Clinical trial protocol

Title
Single Center, Double-Blind, Randomized, Placebo-Controlled, 2-Period/2-Treatment Crossover Study Investigating the Effect of Miglustat on the Nasal Potential Difference in Patients With Cystic Fibrosis Homozygous for the ΔF508 Mutation

Inclusion Criteria

Ages Eligible for Study: 12 Years and above, Genders Eligible for Study: Both

- Aged 12 years and older
- Male or female

- Non-pregnant women who are to remain non-pregnant for 3 months after the end of the study: only women who are surgically sterile, who are in the menopause (no menstruation for at least one year) or those of childbearing potential who are using a reliable method of contraception. Reliable methods of contraception for female patients include the following:
  - Barrier type devices (e.g., female condom, diaphragm and contraceptive sponge) used ONLY in combination with a spermicide
  - Intrauterine devices
  - Oral contraceptive agent
  - Depo-Provera™ (medroxyprogesterone acetate)
  - Levonorgestrel implants Abstention, the rhythm method or contraception by the partner alone are NOT reliable methods of contraception.

For children, a reliable method of contraception must be considered, if appropriate.

- Accepting for the duration of the study and for 3 months thereafter to use a condom and not to procreate a child (males only)
- Cystic fibrosis patients homozygous for the ΔF508 mutation as confirmed by genetic test
- Signed informed consent prior to any study-mandated procedure

Exclusion Criteria

- Any condition prohibiting the correct measurement of the NPD such as upper respiratory tract infection
- Acute upper respiratory tract or pulmonary exacerbation requiring antibiotic intervention within 2 weeks of screening
- Severe renal impairment (creatinine clearance < 30 ml/min as per Cockcroft and Gault)
- Female patients who will not undergo a pregnancy test prior to enrollment in the study
- History of significant lactose intolerance
- History of neuropathy
- History of cataracts or known increased risk of cataract formation
- Presence of clinically significant diarrhea (>3 liquid stools per day for >7 days) without definable cause within 1 month prior to screening
- Any known factor of disease that might interfere with treatment compliance, study conduct or interruption of the results such as drug or alcohol dependence or psychiatric disease
- FEVI <25% of predicted normal
- Oxygen saturation at rest <88%
- Active or passive smoking as measured using the Smokelyzer®
- Hypersensitivity to miglustat or any excipients
- Planned treatment or treatment with another investigational drug or therapy (e.g., gene therapy) within 1 month prior to randomization

**Study start:**
September 2007

**Expected completion:**
December 2008

**Total Enrollment**
25

**Drug**
Miglustat

**Arms**
A: Experimental
  Oral miglustat capsules 200 mg t.i.d. for 1 week and a single 200 mg dose on day 8
  Drug: miglustat

B: Placebo Comparator
  Oral placebo capsules matching in appearance miglustat capsules given t.i.d. for 1 week and a single dose on day 8
  Drug: placebo

**Trial phase**
Phase II

**National monocenter study**