DEPRESSION AND ANXIETY IN PATIENTS WITH CYSTIC FIBROSIS AFTER SIX MONTHS ON ELEXACAFTOR-TEZACAFTOR-IVACAFTOR

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Background

Cystic fibrosis (CF) is a life-limiting disease with chronic, debilitating pulmonary, endocrine, gastrointestinal, and other symptoms. Patients with CF have higher rates of anxiety and depression than the general population[1]. Elexacaftor-tezacaftor-ivacaftor (ETI) has resulted in significant improvement of physical CF symptoms by targeting defects in in the CF transmembrane regulator proteins transcribed by the deltaF508 mutation[2]. However, little is known regarding its effects on mental health. This data is part of a 5-year study monitoring medical and psychiatric symptoms, especially anxiety and depression, in patients taking ETI.

Methods

This is a single center, Nationwide Children's Hospital IRB approved, 5-year longitudinal observational study evaluating the effects of ETI treatment on mood and anxiety. Eligible participants were recruited during routine CF clinic visits at the time of initiation of ETI. Subjects were administered standardized validated measures for anxiety and depression at baseline, 1, 3, 6, 9, 12, 18, 24, 36, 48, and 60 months. Measures include the PHQ-9, GAD-7, adult and pediatric PROMIS Depression and Anxiety Scales. Recruitment and data collections are ongoing.

Table 1: Baseline Characteristics	N = 255[1]
Age (years)	23 (14, 33)
Sex	
Female	125 (49%)
Male	130 (51%)
CF causing mutations	
Homozygous	150 (59%)
Heterozygous	92 (36%)
Other	12 (4.7%)
Severity FEV1pp at baseline (or pre-6mo)	
<40	29 (12%)
40-59	40 (17%)
60-79	62 (26%)
80+	110 (46%)
Compassionate use	17 (6.7%)

[1] Median (IQR); n (%)

Table 2: Change in median PHQ-9 and GAD-7 scores from baseline to 6 months

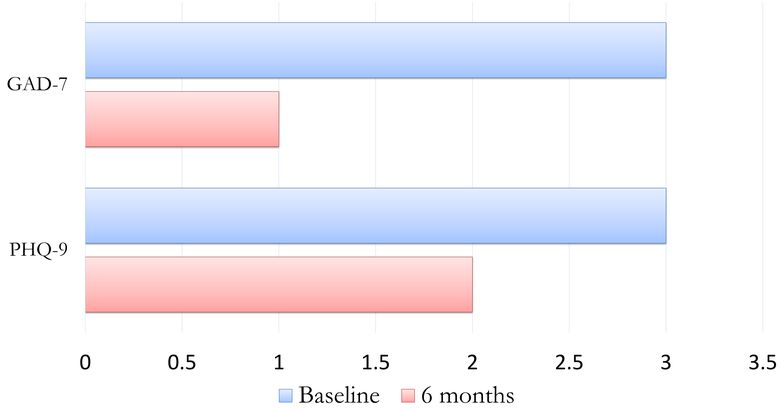
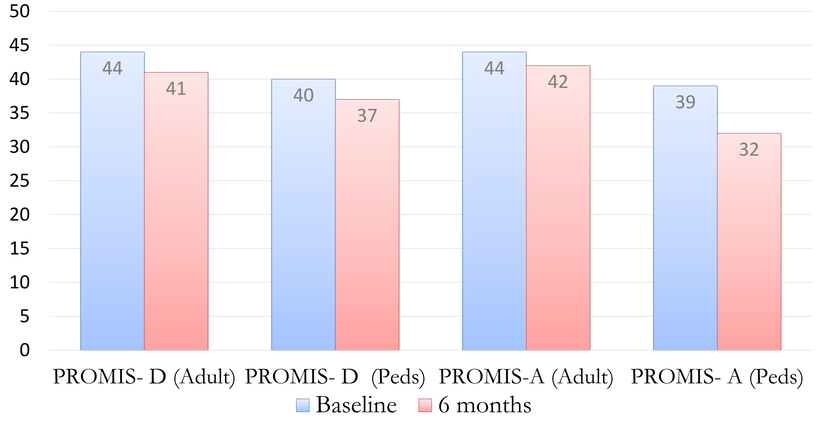


Table 3: Change in median PROMIS scores from baseline to 6 months



Results

At the time of this analysis, 255 subjects (130 males, 125 females), completed anxiety and depression measures at the 6-month mark. Seventy-four of 255 received pediatric measures. Linear mixed-effects model was used to evaluate changes of primary outcomes, PHQ-9, GAD-7, and PROMIS over the study visits. All statistical analyses are performed in R version 4.0 (R Core Team, Vienna, Austria). All baseline scores fell in the within normal range (WNL) and all mental health scores improved over the first 6 months after ETI initiation. However, the decrease in anxiety symptoms on the GAD-7 from baseline to 6 months was the only statistically significant change (estimate = -0.86; 95% CI = -1.53, -0.18; $p < 0.01$). Overall trends were toward stability to slight improvement on all measures, with only 3 respondents reporting shifts from baseline "normal" to "severe" symptoms within the first 6 months. No study participants required emergency or inpatient psychiatric care during this 6-month period.

Discussion

A significant majority of 255 patients with CF demonstrated normal scores on measures of depression and anxiety during their first 6 months on ETI. These results indicate trends toward improvement in mental health upon initiation of ETI in this sample. While this does not reflect each individual case, it indicates that patients with CF collectively may have decreased anxiety and depression during this time period. While improvements in anxiety and depression as CF symptoms improve with ETI treatment make intuitive sense, the first 6 months of this study occurred during the COVID-19 pandemic. Hence, anxiety and depression may also have been affected by social isolation, changes in routine, and fear of contracting COVID-19.

References

1. Quittner AL, et al. (2014). Prevalence of depression and anxiety in patients with cystic fibrosis and parent caregivers. Thorax, 69:1090-97.
2. Middleton PG, et al. (2019). Elexacaftor-tezacaftor-ivacaftor for cystic fibrosis with a single Phe508del allele. NEJM, 381(19):1809-19.