Protocol of clinical study

Title

Open-Label, randomized, phase III trial to evaluate the efficacy and safety of Aztreonam (AZLI) versus TOBI® (TNS, Tobramycin Nebuliser Solution) in an intermittent aerosolized antibiotic regimen in patients with Cystic fibrosis , followed by an open-label, single arm extension.

Inclusion Criteria:

- Males or females aged 6 years and older
- Patients with CF as diagnosed by one of the following:
- Documented sweat chloride ≥ 60 mEq/L by quantitative pilocarpine iontophoresis test, or
- Documented sweat sodium ≥ 60 mmol/L, or
- Two well characterized genetic mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene, or
- Abnormal nasal potential difference with accompanying symptoms characteristic of CF
- Documented PA in an expectorated sputum or throat swab culture within 3 months prior to Visit 1 or at Visit
- Patients must be able to provide written informed consent/assent prior to any study related procedures; parent/guardian must be able to give written informed consent as necessary prior to any study related procedure
- Patients must have received previous treatment with aerosolized antibiotics without demonstration of drug intolerance
- FEV1 ≤ 75% predicted at Visit 1
- Ability to perform reproducible pulmonary function tests
- Chest radiograph at Visit 1 without significant acute findings (eg, infiltrates [lobar or diffuse interstitial], pleural effusion, pneumothorax); or chest radiograph or MRI obtained within the 180 days prior to Visit 1 without acute findings and no significant intercurrent illness; chronic, stable findings (eg, chronic scarring or atelectasis) are allowed

Exclusion Criteria:

- Current use of oral corticosteroids in doses exceeding the equivalent of 10 mg prednisone a day or 20 mg prednisone every other day
- History of sputum or throat swab culture yielding B. cepacia in the previous 2 years
- Current requirement for daily continuous oxygen supplementation or requirement for more than 2 L/minute at night
- Administration of any investigational drug or device within 28 days of Visit 1 or within 6 half-lives of the investigational drug (whichever is longer)
- Known local or systemic hypersensitivity to monobactam antibiotics
- Known allergies/intolerance to tobramycin
- Inability to tolerate inhalation of a short acting beta agonist
- Changes in or initiation of chronic azithromycin treatment within 28 days prior to Visit 1
- Administration of antipseudomonal antibiotics by inhalation, intravenous or oral routes within the 14 days prior to Visit 1
- Changes in antimicrobial, bronchodilator (BD), dornase alfa, or corticosteroid medications within 7 days prior to Visit 1

- Changes in physiotherapy technique or schedule within 7 days prior to Visit 1
- History of lung transplantation
- Abnormal renal or hepatic function or serum chemistry at Visit 1, defined as:
- AST, ALT > 5 times upper limit of normal range (ULN)
- Creatinine > 2 times ULN
- Positive pregnancy test at Visit 1; all women of childbearing potential will be tested
- Female of childbearing potential who is lactating or is not (in the opinion of the investigator) practicing an acceptable method of birth control; female subjects who utilize hormonal contraceptives as one of their birth control methods must have used the same method for at least 3 months before study dosing
- Any serious or active medical or psychiatric illness, which in the opinion of the investigator, would interfere with patient treatment, assessment, or compliance with the protocol

Drug
Aztreonam for Inhalation Solution
Tobramycin Nebuliser Solution

Number of expected inclusions
200 patients

Study start
August 2008

Estimated completion
September 2010

Study phase
Phase III

Study Design
International, multicentre, treatment, randomized, open label, parallel assignment, safety/efficacy study