



British Columbia  
Centre for Excellence  
in HIV/AIDS

# Antiretroviral update from the BC Centre for Excellence

by Carley Taylor

The BC Centre for Excellence in HIV/AIDS recently held an antiretroviral therapy update. One of the key presentations, by Dr. Marianne Harris, was on the side effects of new antiretroviral agents. Dr. Harris broke new antiretroviral agents into three groups: new agents in existing classes, new agents with new targets, and older agents in new formulations.

## New agents in an existing class

New agents in an existing class include the protease inhibitors tipranavir (Aptivus) and darunavir (TMC114; Prezista) and the non-nucleoside reverse transcriptase inhibitor etravirine (TMC125). Both tipranavir and darunavir have been designed for patients who are treatment resistant to other protease inhibitors (PIs). Side effects of tipranavir include elevation in liver enzymes and an increase in lipids. Tipranavir is also associated with reports of clinical hepatitis and fatal and nonfatal intracranial hemorrhage. Due to safety concerns with tipranavir, it's only used for treatment resistance to protease inhibitors, and not for treatment-naïve patients.

Darunavir has been associated with less severe side effects than tipranavir. The most common side effects of darunavir include diarrhea and elevated cholesterol. There have been some reports of severe rash, including Stevens-Johnson Syndrome, but only 0.3 percent of people have discontinued the drug due to rashes. Pancreatitis is also a rare side effect associated with darunavir.

The non-nucleoside reverse transcriptase inhibitor (NNRTI) etravirine is a second generation NNRTI that may be helpful in treating patients with resistance to other NNRTIs. TMC125 will be available through an expanded access program early this year. The most common side effects associated with this drug are diarrhea and rash, although no severe rashes have been observed.

## New types of agents

Two new types of agents are in the early stages of development: integrase inhibitors, which work by blocking the reproduction of HIV once it's inside the CD4 cell; and CCR5 receptor

antagonists that are aimed at a cellular target and not a viral target. Because these new agents are aimed at new targets in the viral replication cycle, they shouldn't have cross-resistance with existing agents.

Two promising integrase inhibitors are in development: MK-0518 and GS-9137. MK-0518 has been shown to be very benign, with no concerns identified in clinical trials. This agent will be available early this year through an expanded access program. GS-9137 is not as far along in its development and has only been evaluated through a 10-day monotherapy study. The study showed that adverse effects were generally mild and resolved on treatment with no serious adverse events. It is expected that GS-9137 may come into clinical trials in Canada this year.

The drug maraviroc, a CCR5 receptor antagonist, appears to be safe in clinical trials to date at doses of less than 300 mg. At higher doses, however, postural hypotension (head rush) appears to be a problem.

## Older agents, new formulations

A number of older agents in new formulations have been developed. These include Truvada (tenofovir/emtricitabine combination), Kaletra (lopinavir/ritonavir combination) and Invirase 500 (saquinavir). Truvada is a fixed-dose combination pill. The emtricitabine (FTC) has mild side effects, and hyperpigmentation appears to be a problem in eight percent of African Americans.

Invirase 500, another PI, is a 500 mg tablet. Preliminary studies comparing Invirase 500 and Kaletra show that Invirase 500 has fewer side effects and a less adverse impact on lipids than Kaletra.

*You can watch Dr. Harris's presentation and the other presentations at the antiretroviral update session by visiting the "Live Broadcast" section of the BC Centre for Excellence's website at [www.cfenet.ubc.ca](http://www.cfenet.ubc.ca).*

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