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Impact of elexacaftor/tezacaftor/ivacaftor therapy on older adults with cystic fibrosis

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Background: Survival of people with cystic fibrosis (CF) has increased over the past few decades and is projected to rise further with the use of effective CF transmembrane conductance regulator (CFTR) modulator therapy. We aimed to assess clinical response of individuals with CF aged 40 and older to elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) therapy, and explore the impact of ELX/TEZ/IVA therapy on liver function tests (LFTs) and cardiovascular risk factors, including serum markers of inflammation, lipid profiles, blood pressure (BP), and noninvasive measurements of central arterial stiffness, including pulse wave velocity (PWV) and augmentation index (AI).
Methods: We conducted a single-center, prospective, observational study between August 2020 and December 2021 of people with CF aged 40 and older prescribed ELX/TEZ/IVA after licensing of this CFTR modulator in the United Kingdom. C-reactive protein (CRP), liver function, serum iron, lipid profile, spirometry, sweat, BP, PWV, and AI were tested at times of clinical stability before commencing ELX/TEZ/IVA therapy and 3 to 6 months thereafter. All permanent and temporary discontinuations of ELX/TEZ/IVA were recorded.
Results: Sixty-five of 73 adults aged 40 and older who commenced ELX/TEZ/IVA (including 31 *phe508del* homozygotes) were studied. Mean percentage predicted forced expiratory volume in 1 scone improved from 54.6 ± 22.9% to 61.0 ± 22.8% ($p < 0.001$), mean weight increased by 1.9 kg ($p < 0.001$), and sweat chloride decreased by 41.4 mmol/L ($p < 0.001$), with the greatest decrease seen in the minimal function group. There was an increase in serum iron levels from 11.9 ± 6.1 mmol/L to 15.7 ± 7 mmol/L ($p = 0.009$). CRP decreased from a median of 3 mg/L (interquartile range 1.0–59) to 1 mg/L (interquartile range 1.0–11.0) ($p = 0.001$). A change in lipid profiles was observed with increases in triglycerides ($p = 0.006$) and apolipoprotein A1 ($p = 0.006$). No statistically significant change was found in serum total cholesterol, high-density lipoprotein, low-density lipoprotein, cholesterol/high-density lipoprotein ratio, or apolipoprotein B or apolipoprotein B/A1 ratio. There were also no significant changes in BP or AI, although PWV increased from 8.6 ± 1.2 m/s to 9.3 ± 2.4 m/s ($p = 0.02$). LFTs showed increases in aspartate aminotransferase (22.6 ± 8.8 IU/L to 23.8 ± 10.7 IU/L; $p = 0.006$) and bilirubin 7.5 ± 6.0 µmol/L to 9.3 ± 5.8 µmol/L ($p < 0.001$).
Conclusions: Individuals with CF aged 40 and older had a response to ELX/TEZ/IVA therapy, measured according to sweat chloride, spirometry, and weight, similar to that of younger individuals with CF in phase III trials. Further research is required to establish the longer-term impact of CFTR modulation on comorbidities including dyslipidemia and other potential risk factors for cardiovascular disease.

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Feasibility of using a modified menstrual tracking app to correlate menstrual cycles and cystic fibrosis symptoms in women with CF: Early findings of the MENSTRUAL study

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Background: The MENstrual Symptom Tracking to Understand and Assess (women) Living with CF (MENSTRUAL) study explores the feasibility of using a modified menstrual tracking smartphone application to track disease-specific symptoms during the menstrual cycle in women with cystic fibrosis (CF).
Methods: In this prospective cohort study, participants were recruited using social media and listservs and through referrals from CF care centers. After completing a virtual training session, participants used a modified period tracking app daily to report whether they had menstrual bleeding and the presence and severity of CF symptoms, such as lung congestion, coughing, and hemoptysis. These symptoms were considered equal and were selected from a preset list developed by women with CF and a multidisciplinary patient-centered team of family practice, ob/gyn, and CF care clinicians. Participants tracked their daily symptoms for 3 consecutive months using the smartphone application. We received institutional review board approval, and all participants provided informed consent.
Results: We were able to modify a smartphone application to track each participant's menstrual cycles and CF symptoms. Seventy-four women with CF participated in this study. Participants were age 18 to 45 and from every region of the United States. Eighty percent of participants reported that it was very easy to track CF symptoms using the application. Participants reported that it took them less than 1 minute to complete the daily track. Only two participants (2.7%) needed additional technical support to use the application. The application allowed us to determine where each participant was in her menstrual cycle and whether she had frequent or severe CF symptoms. Preliminary analysis of the data suggests that, during the luteal phase of the menstrual cycle, there is an increase in the overall number and severity of CF symptoms.
Conclusions: A modified menstrual tracking smartphone application is feasible to study the intersection of menstrual and CF-related symptoms. Although larger studies are needed, these results may inform CF clinical practice by demonstrating that women can use a smartphone application to anticipate menstrual cycle–related changes in CF symptomatology and share this tracking with their CF care clinicians. These results may also help focus future interventions to alleviate symptoms in menstruating women with CF. A menstrual tracking smartphone application could be used to identify trends in menstrual cycles and disease-specific symptoms to promote a personalized approach to CF care and research.
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Characteristics of late diagnosis through newborn screening and effects on growth and pulmonary health outcomes in infants with cystic fibrosis

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Background: Newborn screening (NBS) for cystic fibrosis (CF) was fully implemented in the United States in 2010, but delays in timeliness of evaluation for infants with positive NBS tests persist. We aimed to determine characteristics and effects of late CF care on health outcomes in infants with CF.
Methods: We studied infants enrolled in the Cystic Fibrosis Foundation Patient Registry born from 2010 to 2018 and diagnosed before the age of 1. Exclusions were meconium ileus, prematurity, sweat chloride less than 30 mEq/L, CF transmembrane conductance regulator (CFTR) modulator use before age 1, missing gestational age, and missing ZIP code. Age at first evaluation (AFE) was defined as the earliest age of one (or more) of the following CF events: sweat test, CF center clinical encounter, or care episode lasting longer than 24 hours (hospitalization). We compared initial CF event characteristics and nutritional and pulmonary health outcomes of infants from the youngest (early) to the oldest (late) AFE quartile, matching for covariates chosen a priori of sex, median income according to ZIP code, race, ethnicity, genotype (McKone class), and pancreatic status.
Results: Of 6,879 infants, 3,607 met inclusion criteria. After quartile assignment and matching, 551 infants were in each cohort. Median AFE was