

Holaira presents data supporting new lung denervation procedure

By Amanda Pedersen, Senior Staff Writer

Denervation, the interruption of the nerve connection to an organ or body part, has been used as a surgical intervention to relieve central neck or back pain, and more recently it has gained fame as a potential treatment for hypertension when used in the renal sympathetic nervous system. But one company is taking the principal idea of interrupting nerve pathways and applying it to the lungs.

Earlier this month at the European Respiratory Society (ERS) meeting in Munich, Germany, **Holaira** (Minneapolis) presented the first scientific data on the use of its lung denervation system in a procedure called targeted lung denervation (TLD). Data presented included results of the first two multi-center feasibility studies of the Holaira system in patients with chronic obstructive pulmonary disease (COPD).

"It's a lung denervation system and it's the first lung denervation system there is. Denervation hasn't been used in the lungs before," Lorraine Marshall Wright, a Holaira spokeswoman, told *Medical Device Daily*.

The procedure is similar in principal to denervation that is used in other medical spaces, Wright said, but in the lung, the neural target itself is very different. In this space, the catheter-based system is designed to address COPD by treating the overactive airway nerves during TLD, a one-time bronchoscopic procedure that provides ablative therapy that opens obstructed airways to improve breathing, and has the potential to provide lasting whole lung improvement.

COPD is characterized by a persistent airflow limitation due to a progressive narrowing of the airways interfering with normal breathing, resulting in shortness of breath (dyspnea), wheezing, chest tightness, and a productive cough. A progressive disease, it is estimated that nearly 190 million people worldwide have COPD, Wright said, with more than 15 million adults diagnosed in the U.S.

Wright said that the TLD procedure is designed to treat a broader group of COPD patients than a lot of the current therapies. She also noted that the therapy targets the same neural transmitter that COPD pharmaceuticals block temporarily, but that TLD is intended to be more sustainable. Early evidence suggests that the procedure might be complementary to existing COPD drugs.

The technology was the subject of six abstracts that were presented at ERS including oral presentations on the two multi-center feasibility studies of the Holaira System in patients with COPD.

"Our research indicates that using Holaira's lung denervation system to perform TLD therapy is feasible and safe," said Principal Investigator Dirk-Jan Slebos of the **University Medical Center** (Groningen, the Netherlands). "Furthermore, in this very early phase open label trial, there is evidence for a working therapy as our patients have experienced sustained improvements in their lung function, exercise tolerance and quality of life compared to their pre-procedure condition. We are encouraged about the potential for this new bronchoscopic therapy."

The feasibility studies were conducted at six sites in Austria, France, the Netherlands and South Africa.

The two oral presentations and poster sessions on the TLD procedure were well-attended during ERS, Wright said. "The room was full, some people were actually outside the room viewing the presentations on two monitors," she said.

Concurrent with ERS, Holaira sponsored an educational symposium on TLD that Wright said also was well-attended. "I thought the questions asked during the educational symposium showed a great deal of interest in the procedure," she told *MDD*.

Holaira is now in the process of enrolling patients in a larger randomized Phase II trial at 15 sites in Europe in six different countries, Wright said. The company also is researching the procedure's effect on airway inflammation in COPD patients.

"The potential to inhibit airway inflammation in COPD patients is of clinical interest," said Martin Mayse, chief technology officer and co-founder of Holaira. "Acetylcholine is the primary neurotransmitter in the airways. It is well known to induce bronchoconstriction and mucous secretion, but there is growing evidence it may play a role in airway inflammation as well. By targeting the parasympathetic innervation of the lungs, TLD may not only reduce the amount of bronchoconstriction and mucous secretion, but may decrease inflammation as well. Early findings suggest this, and we are planning to look at this in further detail in subsequent studies."

In April the company reported raising a Series D private equity round that totaled \$42 million. Vertex Venture Holdings led the

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round, with participation from Windham Venture Partners, two strategic investors, and all of Holaira's existing venture investors: Advanced Technology Ventures, Morgenthaler Ventures, Split Rock Partners, and Versant Ventures. Proceeds from that financing is being used to support the first randomized lung denervation clinical trial with a sham control, Holaira noted.

"Until now, COPD patients have had few options for managing their symptoms," said Lincoln Chee, venture partner of Vertex Venture Holdings. "We believe that Holaira's proprietary technology enables a fundamental advance in COPD treatment. We anticipate that this simple bronchoscopic treatment will provide lasting lung function improvement by opening obstructed airways."

Dennis Wahr, president/CEO of Holaira, said the financing signaled a "strong endorsement" from the investment community for the company's product development progress and support for Holaira's upcoming clinical trials for the lung denervation system. "After completion of multiple animal studies and two human feasibility trials, we are ready to initiate the first randomized clinical trial with a sham control for targeted lung denervation therapy," Wahr said. //