Atazanavir and raltegravir—an interesting combination

In general, the protease inhibitor atazanavir (Reyataz) is used at a dose of 300 mg with a small dose (100 mg) of another protease inhibitor, ritonavir (Norvir), both drugs taken once daily. In this combination, atazanavir has anti-HIV activity and works by interfering with a viral enzyme called protease. The purpose of the small dose of ritonavir in this combination is to enhance levels of atazanavir. Ritonavir has this effect by increasing the absorption of atazanavir in the intestine and by delaying the breakdown of atazanavir in the liver. The net effect is that atazanavir levels in the blood are increased for prolonged periods, allowing once-daily dosing. Drugs such as ritonavir, when used in this way, are called pharmacokinetic boosters or enhancers. A drawback of ritonavir is that it can raise levels of cholesterol and triglycerides in the blood, potentially increasing the risk of cardiovascular disease. Also, some people who use ritonavir can get nausea or diarrhea. Atazanavir is made by Bristol-Myers Squibb (BMS) and ritonavir is manufactured by Abbott Laboratories.

Enter raltegravir

Raltegravir is a new drug that belongs to the class of drugs called integrase inhibitors. It works by interfering with an enzyme—integrase—needed by HIV. Raltegravir is made by Merck and Company, Inc. This drug also has the effect of boosting levels of atazanavir in the blood. Scientists at both BMS and Merck have cooperated and conducted a trial of twice-daily atazanavir and raltegravir in HIV negative people. Their findings suggest that both drugs can be used safely on such a schedule. Further studies assessing the anti-HIV effects of atazanavir-raltegravir as part of HAART are underway.

Study details

Researchers recruited 22 healthy HIV negative participants for their study, the design of which was as follows for all participants:

- days 1 to 5: raltegravir 400 mg taken twice daily
- days 6 to 12: atazanavir 300 mg taken twice daily instead of raltegravir
- days 13 to 26: both atazanavir and raltegravir at the doses listed above

After day 26, participants stopped taking the study medicines and were monitored for up to 14 additional days.

The average profile of participants was as follows:

- 27% female, 73% male
- age – 32 years

Results

In general, the amount of atazanavir absorbed fell between 10% and 20% during the period when it was taken with raltegravir compared with the period when it was taken without raltegravir. However, atazanavir levels remained 10-fold greater than the levels needed to suppress HIV.

On the whole, the amount of raltegravir absorbed increased between 40% and 55% when it was taken with atazanavir. However, in some people raltegravir levels did not significantly increase.

Safety

Side effects reported during the study were generally “mild-to-moderate” in intensity, according to the research team. Common side effects seen when both drugs were taken were as follows:
- jaundice (yellowing of the skin and whites of the eyes)
- headache

Three participants quit the study because of side effects that occurred when both drugs were taken, including the following:

- abnormal heat beats (one person)
- mild rash (two people)

The manufacturer of atazanavir, Bristol-Myers Squibb, is conducting another study of atazanavir and raltegravir taken twice daily in HIV positive participants to assess any potential side effects on the heart. If the combination proves safe and effective, it may form a future treatment option for some HIV positive people.

REFERENCE:

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