A laboratory study on the effects of HIV resistance to integrase strand transfer inhibitors (INSTIs) on later HIV treatment options

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This is a plain language summary of a scientific poster that was originally presented by Dr Michelle L. D'Antoni at the 19th European AIDS Conference (EACS) 2023. This plain language summary presents only selected data and is not intended to replace the full poster. Please refer to the poster (available by QR code at the end of this document) for full details. The intended audience for this plain language summary is registered conference attendees.

Background

Integrase strand transfer inhibitors (INSTIs) are one of the four main classes of HIV medicine. Some are recommended in people who have never previously used HIV medicine or who are replacing their current regimen.

HIV can become resistant to medicines, which means that over time, those medicines stop working and HIV may become detectable in the blood (50 or more copies of the virus in 1 milliliter of blood). Resistance results from genetic changes to the virus, these are called resistance mutations. Resistance mutations have been reported with the use of the INSTI, cabotegravir. Single or multiple cabotegravir resistance mutations can appear either alone or in combination with resistance to other HIV medicines. It is important to understand if these resistance mutations may affect how other medicines work once cabotegravir has been given to people with HIV.

This laboratory study summary looks at the effect of INSTI resistance mutations after cabotegravir treatment failure on how well two other INSTIs, bictegravir and elvitegravir, may work in people with HIV.

Why did researchers do this study?

- Researchers wanted to know if other medicines in the same group (bictegravir and elvitegravir) would still work in people with HIV after cabotegravir treatment failure

How did the researchers do the study?

People with HIV who had already received treatment for HIV and provided **blood samples** were identified

Researchers used these blood samples to look for any mutations in the virus. This is the **'viral profile'**

52 samples with a viral profile showing resistance mutations similar to those previously reported after **cabotegravir** treatment failure were selected

Using these 52 samples, researchers tested:

The number of INSTI resistance mutations, similar to those seen after cabotegravir treatment failure, in each sample

How effective cabotegravir, bictegravir and elvitegravir were at stopping HIV that has these mutations from multiplying

If these mutations showed resistance to cabotegravir, bictegravir and elvitegravir

Whether these mutations could affect how well bictegravir and elvitegravir work (i.e., how sensitive the virus is to the effect of the medicine)

In this study, researchers used laboratory tests to measure how much of a medicine was needed to stop the virus from multiplying. This is also called neutralization.

The IC (Inhibitory Concentration) 50 value looks at how much of a medicine is needed to neutralize half of the virus in a sample. Lower IC50 values suggest that less medicine is needed to do this.

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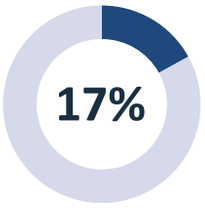
What were the results of the study?

Most HIV samples had more than 1 INSTI resistance mutation similar to those seen after cabotegravir treatment failure

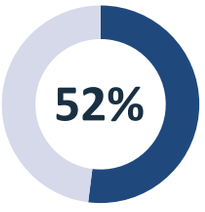
All HIV samples had INSTI resistance mutations, with most having 2 or 3 resistance mutations. This is important because a higher number of resistance mutations can be associated with increased resistance to other medicines.

1 resistance mutation



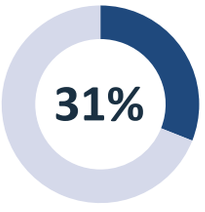
17% of samples had 1 resistance mutation

2 resistance mutations



52% of samples had 2 resistance mutations

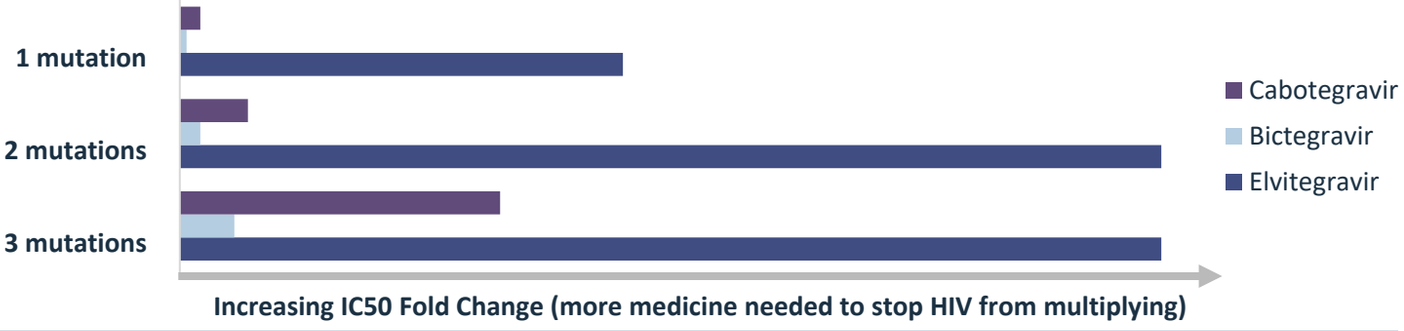
3 resistance mutations



31% of samples had 3 resistance mutations

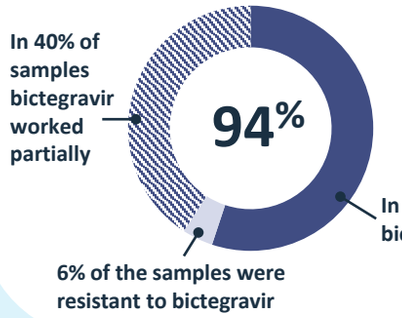
If the HIV sample had 3 resistance mutations, then all the medicines studied were less effective at stopping HIV from multiplying

IC50 fold changes describe how much the IC50 has changed for a particular medicine (i.e., how much more of the medicine is needed to neutralize the virus). In this study, IC50 fold changes for each medicine increased with the number of resistance mutations in the sample.

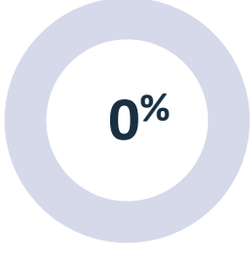


HIV samples were different in how resistant they were to bictegravir and elvitegravir

Resistance was varied in HIV samples with INSTI resistance mutations similar to those seen after cabotegravir treatment failure. Bictegravir worked or partially worked in most samples. All samples were resistant to elvitegravir.



Bictegravir worked in 94% of the samples



100% of samples were resistant to elvitegravir

Poster conclusions

In this lab study of HIV samples with INSTI resistance mutations similar to those seen after cabotegravir treatment failure , the researchers found:

- The number of IC50 fold changes for cabotegravir, bictegravir and elvitegravir increased with the number of resistance mutations in HIV sample
- INSTI resistance mutations similar to those seen after cabotegravir treatment failure strongly reduced how sensitive the HIV samples were to elvitegravir and, to a lesser extent, bictegravir.

Medicines taken after cabotegravir treatment failure should be carefully selected in people with HIV that have cabotegravir resistance mutations because other INSTI medicines may not work in those people.

Reference: D'Antoni ML, et al. EACS 2023, Poster eP.B1.021

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