AIDSmeds in Montreal: Notes from the 16th Conference on Retroviruses and Opportunistic Infections

The biggest HIV science conference of the year proves that there's a lot more to living long and well with HIV than antiretrovirals. We present highlights from the 16th CROI in Montreal.

March 3, 2009 By Tim Horn

For the first time in recent history, antiretroviral (ARV) research was not the focal point of the annual Conference on Retroviruses and Opportunistic Infections (CROI), which took place February 8 to 11 in Montreal. While some delegates walking the halls of the Palais des Congrès grumbled that the lack of new ARV data hinted ominously of a depleted pipeline, the lack of pharmaceutical jockeying provided a little more breathing room for research that might not otherwise have made headlines.

What follows are intriguing highlights from this year's conference, the 16th CROI. For an even more complete list of our coverage—video interviews are still being added—check out our conference page or click on the links below:

Combating Complications

While ARV therapy has tremendously improved the length and quality of HIV-positive people's lives, side effects and a high risk of non-AIDS-related complications remain all too real. In fact, researchers at CROI estimate that half of all premature deaths among people with HIV are not related to AIDS, but instead stem from other medical issues that are becoming increasingly prevalent among those living with the virus. As researchers learn more about these health challenges, they also stumble upon useful clues to prevent and manage them.

Cardio Risk

- Two major studies reported at CROI confirm earlier reports that ongoing use of the protease inhibitor Kaletra (lopinavir/ritonavir)—as well as Lexiva (fosamprenavir), Agenerase (amprenavir) or Crixivan (indinavir)—increases the risk of a heart attack, independent of other factors associated with cardiovascular disease. These studies—plus an Australian clinical trial—also mirror previous reports establishing a link between cardiovascular disease (CVD) and

abacavir (found in Ziagen, Epzicom and Trizivir). Conversely, the results of a government-funded AIDS Clinical Trials Group study failed to find a link between abacavir and a higher risk of a heart attack.

- Seeking to unravel the mystery surrounding heart problems in people taking abacavir, researchers have found that HIV-positive men and women on the drug do not have higher levels of blood vessel inflammation—a possible explanation put forth in the past. But according to another study reported at CROI, those on abacavir may have overly reactive blood clotting factors that may lead to heart attacks.

- 16th CROI delegates also heard new evidence that HIV itself can harden the arteries as much as other risk factors, including age, smoking and diabetes, do. According to University of California in San Francisco (UCSF) researcher Carl Grunfeld, MD, highly specific scans of the carotid arteries of people living with HIV found significant blood vessel thickening compared with HIV-negative controls—a finding that has been overlooked by other groups and may help explain the higher risk of CVD in people with the virus, even without other risk factors.

- Results of one study showed that many risk factors that help raise the risk of death are modifiable, suggesting that behavioral changes and proper medical care can extend life. Whether it's CVD or non-AIDS-related cancers, smoking, low body weight, diabetes or high blood pressure—all of which can be controlled—they each doubled, tripled or quadrupled the risk of death. These findings, researcher Colette Smith, MD, of the University College of London Medical School, argued, "reiterate the importance of addressing traditional, non-HIV specific risk factors in order to further reduce death rates in HIV-positive populations."

- Smoking tops the list of modifiable risk factors targeted by many public health efforts—there's no shortage of data linking cigarettes to substantially higher rates of CVD, cancers and lung disease in relatively young HIV-positive people. But it can be a difficult habit for HIV-positive

people to break, according to one CROI study. While no more than 10 percent of individuals participating in one of two Rhode Island programs abstained from smoking for six months, higher success rates among Hispanics compared with other racial or ethnic groups were encouraging.

Disturbing Cancer Answers

- From the U.S. Centers for Disease Control and Prevention (CDC): Roughly 25 percent of HIV-positive women, with their higher risk of cervical cancer, are not receiving annual Pap smears to screen for abnormalities that can lead to the potentially fatal malignancy. Efforts to step up education and integrated care are very much needed, the CDC presenters argue, to ensure that HIV-positive women are receiving recommended preventive care.

- A California analysis of collected data indicates that HIV-positive people with non-Hodgkin's lymphoma (NHL)—a cancer of the immune system—face a significantly higher risk of death than HIV-negative individuals with the same malignancy. While this CROI report was troubling in light of previous studies showing improved survival in recent years, another encouraging report made many delegates sit up and take notice: By measuring certain protein fragments in the blood, it may be possible to screen individuals to determine their risk for the cancer.

Nervous System Symptoms

- Distal sensory polyneuropathy (DSPN, also known as peripheral neuropathy or PN)—nerve damage that can cause tingling and pain in the feet and hands—affects more than half of all people with HIV. While fewer people are now using ARVs considered to be prime DSPN causes, notably Videx (didanosine) and Zerit (stavudine), people living with HIV are now more likely to suffer from other risk factors for the potentially debilitating condition: diabetes and elevated triglyceride levels.

- Rates of AIDS-related dementia remain at an all-time low, but another—albeit, much milder—central nervous system problem appears to be on the rise: HIV-associated

neurocognitive disorder (HAND). Not surprisingly, aging is a risk factor. One study found at least one symptom of HAND—including problems with remembering, thinking and learning new tasks—in 37 percent of HIV-positive individuals averaging 46 years old, whereas another reported the rate to be in excess of 50 percent in a cohort of HIV-positive individuals averaging 67 years old. An expanding waistline is also associated with HAND, as is a diabetes diagnosis, which increased the risk more than sevenfold.

Treatments to Watch

- Testosterone is present in women as well as men, and a study reported at CROI indicates that long-term testosterone replacement therapy is safe and beneficial for women with low levels of the natural hormone. When the ovaries and adrenal glands are not producing enough testosterone, low-dose replacement therapy—in the form of skin patches applied twice weekly—used for 18 months yielded significant improvements in body composition, bone mineral density and quality of life in a study involving 23 women living with HIV.

- For HIV-positive people with lipoatrophy, Avandia—a member of the "glitazone" drug class approved for the treatment of diabetes—may help reverse fat loss. The encouraging results of a study presented at CROI counter those of several earlier clinical trials, likely because patients in this one were no longer treating their HIV with either zidovudine (found in Retrovir, Combivir and Trizivir) or stavudine (Zerit)—two HIV meds believed to cause lipoatrophy. Unfortunately, the researchers only looked at fat changes in the legs and arms; it is not clear from this study whether Avandia reverses fat loss where many people find it most distressing: in the face.

HIV Treatment News and Views

While not the headlining act, advances—and a few setbacks—in HIV treatment made news at CROI. Three items of note: further evidence to support early HIV treatment, promise from studies of two new boosting agents to replace Norvir (ritonavir) and disappointing yet long-awaited results from two massive studies of the immune-based therapy Proleukin (IL-2).

- Multiple lines of evidence now support initiating ARV therapy earlier than currently recommended. But if guidelines experts are to commit a new recommendation to paper, they

will require research consistently illustrating when treatment should be started based on CD4 cell counts. Two CROI presentations confirm that earlier ARV treatment yields lifesaving benefits, but they did not agree on the best time to begin that treatment. One study suggested that starting ARV therapy when CD4s are between 350 and 450 is best, whereas the second concluded that treatment should be initiated with the CD4 count above 500.

- Two pharmaceutical companies have made progress developing novel agents that can be used in place of Norvir (ritonavir) to boost other HIV drugs in the blood stream. Gilead Sciences, testing GS 9350, and Sequoia Pharmaceuticals, testing SPI-452, each presented data from its Phase I studies involving HIV-negative volunteers. Both companies are now planning to move these promising candidates into studies involving people living with HIV.

- It's official: Proleukin (interleukin-2, IL-2), an experimental immune-based therapy that has been studied for more than 15 years in people with HIV, simply doesn't work. When compared with ARV therapy alone, adding Proleukin to ARV treatment did not protect people from dying or developing an opportunistic infection, although it did produce greater increases in CD4 counts. Two possible explanations for the lackluster results: CD4 cells generated using Proleukin may not be sufficiently functional to ward off infections, or the drug may cause some as yet unidentified damage to the immune system that outweighs whatever benefit it provides in CD4 increases.

Attention to Prevention

Biomedical approaches to prevention—developing microbicides and using medicine such as ARV treatment as pre- and post-exposure prophylaxis—continue to show promise.

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