

# Impact of CFTR modulator therapy on nutritional status, hepatic steatosis, and dyslipidemia

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## Background

- Cystic Fibrosis (CF) is a common genetic disorder that occurs due to a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR)
- CF classically affects the lungs, causing progressive pulmonary disease, but also manifests in disease of the pancreas, liver, intestine, and reproductive organs.
- CFTR modulators are a novel class of medications that restore CFTR function
  - Symdeko and Orkambi are CFTR modulators introduced between 2015-2018 and provide modest improvement in CFTR function.
  - Trikafta was approved in 2019 and is highly effective at restoring CFTR function.
- Patients with CF have been malnourished in the past, but there is starting to be a rise in the number of CF patients who are overweight/obese
- This could be attributed to multiple things including:
  - the initiation of high calorie high fat diet promoting unhealthy eating habits
  - Some studies have shown that modulator therapy can lead to weight gain
- This increases patient’s risk of other problems like insulin resistance and cardiovascular disease
  - CVD is not common in the cystic fibrosis population and typically has low prevalence.
  - There are not many studies regarding lipid levels with modulator treatment

## Objectives

- Determine whether modulator status affects lipid levels
- Determine if addition of Trikafta affects lipid levels

## Methods

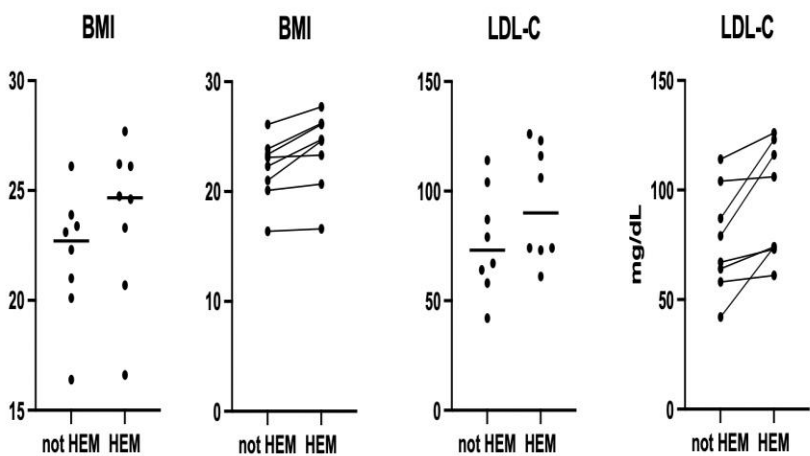
- Retrospective chart review was performed on 30 adults with cystic fibrosis who underwent abdominal MRI to assess the protein density fat fraction (PDFF) while treated with no modulator, a not highly effective modulator (Symdeko or Orkambi), or highly effective modulators (Trikafta).
- Retrospective chart review was used to evaluate BMI and ppFEV1 within 3 months of the MRI.
- Serum lipids were recorded if it was taken within a one-year time period from the MRI with same modulator status.
- Eight patients had data available before and after highly effective modulator
- Eight patients had data available on no modulator versus any modulator treatment.
- A paired Wilcoxon test was used to compare pre and post treatment data.

## Results

**Table I: Before and After Highly Effective Modulator**

N=8	Before Highly Effective Modulator (4 on orkambi or symdeko, 4 on no mod)	After Highly Effective Modulator	P value
ppFEV1	68 32-97	78 36-96	0.0156
BMI	22.7 16.4-26.1	24.7 16.6-27.7	0.0078
PDFF *n=6	3.7 3.0-4.7	4.3 3.0-5.6	0.62
LDL-C	73 42-114	90 61-126	0.0078
HDL-C	48 21-59	52 47-90	0.0391
Triglycerides	90 32-277	84.5 60-237	0.95

**Graph 1: Before and After Highly Effective Modulator Therapy**

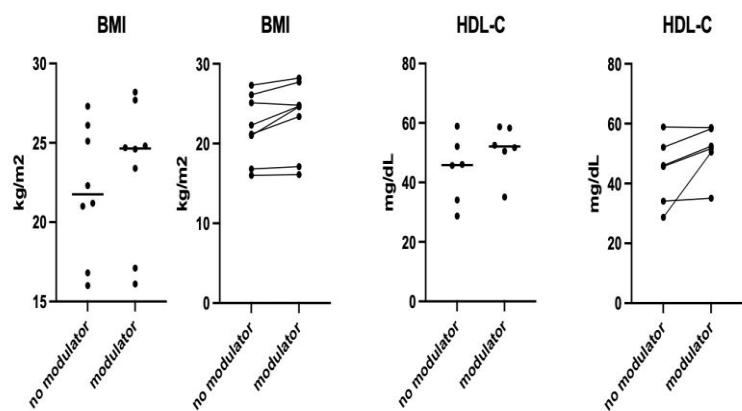


## Results

**Table 2: No Modulator versus Any Modulator**

No Modulator *n=6	No modulator	Any modulator N=3 (trikafta) N=5 (symdeko)	
ppFEV1	74 25-97	73 24-104	0.453
BMI	21.8 16.0-27.3	24.7 16.1-28.2	0.031
PDFF*	3.7 2.1-7.8	4.6 2.6-5.6	0.84
LDL-C *	65 45-104	69 40-106	0.68
HDL-C*	46 29-59	52 35-59	0.0625
Triglycerides *	82 32-132	90 76-201	0.4375

**Figure 3: No Modulator versus any Modulator**



- Pre/post Trikafta- significant increases in median ppFEV1 from 68% to 78% (p=0.0156), median BMI from 22.7 to 24.7 kg/m<sup>2</sup> (p=0.0078), median LDL-C from 73 to 90 (p=0.0078), and median HDL-C (p=0.0391) from 48 to 52.
- No modulator versus any modulator-statistically significant increase in median BMI from 21.8 to 24.7 (p=0.031) and median HDL-C also increases from 46 to 52 with approaching statistical significance (p=0.0625).

## Conclusions

- Treatment with the highly effective CFTR modulator, Trikafta, is associated with elevated levels of HDL-C, LDL-C, and BMI
- Hepatic steatosis did not change as patients transitioned between modulator status
- Limited by sample size and the number of patients that got pre and post scans with lipid levels performed within one year