How Entry Inhibitors Work

OVERVIEW

HIV attacks cells within the body's immune system. To spread, the virus needs to enter these cells and make copies of itself. The copies are then released from these cells and infect other cells. Treatment with entry inhibitors is one way to help stop the virus from replicating and control HIV infection.

Entry inhibitors work by preventing HIV from entering healthy CD4 cells (T-cells) in the body. They work differently than many other ARVs—nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs)—which are active against HIV *after* it has infected a CD4 cell.

Entry inhibitors work by attaching themselves to proteins on the surface of CD4 cells or proteins on the surface of HIV. In order for HIV to bind to CD4 cells, the proteins on HIV's outer coat must bind to the proteins on the surface of CD4 cells. Entry inhibitors prevent this from happening.

There are different types of entry inhibitors—fusion inhibitors, receptor blockers (CCR5 antagonists), and post-attachment inhibitors. Some entry inhibitors target the gp120 or gp41 proteins on HIV's surface. Some entry inhibitors target the CD4 protein or the CCR5 or CXCR4 receptors on a CD4 cell's surface. If entry inhibitors are successful in blocking these proteins, HIV is unable to bind to the surface of CD4 cells and gain entry into the cells.

People with HIV who have become resistant to NRTIs, NNRTIs, and PIs will likely benefit from entry inhibitors because they are a different class of drugs. This is good news for people with HIV who have tried and failed many of the currently approved ARVs.

Entry inhibitors are one of 6 classes of antiretroviral drugs (ARVs) used to treat HIV as part of antiretroviral therapy (ART).

AVAILABLE ENTRY INHIBITORS

Currently, there are several entry inhibitors that the Food and Drug Administration (FDA) has approved for HIV treatment:

- maraviroc (Selzentry) (CCR5 antagonist)
- ibalizumab-uiyk (Trogarzo) (Post-attachment inhibitor)
- fostemsavir (Rukobia) (Attachment inhibitor)

POTENTIAL SIDE EFFECTS

The most common side effects of maraviroc include colds, cough, fever, rash, and dizziness.

The most common side effects of ibalizumab-uiyk include diarrhea, dizziness, nausea, and rash.

The most common side effects of fostemsavir are fatigue, nausea, and diarrhea.

If you are taking an entry inhibitor and start to have uncomfortable side effects, don't stop taking the drug without talking to your healthcare provider first. Pausing or changing ARVs can do more harm than good. The medications may become less effective or the virus may become resistant to the drugs altogether. This means the drugs won't work anymore to treat the virus.

THE BOTTOM LINE

Entry inhibitors are medications that have made HIV management possible. It is important that the appropriate antiretroviral drug (ARV) regimen for HIV treatment is carefully selected, depending on your medical history, other illnesses, prior HIV treatment, stage of infection, and individual preferences.

If your healthcare provider has prescribed entry inhibitors it's important to stick to your treatment plan to manage HIV. If you have side effects from antiretroviral therapy (ART), there are some tips you can try to manage them. More importantly, talk to your healthcare provider for suggestions and recommendations. Your healthcare provider may also change your treatment plan to help relieve side effects.

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