Altis I & II: a pilot open label study of d4T/3TC in treatment-naive and experienced individuals

Christine Katlama, MD, of the Hospital Pitie-Salpetriere in Paris-France, reported 24 week data for both treatment-naive and experienced individuals who were treated with d4T/3TC. The study was designed for those with CD4 count between 50-400 and viral load above 15,000. The d4T dose was either 40 or 30 mg bid (twice per day), and the 3TC dose was 150 mg bid . After 6 months of treatment, the Altis Plus Study began where participants in Altis I and II with HIV RNA above 3,000 were permitted to add ritonavir (n=39); those with HIV RNA below 3,000 remained on d4T/3TC (n=35); follow-up data will be reported. Exclusion criteria included: neuropathy above grade 2; liver enzymes greater than 5 times normal.

Individuals in Altis I had no prior antiretroviral treatment. While, those in Altis II had experience using AZT, ddI, ddC either as monotherapy or in combination. In Altis II, 49% had experience with monotherapy, while 51% had combination experience: 34% with AZT/ddC, 17% with AZT/ddI. The median duration of prior treatment-experience for those in Altis II was 35 months.

Of the Altis II participants (n=41), 41% were asymptomatic and 59% were classified as CDC Group II-III. Of the Altis I participants (n=42), 71% were asymptomatic and 29% were classified as CDC Group II-III.

The median baseline characteristics and changes in CD4 and viral load are:

	Altis I	**Altis II**
CD4 baseline- increase at 24 weeks-	 258 CD4 count (n=42) +108 CD4 (n=42)	 172 CD4 count (n=41) +46 CD4 (n=40)
HIV RNA baseline- peak decrease by wk 4- decrease at 24 weeks- % below 3000 copies- % below 200 copies-	 76,500 copies/ml (4.88 log) (n=42) -2.0 log (n=42) -1.66 log (n=42) 57% 21%	 91,255 copies/ml (4.96 log) (n=41) -1.30 log (n=40) -0.66 log (n=40) 22% 5%

In Altis I, 95% of participants had greater than a .60 log reduction from baseline. The following analysis suggests that baseline viral load may have some predictive value of how low oneÕs viral load might be reduced.

Predictive Factors For Antiviral Response	
Altis I	**% with HIV RNA below 3000 copies/ml**
baseline HIV RNA (copies/ml):	29%

-above 120,000 -40-120,000 -below 40,000	64% 79%
Altis II prior treatment experience: -combination experience -monotherapy experience	**% with HIV RNA reduction greater than 0.60 log** 22% 78%

Commentary--In a recent report on this web site --The Duration of Viral Suppression is predicted by Viral Load During Protease Therapy: a retrospective analysis of individuals in 3 ritonavir clinical studies whose viral load rebounded--the authors address the question of factors predictive of successful therapy.

Adverse Events in the Altis I and II study		
	Grade 1-2	**Grade 3-4**
Hematological - eosinophils - thrombopenia	 3 (3.6%) 1 (1.2%)	 0 0
Elevated AST/ALT (liver enzymes)	 30 (36%)	 6 (7.2)
Increased CPK	5 (6%)	4 (4.8&37;)
Increased LDH Increased amylase/lipase Headaches Neurological symptoms -parasthesias -canal tunnel syndrome Arthralgias/myalgias Rash	18 (21.6%) 8 (9.6%) 3 (3.6%) 8 (9.6%) 1 (1.2%) 3 (3.6%) 6 (7.2%)	1 (1.2%) 1 (1.2%) 1 (1.2%) 0 0 1 (1.2%) 0
Nausea Diarrhea	3 (3.6%) 2 (2.4%)	0 0

Clinical Events- One person in Altis I developed PCP; one person in Altis II developed lymphoma; one person in Altis 2 had Stevens-Johnson Syndrome which study investigators said was due to dapsone.