Merck integrase inhibitor

Selected highlights from the XVI International AIDS Conference, Toronto, Canada, 13-18 August 2006

Most licensed anti-HIV agents interfere with the ability of HIV-infected cells to replicate (make new copies of HIV). These drugs do so by blocking the activity of two enzymes—reverse transcriptase and protease. However, HIV has many other potential enzymes and proteins that can be attacked, such as the enzyme integrase.

Drugs that can interfere with this enzyme are called integrase inhibitors. One company that is investigating the effect of integrase inhibitors is Merck & Co. Inc. In Canada, this company is called Merck Frosst Ltd. The Merck integrase inhibitor has the temporary name MK-0518.

Advantages of MK-0518 include the following:

- It can be taken with or without food.
- It does not interfere with liver enzymes commonly used by medications, which reduces the chances of drug interactions.

In the first phase of clinical trials, researchers conducted short-term (10-day) assessments of exposure to MK-0518. The drug was taken at a dose between 100 and 800 mg twice daily. In that period, potent suppression of HIV—around 100-fold or 2 logs—was noted. Based on these results, researchers decided to commence with other studies of this integrase inhibitor. Here's one Phase II study of MK-0518, where it was used as part of combination therapy. Different doses of MK-0518 were taken together with standard doses of two other anti-HIV drugs:

- tenofovir (Viread)
- 3TC (Epivir, lamivudine)

The doses of MK-0518 that were used were as follows:

- 600 mg twice daily
- 400 mg twice daily
- 200 mg twice daily
- 100 mg twice daily

For comparison, other HIV positive volunteers received efavirenz (Sustiva, Stocrin) together with tenofovir and 3TC without any integrase inhibitor.

Each of the five treatment arms listed above had 38 participants.

All volunteers in this study had never previously used anti-HIV drugs and all had HIV that was sensitive to the effects of efavirenz, tenofovir and 3TC. The average profile of participants at the start of the study was as follows:

- 20% female, 80% male
- age - 37 years
- viral load - 63,000 copies
- CD4+ count - about 300 cells

Results—Six months later

Overall, all five arms of the study had similar results—more than 80% of participants had viral loads below the 50-copy mark after six months.
A noticeable difference was that viral load fell significantly faster among participants who received any dose of MK-0518 compared to those who received efavirenz.

Increases in CD4+ counts were similar in all arms of the study, with an average of at least 100 new cells being noted in participants.

**Side effects**

In general, more side effects were noted in efavirenz users than in the MK-0518 arm, particularly for the following:

- headache—in 9% of MK-0518 users vs. 24% of efavirenz users
- dizziness—in 8% of MK-0518 users vs. 26% of efavirenz users
- abnormal dreams—in 6% of MK0518 users vs. 18% of efavirenz users

Additional side effects seen in at least 5% of efavirenz users included the following:

- nightmares—11%
- vomiting—8%
- lack of motivation to do things—8%
- poor concentration—5%
- anxiety—5%

One side effect that appeared to occur only in participants who received MK-0518 was flatulence, with 6% of users reporting it.

Overall, most symptoms of side effects were described by the study team as “mild-to-moderate.”

Further studies with MK-0518 are planned, as is the development of an expanded access program.

**REFERENCE:**

Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

CATIE provides information resources to help people living with HIV and/or hepatitis C who wish to manage their own health care in partnership with their care providers. Information accessed through or published or provided by CATIE, however, is not to be considered medical advice. We do not recommend or advocate particular treatments and we urge users to consult as broad a range of sources as possible. We strongly urge users to consult with a qualified medical practitioner prior to undertaking any decision, use or action of a medical nature.

CATIE endeavours to provide the most up-to-date and accurate information at the time of publication. However, information changes and users are encouraged to ensure they have the most current information. Users relying solely on this information do so entirely at their own risk. Neither CATIE nor any of its partners or funders, nor any of their employees, directors, officers or volunteers may be held liable for damages of any kind that may result from the use or misuse of any such information. Any opinions expressed herein or in any article or publication accessed or published or provided by CATIE may not reflect the policies or opinions of CATIE or any partners or funders.

Information on safer drug use is presented as a public health service to help people make healthier choices to reduce the spread of HIV, viral hepatitis and other infections. It is not intended to encourage or promote the use or possession of illegal drugs.

Permission to Reproduce

This document is copyrighted. It may be reprinted and distributed in its entirety for non-commercial purposes without prior permission, but permission must be obtained to edit its content. The following credit must appear on any reprint: This information was provided by CATIE (the Canadian AIDS Treatment Information Exchange). For more information, contact CATIE at 1.800.263.1638.

© CATIE

Production of this content has been made possible through a financial contribution from the Public Health Agency of Canada.

Available online at: