The REDUCE EU Study - Endobronchial Thermal Liquid Ablation (ETLA) for the Treatment of Emphysema - A Pilot Study (CSP-12123)

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The primary objective of the study is to assess the feasibility and safety of sequential ETLA treatment in patients with severe emphysema with hyperinflation. The secondary objective of the study is to assess efficacy of sequential ETLA treatment in...

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

Summary

ID

NL-OMON57295

Source
ToetsingOnline

Brief title
REDUCE EU study

Condition

- Respiratory disorders NEC

Synonym
COPD, emphysema

Research involving
Human

Sponsors and support

Primary sponsor: Morair Medtech

Source(s) of monetary or material Support: Morair Medtech

Intervention

Keyword: Bronchoscopy, Emphysema, Lung volume reduction

Outcome measures

Primary outcome

The primary endpoints will assess the feasibility and safety of ETLA.

Feasibility:

• % of procedures where the device operated as intended per IFU

• % of procedures and % of target regions where saline is delivered at the predetermined volume per treatment plan

Safety:

• Incidence of serious adverse events (SAE) associated with the ETLA device and/or procedure through 9 months post-procedure 1 as adjudicated by an independent medical monitor

Secondary outcome

The secondary endpoints will assess the efficacy, feasibility, and safety of ETLA.

Feasibility:

• Target Lobe Volume Reduction (TLVR) as measured by CT scan quantified by the reduction in the volume of the targeted lobe(s) (reported in mL) at the below time points:

o 3 months post-procedure 1 compared to baseline

o 3 months post-procedure 2 compared to the scan at 3 months post-procedure 1

• Cumulative Lobar Volume Reduction as measured by CT scan, quantified by the summation of TLVR through both procedures (reported in mL)

Safety:

• Incidence of all adverse events associated with the ETLA device and/or procedure through 9 months post-procedure 1

Efficacy:

The following endpoints will be compared to baseline at 3 months and 9 months post-procedure 1 and 3 months post-procedure 2.

• RV change (mL, % change in absolute and % predicted)

• FEV1 change (mL, % change in absolute and % predicted)

• 6MWT changes

• SGRQ-C change

Study description

Background summary

Many emphysema patients remain symptomatic with worsening symptoms over time despite optimal pharmacotherapy and pulmonary rehabilitation. Lung volume reduction surgery improves symptoms, exercise tolerance and quality of life beyond improvements seen with optimized medical therapy including pulmonary rehabilitation. However, the procedure is characterized by an increase in mortality, significant morbidity, and may involve lengthy post-operative care.

Bronchoscopic approaches to lung volume reduction (LVR) demonstrate

improvements in pulmonary function and quality of life with less morbidity and mortality than surgery. Valve implants have been shown to induce LVR in patients with hyperinflated diseased lobes with intactfissures (no collateral ventilation) resulting in clinically meaningful and statistically significant improvement in pulmonary function and quality of life. ETLA is a non-implant with a short procedure duration that offers the potential to induce significant LVR of hyperinflated emphysematous regions regardless of collateral ventilation and is able to treat at a subsegmental level. ETLA may provide clinically meaningful improvement in pulmonary function and quality of life to a broad population of severe emphysema patients, addressing a clinical need in patients with collateral ventilation as well as patients with significant intralobar heterogeneity.

The preclinical safety and feasibility of ETLA for lung volume has been established and is presented in the Investigator*s Brochure. It is anticipated that LVR will lead to clinically meaningful improvement in pulmonary function and quality of life. Clinical experience gathered to-date from the Australian First in Human REDUCE study have demonstrated correlation to pre-clinical findings for safety, efficacy, and lung volume reduction in patients regardless of collateral ventilation at the dose proposed for this study. The REDUCE EU Pilot study will primarily evaluate the feasibility and safety of ETLA treatment in patients with severe emphysema. Secondarily, the study will evaluate the efficacy of sequential ETLA treatment.

Study objective

The primary objective of the study is to assess the feasibility and safety of sequential ETLA
treatment in patients with severe emphysema with hyperinflation.

The secondary objective of the study is to assess efficacy of sequential ETLA treatment in patients
with severe emphysema with hyperinflation

Study design

This study is a prospective, single-arm, multi-center pilot study of sequential treatment with endobronchial thermal liquid ablation (ETLA) to assess feasibility, safety, and efficacy in patients with severe emphysema with hyperinflation. ETLA is delivered sequentially over two procedures. Treatment can be unilateral or bilateral over the two procedures, with each procedure limited to treatment in a single lung.

The ETLA dose consists of the following parameters that will remain constant:
- Temperature at 95*C
- Flow rate of 1ml/s

- ETLA ratio of 1.75 (volume of heated saline delivered: conductive and respiratory airway volume 1)
- Number of Subsegments Targetted (estimate) 1-4 subsegments

The cumulative ablation potential (CAP) will not exceed 15% per procedure.

Intervention

Subjects will undergo two (2) ETLA procedures separated by a minimum three (3) month interval. Each procedure will be limited to treatment in a single lung, with either unilateral or bilateral treatment over the two procedures.

All sub-segments are presented to the Investigator in a Treatment Region Selection Tool (TRST). The Investigator will identify and target sub-segments for treatment which are >= 25% destruction %-950 HU (by CT analysis).

The ETLA procedure will be performed under general anesthesia with a paralytic according to the Instructions for Use (IFU). The ETLA generator heats and delivers a predetermined volume of normal saline (0.9% NaCl) to targeted emphysematous lung regions through a connected, disposable catheter.

Study burden and risks

Patients with severe emphysema suffer from a debilitating decline in pulmonary function and have a very poor quality of life, primarily due to hyperinflation. Therapies that reduce hyperinflation and improve pulmonary function and QOL offer meaningful relief for patients.

ETLA treatment is anticipated to benefit a broad population of severe emphysema patients. ETLA is not limited to only treating patients with heterogenous lobes without collateral ventilation (CV-) from incomplete fissures (valves). ETLA allows for treatment of all qualifying emphysematous patients with heterogeneous disease regardless of the presence of collateral ventilation. GOLD stage III & IV heterogeneous emphysema patients with collateral ventilation represent a large percentage of the severe emphysema population that currently have limited treatment options. ETLA is expected to benefit these patients by providing safe, clinically meaningful improvements in pulmonary function and quality of life. Additionally, ETLA can be delivered to any eligible subsegment in a lung, allowing the investigator to treat the most diseased regions regardless of location. The risks associated with the study are minimized by implementing a treatment CAP that is within the established safety threshold. A range of 5 to 15% volume treated per procedure is expected to typically result in clinically meaningful improvement in pulmonary function and QOL.

The intended patient population for the ETLA system are those individuals with

severe and very severe (GOLD stage III & IV) emphysema deemed to be in clinical need of lungvolume reduction. These patients may have the following baseline characteristics: chronic obstructive pulmonary disease with highly destructed parenchymal subsegments, hyperinflation, reduced pulmonary function, reduced exercise capacity, reduced oxygen saturation, reduced quality of life, fatigue, and concomitant disease states such as vascular and/or cardiac disease. This patient population is characterized by a severe emphysema disease state where conservative management has failed. The medical condition and nature of the patient population is such that medical intervention is clinically warranted based on the treating clinician*s medical judgement and patient informed consent. The disease state of the patient may contribute to the probability of adverse procedural effects; however, medical intervention in this patient population is indicated. Without appropriate management, the risks posed to health include substantial decrease in quality of life during end-stage disease.

Valve implantation may be appropriate in highly selected patients with severe COPD and hyperinflation if collateral ventilation from incomplete lobar fissures can be excluded (intact fissure on imaging and Chartis negative during bronchoscopy). Benefits of lung volume reduction in the patient population include improved pulmonary function, reduced lung volumes and hyperinflation, exercise capacity, dyspnea, and health-related quality of life. Current evidence on the safety and efficacy of lung volume reduction procedures for severe emphysema appears adequate to support the use of this procedure.

The side-effects associated with lung volume reduction in general are well known and documented and are further discussed within this document. Valve implantation results were used to assess the ETLA pre-clinical studies. These studies demonstrated adequate evidence of the severity and probability of these events to provide an overall safety profile of the ETLA system.

The safety and performance aspects of the ETLA system have been evaluated using risk analysis techniques. Thresholds and precautions have been implemented wherever possible to mitigate safety risks. The risks associated with the use of the ETLA system are considered reasonable in comparison to the anticipated benefits to patients. As the risks associated with the ETLA system are aligned with the risk profiles of currently available bronchoscopic technologies used to facilitate lung volume reduction in the intended patient population, the ETLA system poses an acceptable level of risk for their intended use.

The anticipated residual risks associated with use of the ETLA system are generally short-lasting and well tolerated. Temporary post-procedural respiratory symptoms are expected to occur and will typically be managed with standard of care measures. Due to the minimally invasive nature of the procedure, the risk profile, by design, has a reduced risk compared to traditional open surgical lung volume reduction techniques, and due to the ability to treat patients with collateral ventilation, provide potential for treatment for a

population with limited alternatives.

Initial assessment of early clinical data has been considered in respect to the risks outlined. Results for these procedures have shown expected adverse reactions that, to-date, are consistent with the frequency and severity outlined in Section 12.2 of the Protocol. Initial clinical data also demonstrate lung volume reduction that is expected to result in clinically meaningful improvements in pulmonary function and quality of life. Refer to Investigator*s Brochure for details. The risks associated with the use of the ETLA system are considered reasonable in comparison to the anticipated benefits to patients with severe emphysema.

Further evidence of anticipated and unanticipated risks will be assessed through tracking of
adverse event rates through clinical studies.

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. Age >= 40 years old
2. Diagnosis of COPD with FEV1/FVC less than 0.7 post-bronchodilation
3. Post-bronchodilator FEV1 >= 20% and <= 49% of predicted value
4. Total lung capacity TLC >= 100% predicted
5. Residual volume (RV) >= 175% predicted
6. 6MWD >= 140 meters
7. Dyspnea scoring >= 1 on the modified Medical Research Council scale (mMRC)
8. PCO2 <= 55 mmHg; PO2 > 45 mmHg on room air
9. Optimized medical management (consistent with GOLD guidelines) as confirmed by the Investigator
10. Non-smoking for 3 months prior to study enrollment, as confirmed by:
• Negative cotinine urine analysis or serum cotinine level of <= 10 ng/ml
OR
• Negative carboxyhemoglobin (COHb) test (<= 2.5%)
Note: Carboxyhemoglobin is required for patients who are using smoking cessation products containing nicotine at screening
11. The patient engages in physical activity beyond activities of daily living (i.e., a walking program, pulmonary rehabilitation)
• On a regular basis for more than 6 weeks, AND
• Is continuing the activity at enrollment, AND
• Agrees to continue the activity throughout study participation
Note: Physical activity level may be based on documentation or patient reporting.
12. Patient must meet ONE of the following criteria for distance from treating hospital:
• Live within approximately 1 hour of the study hospital
OR
• If > 1 hour from study hospital, patient lives within approximately 1 hour of regional care that is sufficient to handle an emergency pulmonary event in COPD patients or must be willing to remain in the hospital for at least 5 days post-procedure
13. Vaccinated for COVID-19, pneumococcus, and influenza (per European Union and Member State guidelines) or documented clinical intolerance or documented patient refusal
14. Cognitively able to provide written informed consent and willing to comply with study requirements
15. Severe emphysematous subsegments eligible for ETLA treatment where the volume of targeted subsegments must meet the minimum Targeted Procedure Volume (TPV), with the total targeted volume allowing for two (2) ETLA procedures. Eligible subsegments are defined as having >= 25% destruction %-950 HU per QCT analysis with a heterogeneity index (HI) >1.2.

Note: Chest CT analysis by QCT Core Lab

Exclusion criteria

1. Body mass index (BMI) < 16 kg/m2 or >= 33 kg/m2
2. DLCO < 20% predicted
3. Chronic bronchitis as defined by cough and sputum production for at least 3 months per year for two consecutive years, in the absence of other conditions that can explain these symptoms
4. 75ml or greater sputum production per day most days of the week
5. Greater than two (2) hospitalizations for COPD exacerbations and/or pneumonia in the 12 months
prior to enrollment
6. Diagnosis of asthma that is confirmed according to the Global Initiative for Asthma (GINA)
guidelines
7. Prior lung volume reduction via endobronchial valves(s), coil(s), vapor and/or polymer. Patients whose valves have been removed > 3 months previously can be treated if a baseline bronchoscopy reveals no airway obstruction or obvious tissue granulation and the reason for valve removal was not for complications e.g., Pneumonia, severe exacerbation, or pneumothorax
8. Pulmonary hypertension:
• History of cor pulmonale
OR
• mPAP >20mm Hg in the 12 months prior to enrollment
OR
• RV estimated systolic pressure >45 mmHg in the 12 months prior to enrollment
Note: Measurements from right heart catheterizations are considered definitive over echocardiography. Patients with a pulmonary hypertension diagnosis must have an echocardiogram or right heart catheterization within the past 12 months
9. Alpha-1 antitrypsin deficiency
10. Uncontrolled diabetes mellitus with an HbA1c >9.0% within 6 months of enrollment
Note: Patients with a diagnosis of diabetes mellitus must have an HbA1c measurement within
the past 6 months.
11. Prior heart or lung transplant
12. Myocardial infarction or stroke within the 12 months of enrollment
13. Diagnosis of heart failure: Left Ventricular Ejection Fraction (LVEF) less than or equal to 40% within 12 months prior to enrollment.
Note: Patients with a heart failure diagnosis must have an LVEF measurement within the past 12 months
14. Heart failure requiring hospitalization, within 6 months prior to enrollment
15. History of bleeding disorders or enhanced predisposition to bleeding
16. History of severe/massive hemoptysis defined as >200ml of blood loss in <24

hours
17. Unable to discontinue anti-coagulants or platelet inhibitors (acetylsalicylic acid [ASA] and non-ASA, including low dose) for at least 7 days prior to each procedure (or as per physician discretion based on the specific agent) and for at least 6 weeks after each procedure
18. Daily systemic steroids equivalent to > 15 mg prednisolone
19. Immunosuppressive drugs, such as for the treatment of cancer, autoimmune disease, or prevention of tissue/organ rejection
20. Pregnant, lactating, or women of childbearing potential who plan to become pregnant within the study duration
21. Currently enrolled in another trial studying an experimental treatment
22. Any disease or condition likely to limit survival to less than one year
23. Concomitant illnesses or medications that may pose a significant increased risk for complications following treatment with ETLA
24. Any condition that would interfere with evaluation or completion of the study including study assessments and procedures, including bronchoscopy
25. Active aspergillus infection, including chronic aspergillus infection, aspergilloma, invasive
aspergillosis, cavitation and/or history of aspergillus cavitation(s) or colonization confirmed by bronchoscopic culture*
26. Clinically significant bronchiectasis as determined by the Investigator
27. Radiological evidence of bronchiectasis in target region(s) and/or cystic radiological bronchiectasis in any region of the lungs*
Note: A valid treatment plan must be feasible without targeting regions for ETLA having radiological evidence of bronchiectasis
28. Clinically significant pulmonary fibrosis*
29. Lung nodule not proven stable unless proven to have benign pathology*
30. Large bulla (defined as > 1/3 volume of a lung)*
31. Prior Lung Volume Reduction Surgery (LVRS), bullectomy, or lobectomy*
32. Remaining lung tissue NOT targeted for ETLA treatment is too highly diseased, defined as %-
950 >= 50%, after both ETLA procedure treatment plans are finalized, as confirmed by QCT analysis
Note: Applies to each lung, each individually assessed, regardless of whether the lung is targeted for
ETLA (unilateral or bilateral treatment)
Note: Chest CT analysis by QCT Core lab
33. Active respiratory infection or recent respiratory infection with resolution < 4 weeks prior to
screening or procedure
34. Recent COPD exacerbation within < 6 weeks prior to screening or procedure

*Assessed by the Radiology Eligibility Reviewer in addition to the site.
Clinical significance stated in the criteria is determined by the Investigator.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2025
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Generic name:	Morair Medtech Endobronchial Thermal Liquid Ablation (ETLA) system
Registration:	No

Ethics review

Approved WMO

Date:	11-02-2025
Application type:	First submission
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
CCMO	NL85280.000.24
Other	TBD