Study design of two Phase III, prospective, multicenter, randomized, controlled clinical trials evaluating the efficacy and safety of Liposomal Cyclosporin A for Inhalation (L-CsA-i) in patients with Bronchiolitis Obliterans Syndrome post single- (BOSTON-1) or double- (BOSTON-2) lung transplantation

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BRONCHIOLITIS OBLITERANS SYNDROME

- Lung transplantation (LTx) recipients have 1-, 5- and 10-year unadjusted survival rates of 80%, 54%, and 32%, respectively[1].
- Most deaths after first post-transplant year are caused by Chronic Lung Allograft Dysfunction (CLAD)[1].
- Bronchiolitis obliterans syndrome (BOS) is the obstructive phenotype and most common form of CLAD[2].
- Incidence of CLAD-BOS following lung transplant is about 10% per year, with a prevalence of 50% at 5 years[3]

Currently there are no proven therapies for the treatment of BOS

THE IDEA BEHIND THE THERAPY

- Inhaled liposomal Cyclosporine A (L-CsA-i) is an investigational formulation of cyclosporine.
- The unique formulation of L-CsA-i, administered via the investigational drug-specific eFlow® Technology nebulizer system, is designed to deliver drug directly to the small airways of the lung.
- Delivering the immunosuppressive therapy directly to the allograft, it can act locally at the site of immune activation.

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TWO PHASE III TRIALS IN CLAD-BOS AFTER LTx

Objective:

Assess the efficacy and safety of L-CsA-i plus standard of care (SoC) in the treatment of CLAD-BOS in single- (BOSTON-1) and double- (BOSTON-2) lung transplant recipients.

Study Design:

Phase III, multicenter, controlled clinical trial

ClinicalTrials.gov:

NCT03657342 - NCT03656926

Location:

Approximately 43 centers worldwide

TREATMENT ARMS

48 weeks of treatment

BOSTON 1: CLAD-BOS in Single Lung Transplantation
110 patients randomized 1:1
L-CsA-i (5mg bid) + SoC
SoC alone

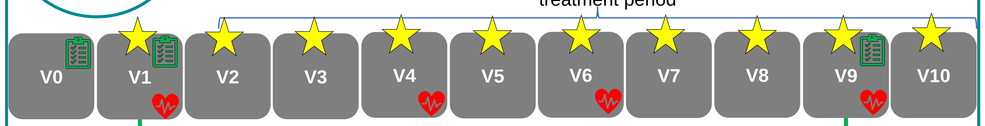
BOSTON 2: CLAD-BOS in Double Lung Transplantation
110 patients randomized 1:1
L-CsA-i (10mg bid) + SoC
SoC alone

Continue treatment until Marketing Authorization

BOSTON 3: Open Label Extension of BOSTON-1 and BOSTON-2
All patients receive L-CsA-i +SoC

VISIT SCHEDULE

Visits scheduled every 4-8 weeks for a total 48-week treatment period



Mandatory on-site
Spirometry Perfomed
QoL Assessment through EQ-5D-5L Questionnaire

KEY INCLUSION/EXCLUSION CRITERIA

Inclusion Criteria:

- ✓ Patients with BOS diagnosis defined as CLAD-BOS phenotype with:
  - a) Screening FEV_1 between 85-51% of personal best FEV_1 value post-transplant **OR**
  - b) Screening FEV_1>85% of personal best FEV_1 associated with EITHER a ≥200mL decrease in FEV_1 in the previous 12 months OR according to medical history showing BOS progression
- ✓ Diagnosis of CLAD-BOS must be made at least 12 months after lung transplantation and a) within 12 months prior to the screening visit **OR** b) more than 12 months from screening and patient must have shown a decline in FEV_1≥ 200ml in the previous 12 months before screening, which is not due to acute infection or acute organ rejection

Exclusion Criteria:

- ✓ Patients with confirmed other causes for loss of lung function, such as acute infection, acute rejection, restrictive allograft syndrome (CLAD –RAS phenotype)
- ✓ Patients with acute antibody-mediated rejection at Screening. In this context, clinically stable patients (as judged by the Investigator) with detectable levels of donor specific antibodies (DSA) at the Screening Visit are eligible for the study
- ✓ Known hypersensitivity to L-CsA or to cyclosporine A

PRIMARY ENDPOINT:

Mean change in FEV1(mL) from baseline to Week 48

SECONDARY ENDPOINTS:

- Mean change in FEV_1/FVC from baseline to Week 48
- Time to Progression of BOS, defined as the earliest of the following:
  - Absolute decrease from baseline in FEV_1≥10% or ≥200 mL and absolute decrease in FEV_1/FVC of >5% **OR**
  - Change in BOS Severity, **OR**
  - Re-transplantation, **OR**
  - Death from respiratory failure

CONCLUSIONS

- These phase III trials will characterize the safety and efficacy of L-CsA-i as add-on therapy to SoC in CLAD-BOS patients after single and double lung transplantation
- Despite the COVID-19 pandemic, BOSTON-1 and BOSTON-2 are ongoing, ensuring the integrity of data collection and safety of enrolled patients

DISCLOSURES

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