Day One of Conference Monday, July 8

Today was the first day of actual conference meetings. I'm writing this report to you from beautiful hot downtown Vancouver, at 3:30 pm, in between afternoon sessions, in the Vancouver Trade and Convention Center. Parked right outside is a passenger ship headed for Alaska.

It is very difficult if not impossible to cover all the important meetings. Frequently, there are 2 and 3 meetings being simultaneously conducted. Sunday, at 9 am I attended a pre-conference meeting sponsored by Merck; at 11:30 to 2 pm, I attended a pre-conference meeting sponsored by Glaxo Wellcome.

The title of the meeting sponsored by Merck was "Changing the Paradigm: Emerging Strategies in the Treatment of HIV disease." David Ho, MD, of the Aaron Diamond AIDS Research Center discussed his work on "viral dynamics and HIV." He talked about the initial burst of virus that generally peaks within the first months after sero-conversion; after which the immune system creates an equilibrium with viral replication, whereby viral load settles in at a level called the "set point." For an in-depth discussion of this concept you can read the article "Viral Load: Important Information," or the more updated booklet recently published by NATAP called "Perspectives on Viral Load and When To Initiate Therapy."

Viral load can settle (at the "set point") at a low, medium or high level for any given individual. However, from the beginning of infection viral replication is very productive. David Ho suggested that individuals should "hit hard and early" with treatment. His reasoning, and the reasoning of other researchers who support this position, is that your immune system is still intact, your CD4s are still preserved, your virus is relatively homogenous and therefore more responsive to therapy. Other researchers recommend taking a more cautious approach. They suggest not spending your treatment options, but that keeping viral load in check at a "lower level" may be adequate. The researchers that recommend "hit early and hard" say other drugs and treatment options will be available. At this point in time, this is a controversial subject, which is discussed in more depth in the NATAP booklet--"Perspectives on Viral Load.....," in the section titled "When to Initiate Therapy??"

At the Merck, and immediately afterwards at the Glaxo Wellcome meeting, John Mellors talked about the correlation between viral load both prior to treatment and subsequent to treatment and its correlation to disease progression and survival. He said viral load, although not the perfect predictor of disease progression because other factors are also involved, is the best predictor of disease progression and mortality. Although, he said, CD4 and viral load together is a better predictor. Again, this is discussed in more depth in the aforementioned NATAP booklet "Perspectives on Viral Load."
On Thursday at a "late-breaker" session, Dr. Roy Gulick of NYU will present updated information on study subjects in the Merck 035 study of AZT/3TC and indinavir in AZT-experienced individuals. But today, Merck talked about the results of a monotherapy study that has previously been presented, wherein a small number of patients showed sustained improvements in CD4 and viral load out to 48 weeks. At the currently recommended dose of 800 mg taken every 8 hours: at 24 weeks 6/14 (43%) subjects had undetectable viral load (under 200 copies, as measured by PCR; at 48 weeks, 7/13 (54%) had undetectable viral load. The median baseline RNA for this group was 70,795 RNA copies, and the median RNA reduction was 2.3 log at 24 weeks and 2.6 log at 48 weeks; the baseline median CD4 was 250, and the median increase in CD4 was 80 at 24 weeks and 85 at 48 weeks. It is important to keep in mind that the amount of individuals upon which this data is based is small. And, at some point in the study, individuals were permitted to add other therapies.

Also, Merck presented previously presented data indicating that multi-drug therapy delayed the development of resistance. This is addressed in more depth in the article "Can HIV be Eradicated from the Infected Individual?" If you can suppress viral replication to a low enough level, resistance is delayed.

At the Glaxo Wellcome meeting, data was presented from the studies of AZT/3TC. An analysis of 4 AZT/3TC studies combined together compared AZT/3TC to the combined control groups of AZT and AZT/ddC; 57/569 (9.9%) individuals taking AZT/3TC progressed to AIDS while 61/316 (19.2%) taking AZT or AZT/ddC progressed to AIDS; that is a 52% reduction in progression to AIDS. Updated data on 1592U89 will be presented at this Conference (see 1592U89--a New Antiviral for HIV in Development).

A constant theme at this Conference is that combination therapy is the best way to treat HIV infection, and that treatment with AZT monotherapy or monotherapy with any approved drug is inadequate. The question remaining is when to start therapy and with what?

At the Agouron sponsored meeting, at 6 am Monday morning, new resistance data was presented for their protease inhibitor, nelfinavir. They took virus from a small number of individuals in which resistance to nelfinavir was "created," and exposed that virus to ritonavir, indinavir, 141W94 (Glaxo Wellcome's protease inhibitor) and saquinavir. They found that the nelfinavir resistant virus was not cross-resistant to any of those other 4 protease inhibitors. Agouron reported the discovery of a unique mutation profile for nelfinavir that differs from that reported previously. There was controversy among observers as to the reliability of the data, but a noted researcher said, "the data is the data." These findings need to be monitored as they could have important implications. Preliminary study results of a small number of individuals taking nelfinavir and d4T were presented. At 5 months, Agouron reported RNA reductions of 1.8 log to 2.4 log, and CD4 improvements of over 100 cells. David Ho presented preliminary data from a small open-label pilot study of AZT/3TC and nelfinavir of treatment-naive individuals. He reported 11/11 subjects had undetectable RNA at 16 weeks. The viral load test he used measured as low as 25 RNA copies; one of the study subjects had 600,000 RNA copies at baseline.

Tonight, I attended an AMFAR reception where Liz Taylor was present to make a
speech. She said the federal government's refusal to support needle exchange programs is "a measured act of pre-meditated murder."