New HIV drug appears to be ‘very potent'

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FROM MONDAY'S GLOBE AND MAIL
AUGUST 13, 2006 AT 11:34 PM EDT

TORONTO — Patients taking a brand new type of HIV drug have shown a quick reduction in the number of viruses circulating in their bloodstream, according to early data from a clinical trial that is to be announced at the International AIDS Conference in Toronto later this week.

The drug belongs to a long-awaited new class of HIV medications known as integrase inhibitors. They work to block the enzyme the virus uses to integrate its genetic material into the DNA of a host's cell and make copies of itself.

As more and more patients develop drug resistance to standard therapies, integrase inhibitors are raising hopes of a new first-line treatment against the AIDS virus.

“For people with resistance to many different drugs, this [early study data] offers them hope,” said Martin Markowitz, one of the trial's investigators and a clinical director at the Aaron Diamond AIDS Research Center in New York.

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But Dr. Markowitz, who is also a professor at Rockefeller University, cautioned that “it is too early to predict where this will lead.”

Merck & Co. is developing the drug, one of two in the new class. Its compound, known for now as MK-0518, is involved in an ongoing clinical trial with 198 HIV patients who had previously been untreated for their infection. The studies are being conducted at 28 different centres around the world, including two in Canada.

At the outset, the patients had to have at least 5,000 copies of the virus in every millilitre of blood. They also had relatively low counts of the immune system's CD4 cells, which HIV attacks. Cell counts averaged between 271 and 314 per microlitre.

(Treatment usually begins when a patient has more than 100,000 copies of the virus or below 350 CD4 cells). Most of the patients in the trial, 160, were given the new oral drug in combination with two other antiretroviral therapies. Thirty-eight were given an existing type of HIV medication as well as the two other antiretroviral agents.

Based on data at six months into the two-year trial, Merck reports that 85 to 95 per cent of patients taking the integrase inhibitor drug regimen have seen their viral loads plummet to less than 50 copies.

Patients' immune-cell counts, meanwhile, increased by 139 to 175. Ninety-two per cent of patients taking the older drug combination showed similar results, but the effect took longer to achieve.

“What is striking is the rapidity with which the patients reached these lower levels [of viral load],” Dr. Markowitz said. “This looks to be a very potent drug.”

But again Dr. Markowitz, a consultant to Merck, noted that “This is a small number of patients, and this is preliminary data.”

The drug's antiviral effect was seen in patients taking the oral drug at doses ranging from 100 milligrams to 600 milligrams twice a day.

A press release from Merck states that side effects in the trial have so far been “mild to moderate, with nausea, dizziness and headache reported most frequently.”

Dr. Markowitz noted that 10 patients have discontinued taking the medication, two for lack of efficacy, seven for reasons not related to the trial and one because of an adverse effect related to liver function.

Mark Wainberg, director of the McGill University AIDS Center and co-host of the Toronto conference, said the results sound encouraging. “For me, these integrase inhibitors are the most promising new class of drugs under development.”

What's more, Dr. Wainberg stressed, the research field desperately needs good news: “It's pretty urgent. People are still dying of AIDS because they are resistant to everything we have to treat them.”

The New Jersey based Merck has been working on its integrase inhibitor since the early 1990s. Gilead Sciences, a pharmaceutical company in California, also has a compound in clinical trials.

Researchers have found integrase inhibitors difficult to develop in part because it requires altering the viral genome without harming the DNA of the host. Dr. Markowitz said it is satisfying to finally see the new drug class move into clinical trials, because it targets the last of three enzymes the virus uses to transform a host cell into an HIV factory.

“We have drugs that target two of three enzymes that HIV requires for its life cycle,” he said. “This is like the third leg of the stool.”

In the Merck trial, for example, the new drug was compared to efavirenz, a reverse transcriptase inhibitor. This type of drug works to block HIV from copying a portion of the host's DNA as a step toward injecting its own genetic material into cell.

The other drug class, and the best known, are protease inhibitors. When the enzyme protease is blocked, HIV makes copies of itself in the host cell that cannot infect new cells. Protease inhibitors, taken in combination with other drugs, was the breakthrough treatment that helped to turn HIV from a certain death sentence to a chronic condition in the mid-1990s.

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