Hep C Protease Inhibitor Telaprevir Interacts With HIV Drugs

March 3, 2011 By Tim Horn

Vertex Pharmaceuticals' hepatitis C virus (HCV) protease inhibitor telaprevir interacts to varying degrees with commonly used HIV antiretrovirals (ARVs), according to new data reported in two presentations at the 18th Conference on Retroviruses and Opportunistic Infections (CROI), held February 28 through March 3 in Boston.

The HCV protease inhibitors currently in late-stage development and gearing up for approval—Vertex's telaprevir and Merck's boceprevir—hold tremendous potential for people living with chronic HCV infection, including people coinfected with HIV. Studies are still needed to fully understand the safety and efficacy of these agents, which will need to be combined with standard pegylated interferon and ribavirin therapy in coinfected patients. One early set of data involving telaprevir reported at CROI painted an encouraging picture—nonetheless, a potential overall concern is the way in which HCV protease inhibitors interact with HIV medications.

Specifically, the concern is that HCV protease inhibitors can cause blood levels of ARVs to become too high or too low, and vice versa. In turn, studies have been needed to look for such interactions, which can be used to determine whether or not some ARVs should be avoided while using HCV protease inhibitors or if dose adjustments are needed.

Several studies were presented at this year's CROI. Reported here are the results of telaprevir-ARV interaction studies. Studies involving boceprevir and HIV medications will be reported separately.

Minimal Interaction With Norvir (Ritonavir)

Results from Phase I study, presented by Varun Garg, PhD, of Vertex and his colleagues, involved HCV- and HIV-negative study volunteers receiving telaprevir—the standard dose of 750 milligrams (mg), three times daily, was used—in combination with twice-daily low doses (100 mg) of Norvir (ritonavir), an HIV protease inhibitor frequently used to boost the levels of other HIV protease inhibitors.

After 14 days of use of both drugs, no significant interactions between Norvir and telaprevir were noted. Unlike its affect on HIV protease inhibitors, Norvir did not boost blood concentrations of telaprevir.

While this is good news in terms of avoiding unwanted drug interactions, it is unlikely that Norvir boosting will allow for telaprevir dose reductions.

Some Interactions With Other ARVs

Rudolph van Heeswijk, PharmD, PhD, of Tibotec and his colleagues looked for interactions between telaprevir and a variety of HIV medications, including Norvir-boosted Reyataz (atazanavir), Norvir-boosted Prezista (darunavir), Norvir-boosted Lexiva (fosamprenavir), Kaletra (lopinavir/ritonavir), Sustiva (efavirenz) and Viread (tenofovir). Three studies, all involving HIV-negative and HCV-negative volunteers, were conducted.

Telaprevir slightly increased blood concentrations of Norvir-boosted Reyataz. Conversely, Novir-boosted Reyataz slightly reduced blood levels of telaprevir. However, this interaction was not considered to be clinically significant. In fact, Norvir-boosted Reyataz is one of the ARV regimens being studied in the HIV/HCV-coinfection study linked above.

An interaction between Sustiva and telaprevir was observed, but a higher dose of telaprevir (1,125 mg, every eight hours) largely offset the interaction. This higher dose of telaprevir, when combined with Sustiva, is also being studied in the HIV/HCV-coinfection study linked above.

Significant interactions were documented in study volunteers receiving telaprevir with Kaletra, Norvir-boosted Prezista and Norvir-boosted Lexiva. Based on these observations, van Heeswijk concluded, telaprevir treatment for HCV is not currently being evaluated for people taking these ARVs.

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