Doctors report interaction between cobicistat and tacrolimus

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Cobicistat is a drug that is used to raise and maintain levels of another drug in the blood. Drugs that are used to raise levels of another drug are called boosters (the technical term is pharmacokinetic boosters). In the history of HIV medicine in the past 15 years, the use of boosters has been relatively common because boosters can allow some drugs to be taken less frequently, such as once daily.

The first commonly used booster was ritonavir (Norvir and in Kaletra). Cobicistat is an analogue of ritonavir; it is similar in structure. Cobicistat is found in the two following medicines:

- Stribild – elvitegravir + cobicistat + tenofovir + FTC
- Genvoya – elvitegravir + cobicistat + TAF + FTC

In these pills, the function of cobicistat is to raise and maintain levels of elvitegravir in the blood so that the entire regimen can be taken once daily. As it is a booster, cobicistat has the potential to raise the level of other drugs in the blood.

A team of doctors, nurses and pharmacists in Chicago has recently reported an interaction between cobicistat and the transplant medicine tacrolimus (Advagraf, Prograf) in a person taking Stribild. The transplant team cautioned other doctors, nurses and pharmacists to be mindful of the potential for interaction between these drugs.

Case details

A 50-year-old man was referred to the infectious disease clinic of the Chicago Medical Center for care because he had recently been diagnosed with HIV. He had a history of higher-than-normal blood pressure and kidney injury despite having undergone two kidney transplants. His current medications were the following drugs that partially suppressed his immune system (allowing the transplanted kidney to survive):

- tacrolimus – 2 mg orally every 12 hours
- prednisone – 5 mg orally every 24 hours

The goal with his dose and schedule of tacrolimus was to keep his tacrolimus levels from falling below 4 to 6 ng/mL.

At his first visit to the clinic, analysis of his blood revealed the following:

- a moderate degree of kidney injury with an eGFR (estimated glomerular filtration rate) of 52 minutes/mL
- HIV viral load – 103,000 copies/mL
- his HIV was either resistant or had partial resistance to a class of HIV medicines called non-nukes (NNRTIs)

Another blood test result—for abacavir hypersensitivity—was not ready. This test is necessary before considering the use of abacavir-containing medicines, as this drug can cause a serious hypersensitivity reaction in susceptible people. Abacavir (Ziagen) is also contained in the following medicines:

- abacavir + 3TC
- Trizivir – abacavir + 3TC + AZT
- Triumeq – dolutegravir + abacavir + 3TC
Of the three fixed-dose formulations listed above, Triumeq is unique in that it is a complete regimen in one pill that is taken once daily and has few potential drug interactions.

The man told his doctor that he was interested in initiating HIV treatment and wanted an entire regimen in one pill. Taking his wishes into account and working with his available lab results, doctors prescribed Stribild. The man’s transplantation team requested that he have weekly blood tests so that they could monitor the levels of tacrolimus in his blood.

**One week later**

One week after initiating therapy with Stribild the man returned to the transplantation clinic for regular monitoring. During his visit he told the clinic staff that he had the following symptoms:

- headache
- sleeping problems
- stomach ache
- his output of urine had decreased

Lab tests that day found that the levels of potassium and the waste product creatinine in his blood were elevated. Furthermore, his level of tacrolimus was elevated, initially at 53 ng/mL. The next day the hospital’s lab repeated the analysis of tacrolimus and found that it was 111 ng/mL.

Taking his symptoms and lab test results into account, doctors concluded that the man very likely had tacrolimus toxicity. They told him to cease taking tacrolimus and Stribild until they could understand what happened and find a solution.

**Afterward**

During the two weeks after he stopped taking Stribild and tacrolimus, the man went to the clinic twice a week for further monitoring and blood tests.

It took about 15 days after he ceased taking tacrolimus for its concentration in his blood to fall to near-normal levels —4 ng/mL. However, levels of creatinine in the man’s blood remained elevated (suggestive of kidney injury). By this time, his abacavir hypersensitivity test result was back and it was negative. This result suggested that he would be at relatively low risk for an abacavir hypersensitivity reaction should doctors prescribe an abacavir-containing medicine (such as Triumeq).

Twenty-seven days after initiating Stribild, the level of creatinine in the man’s blood returned to the normal range. Once this occurred, his doctors prescribed Triumeq once daily. As the component drugs inside Triumeq were not expected to interact with tacrolimus, doctors resumed prescribing tacrolimus, 2 mg orally every 12 hours. Subsequent blood tests revealed stable and safe concentrations of tacrolimus in his blood and no kidney or other issues.

The transplantation and infectious disease teams noted that as more fixed-dose combinations of drugs include cobicistat, “clinicians should be reminded of its multitude of drug-drug interactions.” Furthermore, they added that in HIV-positive people who have transplanted organs and who are using tacrolimus or related compounds (such as cyclosporine), “cobicistat should be avoided.”

---Sean R. Hosein

**REFERENCE:**

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