Cystic Fibrosis Research News

Title:
Clinical efficacy of CFTR modulator therapy in people with cystic fibrosis carrying the I1234V mutation

Lay Title:
CFTR modulators in people with CF and the I1234V mutation

Authors:
Bat El Bar Aluma, Joel Reiter, Ori Efrati, Yael Bezalel, Shlomit Keler, Moshe Ashkenazi, Adi Dagan, Yael Buchnik, Ido Sadras, Malena Cohen-Cymberknoh

Affiliations:
[1]Pediatric Pulmonary Unit and Cystic fibrosis Center, Lily and Edmond Safra Children's Hospital, Sheba Medical Center, Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[2]Pediatric Pulmonary Unit and Cystic fibrosis Center, Hadassah Medical Center and Faculty of Medicine, Hebrew University of Jerusalem, Israel

What was your research question?
Do people with CF and the I1234V mutation benefit from modulator therapies.

Why is this important?
CFTR modulator therapies have been life changing for eligible people with CF (pwCF). However, since modulator in-vitro effects were unclear with this mutation, pwCF carrying the I1234V mutation were not approved for this therapy. This study may therefore offer new hope for this population, and though it is considered rare, with only 28 pwCF listed in the American and European databases, this likely underestimates its true world prevalence as it is the second most common mutation in people of Middle Eastern descent. Furthermore, this study may give hope to pwCF carrying other mutations in whom no in-vitro response was seen.

What did you do?
In this study we collected data from 7 pwCF carrying at least one I1234V variant that had trialled CFTR modulators, off label. Clinical data included sweat chloride values, body mass index, pulmonary function tests (spirometry and lung clearance index), and frequency of pulmonary exacerbations requiring antibiotic treatments. All of these parameters were recorded before and after treatment with CFTR modulators, in order to evaluate efficacy.

Cystic Fibrosis Research News

What did you find?

All clinical parameters investigated showed significant improvement with CFTR modulator therapy. Furthermore, chronic *pseudomonas* airway infection was eradicated in one patient. Remarkably, a female subject that previously required in vitro fertilization (IVF) treatments to conceive, was able to conceive naturally while on modulators, and completed two healthy pregnancies.

What does this mean and reasons for caution?

In this study we demonstrated the efficacy of CFTR modulator therapy in pwCF carrying the I1234V mutation, in whom no in-vitro response was seen till now, and hopefully more pwCF will be able to benefit from this therapy. Every study has its limitations- in our study we had a small number of subjects. In Israel, there are only 10 pwCF with this mutation and not all of them were able to receive off label modulator therapies.

What's next?

This study emphasized the need for a randomized controlled trial. However, the current number of registered pwCF with this mutation, may prevent this from happening in the near future – as such, we hope this study will lead to treatment approval pending such a study.

Original manuscript citation in PubMed

https://pubmed.ncbi.nlm.nih.gov/38443268/

cfresearchnews@gmail.com