevirapine triple therapy in treatment-naive individuals.

These results are after at least 1 year of treatment (median 16 months, range 12-18 months).

		PLASMA -VIRAL LOAD				LYMPH NODE -VIRAL LOAD	
	N	CD 4	plasma RNA	below 500 copies	below 20copies	below 7 log	
Untreated	(10)	410	4.68 log	0/10	0/10	8.31 log	0/10
AZT/NVP	(5)	280	4.43	0/5	0/5	7.86	1/5
AZT/ddI	(4)	495	2.91	2/4	0/4	7.43	0/4
NVP/AZT/ddI	(6)	555	3.73	2/6	1/6	7.04	3/6*

* 2/6 in the triple therapy group were defined as non-compliant: therefore, in column #3, for those who were compliant with taking study drugs 2/4 were below 500 plasma RNA copies; in the fourth column 1/4 were below 20 copies; in the 6th column 3/4 were below 7 log (undetectable-explained below) and Dr. Harris reported that the 4th person was just above detectability (12,000 copies per mg of tissue).

The Roche Amplicor PCR test was used for the plasma RNA testing in column #3 of the chart with a lower limit of detection of 500 copies/ml (or, 2.7 log). The Roche ultra-direct assay (lower limit of detection of 20 copies; or, 1.3 log) was used for the values in column #4. The Chiron bDNA 1st generation test (lower limit of detection of 10,000 copies) was used for the lymph node RNA values in the last column. This test was used because it was the only one available at the time the study was conducted. The results are encouraging, but since the lower limit of detection of the lymph nose test was so high we don't know the true level of virus burden in the lymph node. Unlike blood samples where

you can save the sample and run another test, the lymph node sample is lost after one test. Future lymph node studies will use technology that allows measuring to lower levels of detection.

The CD4 and plasma RNA values in the chart above were done on the same day as the lymph node biopsies. So, all chart values were obtained on the same day. Unfortunately, no lymph node viral burden values were obtained at the baseline of the study prior to study treatment.

The plasma RNA declines during the course of therapy in the study correlate (statistically significant) with the reductions in lymph node viral burden (RNA). The plasma RNA levels done on the day of the lymph node biopsies indicate a trend in correlation with the lymph node RNA levels.

The language currently used for expressing the values of viral burden in lymph tissue is foreign to me and others, and is not easily understood; but, the actual values follow. The 8.31 log value in column #5 equals 206 million copies per gram of lymph tissue or 206,000 copies per mg of lymph tissue; the 7.86 log value equals 72 million copies per gram of tissue or 72,000 copies per mg of tissue; 7.43 log equals 27 million copies per gram of tissue or 27,000 copies per mg of tissue; 7.04 log equals 11 million copies per gram of tissue or 11,000 copies per mg of tissue. In the last column, 7 log (undetectable-10,000 copies) is equal to 10 million copies per gram of tissue or 10,000 copies per mg of tissue.

As we are able to reduce plasma viral load to undetectable levels, it becomes vitally important to be able to evaluate viral burden in other organs or compartments of the body to obtain a closer assessment of the effect of antiretroviral therapy. Treating physicians, researchers, people with HIV or AIDS, insurance re-imbursers and others will want to know the full extent of the effect of treatment. Eventually, we may learn that lowering plasma viral load to below 20 copies correlates with viral suppression or possibly eradication in certain or all sites; if that correlation emerges, we may only have to measure plasma RNA.