Testing Drug Efficacy in Cystic Fibrosis Through N-of-1 Trials

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 6 years and over
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

- Signed informed consent (and assent when applicable)
- Willing and able to adhere to the study visit schedule and protocol requirements
- Male or Female ≥6 years old and within the FDA-approved range for the proposed modulator drug
    - Ivacaftor: ≥4 months old
    - Lumacaftor/Ivacaftor: 2 years old
    - Tezacaftor/Ivacaftor: 12 years old
    - Elexacaftor/Tezacaftor/Ivacaftor: ≥12 years old
- At least one rare CFTR variant (incidence of <5% of the CF population)
- Documentation of a CF diagnosis as evidenced by one or more clinical features of CF plus at least one of the following:
    - Sweat Chloride ≥60mmol/L by quantitative pilocarpine iontophoresis
    - Two mutations in the CFTR gene
    - Abnormal nasal potential difference (NPD) testing supportive of a CF diagnosis
- FEV1 > 50% predicted for age
- Stable chronic CF therapies with no changes in >28 days (except for chronic cycled inhaled antibiotics such as tobramycin)
- Prescribed CFTR modulator by a licensed physician
- No contraindication to treatment with the selected drug at the time of treatment initiation

Exclusion Criteria:

- Presence of any condition or abnormality that, in the opinion of the Investigator, would compromise the safety of the patient and/or quality of the data
- For women of child bearing potential:
    - Positive pregnancy test or known pregnancy at Visit 1
    - Lactating
    - Unwilling to practice a medically acceptable form of contraception (acceptable forms include abstinence, hormonal birth control, intrauterine device, or barrier method plus a spermicidal agent), unless surgically sterilized or postmenopausal during the study
- BMI < 10th percentile for age (if <18 years old) or < 20kg/m2 (if ≥18 years old)
- FEV1 ≤ 50% predicted for age
- Growth of CF pathogens from sputum cultures that are associated with unstable disease (e.g., nontuberculous mycobacteria, Burkholderia spp) within six months of enrollment
- Concomitant use of CYP3A inducers or inhibitors (e.g., voriconazole, fluconazole, rifampin) or prednisone (>20mg daily)
- Concomitant conditions:
    - Poorly controlled diabetes mellitus (HbA1c >8.5 or glucosuria as noted below)
    - Advanced CF liver disease (cirrhosis with portal hypertension, ascites, or abnormal liver laboratory testing as noted below)
    - End stage renal disease
    - History of organ transplantation
    - Additional medical conditions that in the opinion of the Investigator place the patient at risk of participation or may impact the patient's ability to complete the trial (e.g., uncontrolled depression, anxiety disorder, poor adherence to CF therapies, active ABPA)
- Any of the following abnormal laboratory values at the Screening Visit:
    - CBC
    - WBC >15,000 K/mcL or ANC <1,500 K/mcL
    - Hemoglobin <10 gm/dL
    - Platelets <50,000 K/mcL
    - Chemistries
    - >2+ Glucosuria
    - Clinically significant abnormalities as assessed by the Investigator
    - Glomerular filtration rate ≤50 mL/min/1.73 m2 (calculated by the Counahan-Barratt equation)
    - Hepatic Function Testing / Coagulation Testing

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  - ≥3 × upper limit of normal (ULN) aspartate aminotransferase (AST)
  - ≥3 × ULN alanine aminotransferase (ALT)
  - ≥3 × ULN gamma-glutamyl transpeptidase
  - Total or direct bilirubin >2 × ULN
  - INR > 1.5 x ULN
  - Positive pregnancy test

Conditions & Interventions

Interventions:
DRUG: CFTR Modulators
Conditions:
Cystic Fibrosis
Keywords:
CFTR modulators, cystic fibrosis, HNE, human nasal epithelial cells, NPD, nasal potential difference, air-liquid interface, N-of-1

More Information

Description:
The purpose of this study is to validate and utilize a personalized medicine approach to identify potential treatments with current FDA approved CFTR modifiers for non-approved CF gene mutations. The study will perform ex vivo testing of CFTR function and current marketed CFTR modulating drugs on expanded nasal cells at Cincinnati Children's Human Nasal Epithelium (HNE) Core Laboratory. The results will be confirmed and translated into bedside care through an N of 1 trial to determine effectiveness of treatment.

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