Table 1 (abstract 195):
Median vitamin levels and percentage of participants with subtherapeutic or supratherapeutic levels before and after elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) initiation. IQR: interquartile range, PT: prothrombin time *$p < 0.05$.

Serum marker	Median [IQR] pre-ELX/TEZ/IVA	Median [IQR] post-ELX/TEZ/IVA	Percent subtherapeutic pre-ELX/TEZ/IVA	Percent subtherapeutic post-ELX/TEZ/IVA	Percent supratherapeutic or elevated pre-ELX/TEZ/IVA	Percent supratherapeutic or elevated post-ELX/TEZ/IVA
Vitamin A (mcg/L)	440.00 [332.25 - 494.12]	433.30 [314.2 - 502.5]	9%	13%	1%	0
Vitamin D (ng/mL)	26.50 [21.50 - 32.00]	27.67 [22.50 - 34.00]	80% *	63% *	1%	0
Vitamin E (mg/L)	8.80 [6.05 - 10.20] *	6.70 [5.133 - 8.033] *	17%	19%	1%	0
PT (sec)	14.00 [13.60 - 14.65]	14.00 [13.60 - 14.40]	0	0	20% *	7% *

after initiation were used to determine the proportion of participants with one or more vitamin levels in the supratherapeutic or subtherapeutic range. Proportions were compared using the McNemar's chi-square test. A two-sided $p < 0.05$ was considered statistically significant, and all analyses were completed in R version 4.1.2.

Results: Seventy-two participants met inclusion criteria for enrollment, and 54 (75%) had follow-up vitamin levels after ELX/TEZ/IVA was started. Median age at ELX/TEZ/IVA initiation was 15.9 (95% CI, 13.5–17.8), 61% were homozygous for F508del, 54% were male, and 88% were Caucasian. Median baseline body mass index was 20.8 kg/m^2 (95% CI, 18.8–22.6), and median baseline percentage predicted forced expiratory volume in 1 second was 101% (95% CI, 93–110%). There were no significant differences in median vitamin A or D level or PT before and after ELX/TEZ/IVA initiation (Table 1). Median vitamin E level decreased from 8.8 mg/L to 6.7 mg/L ($p < 0.005$). The percentage of participants with subtherapeutic vitamin D levels decreased from 80% to 63% afer ELX/TEZ/IVA initiation ($p = 0.007$), and the percentage with high PT levels decreased from 20% to 7% ($p = 0.046$). There was no significant difference in the proportion of participants with subtherapeutic vitamin A or E levels. There were no measured vitamin A, D, or E levels in the supratherapeutic range after ELX/TEZ/IVA initiation.

Conclusions: Our results demonstrate a greater proportion of participants with vitamin D and PT within the normal range after ELX/TEZ/IVA initiation. By contrast, median vitamin E level decreased significantly, and there was no significant change in vitamin A level. No vitamin A, D, or E levels were in the supratherapeutic range after ELX/TEZ/IVA initiation. There are several possible explanations for our results. First, although it was assumed that participants continued vitamin supplementation after ELX/TEZ/IVA initiation, we were unable to verify this. It is possible that, as participants' health improved on ELX/TEZ/IVA, they stopped taking vitamin supplements. We continue to investigate how vitamin intake has changed after ELX/TEZ/IVA initiation. Alternatively, greater exposure to sunlight or dietary changes could have contributed to our findings. Data collection and analysis at the second study site are ongoing and may help clarify these relationships.

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Liver function test abnormalities in people with cystic fibrosis treated with elexacaftor/tezacaftor/ivacaftor

C. Colombo[1,2], L. Zazzeron[2], L. Claut[2], C. Rizza[1], A. Malfitano[1], G. Alicandro[1,2].
[1]*Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy;* [2]*Cystic Fibrosis Center, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*

Background: A high prevalence of abnormalities and fluctuation in liver function tests (LFTs) have been reported in people with cystic fibrosis (PwCF) that may be a confounder when monitoring CF transmembrane conductance regulator (CFTR) modulator safety. Triple combination with elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) can induce mild, transient increases in LFT results and, much more rarely, clinically relevant drug-induced liver injury with jaundice and even irreversible decompensation, especially in patients with advanced liver disease. Thus, close monitoring and specific thresholds to decrease dosing or to discontinue medication have been recommended. The aim of this study was to characterize the emergence of abnormalities on LFTs in PwCF after initiation of ELX/TEZ/IVA and to evaluate those considered clinically relevant.

Methods: After approval in Italy in July 2021, ELX/TEZ/IVA was started in 56 PwCF at the reference CF center of the Lombardia region. LFTs were prospectively conducted before and 1, 3, and 6 months after starting ELX/TEZ/IVA. Alanine transaminase (ALT), gamma-glutamyl transferase (GGT), and total bilirubin were measured and expressed as multiples of the upper limit of normality (ULN). Incidence rates (per 100 patient-months) of LFT elevation (>ULN) were computed in patients with normal pretreatment LFT results, and rates of further increments in LFT were computed in those with abnormal pretreatment LFT.

Results: Fifty-six patients were included (27 male; 25 F508del homozygous; median age 20, range 13–36); 18 patients had pretreatment values of ALT, GGT, or bilirubin greater than the ULN, four had cirrhosis, which was associated with portal hypertension in two. Thirty-eight patients were followed for 6 months, 17 for at least 3 months, and one for 1 month. Table 1 reports the number, rates, and corresponding 95% confidence intervals of high LFT results in patients with normal pretreatment LFT and increments above pretreatment values in patients with abnormal pretreatment LFT. During follow-up, ALT values more than three times as high as the ULN were observed in three patients, GGT values more than three times as high as the ULN in one patient, and bilirubin values more than twice as high as the ULN in four patients, all except one with concomitant Gilbert syndrome. None discontinued treatment, although three reduced ELX/TEZ/IVA dose. Most LFT elevations occurred within the first month of treatment and remained above the ULN thereafter.

Conclusions: LFT elevations after ELX/TEZ/IVA introduction is a relatively frequent adverse event but does not appear to be clinically relevant in most cases, even in patients with advanced liver disease. Longer follow-up is needed to have a clear picture of the safety of ELX/TEZ/IVA.

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.

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

J. Torres[1], A. Singla[2], J. Abraham[3], M. Derleth[2]. *[1]Internal Medicine, University of Washington, Seattle, WA; [2]Division of Gastroenterology, University of Washington, Seattle, WA; [3]Division of Gastroenterology, University of Michigan, Ann Arbor, MI*

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

C. Dress[1], E. Hente[1], K. Swegheimer[1], M. Hjelm[1,2], C. Siracusa[1,2], W. Hardie[1,2], T. Boat[1,2]. *[1]Division of Pulmonary Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; [2]Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH*

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].