Title:
Drug-drug interactions with CFTR modulator therapy in cystic fibrosis: Focus on Trikafta®/Kaftrio®

Lay Title:
Examining the potential for drug interactions with Trikafta®/Kaftrio® in people with cystic fibrosis

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What was your research question?
When Trikafta®/Kaftrio® is administered with other medications are there combinations that should be avoided or require adjustments in dosing to ensure efficacy and safety?

Why is this important?
Trikafta®/Kaftrio®, a combination of three medications, is a relatively new treatment that can improve meaningful outcomes including lung function and quality of life in up to 90% of people with cystic fibrosis (pwCF). However, this medication is prone to many drug interactions when combined with other medicines, which might result in a reduced treatment benefit an/or an increased risk of side effects. pwCF patients often require medications for other reasons and these reasons are expected to increase as survival improves with Trikafta®/Kaftrio®. In this paper we identify known and predicted drug-drug interactions with Trikafta®/Kaftrio® and provide advice to manage these interactions.

What did you do?
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We searched electronic databases of medical articles as well as databases containing information about medications to identify any potential interactions that could exist between Trikafta®/Kaftrio® and other medications. We describe the strength of the evidence for each interaction. We provide suggestions for those combinations that may be managed by adjusting the dose and those that should be avoided altogether.

What did you find?
We identified 86 potential interactions between Trikafta®/Kaftrio® and other medications. Thirteen interactions were supported by 14 studies found through our search. The remaining potential interactions are probable interactions that need further study. These interactions were with medications taken for a range of illnesses such as seizures, infections, and cardiovascular disease. In some cases, the combination therapy increases the risk of side effects of Trikafta®/Kaftrio® that could be managed by reducing the dose, while other combinations reduce the benefits of Trikafta®/Kaftrio® and should be avoided. Trikafta®/Kaftrio® also can increase the risks of side effects or treatment failure of other medications in combination as well.

What does this mean and reasons for caution?
Our work suggests that the effectiveness and safety of the Trikafta®/Kaftrio® can be affected by medications taken for other health issues. Similarly, Trikafta®/Kaftrio® can affect the effectiveness and safety of other medication. As pwCF go through life and experience other health issues that require medication, their care-givers should be aware of the potential for drug-drug interactions and consider the mitigation strategies proposed.

What’s next?
Most of the medications we found that could interact with Trikafta®/Kaftrio® were based on an understanding of how these drugs are processed by the human body rather than studies describing the effects of these drug combinations. More research is needed to describe the severity of these interactions and how clinical outcomes might be affected as a result.

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