European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

Title:

A case of Elexacaftor-Tezacaftor-Ivacaftor induced rash resolving without interruption of treatment

Lay Title:

CFTR modulators: A case where Triple therapy induced rash resolved on its own, without stopping the drug

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What was your research question?

Is there any need to stop Elexacaftor-Tezacaftor-Ivacaftor (ELX-TEZ-IVA) in the event of a rash?

Why is this important?

Cystic fibrosis transmembrane conductance regulator (CFTR) modulators have revolutionized treatment for cystic fibrosis (CF). A major side-effect of the latest CFTR modulator, ELX-TEZ-IVA, can be the development of a rash. There is considerable variability of this rash. Often the drug is stopped or re-introduced in small doses to counteract this side-effect. Stopping the drug can lead to loss of lung function and the development of chest infections. Therefore, it is important to know if stopping the drug really stops the rash as clearly, if it is not the case, the risks of stopping, ELX-TEZ-IVA therapy outweigh the benefits of doing so. The scientific rationale seems to be generally lacking with no clear understanding of the mechanism by which this rash takes place.

What did you do?

We reported a case where ELX-TEZ-IVA triple therapy was not stopped in a patient despite the rash and show that the rash resolved on its own with some minimal supportive therapy that included emollient creams and antihistamines. We summarised other cases reporting

their approach to the rash and trying to understand the immunological mechanism of this rash.

What did you find?

On summarising all the cases reported this far and comparing it with our case, we noted that there seems to be a wide variation in this side-effect. From our case, it suggests that there was no need to stop the drug to deal with the rash, as it seemed to resolve on its own. We question the scientific rationale for either stopping the drug entirely or giving small doses of it to counteract this rash. Understanding the biological mechanism of the rash is key to dealing with it more effectively rather than arbitrarily stopping the drug entirely. We speculate that if the offending component of triple therapy is known, it might be worth stopping just that instead of the whole drug.

What does this mean and reasons for caution?

We advocate for further systematic reporting of this side-effect and approaches to its management which might help us better understand why the rash occurs and why it varies between patients. We speculate that this data might help triaging patients effectively based on rash severity and informing when the drug must be stopped entirely. However, there are still not enough case reports as to which component of triple therapy is causing the rash. Stopping the drug entirely or giving small doses of the drug to deal with this side-effect can affect lung function and should be considered carefully.

What's next?

Further research into the biological basis of this drug reaction is required to understand whether desensitization or stopping the drug has a role in dealing with this side-effect.

Original manuscript citation in PubMed

https://pubmed.ncbi.nlm.nih.gov/35840534/

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