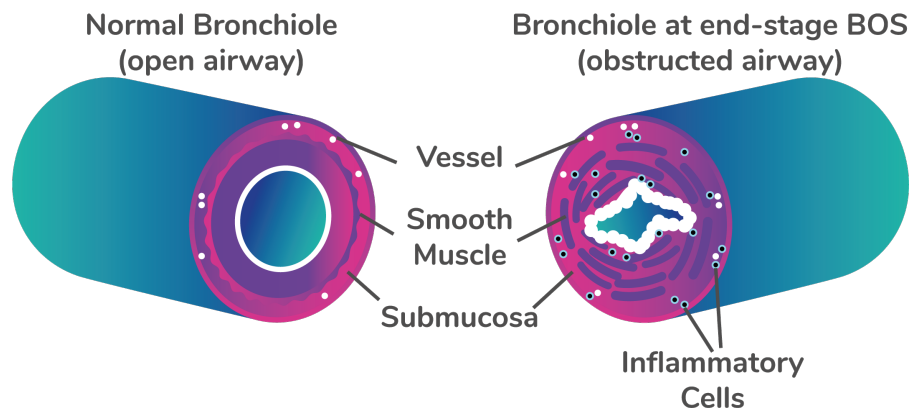


What is Chronic Lung Allograft Dysfunction (CLAD) – Bronchiolitis Obliterans Syndrome (BOS)?

- Chronic Lung Allograft Dysfunction (CLAD) is a severe lung disease where the immune system attacks the airways of the lungs, also known as chronic rejection. There are various types, the most common is Bronchiolitis Obliterans Syndrome (BOS).¹
- BOS may be diagnosed through pulmonary function tests. The Forced Expiratory Volume at 1 second (FEV₁) is measured for decline after lung transplantation. Chest x-ray, computerized tomography (CT) scan, and lung biopsy are other methods used to diagnose BOS, or in the alternative, to exclude BOS because of other potential causes for the decline in FEV₁, such as infection.
- Lung tissue shows inflammation, scarring and narrowing of the airways.
- BOS is a rapidly progressive inflammatory disease that irreversibly destroys the airways of the lung and can lead to respiratory failure and death within 2 to 4 years after diagnosis.²
- BOS may manifest in patients following lung transplantation.
- Incidence of BOS following lung transplant is about 10% per year, with a prevalence of 50% at 5 years.³



What is the BOSTON Development Program?

- The BOSTON development program is evaluating Liposomal Cyclosporine A for Inhalation (L-CsA-i) for the treatment of CLAD-BOS. If approved, L-CsA-i would be the first available treatment for CLAD-BOS.
 - Two global Phase 3 randomized controlled studies are currently evaluating the safety and efficacy of L-CsA-i in CLAD-BOS adult patients following lung transplantation.
 - BOSTON-1 study is for CLAD-BOS in adults after single lung transplant.
 - BOSTON-2 study is for CLAD-BOS in adults after double lung transplant.
 - Study sites are in the US, Austria, Belgium, France, Germany, Spain, UK, and Israel.
 - In each study, approximately 110 patients will be followed for up to 48 weeks.
 - Study information is available on www.ClinicalTrials.gov or at www.studyforbos.com.

Who can Participate?

- Individuals who are interested should talk to their doctors about the study.
- These individuals will need to consent to participate in the study, prior to a screening visit. If they qualify, they will be randomized and assigned to one of two groups.
 - One group of participants will receive standard of care and the investigational inhaled L-CsA-i.
 - One group will receive their standard of care regimen only and no study medication.
 - Regardless of the treatment allocation, all participants will continue to receive their standard of care regimen for maintenance of the lung allograft. For evaluation, the two groups will be compared.
- Primary study endpoint: Change of FEV₁ over time.
- Secondary endpoint: progression free survival.

What is Liposomal Cyclosporine A for Inhalation (L-CsA-i)?

- L-CsA-i is a liposomal formulation of cyclosporine A designed for inhaled delivery to the lungs via a customized Investigational eFlow[®] Technology nebulizer system (PARI Pharma GmbH).
- Cyclosporine A is a well-known immunosuppressive drug.
- Liposomal Cyclosporine A is an investigational formulation preparation of cyclosporine A that is enclosed within tiny droplets called liposomes.
- L-CsA is inhaled into the lungs using a drug-specific nebulizer system.
- Research studies are being performed to evaluate the safety and efficacy of inhaled L-CsA as a treatment for BOS when added to the standard of care regimen after lung transplantation.
- L-CsA-i has received orphan drug designation for the treatment of BOS from FDA and EMA, and Fast Track designation from FDA.
- Drug-device combination inhalation therapies are designed to deliver dosing to the small airways of the lung and minimize overall systemic drug exposure.

About Zambon S.p.A

Zambon is a multinational pharmaceutical company that focuses on innovation and development with the aim to improve patients' lives. Based on a valuable heritage and strongly focused on the future, its goal is to improve people's health through the development of innovative and quality healthcare solutions.

Zambon products are commercialized in 87 countries. The company has 20 subsidiaries in three different continents – Europe, America and Asia – and owns manufacturing units in Italy, Switzerland, China and Brazil. The company today has a strong focus on the treatment of rare diseases and specialties, on top of respiratory, pain management and women's care. Zambon was established in 1906 in Italy and today counts 2,500 employees all over the world. For further information, please visit www.zambon.com.

1. Verleden GM, et al. *J Heart Lung Transplant*. 2019; 38(5):493-503. ([https://www.jhltonline.org/article/S1053-2498\(19\)31432-9/fulltext](https://www.jhltonline.org/article/S1053-2498(19)31432-9/fulltext)).
2. Chambers DC, et al. *J Heart Lung Transplant*. 2018;37(10):1169-1183.
3. Ruttens D, et al. *PLoS ONE*. 2018; 13(4): e0193564. <https://doi.org/10.1371/journal.pone.0193564>.

For more information about the BOSTON-1 and -2 studies

