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**P236 Investigating the impact of elexacaftor/tezacaftor/ivacaftor therapy on longitudinal oropharyngeal microbiome dynamics in children with cystic fibrosis**

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Introduction

Elexacaftor/tezacaftor/ivacaftor (ETI) significantly improves pulmonary function and reduces pulmonary exacerbations in ∼90% of people with cystic fibrosis (PwCF). ETI decreases sputum abundances of typical CF bacterial pathogens among PwCF 12 yo and older, but eradication was rare. Most PwCF produce less or no sputum on ETI. Accordingly, alternative airway sampling methods such as oropharyngeal (OP) swabs have supplanted sputum as the most common method to monitor infections. It is unknown how long-term ETI impacts airway microbiota in children with CF (CwCF) under 12 yo. The PROMISE pediatric clinical sub-study prospectively describes clinical outcomes in CwCF 6–11 yo on ETI.We will use OP swabs collected from this cohort to describe the impact of ETI on OP microbiota over time.We hypothesize that 1) ETI therapy will persistently decrease abundances of typical CF pathogens and increase microbial diversity in OP swabs from 6–11 yo CwCF, and 2) sequencingbased identification methods will identify persistent typical CF pathogens longer than will culture-based methods.

Section snippets

Methods

OP swabs (n = 336)were collected before and at 1 and 3-months after initiating ETI from CwCF ages 6–11 yo (n = 112) in the PROMISE pediatric cohort. Shotgun metagenomic sequencing and 16S rRNA qPCR are used to define microbial abundance, community structure, and alpha- and beta-diversity metrics over time in these swabs.We are comparing results of routine clinical bacterial cultures and of DNA-based, culture-independent analyses in paired, concurrent OP swabs to determine the relative

Conclusions

We will provide a detailed description of microbiota dynamics in CwCF on ETI therapy using the most common current CF respiratory sample type, OP swabs, using both culture-independent and culture-based methods. At the conference, we will present the results of these analyses up to 3 months post-ETI.