



# in the news

The 15<sup>th</sup> Conference on Retroviruses and Opportunistic Infections (CROI) was held in Boston from February 3<sup>rd</sup> to 6<sup>th</sup>, 2008.

**Dr. Harold Dion**, co-editor-in-chief of *Relay*, was there.

## Heart disease and ARVs

The most surprising results at CROI came from the DAD study (Data Collection of Adverse Effects on Anti-HIV Drugs). This study is a collaboration between 11 groups collecting clinical data on more than 33,000 HIV-infected persons from Europe, Australia and the United States. Previously published data from this study established a link between protease inhibitors (PIs) and the risk of developing cardiovascular (CV) disease.



In order to better understand this increased risk, the researchers then looked at whether nucleoside reverse transcriptase inhibitors (NRTIs) were also associated with a higher risk of CV disease. They hypothesized that zidovudine (AZT) and stavudine (d4T) would increase risk because of their association with **dyslipidemia** (high cholesterol and triglycerides) and insulin resistance (or pre-diabetes — see In Brief on page 7), two factors known to increase CV risk.

To date, 517 cases of myocardial infarction (MI or heart attack) have been reported in the study. Researchers analyzed the data to see whether, for each of the different NRTIs, total length of time on the drug, recent exposure (currently under treatment or under treatment in the past six months) or previous exposure (treatment stopped more than six months before) had an impact on CV risk. Tenofovir and emtricitabine (FTC) were not evaluated.

Unexpectedly, results showed that recent use of abacavir (ABC) or didanosine (ddl) were associated with a significant increase in CV risk (90% and 49% increases, respectively) but that AZT, d4T and 3TC were not. Tenofovir and emtricitabine (FTC) were not evaluated as there were not enough patients included in the study who were taking these drugs. Neither previous treatment nor total length of treatment increased the risk.

The authors stressed the importance of putting these results in perspective. First, this was an observational study, and only a randomized clinical trial can really confirm the link between use of a particular product and a specific side effect. As well, the absolute risk of MI in the group as a whole was still quite low (1.6% over 5 years) and was seen mainly in people already at risk for cardiovascular disease (male sex, age over 45, diabetes, high blood pressure and dyslipidemia). Lastly, these results have never before been reported in other studies.

More data are needed before these results influence clinical practice. In the meantime, the authors feel that the two NRTIs in question, abacavir and ddl, may not be an ideal first choice of treatment for people with risk factors for CV disease if other treatment options are available. As well, the authors state that people with cardiovascular risk factors who are already on these treatments may benefit from a change in regimen if an equally effective and tolerable alternative is available. Some researchers, commenting on the study, emphasize that this type of study can show trends but cannot show cause and effect because too many variables are at play. They recommend waiting for more specific results before changing people's regimens.

## PI regimens

Current guidelines from the Department of Health and Human Services (DHHS) in the U.S. recommend atazanavir (Reyataz<sup>®</sup>) boosted by ritonavir (Norvir<sup>®</sup>) as one of the preferred PI regimens (the boosted regimen is referred to as ATV/r). However, until now, the data supporting this recommendation came primarily from very small studies.

At CROI, Dr. Molina and colleagues presented results from the CASTLE study comparing ATV/r (Reyataz) and LPV/r (Kaletra<sup>®</sup>), combined with tenofovir (Viread<sup>®</sup>) and emtricitabine (Emtriva<sup>®</sup>), in 883 treatment-naive people (who have never taken antiretrovirals before). Before starting treatment, the two groups had similar characteristics (average CD4 cell counts of about 200, and 50% with viral load of >100 000 copies/mL).

After 48 weeks, people on both treatments showed comparable results. Nearly the same number of people in each group had undetectable viral loads (< 50 copies/mL: tests cannot detect the virus at less than 50 copies/mL) — 78% of those on boosted atazanavir, and 76% on Kaletra. CD4 counts increased by 203 cells in the ATV/r group and by 213 cells in the LPV/r group. There were very few treatment interruptions due to side effects, and these were essentially equal between the two treatment groups (2% and 3%). Jaundice and increases in bilirubin (a liver enzyme) were more frequent in the ATV/r group, while nausea and diarrhea were more frequently associated with LPV/r. Fewer people receiving boosted Reyataz needed to start a treatment for hyperlipidemia (2% vs 7% with Kaletra).

These results confirm that treatment with ritonavir-boosted Reyataz is at least as effective as treatment with Kaletra in treatment-naive patients over one year and that it has certain benefits for some people (fewer GI symptoms and a better lipid profile). **R**