Lung Function Improvement after Bronchoscopic Lung Volume Reduction with Pulmonx Endobronchial Valves used in Treatment of Emphysema

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The purpose of this study is to assess the safety and effectiveness of bronchoscopic lung volume reduction (BLVR) using the PulmonxEndobronchial Valve (EBV) in treated study participants compared to control participants to support a premarket…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON42116

Source
ToetsingOnline

Brief title
LIBERATE STUDY

Condition

- Respiratory disorders NEC

Synonym
COPD emphysema

Research involving
Human

Sponsors and support

Primary sponsor: PulmonX International Sarl

Source(s) of monetary or material Support: Door industrie zie hieronder (PulmonX)

Intervention

Keyword: bronchoscopy, COPD, emphysema, lung volume reduction

Outcome measures

Primary outcome

Primary effectiveness endpoint:

The percentage of study participants in the EBV treatment arm meeting the clinically significant threshold of 15% or higher improved forced expiratory volume in one second (FEV1), obtained immediately following bronchodilator therapy, as compared to the percentage in the control arm at 1 year post-procedure.

Primary safety Endpoint:

Evaluation of the short- and long-term adverse events profile of the EBV treatment arm during the treatment period, defined as the day of the study procedure until 45 days after the study procedure (short), and in the post-treatment period, defined as 46 days after the study procedure until the 1-year follow-up visit (long).

Secondary outcome

Secondary Effectiveness Measures:

Treatment Lobe Volume Reduction (TLVR) for the Treatment Arm

* TLVR, measured as the *absolute change from baseline* for treated lobe volume as seen via HRCT (high resolution computed tomography), will be evaluated at 45 days and 1 year.

* TLVR, measured as the *percentage change from baseline* for treated lobe volume as seen via HRCT, will be evaluated at 45 days and 1 year.

St. George*s Respiratory Questionnaire (SGRQ)

* Difference between study arms in *absolute change from baseline* for SGRQ score at 1 year.

FEV1

* Persistence of treatment effect will be evaluated by determining the difference between study arms for *absolute change from baseline* for FEV1 at 45 days, 6 months, and 1 year.

* Persistence of treatment effect will be evaluated by determining the difference between study arms for *percentage change from baseline* for FEV1 at 45 days, 6 months, and 1 year.

6-Minute Walk Distance (6MWD)

* Difference between study arms in *absolute change from baseline* for 6MWD at 1 year.

* Difference between study arms in *percentage change from baseline* for 6MWD at 1 year.

Study description

Background summary

Patients with severe emphysema suffer from severe dyspnea and a poor quality of life, with no current effective medical treatment. Only for a very small, highly selective group of COPD patients, very invasive surgical procedures like lung volume reduction surgery (LVRS) or lungtransplantation are available.

Minimally invasive bronchoscopic lung volume reduction (BLVR) techniques through the implantation of one-way valves have now been established as a means of treating the hyperinflation of emphysema for a group of selected patients.clinical evidence indicates that by achieving lobar occlusion in the absence of collateral ventilation, significant lung volume reduction can be obtained with associated good clinical responses. The Chartis Pulmonary Assessment System which assesses collateral ventilation has shown 75% accuracy in predicting response.

Study objective

The purpose of this study is to assess the safety and effectiveness of bronchoscopic lung volume reduction (BLVR) using the Pulmonx Endobronchial Valve (EBV) in treated study participants compared to control participants to support a premarket approval application to FDA.

Study design

This will be a multi-center, prospective, randomized, controlled study with EBV treatment statistically evaluated using Intent-to-Treat (ITT) analyses. A maximum of 183 study participants, who meet study entry criteria, consisting of screening eligibility criteria, baseline eligibility criteria, and procedure eligibility criteria, will be enrolled at a maximum of 22 centers.

Intervention

The Pulmonx Zephyr Endobronchial Valve (EBV) is an implantable bronchial valve intended to decrease volume in targeted regions of the lung. It is indicated for the treatment of patients with hyperinflation associated with severe heterogeneous emphysema in regions of the lung that have little or no collateral ventilation as assessed by the Chartis System.

Study burden and risks

The patients that will be included in the study will have to come to our outpatient clinic, perform pulmonary function testing, a 6 min walking test, HRCT scanning, thoracic x-ray, fill in questionnaires and testing of blood samples and arterial blood gas. For the actual treatment with bronchoscopy under general anesthesia the patients will stay 6 nights in our hospital. For the follow-up, the patients will visit the hospital (7x or 5x), which will include 1 CT scan and pulmonary function tests, questionnaires and exercise testing (6MWT). The included patients will have to put large effort in the study, but is in balance with the expected outcome and very limited compared 'alternative' treatments like highly invasive surgery: Lung volume reduction

surgery or Lung transplantation. All included patients have a severe limitation of their activities of daily living. With the development and validation of the use of the lung volume reduction treatment with the placement of valves, does it seem possible to give relieve of shortness of breath and improvement in exercise performance. Furthermore, this technique can be used as a 'bridge' to lung transplantation in future, or will be the only possible therapeutic tool available by them. The risks are not bigger than the risks any individual has for the investigations described. The treatment with the valves and inducing the significant volume reduction the major risks involved are: Pneumothorax (1 in 4 patients) for which chest drainage is required, transient (1-3 days) chest pain (1 in 2 patients), transient (1-7 days) and dyspnea (1 in 4 patients).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Signed Screening or Study Procedure Informed Consent using a form that was reviewed and approved by the IRB;
2. Age 40 to 75 years;
3. BMI less than 35 kg/m2;
4 Stable with less than 20 mg prednisone (or equivalent) per day;
5 Nonsmoking for 4 months prior to screening interview.
6.Completed a supervised pulmonary rehabilitation program less than equal to 6 months prior to the baseline exam or is regularly performing maintenance respiratory rehabilitation if initial supervised therapy occurred greater than 6 months prior
7.FEV1 between 15% and 45% of predicted value at baseline exam
Post-rehabilitation 6-minute walk distance between 100 meters and 500 meters at baseline exam
8.Current Pneumococcus vaccination & Current Influenza vaccination
9.Little or no collateral ventilation (CV-) as determined using the Chartis System

Exclusion criteria

1. Currently enrolled in another clinical trial studying an experimental treatment;
2. Previously enrolled in this study for which protocol required follow up is not complete;
3. Clinically significant (greater than 4 tablespoons per day) sputum production;
4. Two or more COPD exacerbation episodes requiring hospitalization in the last year at screening;
5. Two or more instances of pneumonia episodes in the last year at screening;
6. Unplanned weight loss >10% usual weight <90 days prior to enrollment;
7. History of exercise-related syncope;
8. Myocardial Infarction or congestive heart failure within 6 months of screening;
9. Prior lung transplant, LVRS, bullectomy or lobectomy;
10. Clinically significant bronchiectasis;
11. Unable to safely discontinue anti-coagulants or platelet activity inhibitors for 7 days;
12. Uncontrolled pulmonary hypertension (systolic pulmonary arterial pressure > 45 mm Hg) or evidence or history of CorPulmonale as determined by recent echocardiogram (completed within the last 3 months prior to screening visit);
13. Pulmonary nodule requiring surgery as noted by chest X-ray or CT scan;
14. HRCT collected per CT scanning protocol within the last 3 months of screening date and evaluated by clinical site personnel using 510k cleared CT software shows:
a Parenchymal destruction score of greater than 75% in all three right lobes or both left lobes
b Emphysema heterogeneity score less than 15%
c Large bullae encompassing greater than 30% of either lung
d Insufficient landmarks to evaluate the CT study using the software as it is intended;
15. Left ventricular ejection fraction (LVEF) less than 45% as determined by recent echocardiogram (completed within the last 3 months prior to screening visit);
16. Resting bradycardia (<50 beats/min), frequent multifocal PVCs, complex ventricular

arrhythmia, sustained SVT;
17. Dysrhythmia that might pose a risk during exercise or training;
18. Post-bronchodilator FEV1 less than 15% or greater than 45% of predicted value at screening;
19. TLC less than 100% predicted (determined by body plethysmography) at screening;
20. RV less than 175% predicted (determined by body plethysmography) at screening;
21. DLCO less than 20% predicted value at screening;
22. 6-minute walk distance less than 100 meters or greater than 450 meters at screening;
23. PaCO2 greater than 50mm Hg (Denver greater than 55 mm Hg) on room air at screening;
24. PaO2 less than 45 mm Hg (Denver less than 30 mm Hg) on room air at screening;
25. Elevated white cell count (>10,000 cells/mcL) at screening;
26. Presence of alpha-1 anti-trypsin deficiency as determined by local laboratory ranges;
27. Plasma cotinine level greater than 13.7 ng/ml (or arterial carboxyhemoglobin > 2.5% if using nicotine products) at screening;
28. Any disease or condition that interferes with completion of initial or follow-up assessments.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-03-2015
Enrollment:	24
Type:	Actual

Medical products/devices used

Generic name:	Endobronchial one-way valve (Zephyr)
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	03-03-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-05-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-04-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-12-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-09-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT01796392
CCMO	NL50814.042.14