RITONAVIR + SAQUINAVIR

Abstract (Birmingham, England)

At the 3rd International Congress on Drug Therapy in HIV Infection, in early November '96, Dr. William Cameron of the University of Ottawa in Canada presented data from extended follow-up of participants in both Groups I and II, for the aforementioned study of individuals receiving the combination of the two protease inhibitors.

The data for Group I (treatment arm A--400 mg bid RTV+400 mg bid SQV, and treatment arm B--600 mg bid RTV+400 mg bid SQV) extends to 20 weeks. The data for Group II (treatment arm C--400 mg tid RTV+400 mg tid SQV, and treatment arm D--600 mg bid RTV+600 mg bid SQV) extends to 12 weeks for this data set.

For the participants in treatment arm A, the median CD4 increase from baseline and median viral load decrease at 20 weeks are 75 CD4 and 3.21 log. For the participants in arm B, the median CD4 increase was 120 cells from baseline; the median decrease from baseline in viral load was 3.17 log. About 80% of the 51 evaluable participants from arms A and B were below the limit of detection, for viral load, of 200 copies/ml.

The participants in treatment arm C, at 12 weeks, experienced a median reduction in viral load from baseline of 2.68 log, and a median increase from baseline in CD4 of about 100. The participants in arm D experienced a median CD4 increase of 120, and a median reduction in viral load of 2.73. At 12 weeks, for arms C and D, the proportion of evaluable study participants below the limit of detection, for viral load, was 75% and 70%, respectively.

Commentary: The differences in viral load and CD4 between groups or arms are not statistically significant. It is uncertain which of the dose regimens may be superior simply by comparing CD4 and viral load differences.

Safety and Tolerability
Table 6

RTV dose (mg):	**400 bid**	**600 bid**	**400 tid**	**600 bid**
SQV dose (mg):	**400 bid (n=35)**	**400 bid (n=36)**	**400 tid (n=34)**	**600 bid (n=34)**

ADE (at least moderate and possibly related)				
Circumoral parasthesia	1	3	0	3
Diarrhea	4	6	4	9
Asthenia	1	3	8	8
Nausea	5	5	2	7
Taste perversion	1	0	2	2
Peripheral parasthesia	1	4	0	1
Lab event (grade 3 or 4)				
SGOT (AST) Increase	1*	1	2	5
SGPT (ALT)	1*	2	2	6
GGT	2	4	1	5
Triglyceride	5*	9	10	9
Discontinuation due to ADE	1	4	5	0
*Includes one patient that dose escalated to 600mg bid RTV				

Transaminase Elevations

Table 7

Category	**Pts with**	**Total patients**

	grade 3/4 SGPT (ALT)	
All patients	11	139
By treatment assignment:		
RTV 400 bid+SQV 400 bid	1	35
RTV 600 bid+SQV 400 bid	2	36
RTV 400 tid+SQV 400 tid	1	34
RTV 600 bid+SQV 600 bid	7	34
By baseline liver status		
Normal baseline SGPT and HBsAg- and HCV ab-	2	85
Abnormal baseline SGPT	7	41
Hep Bs Ag+	4	7
Hep C Ab+	4	10

Commentary: In table 6, the side effects and lab abnormalties profiles are more favorable for the 400/400 bid group. Note the discontinuations in the 400/400 tid group. The 600/600 group have the highest incidence of ADEs and lab abormalities. In table 7, participants with normal baseline LFTs (SGPT) and who are Hepatitis B and Hepatitis C antibody negative, have a lower incidence of elevations of LFTs. Those with Hepatitis B or C antibody at baseline indicate higher incidence of elevated LFTs. But, it appears to be the 600/600 bid regimen that causes the highest incidence of LFT elevation. 20 weeks data is normally too short upon which to base treatment decision making. However, when selecting a dose regimen, you may want to consider both--the combination's efficacy (CD4 and viral load) as well as the safety and tolerability profile.

Cameron showed a graph indicating that the drug concentration in the plasma (blood levels) of 600 mg bid dose of ritonavir is higher than the plasma concentrations of 400 mg bid ritonavir. Additionally, the chart indicated using 600 mg bid ritonavir raises the both the plasma concentration level and trough level of saquinavir above those resulting from combining only 400 mg bid ritonavir with the same dose of saquinavir.