An Evaluation of the AeriSeal System for CONVERTing Collateral Ventilation Status in Patients with Severe Emphysema: The CONVERT II Trial

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This study is to investigate the safety and effectiveness of the AeriSeal system in limiting collateral ventilation within a target lung lobe. And to achieve lung volume reduction using Zephyur Vavles and assess lung function, hyperinflations and...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Observational non invasive

Summary

ID

NL-OMON57001

Source
ToetsingOnline

Brief title
CONVERT II Trial

Condition

- Bronchial disorders (excl neoplasms)

Synonym
COPD emphysema

Research involving
Human

Sponsors and support

Primary sponsor: Pulmonx Corporation

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

Intervention

- No intervention

Keyword: aeriseal, COPD, endobronchial valves, fissure

Explanation

N.a.

Outcome measures

Primary outcome

The percentage of study subjects that successfully convert from CV+ in the
treated lobe to having little to no collateral ventilation (CV-) by Chartis at
45 days post-AeriSeal treatment (index or repeat, if performed).

Secondary outcome

The following endpoints will be assessed in Converters (subjects that
successfully converted from CV+ status to CV-) from Baseline to Month 6 after
placement of Zephyr Valve:
• Post-bronchodilator FEV1: percentage of subjects achieving a >= 12% increase
• RV: percentage of subjects achieving a >= 310 mL decrease
• TLVR by HRCT: percentage of subjects achieving a >= 350 mL decrease
• SGRQ total score: percentage of subjects achieving a >= 4-point decrease

Additional endpoints
The following endpoints will be assessed in all subjects from Baseline to the
timepoint indicated.
• Post-bronchodilator FEV1: absolute, percent and percent predicted change
(Month 3, 6, 12, 24), percentage of subjects achieving a >= 12% increase (Month
3, 12, 24)
• RV: absolute and percent change (Month 3, 6, 12, 24) and percentage of
subjects achieving a >= 310 mL decrease (Month 3, 12, 24)
• TLVR by HRCT: absolute change (Day 45, Month 6, 12), percentage of subjects
achieving a >= 350mL decrease (Day 45, Month 12), and percentage of subjects
achieving a >= 50% decrease (Day 45, Month 6, 12)
• RV/TLC ratio: absolute change (Month 3, 6, 12, 24)
• FVC: absolute and percent change (Month 3, 6, 12, 24)
• DLCO: absolute and percent predicted change (Month 6, 12)
• CAT score: absolute change and percentage of subjects achieving a >= 2-point
decrease (Month 3, 6, 12)
• mMRC score: absolute change and percentage of subjects achieving a >=1-point

decrease (Month 3, 6, 12)
• SGRQ total score: absolute change (Month 3, 6, 12) and percentage of subjects
achieving a >= 4-point decrease (Month 3, 12)
• 6MWT: percentage of subjects achieving a >= 26 m increase in 6MWD (Month 6,
12)</p>

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 for patients who are not eligible for treatment with valves due to the presence of collateral ventilation.

This is a prospective, open-label, multi-center, single-arm study planned to enroll 200 subjects with heterogeneous emphysema and collateral ventilation (CV) in the target lobe. Subjects will undergo instillation of AeriSeal Foam in the target lobe and subsequent assessment CV status using Chartis Pulmonary Assessment System (Pulmonx Corporation, Redwood City, CA, USA). Subjects with CV- status will then undergo placement of Zephyr Valve (Pulmonx Corporation, Redwood City, CA, USA) in the target lobe.
The study hypothesis is that the instillation of AeriSeal Foam will block collateral ventilation and isolate the target lobe such that subsequent placement of Zephyr Valves will result in reduction of hyperinflation and improvement in lung functions and health-related quality of life.

Study objective

This study is to investigate the safety and effectiveness of the AeriSeal system in limiting collateral ventilation within a target lung lobe. And to achieve lung volume reduction using Zephyur Vavles and assess lung function, hyperinflations and quality of life. And to assess the long-term safety of the AeriSeal System.

Study design

A multicenter, prospective, single-arm, pivotal trial.

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 CV- conversion 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.

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Trial sites

Trial sites in the Netherlands

Universitair Medisch Centrum Groningen
Target size: 15

Listed location countries

Australia, Italy, Denmark, Austria, United Kingdom, United States, Germany, France, Netherlands

Eligibility criteria

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

Inclusion criteria

1. Subject is willing and able to provide informed consent and to participate in the study.
2. Subject is aged >= 40 and <= 80 years at the time of the ICF signature date.
3. Subject has completed a documented pulmonary rehabilitation (in clinic or home-based) program within 12 months prior to Baseline.
4. Subject has stopped smoking for at least 8 weeks prior to the ICF signature date as confirmed by carboxyhemoglobin or cotinine levels.
5. Subject has an HRCT from the screening within 3 months of the ICF signature date with the following findings at -910 Hounsfield Units:
a. At least one (1) lobe with segmental emphysema destruction score >= 50%.
b. Subject has heterogenous emphysema, defined as difference in emphysema destruction score of >= 15 between the density scores of the target lobe and the ipsilateral non-target lobe(s) per QCT report with % voxel density of < -910 HU. For non-target lobes
that include the RML, calculate the combination of non-target lobes as a single density score using volume-weighted percent.
c. LUL, LLL, RUL, RLL, or RUL+RML are targets for valve intervention.
d. Subject has a gap in the interlobar fissure that corresponds to one or more

segments and the fissure(s) contacting the target lobe is >= 80% complete per QCT report.
e. Subject has 98% of the fissure gap confined to a maximum of 3 segments within the target lobe per Fissure Targeting Report (FTR).
6. Subject has 6MWD >= 150 m and <= 450 m.
7. Subject has clinically significant dyspnea with an mMRC score of >= 2.
8. Subject has post-bronchodilation FEV1 >= 15% predicted and <= 45% predicted.
9. Subject has an FEV1/FVC ratio of < 0.7.
10. Subject has post-bronchodilation TLC, measured by body plethysmography, >= 100% predicted.
11. Subject has post-bronchodilation RV >= 175% predicted, measured by body plethysmography.
12. Subject has post-bronchodilation DLCO >= 20% predicted.
13. Subject has received preventative vaccinations against potential respiratory infections, including COVID-19, consistent with local recommendation or policy.
14. Subject is on optimal medical management for more than one month prior to the ICF signature date.
15. Subject has collateral ventilation (CV+) as confirmed per the Chartis assessment prior to the AeriSeal Index Procedure.

Exclusion criteria

1. Subject has prior lung volume reduction surgery, lobectomy or pneumonectomy, lung transplantation, airway stent placement, pleurodesis, or BLVR of any type, except BLVR using Zephyr Valve with < 50% TLVR at 6 months, followed by valve removal > 6 months prior to ICF signature date.
2. Subject has visible radiological abnormality on HRCT scan such as pulmonary nodule greater than 0.8 cm in diameter (does not apply, if present for 2 years or more without increase in size or if deemed benign by biopsy) or active pulmonary infection (e.g., unexplained parenchymal infiltrate, significant interstitial lung disease or significant pleural disease).
3. Post-COVID-19 pathology on CT, including ground glass opacities with or without consolidation, adjacent pleura thickening, interlobular septal thickening, or air bronchograms.
4. Large bullae encompassing greater than 1/3 of the total lung.
5.Subject had 3 or more COPD exacerbations requiring hospitalization within 12 monthspreceding theICFsignature date or a COPD exacerbation requiring hospitalization within 8 weeks of the ICF signature date. Subjects may be re-considered for future enrollment.
6.Subject has asthma as their primary diagnosis.
7.Subject has chronic bronchitis(defined as greaterthan 4 tablespoons of sputum production perday) as their primary diagnosis.
8.Subject has clinically significant bronchiectasis.
9.Subjectswithevidence of active respiratory infectionshould be considered

forenrollmentonlyafter satisfactory resolution.
10.Subject requires invasive ventilatory support. Note: The use of Continuous Positive Airway Pressure (CPAP) or BiPAP devices for sleepapnea is permitted.
11.Subject has severe gas exchangeabnormalities as defined by any one of the following tests,conducted at rest, on room air, as tolerated.
•PaCO2>= 50 mm Hg (7.3 kPa)
•PaO2 < 45 mm Hg (6.0 kPa)
12.Subject has pulmonary hypertension, defined as mean pulmonary systolic pressure > 45 mmHg.
13.Subject has known documented alpha-1 antitrypsin deficiency.
14.Subject has clinically significant hematological disorder.
15.Subject has recent significant unplanned or unexplained weight loss or other relevantcomorbidities considered by the investigator to be potentially confounding or limiting to thesubject*s participation in the study.
16.Subject has non-atrial arrhythmias or conduction abnormalities on EKG.
17.Subjecthashigh cardiac risk after undergoing cardiac risk assessmentin accordance withpublished guidelines (Fleisher 2007)or hasischemic heart disease, congestive heart failure,cerebrovascular disease (stroke or TIAwithin 6 months of the ICF signature date),or serumcreatinine > 2.0 mg/dL (177 µmol/L).
18.Subject has uncontrolled exercise induced syncope.
19.Subject has evidence of severe diseasewhich in the judgment of theinvestigator may compromise the anticipated treatmenteffect or the subject*s survivalfortheduration ofatleast 12 months.
20.Subject has any other condition that theinvestigator believes would interfere with the intent ofthe study or would make participation not in thebest interest of the subject including but notlimited to alcoholism, high risk for drug abuse, or noncompliance in returning forfollow-up visits.
21.Subject cannot toleratecorticosteroids or relevant antibiotics.
22.Subject use of systemic corticosteroids > 20 mg/day prednisolone or equivalent within four (4)weeks of the ICF signature date. Subjects may be re-considered for future enrollment.
23. Subject use of immunosuppressive agents within four (4) weeks of the ICF signature date. Subjects may be re-considered for future enrollment.
24. Subject is unable to temporarily discontinue heparins and oral anticoagulants (e.g., warfarin, dicumarol) according to local pre-procedural protocols. Note: Antiplatelet drugs including aspirin, thienopyridines and ticagrelor are permitted.
25. Subject has allergy or sensitivity to medications required to safely perform bronchoscopy under conscious sedation or general anesthesia.
26. Subject has known allergy to the following device components: Polyether block amide (PEBAX), Polyvinyl Alcohol or Glutaraldehyde, Nitinol (nickel-titanium) or its constituent metals (nickel or titanium) or Silicone.
27. Subject is a female who is pregnant (positive βHCG Pregnancy test), breast-feeding, or planning to be pregnant in the next 12 months.
28. Subject has Body Mass Index < 18 kg/m2 or > 35 kg/m2.
29. Subject participated in an investigational study of a drug, biologic, or device not currently approved for marketing within 30 days prior to the ICF

signature date. Note: 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.

Study design

Design

Study phase:	N/A
Study type:	Observational non invasive
Intervention model:	Single
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-11-2024
Enrollment:	15
Duration:	36 months (per patient)
Type:	Actual

WORLD

Recruitment status:	Recruiting
Start date (anticipated):	22-02-2024
Enrollment:	200
Type:	Actual

Medical products/devices used

Product type:	N.a.
Registration:	Yes - CE intended use

IPD sharing statement

Plan to share IPD: Yes

Plan description
N.a.

Ethics review

Approved WMO Date:	22-05-2024
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-09-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-04-2025
Application type:	Amendment
Review commission:	METC UMCG

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	NCT06035120
CCMO	NL85762.042.23
Research portal	NL-005093