Table 1 (abstract 196):
Rate of liver function test elevation after elexacaftor/tezacaftor/ivacaftor treatment according to pretreatment values.

Pre-treatment LFT values (number of patients)	LFT	No. of events	Rate (No. of events per 100 patient-month) [95% CI]
< ULN (n= 38)	ALT elevation (>ULN)	18	9.7 [5.7-15.3]
	GGT elevation (>ULN)	7	3.8 [1.5-7.8]
	Total bilirubin elevation (>ULN)	14	7.5 [4.1-12.6]
> ULN (n= 18)	ALT increment above pre-treatment value	9	9.6 [4.4-18.2]
	GGT increment above pre-treatment value	13	13.8 [7.4-23.6]
	Total bilirubin increment above pre-treatment value	17	18.1 [10.5-29.0]

CI: Confidence Interval. ETI: Elexacaftor, Tezacaftor and Ivacaftor. LFT: Liver Function Test. ULN: Upper Limit of Normality.

197

Rare prevalence of colonic sessile serrated lesions in people with cystic fibrosis

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Background: People with cystic fibrosis (PwCF) have higher rates of early colon polyp development and progression to colorectal cancer than the general population, especially those who have undergone solid organ transplantation. In response, the Cystic Fibrosis Foundation developed colorectal cancer (CRC) screening guidelines in 2017 recommending initiation of earlier first screening colonoscopy and shorter re-screening intervals than in the general population. The exact mechanism for how PwCF develop more polyps and whether different polyp types occur at similar prevalence rates as the general population is unclear. Recent studies suggest that sessile serrated lesions (SSLs) have a prevalence in the general population of 8.2% [1], but a detailed review of prior literature suggests that PwCF may have different polyp type distributions [2]. We developed a database of colonoscopy results in PwCF to better characterize the prevalence of SSLs.

Methods: In this retrospective chart review, patients were identified through the University of Washington Cystic Fibrosis Foundation Patient Registry. Inclusion criteria were diagnosis of CF, and exclusion criteria were age younger than 18. Patients' electronic medical records (EMRs) were accessed using the University of Washington Epic EMR system, including linked archival data systems to access partner health system data on the selected patients. The colonoscopy reports were systematically reviewed for selected variables including patient age at time of procedure, date of colonoscopy, bowel preparation quality, cecal intubation, polyp quantity, polyp size, polyp location within the colon, and whether cancer was present. Statistical analysis was performed to compare data with that of the general population.

Results: Seven hundred fifty-seven patients were identified from the CF registry, of whom 170 had available records of prior colonoscopy for any indication; 52.9% were women and 47.1% men. Mean age at time of colonoscopy was 43.2. From these patients, 288 colonoscopy reports were reviewed, and 270 polyps, of all types, were identified. Two patients were found to have solitary SSLs (Table 1). SSL prevalence was 1.2%, significantly lower than what has been described in the general population ($p < 0.05$). There were 41 colonoscopies in our database from before 2010, from which 14 polyps were found; none of these polyps were hyperplastic or other serrated polyp types.

Table 1.
Characteristics of two people with cystic fibrosis found to have a sessile serrated lesion (SSL). CRC = colorectal cancer; CFRD, cystic fibrosis–related diabetes.

Variable	Patient 1	Patient 2
Year SSL discovered	2016	2015
Age at colonoscopy	>50 years old	>50 years old
Polyp Location	Right Colon	Right Colon
Size of SSL	<5mm	<5mm
Lifetime total polyps	13	15
Polyp on first colonoscopy	Yes	No
3 or more polyps (any colonoscopy)	Yes	Yes
Sex	Male	Male
Lung Transplant	Yes	No
FEV1 (% Predicted) at time of colonoscopy	39	105
Family History of CRC	No	No
Personal History of CRC	No	No
History of DIOS	Yes	No
Pancreatic Insufficiency	Yes	Yes
CFRD	Yes	Yes

Conclusions: At our center, PwCF had a significantly lower prevalence of SSLs than what has been described in the general population. Patients who developed SSLs appear to follow age-dependent trends typically seen in the general population. Low SSL prevalence may shed light on the tumor biology of PwCF. Low prevalence of SSLs in PwCF may affect the utility and advantage of more-expensive stool DNA tests over fecal immunochemical tests for CRC screening.

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198

Weight and body composition of school-aged children with cystic fibrosis and extended modulator therapy

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Background: Body mass index (BMI) greater than the 50th percentile has long been the nutritional target for children with cystic fibrosis (CF), but increasing numbers of children have become overweight or obese [1].

Although previous studies have found that higher BMI is correlated with better lung function, newer research highlights that *lean* body mass is associated with good lung function and health [2]. A high percentage of body fat and low skeletal muscle mass is common in individuals with CF at all BMI levels, suggesting that BMI is a suboptimal marker of nutritional status [3]. The effect of modulators on body composition in children with CF has not been comprehensively documented. Based on previous studies, largely in adolescents and adults, we hypothesize that children with CF on modulator therapy will experience a sustained increase in fat mass. The effect of extended modulator therapy on skeletal muscle mass is unknown.
Methods: This abstract uses baseline data from a longitudinal, observational study that assessed the BMI and body composition of children aged 6 to 11 with CF who were poised to initiate elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) therapy and who had ($n = 27$) or had not ($n = 10$) been treated with modulator therapy. Modulator treatment and BMI data were extracted from the medical record, and body composition was assessed using bioelectrical impedance analysis (BIA) using InBody 770 equipment.
Results: Significant differences were noted at baseline assessment between those who were on modulator treatment before enrollment and those naïve to modulator therapy (Figure 1). Children in the previous modulator treatment group had been on therapy for an average of 3.7 years (range 1.9–4.5 years). Those naïve to modulator were younger on average at study enrollment (8.4 vs 9.7 years, $p = 0.05$). Children previously on modulators were noted to have higher BMI (mean BMI percentile 73% vs 54%, $p = 0.07$), fat mass index (5.03 vs 3.15 kg/m^2, $p = 0.01$), and percentage body fat (25.5% vs 16.9%, $p = 0.007$) than those naïve to modulators. Lean BMI (13.9 vs 13.7 kg/m^2, $p = 0.45$) and skeletal muscle mass index (7.1 vs 6.9 kg/m^2, $p = 0.31$) were comparable.

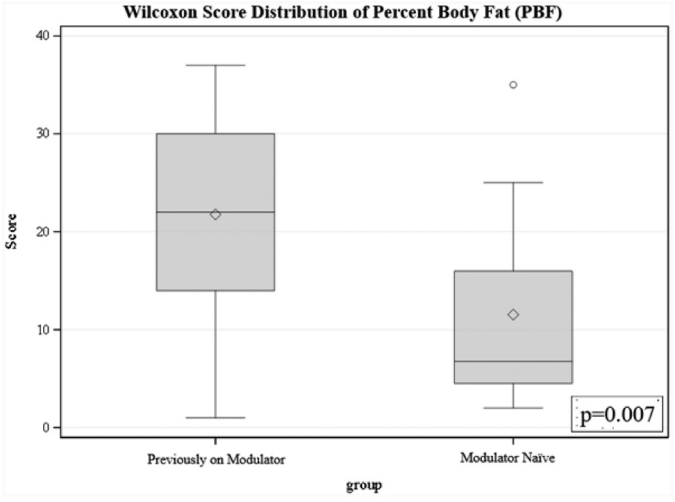

Figure 1. Score distribution of percentage body fat of individuals on modulator therapy and those who were modulator naïve

Conclusions: Our baseline data offered a novel opportunity to identify modulator effects over several years on body weight and composition for children with CF. Data suggest that extended modulator therapy is associated with a persisting increase in body weight and fat mass but not skeletal muscle mass of prepubescent children. These data suggest a need for nutritional and physical activity interventions to optimize overall improvement with modulator therapy. The further effect of ELX/TEZ/IVA therapy on weight, body composition, and muscle strength is being evaluated.
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199

Persistent immaturity of the developing gut microbiome in infants with cystic fibrosis

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Background: The gut microbiome of infants with cystic fibrosis (CF) is characterized by the altered abundance of beneficial bacterial taxa coincident with a developmental delay in maturation in the first year of life [1]. There is an inflection point of microbiome stability after 12 months of age in healthy infants [1,2]. We sought to explore the functional capacity of the CF gut past the first year of life to understand how gut microbiome dysbiosis affects long-term health in CF.
Methods: We performed whole-genome shotgun sequencing on 192 stool samples from 40 infants with CF through 3 years of age and compared metagenomic taxonomic and functional profiles with published data including 4003 samples from 714 infants [1–6]. We then used supervised and unsupervised machine learning methods to understand the developmental trajectory and key contributing taxa [1,7,8].
Results: Our analysis revealed persistent delays in microbiome development in CF through 36 months of life. We identified distinct developmental community states through which the CF microbiome failed to transition, defined by depleted levels of immune-modulatory taxa including *Bacteroides* and members of the phylum *Firmicutes* known to produce short-chain fatty acids [9].
Conclusions: We identified key developmentally delayed microbiome states in the gut of infants with CF that could be targeted using future microbiota-directed therapeutic interventions to improve gut and systemic health in CF.
Acknowledgements:

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