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Cystic Fibrosis Research News

Title:
Elexacaftor-tezacaftor-ivacaftor pharmacokinetics with concurrent tacrolimus administration after lung transplant

Lay Title:
Concentrations of elexacaftor-tezacaftor-ivacaftor After Lung Transplant

Authors:
Jennifer S Guimbellot *et al.*

Affiliations:
Department of Pediatrics, Section of Pulmonary and Sleep Medicine, University of Arkansas for Medical Sciences, Little Rock, AR, USA.

What was your research question?
The question that the study aimed to answer is if Elexacaftor-tezacaftor-ivacaftor (ETI) levels in the blood differ between CF patients with and without lung transplant. . If ETI levels are too low, the drug may not work effectively; if ETI levels are too high, there could be harmful side effects.

Why is this important?
ETI has improved the health of people with CF, but its use in lung transplant recipients is uncommon. These recipients take immunosuppressants, like tacrolimus, to prevent organ rejection. Tacrolimus has certain properties that may make it interact with ETI, which could change the concentrations of either drug in the body. Transplant patients were not included in clinical trials of ETI, so it is less clear how ETI might affect them. These patients seem to have more side effects from ETI and stop ETI more often than non-transplant patients, which could be related to differences in ETI concentrations between them.

What did you do?
We included twelve lung transplant recipients with CF and fourteen people with CF without transplant, who were all taking ETI. The lung transplant recipients were taking tacrolimus, which is a drug to suppress the immune system for people with transplants. We collected multiple blood samples over 12 hours to measure ETI levels in patients in these two groups (transplant and non-transplant). People who were taking other medications that would have drug interactions with either tacrolimus or ETI could not be in the study.

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What did you find?

We did not find significant differences in the ETI concentrations in the blood between the two groups. We did not find any evidence that differences in ETI concentrations explain why transplant patients have more side effects or lack of benefit. While tacrolimus has been shown to have some increase in concentrations when ETI is started, the tacrolimus levels were manageable in our study with routine medical monitoring.

What does this mean and reasons for caution?

Doctors who prescribe ETI may be unsure about giving it to transplant recipients because of potential drug interactions and side effects. This study provides evidence that ETI seems to have similar concentrations in the blood even when taken with tacrolimus. ETI may be beneficial for some transplant patients to treat organ disease from CF outside of the lung, like sinus or gut symptoms. Our study was limited by its sample size, so we cannot be certain that there is no effect of tacrolimus on ETI levels, but the effect was not large enough to be detected in our study.

What's next?

Additional studies are needed to understand why transplant patients have more difficulty with ETI.

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cfresearchnews@gmail.com