Cystic Fibrosis Research News

Title:
Impact of chronic medication de-escalation in patients with cystic fibrosis taking elexacaftor, tezacaftor, ivacaftor: A retrospective review

Lay Title:
Impact of the De-escalation of Supportive Therapies in Patients with Cystic Fibrosis Taking Elexacaftor, Tezacaftor, Ivacaftor

Authors:
Emma L. Guenther[1], Karen S. McCoy[2], Mariah Eisner[3], Shasha Bai[4], Christopher J. Nemastil[2], Kimberly J. Novak[1], Terri Johnson[2], Emily M. Stephan[1]

Affiliations:
[1]Department of Pharmacy, Nationwide Children's Hospital, Columbus, OH
[2]Department of Pulmonology, Nationwide Children's Hospital, Columbus, OH
[3]Biostatistics Resource at Nationwide Children's Hospital, Columbus, OH
[4]Pediatric Biostatistics Core, Department of Pediatrics, Emory University, Atlanta, GA

What was your research question?
The goal of this study was to evaluate the effect of de-escalating cystic fibrosis (CF) supportive therapies in patients on stable on elexacaftor/tezacaftor/ivacaftor (ETI). Patients were included in this study if they were 6 years of age or older and had either one copy or two copies of F508del.

Why is this important?
Those living with CF commonly need to take multiple supportive therapies daily. While historical care focused on the management of symptoms, cystic fibrosis transmembrane regulator (CFTR) modulators were developed over the past decade. The newest CFTR modulator, ETI, has shown great promise. Due to the timely and costly nature of these supportive therapies and the vast improvement seen with ETI, we anticipated that patients would desire to discontinue many of their supportive CF therapies once on ETI. Therefore, we needed to evaluate the safety of discontinuing these supportive therapies.

What did you do?
In order to collaborate with patients and caregivers to prevent abrupt therapy discontinuation, our multidisciplinary workgroup at Nationwide Children's Hospital (NCH)

developed a de-escalation algorithm. Medication cost and burden, along with patient safety, were considered when designing the algorithm. Quarterly, if the patient was stable on ETI, CF supportive therapies could be de-escalated based on the algorithm. The algorithm did not have to be followed precisely, as providers engaged patients and caregivers in shared decision making. Then, a retrospective chart review was conducted to evaluate the effect of de-escalating CF supportive therapies in patients on ETI.

What did you find?

A total of 174 patients were included in the study, of which 139 de-escalated at least one supportive therapy. Despite the de-escalation of supportive therapies, lung function increased then remained stable from month-1 to month-12 post-initiation of ETI. Lung function improved in all subgroups regardless of lung function at baseline, genotype, age, de-escalation, and adherence to de-escalation algorithm. During this period, patients were able to decrease the number of CF supportive therapies by 50%. In addition, BMI increased, sweat chloride levels decreased, the percentage of patients who grew *Pseudomonas* decreased, and hospital admissions decreased after starting ETI.

What does this mean and reasons for caution?

The de-escalation of supportive therapies for patients stable on ETI therapy had similar outcomes to continuing those therapies. Lung function initially increased and was sustained throughout the study independent of CF supportive therapies taken by the patient. This suggests that supportive CF therapies may be able to be discontinued within the context of a de-escalation algorithm while maintaining pulmonary stability. However, not everyone will be able to safely de-escalate supportive therapies due to differing lung function and response to medications.

What's next?

While this study showed favorable outcomes, more studies are needed to evaluate the safety of de-escalating supportive therapies. A similar study is currently underway to determine if it is safe to de-escalate either inhaled hypertonic saline or dornase alfa.

Original manuscript citation in PubMed

https://pubmed.ncbi.nlm.nih.gov/37069044/