Ritonavir + AZT + ddC

Abstract (Birmingham, England) November 1996

This is the 72-week follow-up data of this study, reported by Dr. Jean-Pierre Chauvin of Abbott-France.

This is an open-label pilot study of antiretroviral-naive individuals with moderately advanced HIV. All study participants received open-label 600 mg twice per day (every 12 hrs) of ritonavir for 14 days followed by the addition of 200 mg three times per day (every 8 hrs) of AZT and 0.75 mg three times per day of ddC. Study participants initiated therapy with the ritonavir liquid formulation, and were switched to the oral gel capsule formulation of ritonavir after 54 weeks.

A total of 32 patients were enrolled with the following entry criteria: baseline CD4 counts of between 50 and 250; or, a drop of 200 cells to a level of less than 350 cells over a recent 6 month period; or, 250 to 350 cells with symptoms.

Mean and median baseline CD4 counts were 170 and 152, respectively; mean plasma viral load and cellular viral load levels were 4.7 log (about 50,000 copies/ml-- the Roche RT-PCR test with lower limit of detection of 200 copies/ml), and 3.2 logs per 107 cells (peripheral blood mononuclear cell culture), respectively.

Chauvin reported 11 patient discontinuations after 24 weeks-- 6 with ritonavir-related adverse events and 5 with non-ritonavir related adverse events; 21 completed 24 weeks; subsequently, there were 4 additional discontinuations as 17 completed 72 weeks.

Plasma Viral Load. At 72 weeks, the mean reduction in viral load was about 1.9 logs from baseline for 17 evaluable study participants, compared to decreases of 1.94 at 24 weeks, and 1.6 at 52 weeks. The proportion of patients with viral load below the lower limit of detection (200 copies/ml) was about 52% (n=17) at 72 weeks, compared to about 48% at 28 weeks, and 22% at 52 weeks.

Mean cellular viremia (infectious cells) was about 2.5 logs below baseline at 72 weeks, compared to decreases of 1.06 logs at week 2, 2.41 logs at week 24, and about 2.4 logs at 52 weeks. About 70% of patients (n=17) had negative HIV cell cultures (defined as less than 5 infectious cells per 107 PBMC) at week 72, compared to about 60% at week 60 (n=15).

CD4. The mean CD4 increases from baseline were about 160 at week 72 (n=17), compared to increases of 130 at week 24, and 170 at week 52.

The dose escalation method, which is now recommended for ritonavir, was not used in this study. A total of 6 patients discontinued due to GI intolerance; two patients discontinued due to liver toxicity (one grade III, one grade IV); several patients experienced elevated triglyceride levels.

Commentary: When comparing viral load changes and the proportion with undetectable viral load from the time point of prior to 52 weeks and after 52 weeks, bear in mind that at about 52 weeks, patients were switched from the oral liquid ritonavir to the gel capsules. Apparently, compliance may have improved after the switch to the gel capsule.