Fissure Closure with the AeriSeal System for CONVERTing Collateral Ventilation Status in Patients with Severe Emphysema; A Multicenter, Prospective Trial

Published: 18-02-2021
Last updated: 16-11-2024

The primary objective of this prospective study in subjects with severe emphysema is to evaluate the utility of the AeriSeal System to occludecollateral air channels in a target lung lobe with collateral ventilation (CV+) and convert the target lung...

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

Summary

ID

NL-OMON52333

Source
ToetsingOnline

Brief title
CONVERT trial

Condition

- Respiratory disorders NEC

Synonym
COPD, emphysema

Research involving

Human

Sponsors and support

Primary sponsor: Pulmonx Corporation
Source(s) of monetary or material Support: PULMONX

Intervention

Keyword: aeriseal, COPD, endobronchial valves, fissure

Outcome measures

Primary outcome

Stage 1 (Post-AeriSeal):

The Primary AeriSeal Endpoint is the percentage of study subjects that are successfully converted from a positive collateral ventilation status (CV+) in the treated lobe to having little to no collateral ventilation (CV-) by Chartis in the treated lobe, six (6) weeks after delivery of AeriSeal.

Stage 2 (Post-Zephyr Valves):

The Primary Zephyr Valve Endpoint is the percent of subjects achieving Treated Lobar Volume Reduction (TLVR) >= 350 mL at 45- days post successful lobar occlusion with Zephyr Valves.

Secondary outcome

Secondary:

o Post-Bronchodilator Forced Expiratory Volume in 1 second (FEV1) change from Baseline to 3-months (Absolute and Percent).

o Residual volume (RV) change from Baseline to 3-months (Absolute and Percent).

Additional:

o Post-Bronchodilator Forced Expiratory Volume in 1 second (FEV1) change from Baseline to 6 and 12 months (Absolute and Percent).

o Residual volume (RV) change from Baseline to 6 and 12 months (Absolute and Percent).

o Six-Minute Walk Distance (6MWD) change from Baseline to 3-months, 6-months and 12 months.

o St. George*s Respiratory Questionnaire (SGRQ) score change from Baseline to 3-months, 6-months and 12 months.

o Modified Medical Research Council Dyspnea Score (mMRC) change from Baseline to 3-months, 6-months and 12 months.

o Absolute and percent changes in TLC and IC from Baseline to 3-months, 6-months and 12 months.

o Changes in RV/TLC and IC/TLC from Baseline to 3-months, 6-months and 12 months. (Absolute and Percent).

o TLVR at 6-Months and 12 months.

Study description

Background summary

Patients with severe emphysema and hyperinflation may be eligible for treatment with endobronchial valves and may lead to improvement of lung function, exercise capacity and quality of life. This is only possible if there is no collateral ventilation between the treatment target lobe and the contralateral lobe.
Most patients have collateral ventilation and cannot be treated with valves. If the collateral ventilation could be blocked, patients might be eligible for treatment.

This study is to investigate the feasibility of closing the collateral ventilation channels by AeriSeal to convert positive collateral ventilation to negative collateral ventilation, to see if treatment with endobronchial valves is possible after closure of the collateral channels.

Study objective

The primary objective of this prospective study in subjects with severe emphysema is to evaluate the utility of the AeriSeal System to occlude collateral air channels in a target lung lobe with collateral ventilation (CV+) and convert the target lung lobe to having little to no collateral ventilation (CV-). A secondary objective is to perform bronchoscopic lung volume reduction (BLVR) with placement of commercially available Zephyr Valves in the target lobe, successfully converted from positive collateral ventilation (CV+) status to having little to no collateral ventilation (CV-). Subjects who are successfully converted to CV- after treatment with AeriSeal will follow the standard of care for CV- emphysema and be treated with the CE marked Zephyr Valve(s) according to the Zephyr IFU, to achieve lung volume reduction.

Study design

This is a prospective, open-label, multi-center, single-arm study to be conducted at up to 15 investigational sites.

Intervention

1) Stage 1 will address the closure of the lobar fissure gaps (or collateral air channels) to block collateral ventilation with the AeriSeal System
2) Stage 2 will include successfully converted subjects; CV+ to CVconversion in Stage 1. Converted CV- target lobes will follow standard of care and receive CE marked Zephyr Endobronchial valves per the Zephyr IFU to perform bronchoscopic lung volume reduction (BLVR).

Study burden and risks

It is possible that the patients will not receive any benefit from participation in this trial if the procedure will not lead to a conversion to CV(-). Risks associated with the Chartis measurement and the placement of EBVs mainly include the risk associated with routine bronchoscopy, like sore throat and bronchitis. The placement of the EBV is associated with an increased risk of a pneumothorax. The specific risks to the use of the transbronchial administration of AeriSeal include infective COPD exacerbation and pneumonia. The patients who will participate in this trial have limited treatment options. Due to the phenotype of the COPD and emphysema with incomplete fissures there are no other possible regular bronchoscopic interventions at the moment.

Patients will only be offered entry into the CONVERT trial if the consensus decision of the bronchoscopic intervention is that participating in this trial is the best option for the patient. Other trials have shown that bronchoscopy is a very safe procedure in severe emphysema patients. The injection of AeriSeal could potentially successful convert CV(+) to CV(-) and consequently the patient can be treated with the EBV. Potentially, BLVR could result in the majority of patients in a clinical significant increase in FEV1 and FVC, with decreasing RV, resulting in a significant reduction in dyspnea and improvement in quality of life, and a better exercise tolerance.

Contacts

Public
Pulmonx Corporation

Chesapeake Drive 700
Redwood City CA 94063
US
Scientific
Pulmonx Corporation

Chesapeake Drive 700
Redwood City CA 94063
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion Criteria

1. Subject is willing and able to provide Informed Consent and to participate
in the study.
2. Subject is >= 40 and <= 75 years of age at the time Informed Consent signature.
3. Subject has at least one lobe with >= 50% emphysema destruction (at *910 HU)
as determined
by QCT.
4. Subject has a diagnosis of homogenous or heterogeneous emphysema, confirmed
by HRCT
scan. Heterogeneous emphysema defined as >= 15% difference (at -910 HU) in
emphysema
destruction score of adjacent lobes by HRCT.
5. Subject has a gap in the interlobar fissure that corresponds to one or more
segments as
determined by QCT.
6. Subject has clinically significant dyspnea with a mMRC Dyspnea score >= 2.
7. Subject has a Six-Minute Walk Distance >= 250 meters.
8. Subject has post-bronchodilator FEV1 >= 15% predicted and <= 50% predicted.
9. Subject has post-bronchodilator Total Lung Capacity >= 100% predicted.
10. Subject has post-bronchodilator Residual Volume >= 150% predicted if
heterogeneous
emphysema and >= 200% predicted if homogeneous emphysema.
11. Subject has stopped smoking for at least eight (8) weeks prior to Screening
visit as confirmed
by carboxyhemoglobin or cotinine levels.
12. Subject has received preventive vaccinations against potential respiratory
infections
consistent with local recommendations or policy.

Exclusion criteria

Exclusion Criteria
1. Subject has severe bullous emphysema where bulla is >= 1/3 of the total lung
volume.
2. Subject has had prior lung volume reduction surgery, prior lobectomy or
pneumonectomy,
prior lung transplantation, prior airway stent placement, prior ipsilateral
pleurodesis, or prior
endobronchial lung volume reduction therapy of any type.
3. Subject has evidence of active respiratory infection.
4. Subject has an ongoing COPD exacerbation or bronchospasm.
5. Subject has a known allergy to the device components:
a. Polyether block amide - PEBAX®
b. Polyvinyl Alcohol
c. Glutaraldehyde
d. Nitinol (nickel-titanium) or its constituent metals (nickel or titanium)

e. Silicone
6. Subject requires ventilatory support (invasive or non-invasive).
7. Subject has post-bronchodilator Diffusion Capacity (DLCO) < 20% predicted.
8. Subject cannot tolerate corticosteroids or relevant antibiotics.
9. Subject has other relevant comorbidities as judged by the Investigator or is deconditioned
and cannot tolerate the stress of post-treatment inflammatory response.
10. Subject has had three (3) or more COPD exacerbations requiring hospitalization during the
year prior to Informed Consent signature.
11. Subject has severe gas exchange abnormalities as defined by any one of the following (test
conducted at rest on room air as tolerated, or on up to 4 L/min supplemental O2)
a. PaCO2 >= 55 mm Hg (7.3 kPa)
b. PaO2 < 45 mm Hg (6.0 kPa)
c. SpO2 < 90%
12. Subject has uncontrolled pulmonary hypertension, defined as peak pulmonary systolic
pressure > 45 mm Hg on echocardiogram or right heart catheterization.
13. Subject use of systemic steroids > 20 mg/day prednisolone or equivalent within 4 weeks of
Informed Consent signature.
14. Subject use of immunosuppressive agents within four (4) weeks of Informed Consent
signature.
15. Subject whose use heparins and oral anticoagulants (e.g., warfarin, dicumarol) cannot be
discontinued according to local pre-procedural protocols. Note: antiplatelet drugs including
aspirin and clopidogrel are permitted.
16. Subject*s CT scan indicates the presence of any the following radiologic abnormalities:
a. Pulmonary nodule on CT scan greater than 0.8 cm in diameter (Does not apply if
present for one (1) year or more without increase in size or if proven benign by biopsy).
b. Radiologic picture consistent with active pulmonary infection, e.g., unexplained
parenchymal infiltrate.
c. Significant interstitial lung disease.
d. Significant pleural disease.
17. Subject*s baseline EKG indicates non-atrial arrhythmias or conduction abnormalities.
18. Subject has high cardiac risk after undergoing cardiac risk assessment in accordance with
published guidelines18 or ischemic heart disease, congestive heart failure, renal failure, or

cerebrovascular disease.
19. Subject has clinically significant asthma (reversible airway obstruction), chronic
bronchitis, or bronchiectasis.
20. Subject has allergy or sensitivity to medications required to safely perform bronchoscopy
under conscious sedation or general anesthesia.
21. Subject participated in an investigational study of a drug, biologic, or device not currently
approved for marketing within 30 days prior to Screening visit. Subjects being followed as
part of a long-term surveillance of a non-pulmonary study that has reached its primary
endpoint are eligible for participation in this study.
22. Subject has Body Mass Index (BMI) < 18 kg/m2 or > 35 kg/m2.
23. Subject is a female who is pregnant, breast-feeding, or planning to be pregnant in next 12
months.
24. Subject has clinically significant abnormal screening laboratory test results per the
Institution specific reference laboratory normal values for the following:
a. White blood cells (total)
b. Hematocrit
c. Platelets
d. Prothrombin time or INR
e. Partial thromboplastin time
f. Positive β-HCG Pregnancy test (if female)
25. Subject has evidence of severe disease which in the judgment of the Investigator may
compromise survival for the duration of the study (at least 12 months) e.g.:
a. HIV/AIDs
b. Active malignancy
c. Stroke or Transient Ischemic attack (TIA) within 12 months of Screening visit
d. Myocardial infarction within six (6) months of the Screening visit
e. Congestive heart failure within six (6) months of the Screening visit defined as
clinical evidence of right or left heart failure or left ventricular ejection fraction <
45% on echocardiogram
26. Subject has uncontrolled diabetes mellitus.
27. Subject has any other condition that the Investigator believes would interfere with the intent
of the study or would make participation not in the best interest of the subject including
but not limited to alcoholism, high risk for drug abuse, or noncompliance in returning for

follow-up visits.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	22-03-2021
Enrollment:	15
Type:	Actual

Medical products/devices used

Generic name:	AeriSeal
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	18-02-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-10-2022
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	NCT04559464
CCMO	NL75325.042.20