Analyzing Effects of Cystic Fibrosis Transmembrane Conductance Regulator Modulator Therapy on Nutritional Status in Pediatric Cystic Fibrosis Patients

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Background: Cystic Fibrosis (CF) is a multifaceted genetic disease affecting multiple organs systems throughout the body. One significant problem for CF patients is the challenge to achieve normal growth and nutrition, which can poorly impact lung function. Optimizing body mass index (BMI) percentile has been shown in previous studies to contribute to improved lung function. This study aims to determine the percent of CF pediatric patients on CFTR modulators that reached their nutritional target (BMI-percentile) as compared to patients not on modulator therapy.

Methodology: A single-center, retrospective review of pediatric CF patients on either lumacaftor-ivacaftor or tezacaftor-ivacaftor therapy from January 1, 2018 to July 30, 2019. This population was matched with a historically similar CF patient population not on modulator therapy from October 1, 2013 to June 30, 2015. Groups were matched in accordance with age, gender, and lung function (ppFEV1). Nutritional targets collected included BMI-percentile, height, and weight, each assessed prior to and at 1, 3, 6, 9 and 12 months following CFTR modulator initiation or study inclusion.

Results: After 12 months of dual-modulator therapy, the group initiated on either lumacaftor-ivacaftor or tezacaftor-ivacaftor saw a 23% increase in patients achieving a BMI-percentile ≥ 50, whereas, those not on modulator therapy saw a net neutral effect with no overall increase in the percent of patients achieving this nutritional target. Additionally, patients in the modulator group had a median increase in BMI-percentile of 10.5% at 12 months, as compared to historically matched patients who saw a fluctuation in BMI-percentile that resulted in 0.1% decrease from baseline. Median difference in weight over 12 months, also favored the modulator arm with an increase in weight of 5.3 kg, as compared to 3.3 kg in the historically matched population.

Conclusion: Initiating CFTR modulator therapy, lumacaftor-ivacaftor or tezacaftor-ivacaftor, as compared to no modulator therapy, increased the percent of patients achieving a key nutritional target that has been associated with improved overall lung function. Additionally, over a 12 month period, modulator therapy revealed improvements in weight and height in pediatric CF patients, when compared to patients not receiving modulator therapy. It would be beneficial to test these correlations in a larger patient population, as well as in patients on the new triple modulator therapy, elexacaftor-tezacaftor-ivacaftor, to assess whether these nutritional benefits could be considered a class effect for modulator therapies.