



# Cystic Fibrosis Research News

## **Title:**

Anti-inflammatory effects of lenabasum, a cannabinoid receptor type 2 agonist, on macrophages from cystic fibrosis.

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## **What was your research question?**

Cystic fibrosis (CF) lung disease is characterized by excessive inflammation causing damage to the lungs. Following infection, macrophages, a type of white blood cells, migrate to the lungs, engaging to kill the pathogen. Lenabasum is a novel synthetic small molecule that has been shown to switch off inflammation in many diseases. This study aimed to evaluate the efficacy of lenabasum in resolution of macrophage-driven inflammation in CF.

## **Why is this important?**

Lenabasum works independently from the type of CFTR mutation. Successful resolution of inflammation by lenabasum would offer its universal therapeutic use to manage inflammation for all patients carrying any type of CFTR mutation.

## **What did you do?**

In the lungs, macrophages identify the bacteria and internalize them to kill them and keep the lungs clean. In addition, macrophages release agents that are toxic to surrounding bacteria. Unfortunately, excessive release of these toxic agents is detrimental to the lungs. We developed a laboratory model to study macrophage responses to infectious bacteria. We obtained blood samples from patients with CF and healthy donors. We then isolated monocytes, the precursor cells of macrophages and differentiated them to macrophages. Lenabasum was administered to macrophages at different doses in laboratory settings. Macrophages were then evaluated by their toxicity and ability to kill and clear bacteria.

## **What did you find?**

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Our three key findings from this study were

- a) Lenabasum enhanced the capability of the macrophages to kill bacteria
- b) Lenabasum was able to increase the percentage of CF macrophages that were not inflammatory, rather limit detrimental inflammation.
- c) Lenabasum reduced the release of toxic agents by CF macrophages, which would lower the chance of lung cell damage.

## **What does this mean and reasons for caution?**

Our findings indicate lenabasum may prove to be useful in the treatment of patients with CF. Lenabasum enhanced the ability of CF macrophages to kill bacteria and reduced excessive inflammation that can contribute to lung disease progression. However, our studies were undertaken in the laboratory test tubes using white blood cells obtained from patients with CF and controls. A clinical trial is required to assess lenabasum as a treatment for individuals with CF.

## **What's next?**

The next phase of our findings is to conduct clinical trials of lenabasum where we will treat patients and measure multiple clinical outcomes such as, lung function, pulmonary exacerbation and hospital admission rates to assess the level of improvement due to the treatment.

## **Original manuscript citation in PubMed**

<https://pubmed.ncbi.nlm.nih.gov/32387042/>