Study Protocol

Title:

Orkambi in Patients with Cystic Fibrosis and Severe Liver Disease

Clinical Trial Protocol Version 3.0 (Amendment)

8 November 2021

Protocol amendment

Patients with cystic fibrosis and severe liver disease will continue to be recruited as per the Clinical Trial Protocol Version 2.0 (22 May 2020). This amended protocol will include patients who are already on full dose Orkambi, without liver disease as well as those with mild to severe liver disease (cirrhosis and portal hypertension). It is very unlikely that patients with severe liver disease have been commenced on Orkambi, as they would have been a part of this clinical trial (Version 2.0).

The aim of this study is to examine the pharmacokinetics of Orkambi in patients without severe liver disease as compared to those with severe liver disease.

Stool samples and blood samples (with consent) will be obtained. The target will be to collect samples from approximately 30 patients, 10 from each age group (i.e., 2-5 years, 6-11 years, >12 years).

Sample collection

Baseline

- Baseline information will be retrospectively collected
- Lung function
- Bloods – Full blood count (FBE), CHEM20 (including liver function tests - ALT, AST, GGT, ALP, albumin, bilirubin), coagulation tests, ammonia levels
- Imaging – abdominal ultrasound and elastography
- Growth measurements – weight, length, BMI
- Medication list including CYP3A inducers/inhibitors
- Previous sputum microbiology – over the last 12 months
- Ophthalmology examination (eye tests) to exclude cataracts

Blood pharmacokinetic collection

- For patients without ready intravenous access (i.e. a portacath or peripherally inserted central catheter [PICC]), a single blood test will be obtained between 1 to 12 hours after the morning Orkambi dose
- For patients with intravenous access and who are inpatients in the hospital, a full pharmacokinetic profile will be opportunistically obtained at 0, 2, 4, 6, 8 and 24 hours
- During the blood test, a full blood count (FBE), CHEM20 (including liver function tests - ALT, AST, GGT, ALP, albumin, bilirubin), coagulation tests and ammonia levels may also be collected
- Where possible, bloods tests will be taken opportunistically with the patients' annual bloods, other blood tests or in conjunction with formal clinical trials

Faecal pharmacokinetic collection

- The first faecal sample of the day will be collected
- A second faecal sample will be collected opportunistically from the inpatients as able