

Cystic Fibrosis Research News

Title:

Association between CFTR modulators and changes in iron deficiency markers in cystic fibrosis

Lay Title:

Impact of modulator therapy on iron deficiency in cystic fibrosis

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What was your research question?

What is the effect of moderately-effective and highly-effective modulator therapy (MEMT and HEMT) on lab tests for iron deficiency (ID) and anemia in people with cystic fibrosis (pwCF)? We hypothesized that HEMT would be associated with improvement in iron labs and hemoglobin.

Why is this important?

Cystic fibrosis (CF) is associated with lung disease; however, nutritional deficiencies are a major source of illness and poor quality of life in pwCF. One of these nutritional deficiencies is ID, which has been reported to occur in up to 80% of pwCF.

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The availability of modulator therapies, particularly HEMT, has greatly improved health and quality of life for the subset of pwCF with highly-responsive mutations. We need to better understand how these modulator therapies impact health in pwCF outside of the lung, such as in the case of ID.

What did you do?

We reviewed prior medical records of 568 CF patients, aged 18 years and older, from 4 CF Care Centers across the United States, spanning from 2012-2022. We focused on patients who had lab testing for ID (transferrin saturation [TSAT], serum iron, ferritin) or anemia (hemoglobin), and the specific modulator therapy prescribed to the patient at the time of the lab tests. We compared the effects of HEMT and MEMT versus off modulator therapy on ID lab results and hemoglobin result. In assessing this effect, we accounted for potential confounders such as age, lung function, body mass index, presence of diabetes, presence of pancreatic insufficiency, and other factors that may impact the lab results. We also assessed these effects in subgroups of male versus female patients, those with higher versus lower body mass index, patients with better versus worse lung function, and others.

What did you find?

We found that HEMT was associated with improvements in ID lab results (including TSAT and serum iron, but not ferritin) and hemoglobin. The degree of improvement was similar to what was seen in the intravenous iron repletion studies, supporting that this is a clinically significant improvement. Men on HEMT had more significant improvements in ID lab results and hemoglobin compared to women on HEMT. Other subgroups that had more significant responses included those with worse lung function ($FEV_1 < 40\%$) and lower body mass index (< 18.5).

MEMT was overall not associated with improvements in ID lab results, but was associated with modest improvements in hemoglobin.

Even with HEMT therapy, $> 30\%$ of patients were ID at some point during the study period.

What does this mean and reasons for caution?

HEMT is associated with improvements in iron deficiency and anemia. This is further evidence of the impact of modulators on CF outside of the lung. We still saw differences in response



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when looking at male versus female patients, suggesting a need to more clearly study these population differences.

MEMT was not associated with improvements in iron deficiency and only modest improvements in anemia. This effect is similar to the differences in the lung function improvement seen with HEMT versus MEMT.

Patients not taking modulator therapies have the highest risk for ID and anemia. But the rates of ID remained high in all patients, regardless of modulator therapy or type of modulator therapy.

What's next?

While we saw improvements in ID lab results and hemoglobin results, there are subgroup differences which require further study. We observed high rates of ID regardless of modulator therapy type, indicating that ID remains a common problem in CF.

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