Integrase inhibitors

The first integrase inhibitor for HIV treatment, raltegravir (Isentress), has been used for different purposes—from part of an initial regimen to more complex regimens for treatment-experienced people. For some patients, raltegravir’s twice-daily dosing requirement may be considered a disadvantage in an era when there are several options offering an entire regimen in a single tablet. Still, raltegravir is noteworthy for having few interactions with other drugs and is relatively well tolerated.

The second integrase inhibitor, elvitegravir, is available as part of an entire regimen in one pill (Stribild). In addition to elvitegravir, Stribild contains the anti-HIV drugs tenofovir (Viread) and FTC (emtricitabine, Emtriva). Stribild also contains a novel drug called cobicistat, which is a boosting agent (also known as a pharmacoenhancer). The purpose of cobicistat is to raise and maintain levels of elvitegravir in the blood so that Stribild can be taken once daily. Stribild is roughly equivalent in strength to other commonly used combinations for HIV treatment. It must be taken with food and the presence of cobicistat results in the potential for interactions between many other commonly used medications.

Enter dolutegravir

Dolutegravir is a second-generation experimental integrase inhibitor. Dolutegravir (sold under the brand name Tivicay) has been licensed for use in the U.S. Approval in Canada and the European Union is likely in the coming months. In one clinical trial, when taken as part of combination therapy, dolutegravir was considered statistically superior to a regimen called Atripla—a single pill taken once daily containing efavirenz (Sustiva, Stocrin) + tenofovir + FTC—in participants new to HIV therapy. In the same population, dolutegravir-based regimens were considered roughly equivalent to raltegravir-containing regimens.

In Sailing, the latest clinical trial with dolutegravir, the drug was compared to raltegravir in treatment-experienced participants who had never previously used an integrase inhibitor. Researchers found that, in general, once-daily dolutegravir-based regimens were more potent than raltegravir-containing regimens. Further details about this particular clinical trial appear later in this issue of TreatmentUpdate.

Dolutegravir likely has at least these advantages:

- It can be taken once daily (50 mg) without the need for also taking a booster.
- It does not need to be taken with food.
- It is generally well tolerated.
- In some cases it can be used against HIV that has developed resistance to elvitegravir or raltegravir.

Note that when dolutegravir is taken by people who have HIV that is somewhat resistant to integrase inhibitors, it will likely have to be taken twice daily. Prior to prescribing dolutegravir, and particularly in the case of treatment-experienced patients, doctors will have their patients’ blood analysed for the degree of resistance to this drug. Also, each patient’s treatment history needs to be taken into account.

—Sean R. Hosein

REFERENCE:

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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.

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