Safety and feasibility of targeted lung denervation in patients with moderate to severe COPD

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Publication: European Respiratory Journal. Volume 44 / Supplement 58 / September 2014

Background: Acetylcholine derived from parasympathetic nerves is a well-validated target to treat patients with COPD. Targeted lung denervation (TLD) is a novel bronchoscopic therapy that ablates parasympathetic pulmonary nerves along the main bronchi.

Aim: Evaluate safety and feasibility of TLD in COPD patients.

Methods: A first-in-human, prospective, multicenter, study in COPD patients ($FEV_1/FVC<0.70$; FEV_1 30-60% predicted) was performed (NCT01483534). Patients underwent TLD using a catheter based lung denervation system (Holaira, Inc., USA) delivered during two rigid bronchoscopies 30 days apart, in an outpatient setting. Follow-up bronchoscopy to assess airways was performed 90 days post 2nd treatment. Feasibility was defined as ability to deliver treatment to the airway and safety determined by registration of all adverse events (AE) out to 365 days after TLD.

Results: Twelve patients (FEV_1 33.8±9.4 % predicted, age 62.9±11.4 yrs) were treated at a 20W energy dose and 10 (FEV_1 34.5±6.3 % predicted, age 64.4±8.9 yrs) at 15W. The procedure time was 49±15 mins per lung. TLD was 100% technically successful. No serious AEs directly related to TLD and no unexpected AEs occurred. Sixteen serious AEs were observed; 8 COPD exacerbations, 2 respiratory infections, 1 flu, 1 myocardial infarction, 1 chest pain, 1 drug reaction, 1 episode of gastroparesis, and 1 stomach cancer. Ten of these were in the 15W group with 7 in one single patient. Follow-up bronchoscopy showed asymptomatic local airway wall effects post TLD in 5 patients in the 20W group, but not in the 15W group.

Conclusion: TLD is technically feasible with an acceptable rate of AEs and no unexpected AEs in COPD patients.