Evaluation of the Innovative Pulmonary Solutions (IPS) System for Targeted Lung Denervation (TLD) Therapy in patients with moderate to severe Chronic Obstructive Pulmonary Disease (COPD) - A Safety Study

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Evaluate the safety and technical feasibility of TLD Therapy in the treatment of patients with moderate to severe Chronic Obstructive Pulmonary Disease (COPD).

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

Summary

ID

NL-OMON39206

Source
ToetsingOnline

Brief title
Targeted Lung Denervation in COPD

Condition

- Respiratory disorders NEC

Synonym
chronic bronchitis, COPD

Research involving
Human

Sponsors and support

Primary sponsor: Holaira, Inc. (IPS)
Source(s) of monetary or material Support: industrie;zie onder

Intervention

Keyword: Bronchoscopy, COPD, RF ablation, Vagal nerve

Outcome measures

Primary outcome

Primary Safety Endpoint: Freedom from documented and sustained worsening of

COPD directly attributable to the investigational device or procedure to

180-days post TLD Therapy.

Secondary outcome

Technical Feasibility (performance) Endpoint: The ability of the IPS System to

access the target treatment area and deliver RF energy to the target treatment

site as confirmed by the IPS Console.

Study description

Background summary

It is well known that increased smooth muscle tone in patients with Chronic Obstructive Pulmonary Disease (COPD) is due in part to increased parasympathetic drive. Pharmacologic blockade of vagus nerve input to airway smooth muscle in the human lung leads to improvements in lung function and overall health status. Once daily-inhaled tiotropium improves peak flow by 25% and causes a 9% sustained improvement
in the forced expiratory volume in one second (FEV1) in patients with COPD with a baseline FEV1 <= 65% of predicted. It is also known that mechanical disruption of the vagus nerve as it passes between the brain and the lung can also lead to improvements in pulmonary function. Intrathoracic bi-lateral vagotomy was investigated as a treatment for COPD and asthma as early as the 1940s, and most recently in the 1980s. In patients with severe COPD, surgical resection of the vagus nerve led to a 30% improvement in FEV1 in one patient with severe COPD.

In severe asthma, vital capacity (VC) has also been shown to improve from 2.36 L to 2.79 L (18%) and maximal voluntary ventilation (a parameter linearly related to FEV1) increased from 43 L/min to 50 L/min (16%). Prior to vagotomy, histamine caused a 25% reduction in VC compared to only 9% after vagotomy. Sputum production was essentially stopped in 8/11 patients with heavy sputum. However, due to a high risk of procedure related mortality (as high as 28%) following bilateral thoracotomies, surgical resection of the vagus nerve in the lung has never been routinely practiced. More recently, knowledge of the long-term effects of lung denervation has been demonstrated in two patient populations: 1) lung transplant patients; and, 2) patients who received sleeve resections (removal of the mainstem bronchus and associated airway nerve trunks) as treatments for lung cancer. Lung transplant recipients have both vagus nerve fibers and bronchial arteries severed during surgery. In the early days of lung transplantation, there was a concern that lung denervation would lead to worsened physiologic function (i.e. decrease of Hering-Breuer reflex, decrease of cough reflex). These issues have not been observed did not come to bear, and lung transplant patients have not been found to have to have any clinical issues due to their lung denervation. In lung cancer patients, it has been shown that there is no difference in outcomes, stage by stage, for patients who received a sleeve resection versus a traditional pneumonectomy for treatment. It is generally believed that airway nerve trunk branches of the vagus nerves that influence airway smooth muscle constriction do not re-grow following transplantation, though there is some evidence that afferent sensory pathways may regenerate over time. We hypothesize that Targeted Lung Denervation Therapy will be a safe method to ablate the nerve trunks that travel parallel to and outside of the main bronchi and into the lungs to achieve Targeted Lung Denervation.

Study objective

Evaluate the safety and technical feasibility of TLD Therapy in the treatment of patients with moderate to severe Chronic Obstructive Pulmonary Disease (COPD).

Study design

This study is prospective, multi-center (3 centers), single-arm (non-randomized) safety and technical feasibility study.

Intervention

Bronchoscopically guided Targeted Lung Denervation (TLD) Therapy with the Innovative Pulmonary Solutions (IPS) System.

Study burden and risks

Risks associated with the IPS System are minimized by design. Risks are minimized under this protocol due to:
- Operators with a high degree of experience in interventional bronchoscopy
- Extensive non-clinical evaluation of the device and therapy (animal and bench top testing)
- The use of standard medical grade materials in the manufacture of the device
- The well-established nature of the bronchoscopic procedure and technique used to perform this procedure
- Use of RF energy which is well understood in medical applications
Based upon literature review and pre-clinical evaluations performed to date, it is expected that TLD therapy may provide some benefit to the subject; however, this procedure has not been performed in human subjects and the actual benefits are not known. There may be no direct benefits of study participation.
However, subject participants will undergo an enhanced level of clinical scrutiny of pulmonary health compared to routine clinical care, which may provide some indirect health benefits.
A more comprehensive Risk-Benefit assessment is included in the Investigator*s Brochure provided as Appendix A.

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

FEV1 30% - 60% of predicted
FEV1/FVC <70%
Positive change in FEV1 of greater than 15% following administration of ipratropium
Non-smoking for a minimum of 6 months and a minimum of 10 packyears of smoking

Exclusion criteria

Asthma
Prior lung transplant, LVRS, median sternotomy, bullectomy or lobectomy
Presence of a pacemaker, internal defibrillator or other implantable electronic devices

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-11-2011
Enrollment:	11
Type:	Actual

Ethics review

Approved WMO Date:	25-08-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-12-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-06-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-10-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-05-2013
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
CCMO	NL36608.042.11