Resistance to integrase inhibitors

HIV has the ability to mutate (or change) and develop the capacity to resist the effects of treatment. The chance of such changes greatly increases when doses of treatment are missed or skipped.

Researchers in North Carolina have been studying HIV’s ability to resist treatment, particularly the class of medicines called integrase inhibitors. Members of this class are as follows:
- raltegravir
- elvitegravir
- dolutegravir

In this recent study, U.S. researchers analysed HIV in blood samples from 3,022 participants that had been collected to assess HIV’s ability to resist drugs. The type of resistance testing done was genotypic testing. This type of testing can identify known mutations in genes that allow HIV to resist the effect of therapy.

Researchers found that about 16% of participants had HIV with at least one major mutation in the integrase gene. Common mutations were as follows:
- N155H
- Q148H/K/R

These mutations were equally common.

Based upon these and other findings, the researchers predicted that high-level resistance (this would very likely lead to treatment failure) to the following drugs was present in the following proportion of participants in their study:
- raltegravir - 15% of participants had high-level resistance to this drug
- elvitegravir - 13% of participants had high-level resistance to this drug
- dolutegravir - 2% of participants had high-level resistance to this drug

The 2% figure above was derived from all 3,022 participants. However, among participants who had at least one major mutation to integrase inhibitors, 12% had high-level resistance to dolutegravir. In other words, it is very likely that dolutegravir would not have been an effective treatment option for these people because of the development of cross-resistance.

About cross-resistance

Bear in mind that exposure to a failing regimen containing an integrase inhibitor can, in some cases, lead to the development of mutations in HIV that can cause not only resistance to the integrase inhibitor being used but also cross-resistance to other integrase inhibitors that have not yet been used. In the present study, some people using raltegravir not only developed resistance to this drug but also cross-resistance to other integrase inhibitors—even though they had never used these other drugs (elvitegravir and, to a lesser extent, dolutegravir). Cross-resistance is also an issue with other classes of HIV drugs.

The study took place over four years between January 2009 and December 2012. During this time, raltegravir is likely the integrase inhibitor that patients would have used. Elvitegravir was only approved four months prior to the study, so it is unlikely that elvitegravir users would have been part of it. Also, because anyone who participated in a clinical trial of integrase inhibitors was excluded, it is extremely unlikely that anyone in the study was exposed to dolutegravir, which was only approved in the U.S. in August 2013.
Additional findings

Researchers found that there were 239 participants with a high degree of resistance to integrase inhibitors. These participants were very treatment experienced, and HIV resistance testing revealed that they appeared to have limited treatment options. Among these 239 participants, here are some additional results of resistance testing:

- nukes – 14% did not have a nuke that was fully active against HIV
- non-nukes – 27% did not have a non-nuke that was fully active against HIV
- protease inhibitors – 5% did not have a protease inhibitor that was fully active against HIV

Overall, the study’s findings underscore the need to screen patients for resistance testing, particularly those whose integrase-based regimens may be failing.

CATIE’s Positive Side magazine has a very useful resource to help people understand HIV and its ability to resist therapy.

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: