A Retrospective Chart Review Study of Patients With Chronic Lung Allograft Dysfunction-Bronchiolitis Obliterans Syndrome (CLAD-BOS) Post Lung Transplantation – "BOSTON EVOLUTION"

First published: 16/06/2026

Last updated: 23/07/2026

Study Finalised

Administrative details

EU PAS number

EUPAS1000001016

Study ID

1000001016

DARWIN EU® study

No

Study countries

Belgium

Spain

United States

Study description

A retrospective, multinational, multicenter chart review study of adult patients with clinically diagnosed Chronic Lung Allograft Dysfunction-Bronchiolitis Obliterans Syndrome (CLAD-BOS) after lung transplantation. All data retrospectively collected from patient records starting from lung transplantation date through last date of available data.

Study status

Finalised

Research institutions and networks

Institutions

Fortrea - Real world Intelligence & Late Phase Solution

Germany

United Kingdom (Northern Ireland)

First published: 15/12/2015

Last updated: 31/10/2023

Institution | **Non-Pharmaceutical company** | **ENCePP partner**

Zambon

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Contact details

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Primary lead investigator

Paola Castellani

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 30/11/2023

Actual: 30/11/2023

Study start date

Planned: 18/05/2024

Actual: 27/06/2024

Data analysis start date

Planned: 14/01/2025

Actual: 12/05/2025

Date of final study report
Planned: 15/04/2025

Actual: 16/04/2026

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Zambon SpA, Via Lillo del Duca, 10 Bresso (MI) 20091 Italy

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Other study registration identification numbers and links

Protocol version identifier: Z8000N01

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Disease epidemiology

Other

If ‘other’, further details on the scope of the study

Study to describe natural disease evolution and clinical outcomes. Data collection methods: The study data sources consisted of medical records (including electronic and/or paper) and patient notes for the study patients.

Data collection methods:

Secondary use of data

Study design:

This was a retrospective, multinational, multicenter chart review study of adult patients with clinically diagnosed CLAD BOS after lung transplantation. All data were retrospectively collected from patient records, starting from the lung transplantation date through the last date of available data;

Main study objective:

The primary objective of this study was to evaluate the FEV1 trajectory of patients diagnosed with CLAD BOS.

Study Design

Non-interventional study design

Other

Non-interventional study design, other

Retrospective chart review study

Population studied

Short description of the study population

Adult patients aged ≥ 18 years who are recipients of a lung transplant and diagnosed with CLAD-BOS following transplantation.

Age groups

- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

Estimated number of subjects

284

Study design details

Setting

The study was conducted at 6 sites located in the US and EU regions, with patient enrollment distributed nearly equally between the 2 regions. Eligible patients were identified through retrospective chart reviews of medical records at the participating study sites. The records were screened chronologically, starting with patients diagnosed with CLAD BOS from 01 January 2013. Patients who met the eligibility criteria were included in the study.

Comparators

Not applicable

Outcomes

Primary outcome: To evaluate the FEV1 trajectory of patients diagnosed with CLAD-BOS

Secondary outcomes:

1. To describe demographics of patients diagnosed with CLAD-BOS
2. To describe clinical characteristics following lung transplantation for patients diagnosed with CLAD-BOS
3. To evaluate the trajectory of other relevant spirometry parameters (i.e., FVC, FEV1/FVC, FEF25-75%)
4. To evaluate the OS of patients diagnosed with CLAD-BOS
5. To evaluate the time to first CLAD-BOS progression
6. To evaluate the cumulative incidence of CLAD-BOS progression
7. To evaluate the rate of hospitalization due to respiratory failure after CLAD-BOS onset
8. To evaluate the incidence of concomitant respiratory disease
9. To evaluate the incidence of concomitant non-respiratory disease
10. To describe the use of concomitant treatments and procedures for CLAD-BOS

Data analysis plan

Descriptive summary statistics for continuous variables included the number of observations, mean, SD, median, Q1, Q3, minimum, and maximum values. Two-sided 95% confidence intervals (CIs) were presented where applicable.

Descriptive summary statistics for categorical variables included frequency and percentages.

The trajectories of FEV1, FVC, FEV1/FVC, and FEF25-75% over time were characterized using a linear mixed model (LMM) for repeated measurements with random coefficients and an unstructured covariance matrix.

For time-to-event outcomes, including overall survival (OS), cumulative event-free survival times were evaluated using the Kaplan-Meier (KM) method. The KM graphs were presented along with the number of patients-at-risk at specified timepoints. Patients who were free from the event were censored at the last available date.

Count data (CLAD-BOS progression, hospitalization rates) per patient-year and 95% CIs were estimated using negative binomial regression models, including an offset for patient follow-up time.

Planned subgroup analyses of main outcomes were performed by region (EU/US), age (<55 years, ≥55 years), sex (male/female), race (White, Black or African American, Asian, Other, Not collected locally), FEV1/FVC ratio (<0.7, ≥0.7), rate of decline (<Q1, ≥Q1-<median, ≥median-<Q3, ≥Q3), Baseline Lung Allograft Dysfunction (yes/no), azithromycin use (yes/no), transplant type (single, bilateral). No multiplicity adjustments were applied due to the descriptive nature of the analyses.

Post-hoc analyses were conducted to further explore the disease trajectory and treatment effects in specific subpopulations and from the clinical diagnosis of BOS. The post-hoc analyses included alternative modeling approaches for FEV1 trajectory (linear spline mixed-effects models), alternative baseline definition

using diagnosis date, and time-dependent Cox proportional hazards models for OS.

Analyses were performed using SAS, V. 9.4 or higher (SAS Institute, Cary, NC).>

Summary results

This study provides the most comprehensive description to date of the natural history and progression of CLAD-BOS following lung transplantation. It highlights a significant decline in lung function among patients with CLAD-BOS over a 3-year period, with spirometry parameters such as FEV_1, FVC, FEV_1/FVC, and FEF_{25-75}% showing progressive deterioration. The analysis confirms that, after disease onset, patients experience a rapid initial decline in lung function during the first 24 weeks, followed by a slower, progressive deterioration over subsequent years. This pattern was consistent across analytical approaches. Sensitivity analyses further supported the robustness of these findings. Posthoc analyses using the clinically diagnosed date of CLAD-BOS as the starting point, instead of the pre-specified algorithmic onset date, confirmed the same disease trajectory, an initial steep decline followed by slower progression, with only minor differences in estimated values. This consistency reinforces the reliability of the overall disease course characterization. Slight variations were observed, including a marginally greater FEV_1 decline at early timepoints and a shorter median OS (approx. 10 months less), when analyses were anchored to the clinical diagnosis date. Survival analyses demonstrated a clear difference by transplant type, with markedly longer median OS in bilateral versus single lung transplant recipients. The overall median survival from CLAD-BOS onset was 77.5 months, consistent with previously reported outcomes in this population. In summary, the study delineates a consistent pattern of disease progression characterized by an early, steep decline in lung function followed by stabilization or gradual deterioration over time. These data clearly indicate that the optimal therapeutic window for treating CLAD-BOS is at the early stage of the diagnosis and provide a strong scientific rationale for initiating treatment in

these patients as early as possible.

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data sources (types)

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

Not applicable