

Cystic Fibrosis Research News

Title:

Immunogenic adverse events to CFTR modulators – an international survey

Lay Title:

Drug allergy to CFTR modulators – an international survey

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What was your research question?

CFTR modulator therapy is a life-long transformative treatment. For many people with CF (pwCF) it provides an improved quality of life and increased life expectancy. CFTR modulator therapy is usually well-tolerated, but there are pwCF with CFTR modulator related drug allergy and treatment interruptions. We wanted to find out how many people are affected, what their reaction was and whether they were re-exposed to CFTR modulators after an allergic reaction.

Why is this important?

The frequency of drug allergy to CFTR modulators is unknown. In the clinical studies that led to the licensing of elexacaftor/tezacaftor/ivacaftor main side effects were skin rashes and elevated liver function tests. 1.2 – 1.6% of the enrolled study participants had to stop taking



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the life-changing medicine. However, until now there is no real-world data on the frequency of drug allergy to CFTR modulators.

What did you do?

We designed a survey and send it to all ECFS CTN trial sites in Europe and beyond. We asked for detailed information on pwCF that had to stop CFTR modulator therapy due to suspected drug allergy and included questions on how they reacted to CFTR modulator therapy (e.g. rash, signs of liver injury, drug fever etc.).

What did you find?

Clinicians from 89 CF centers treating approximately 12000 to 17500 pwCF in 28 countries participated in the survey. 37 centers reported individuals suffering from a suspected drug allergs to CFTR modulators. The most important results were that only 2/3 of pwCF with a suspected drug allergy were re-exposed to the modulator treatment, but of those re-exposed only 1/3 had a second reaction and only a small fraction of those with a second reaction had to completely stop taking CFTR modulator treatment. The most common reactions were skin rashes or elevated liver enzymes.

What does this mean and reasons for caution?

Manifest drug allergy to CFTR modulators is very rare, but very relevant for the affected individual. Many people with suspected drug allergy to CFTR modulators could potentially tolerate them after re-exposure. The underlying disease mechanisms are not well understood and need to be studied in detail to safely re-expose pwCF with a suspected drug allergy to CFTR modulators.

What's next?

For those pwCF with proven drug allergy and complete withdrawal from CFTR modulator therapy, specific underlying immune mechanisms need to be understood. The "Allergies related to CF" (ART-CF) project will try to get a better understanding of the immunological basis of allergic reactions to CFTR modulator therapy.

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