

The Zephyr[®] Endobronchial Valve System

A Minimally Invasive Bronchoscopic Treatment Option for Severe Emphysema



zephyr[®]
valve

Severe Emphysema: The Clinical Need

Emphysema, an advanced form of chronic obstructive pulmonary disease (COPD), is a progressive, debilitating disease characterized by irreversible destruction of alveolar tissue. This results in reduced elastic recoil, progressive lung hyperinflation, and gas trapping.

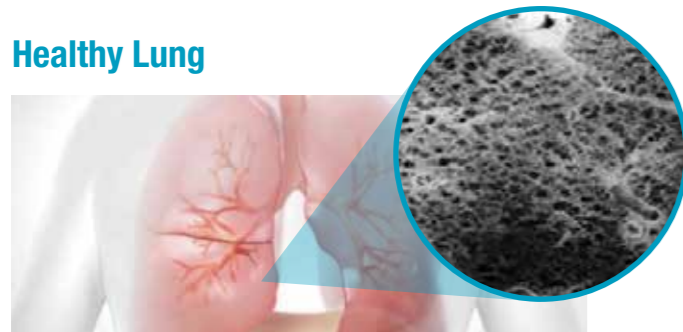
Breathlessness is the predominant and most troublesome symptom experienced by the majority of patients with severe emphysema.¹

As a result, it becomes increasingly more difficult for patients to perform everyday tasks such as bathing,

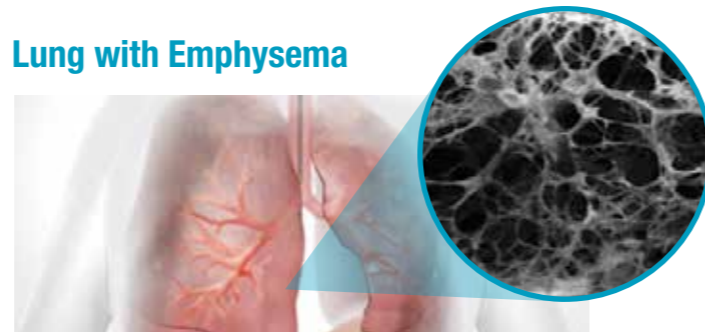
dressing, walking or climbing stairs.²

This can lead to social isolation and depression.³ Severe emphysema also reduces life expectancy.^{4,5} The quality of life for patients with emphysema is reported to be worse than those with lung cancer.⁶

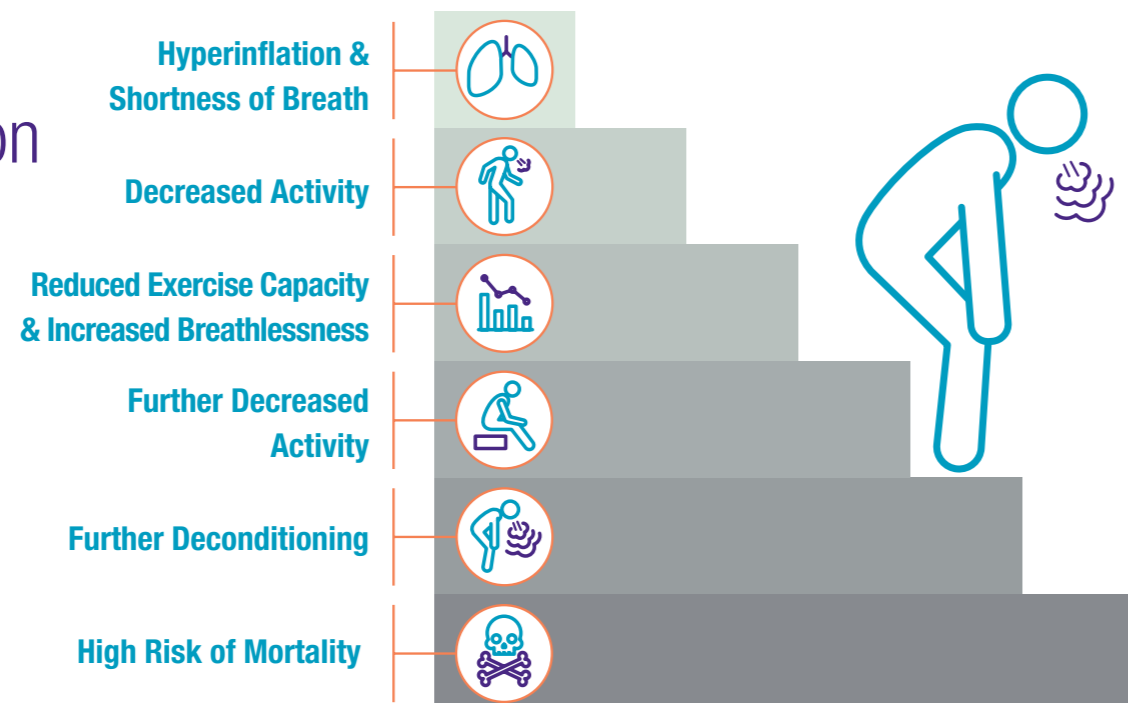
Healthy Lung



Lung with Emphysema



Disease Progression



Adapted from Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD)⁷

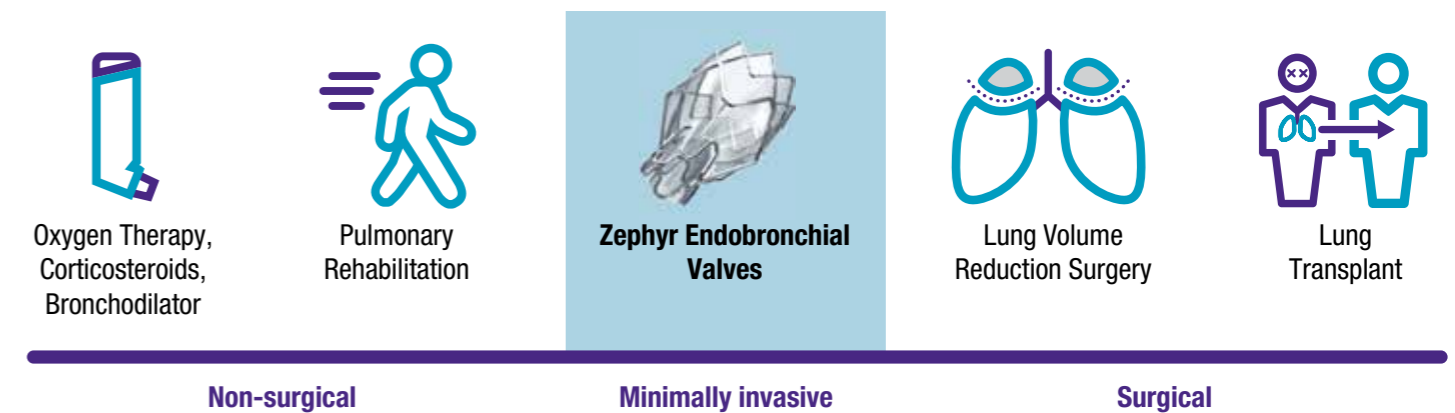
Current Treatment Options: The Zephyr Valve is a Breakthrough Medical Device for Severe Emphysema

Severe emphysema is currently treated with drugs (inhaled bronchodilators and inhaled corticosteroids), smoking cessation, pulmonary rehabilitation, oxygen therapy, lung volume reduction surgery (LVRS), or lung transplantation.⁷

None of these medical therapies reverse or remove the hyperinflation caused by the alveolar destruction and thus have limited impact on patient symptoms of dyspnea and exercise intolerance.⁸ Consequently, patients with severe emphysema remain significantly disabled.

Once medical therapy has achieved maximal benefit, the only remaining current treatment options are procedural, including lung volume reduction surgery and lung transplantation. These options are known to have high-risk complications.^{9,10}

As the disease progresses, treatments can become more invasive.



Proven to Help Emphysema Patients Breathe Easier, Do More, and Enjoy Life¹¹

The Pulmonx Zephyr Valve treatment is an alternative, breakthrough technique to achieve lung volume reduction using a minimally invasive approach. The Zephyr Endobronchial Valve is an FDA-designated “breakthrough medical device,”¹² indicated for bronchoscopic treatment of patients with hyperinflation associated with severe emphysema in regions of the lung that have little to no collateral ventilation (CV).

The Zephyr Valve System

The Zephyr Endobronchial Valve is an implantable device intended to occlude all airways feeding the hyperinflated lobe of the lung that is diseased with emphysema. When the lobe is occluded properly and isolated from airflow, trapped air in that lobe escapes only through the Zephyr Valves until the lobe volume is reduced. The remaining lobes are then able to expand more fully and work more efficiently, improving overall lung function.

Patients who have received the Zephyr Valve treatment experienced an increased exercise capacity – they could walk farther, could do more daily life activities, such as walking, gardening, and getting ready in the morning, with less shortness of breath – increased lung function, and a better quality of life.¹¹

The Zephyr Valve System

- The Zephyr Valve:** available in 4 sizes, the 4.0 EBV, 4.0-LP EBV, 5.5 EBV and 5.5-LP EBV. The low profile (LP) sizes are for deployment in shorter airways.
- The Endobronchial Delivery System (EDC):** available in corresponding sizes, 4.0 and 5.5. The 4.0 EDC is also available in a “J” configuration to access more challenging anatomies.

Available in 4 Sizes*:



Zephyr Endobronchial Valve (EBV)		
DESCRIPTION	DIAMETER RANGE	CATALOG NUMBER
Zephyr 4.0 Endobronchial Valve	4.0 - 7.0 mm	EBV-TS-4.0
Zephyr 4.0-LP Endobronchial Valve	4.0 - 7.0 mm	EBV-TS-4.0-LP
Zephyr 5.5 Endobronchial Valve	5.5 - 8.5 mm	EBV-TS-5.5
Zephyr 5.5-LP Endobronchial Valve	5.5 - 8.5 mm	EBV-TS-5.5-LP

Zephyr Delivery Catheter	
DESCRIPTION	CATALOG NUMBER
Zephyr 4.0 Delivery Catheter	EDC-TS-4.0
Zephyr 4.0-J Delivery Catheter	EDC-TS-4.0-J
Zephyr 5.5-DM Delivery Catheter	EDC-TS-5.5-DM

* Not all product models available in all geographies

Zephyr Valve Body of Clinical Evidence

The Zephyr Valve is the most studied endobronchial device for emphysema and has consistently been shown to be a safe and effective treatment for patients with severe emphysema.

Patients treated with Zephyr Valves have shown significant clinical and statistical improvements in lung function, exercise capacity, and quality of life compared to medical management alone.

Zephyr Valves have been clinically proven in:

- Heterogeneous and homogeneous emphysema
- Upper lobe and lower lobe predominant emphysema

With proper patient selection, the magnitude of clinical improvement with the Zephyr Valve treatment is comparable to lung volume reduction surgery – with less morbidity.^{9,10,13}

Consistent Clinical Findings Across 4 Randomized Controlled Trials

RCT	Design	Sample size & follow-up period	Procedural Success (TLVR%)	Difference EBV vs Control Groups (ITT)		
				LUNG FUNCTION (FEV ₁ %) MCID = 10%-15%	EXERCISE CAPACITY (6MWD) MCID = 26 m	QUALITY OF LIFE (SGRQ) MCID = -4 PTS
LIBERATE ¹¹	2:1 Randomization Heterogenous only Multicenter	n=190 12 months	84%	18.0% p<0.001	39 m p=0.002	-7.1 pts p=0.004
TRANSFORM ¹⁴	2:1 Randomization Heterogenous only Multicenter	n=97 6 months	90%	29.3% p<0.001	79 m p<0.001	-6.5 pts p=0.031
IMPACT ¹⁵	1:1 Randomization Homogenous only Multicenter	n=93 6 months	89%	16.3% p<0.001	28 m p=0.016	-7.5 pts p<0.001
STELVIO ¹⁶	1:1 Randomization Heterogenous & Homogenous Single Center	n=68 6 months	88%	17.8% p=0.001	74 m p<0.001	-14.7 pts* p<0.001

* Completed cases, all other values listed are ITT population

Complications of endobronchial valve treatment can include, but are not limited to, pneumothorax, worsening of COPD symptoms, pneumonia, dyspnea, and, in rare cases, death.

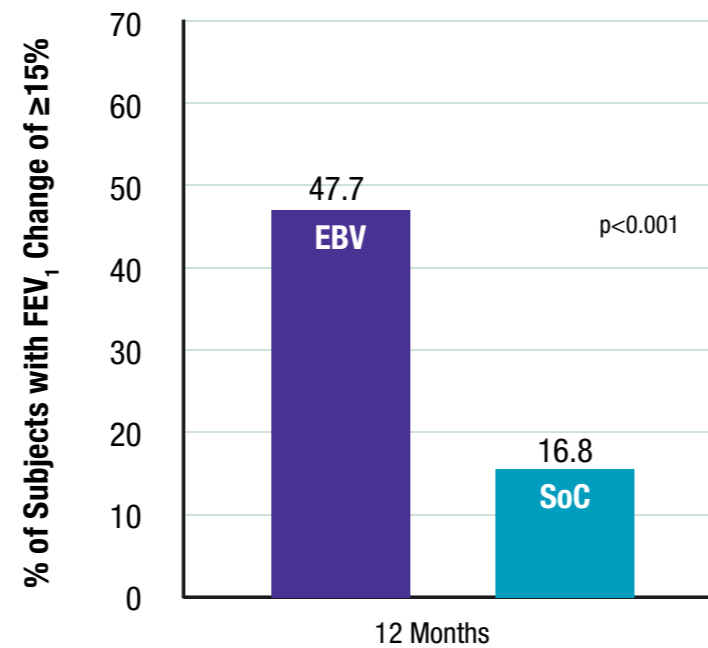


The LIBERATE Study

Study Design¹¹

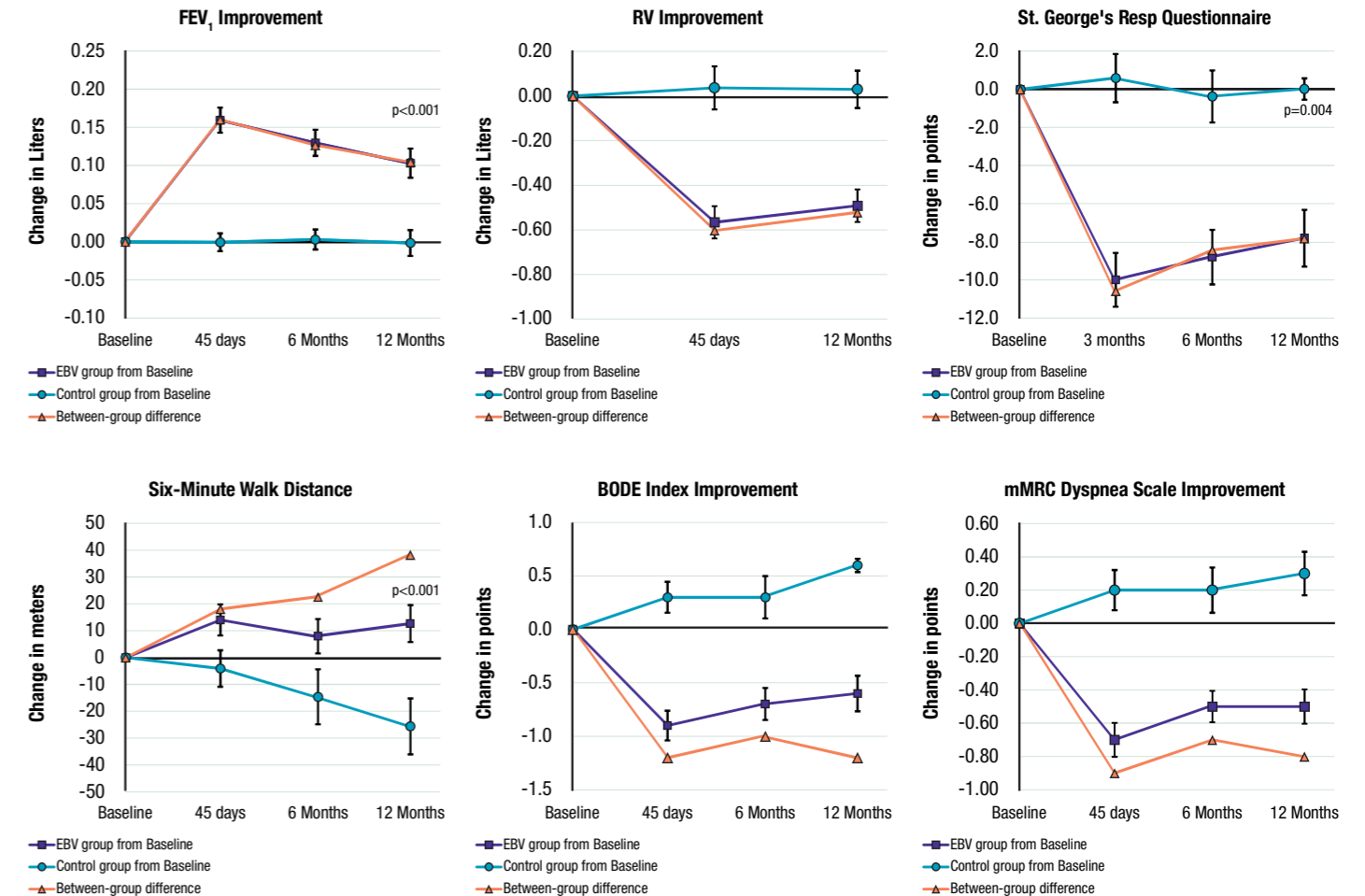
- First multicenter RCT to evaluate effectiveness and safety of Zephyr Endobronchial Valves in patients with little to no collateral ventilation (CV) out to 12 months
- 190 severe emphysema subjects with hyperinflation (Average RV 225% pred.; FEV₁ 27% pred.; DLCO 34% pred.) randomized 2:1 EBV to Standard of Care (SoC)
- Zephyr EBV n=128 : SoC n=62

Primary Endpoint



Percent of Subjects with FEV₁ Change from Baseline to 12 months of ≥15%

Key Secondary Endpoints



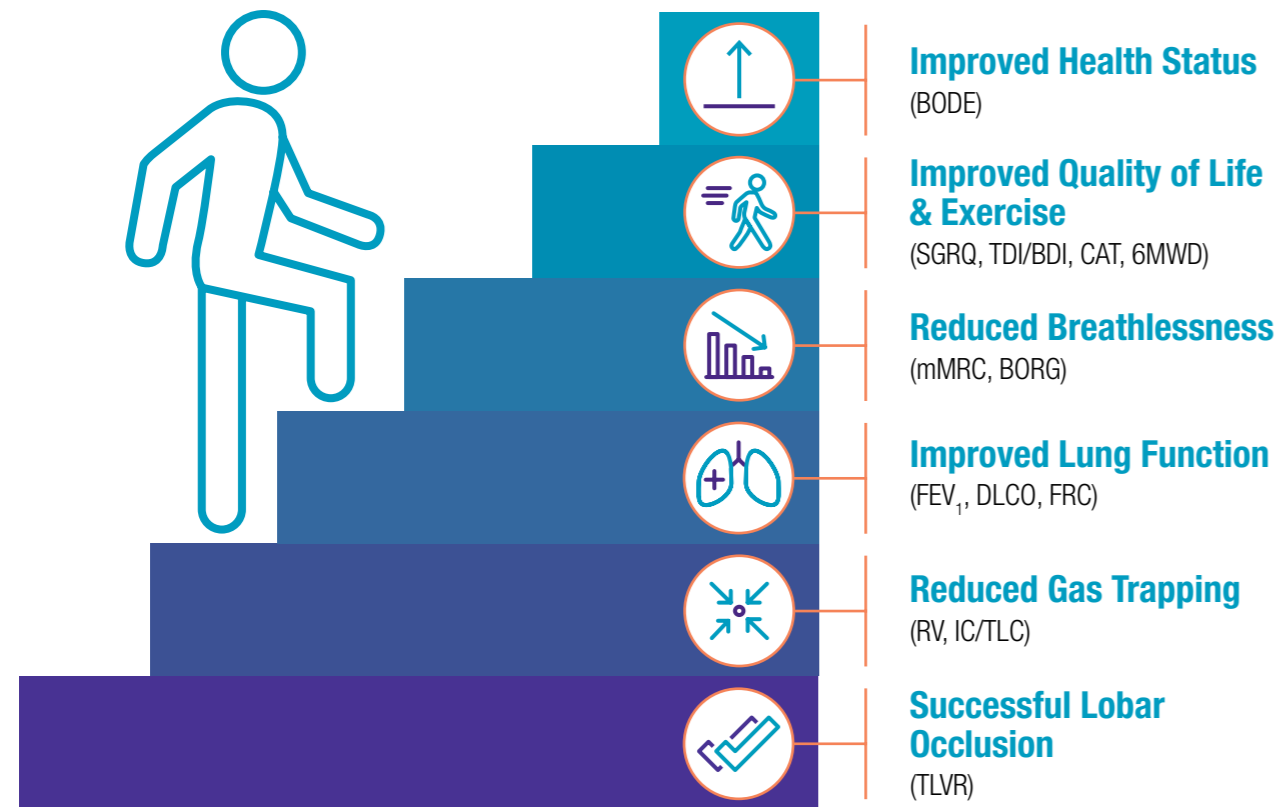
Safety: Pulmonary Serious Adverse Events Occurring in at Least 3.0% of Subjects in Either Group

	Treatment Period (0 - 45 days)		Longer-term Period (46 Days - 1 year)	
	EBV (N=128)	SoC (N=62)	EBV (N=122)	SoC (N=62)
Death	3.1%	0.0%	0.8%	1.6%
Pneumothorax	26.6%*	0.0%	6.6%	0.0%
COPD exacerbation	7.8%	4.8%	23.0%	30.6%
Pneumonia	0.8%	0.0%	5.7%	8.1%
Respiratory failure	1.6%	0.0%	0.8%	3.2%

*Statistically different from SoC

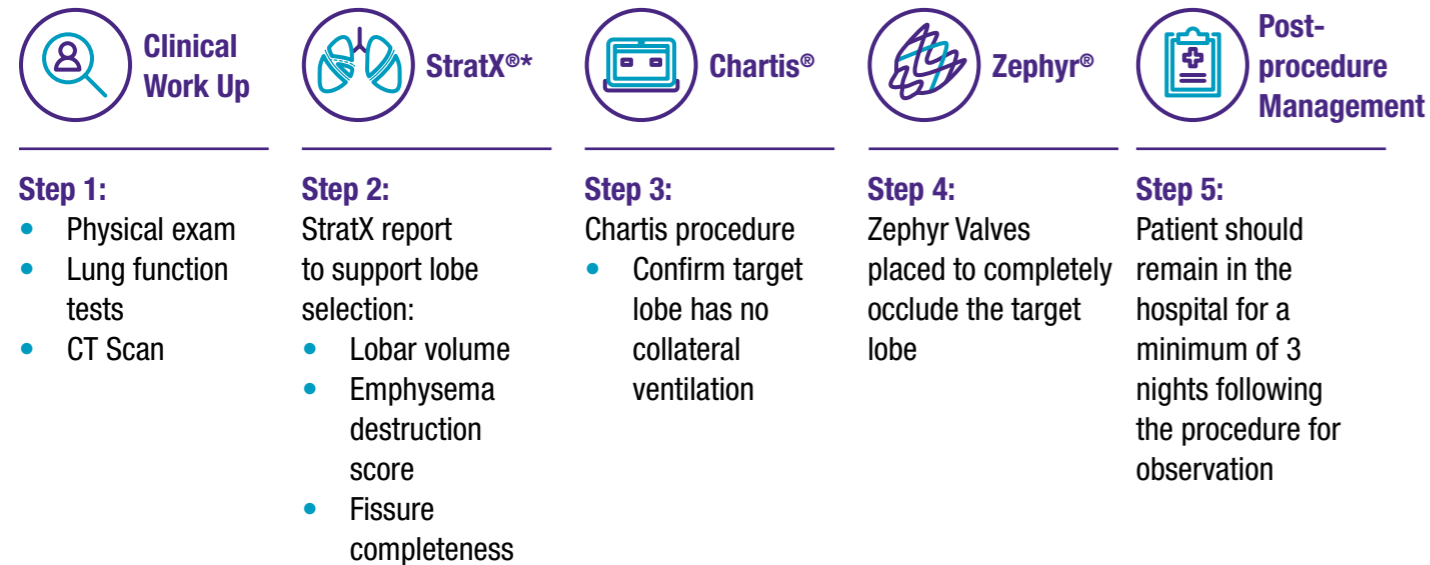
- Increased SAE rate with EBV treatment compared to standard of care in the short-term (first 45 days post-treatment)
- Reduced SAE rate long-term (46 days to 12 months) with EBV treatment compared to standard of care
- 5 of 8 subjects experiencing a pneumothorax in the longer-term period had recently undergone a secondary bronchoscopy for valve replacement and/or removal

Zephyr Treatment Leads to Improved Health Status



Criner, CJ et. al. Am J Respir Crit Care Med, 2018; 198(9), 1151-1164 and data on file at Pulmonx.¹¹

Patient Selection & Treatment Process



* StratX not available in all geographies

Patient Selection

Appropriate patient selection is critical to the success of Zephyr Valve treatment. Over time, clinical trial data have helped define the successful patient profile.

Zephyr Valve treatment is for patients with pulmonary emphysema with a diagnosis of hyperinflation determined by CT scan, severe or very severe emphysema (FEV₁

15-45% predicted) who are symptomatic despite optimal medical management. In addition, candidates should have residual volume indicating hyperinflation (RV ≥ 175% predicted). Zephyr Valves can be used to treat patients with heterogenous or homogeneous emphysema and can be used in upper lobe or lower lobe predominant disease.

Suggested Patient Selection

Inclusion Criteria	
ASSESSMENT	INCLUSION CRITERIA
Medical history and physical examination	<ul style="list-style-type: none"> Consistent with emphysema BMI <35 kg/m² Stable with ≤20 mg prednisone (or equivalent) qd
Radiographic	<ul style="list-style-type: none"> Evidence of emphysema on High Resolution Computed Tomography (HRCT) scan
Pulmonary function	<ul style="list-style-type: none"> Forced expiratory volume in one second (FEV₁, % predicted) ≤45% predicted ≥15% Total lung capacity (TLC) ≥100% predicted post-bronchodilator Residual volume (RV) ≥175% predicted post-bronchodilator
Exercise	<ul style="list-style-type: none"> 6-Minute Walk Distance ≥100 m and <500 m
Smoking	<ul style="list-style-type: none"> Nonsmoking for 4 months prior to initial interview and throughout evaluation for the procedure
Collateral ventilation	<ul style="list-style-type: none"> The lobe targeted for treatment must have little to no collateral ventilation (as measured by StratX and Chartis)

Exclusion Criteria
<ul style="list-style-type: none"> Prior lung transplant, LVRS, median sternotomy or lobectomy Congestive heart failure: Left Ventricular Ejection Fraction <45%; unstable cardiac arrhythmia, myocardial infarction or stroke Known allergies to Nitinol, Nickel, Titanium or Silicone Large bullae >30% of either lung Medical conditions or other circumstances make it likely that the patient will be unable to complete the preoperative and postoperative pulmonary diagnostic and therapeutic program required for the procedure Contraindications for bronchoscopy; patient characteristics that may carry a high risk for postoperative morbidity and/or mortality Severe hypercapnia (PaCO₂ ≥50 mm Hg on room air) and/or severe hypoxemia (PaO₂ ≤45 mm Hg on room air) Uncontrolled pulmonary hypertension (sPAP >45 mm Hg)

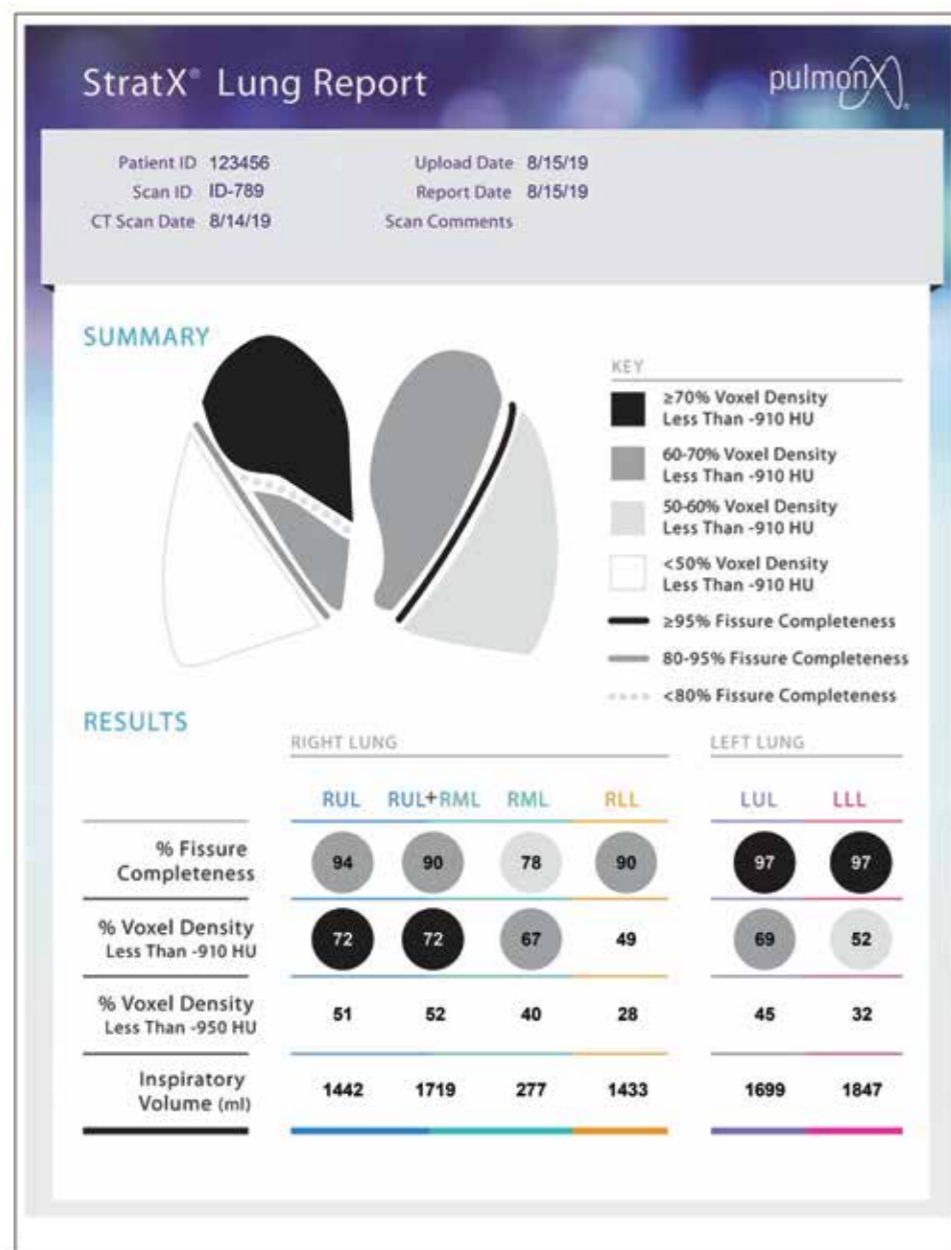
Note: Patients in whom the targeted lobe for treatment is not the most diseased (due to factors such as collateral ventilation or other abnormalities), and the contralateral lung has >60% emphysema destruction score (at -910 HU) could be at higher risk for a complex pneumothorax (defined as requiring removal of all valves or resulting in death) if a pneumothorax occurs. In the event the most diseased lobe is not the target lobe, Zephyr Valve treatment should only be performed after careful consideration and appropriate discussion of the risk with the patient. Patient should be observed more carefully post-procedure.

StratX Lung Analysis Platform

The StratX Lung Analysis Platform is a cloud-based quantitative CT analysis service that provides information on emphysema destruction, fissure completeness, and lobar volume to help identify target lobes for Zephyr Valve Treatment. Patients with fissure completeness scores of <80% are considered positive for collateral ventilation

(CV+) and should not be treated with Zephyr Valves. Patients with fissure completeness scores >80% are likely to be negative for collateral ventilation (CV-) and may be good candidates for Zephyr Valve treatment.¹⁷ CV status in these patients should be confirmed with the Chartis Pulmonary Assessment System.

StratX is used in combination with the Chartis Pulmonary Assessment System and can help properly identify patients appropriate for Zephyr Valve treatment.



Chartis Pulmonary Assessment System

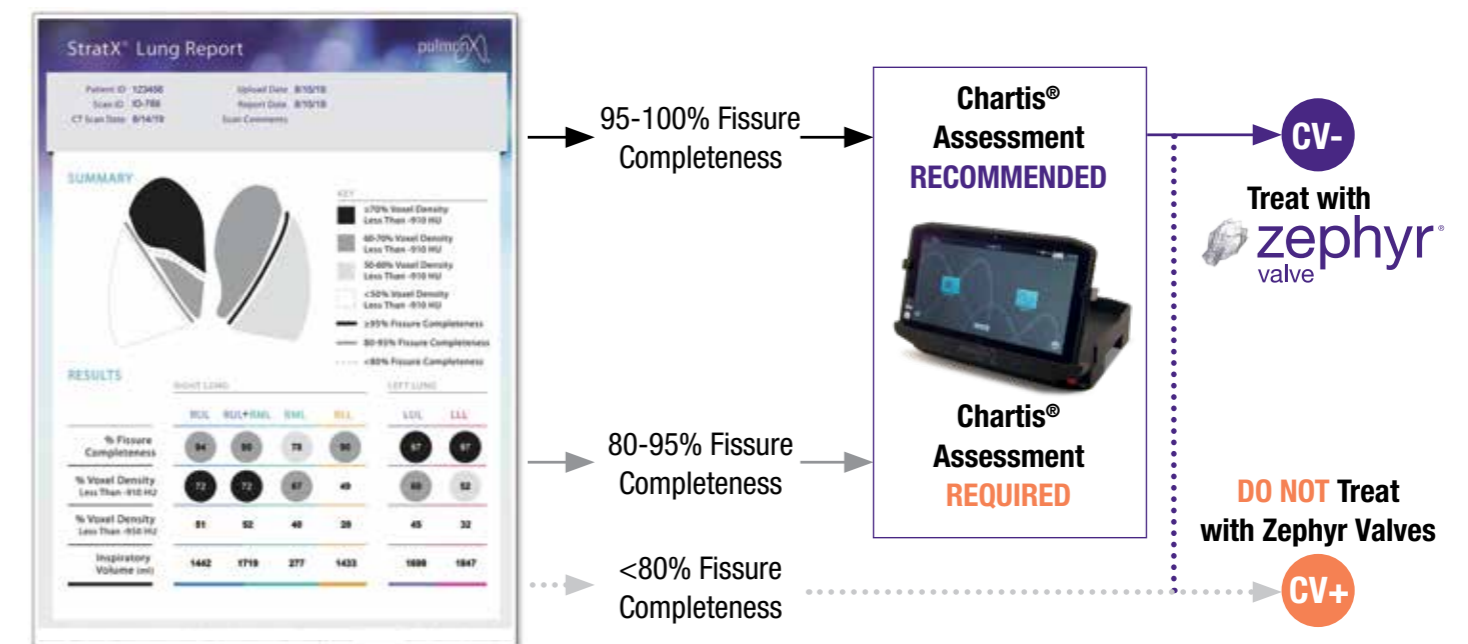
The Chartis Pulmonary Assessment System is a proprietary balloon catheter and console with flow and pressure sensors used to assess the presence of collateral ventilation (CV) within isolated lung units.

The Chartis System consists of a single-patient-use catheter with a central lumen and a balloon at its tip and a console to allow for the assessment of airflow in the targeted lobe.

When the balloon is inflated, the target lobe is blocked, and the air can only escape through the catheter's central lumen. Airflow and pressure are displayed on the Chartis Console allowing for a simulation of an 'occluded lobe' and the measurement of any collateral ventilation in the targeted lobe.



Optimal Approach for CV Assessment¹⁸



Zephyr Procedure

Zephyr Valves are implanted using a bronchoscope, using either general anesthesia or conscious sedation. The procedure time is typically 30-60 minutes. Multiple valves (typically 3 to 5 valves) of varying sizes may be placed in segmental airways to completely occlude the entire lobe with the goal of target lobe volume reduction (TLVR).

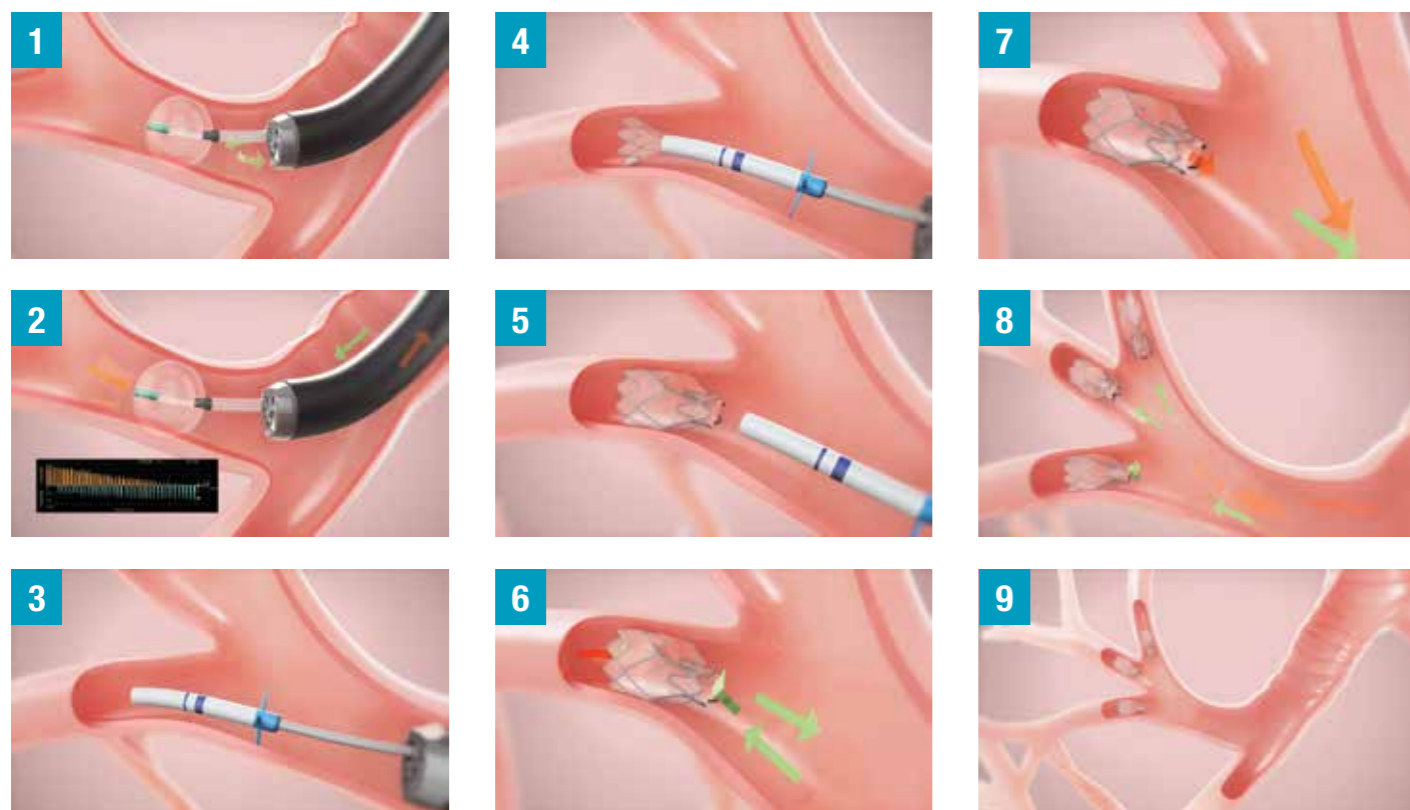
The Zephyr Valve can be removed and retracted through the bronchoscope if needed.

Post-Procedure Management

After the procedure, the patient will stay at least 3 nights in the hospital under observation. This is important to monitor if the patient is experiencing any side effects post-procedure. The major significant side effect associated with the Zephyr Valve procedure in the short-term is pneumothorax. Targeted lobar deflation likely causes inflation of the ipsilateral lobe, which can result in a tear of the already compromised parenchymal tissue of the emphysematous ipsilateral lobe, resulting in a pneumothorax.

In the LIBERATE Clinical Study, subjects experiencing a pneumothorax attained the same level of benefit over the long-term as those without pneumothorax.¹¹

Patients should also be monitored for pneumonia, COPD exacerbations, and respiratory failure, as these events have been observed in patients treated with Zephyr Valves.



Guidance Documents for the Management of Patients with COPD

Patient Benefits

In a clinical study,¹¹ patients treated with the Zephyr Valve compared to patients on medication alone were able to:



Return to activities that were previously limited



Feel **less shortness of breath**



Walk longer distances



Have **more energy**



Feel **more confident** leaving their home

Complications of endobronchial valve treatment can include, but are not limited to, pneumothorax, worsening of COPD symptoms, pneumonia, dyspnea, and, in rare cases, death.

Multiple independent networks have concluded that with proper patient selection, the Zephyr Valve procedure should be considered in the treatment of severe emphysema. These networks include:

- Global Initiative for Chronic Obstructive Lung Disease (GOLD)^{7,19}
- National Institute for Health and Care Excellence (NICE)²⁰
- Australian Lung Foundation (COPD-X)
- German Respiratory Society (DGP)
- Austrian Respiratory Society (OGP)
- National Health Care Institute of the Netherlands (Zorginstituut Nederland)

Of particular interest are the GOLD and NICE recommendations.

In the 2017 GOLD Update, endobronchial valve treatment is recommended for select patients who are still symptomatic despite optimal medical management and who have hyperinflation and the absence of collateral ventilation.⁷

In the updated 2020 GOLD Report, endobronchial valves, endobronchial valve treatment was elevated to “Evidence A”

affirming that endobronchial valves, like the Zephyr Valve, are a proven, viable minimally-invasive treatment option for severe emphysema.¹⁹

The NICE Final Guidance (2017) recommends a change from “special measures” to “standard measures” for the use of endobronchial valve insertion to reduce lung volume in emphysema.²⁰ In 2018, NICE updated the guidelines to include a review of the LIBERATE study. The current guidance states:

“Current evidence on the safety and efficacy of endobronchial valve insertion to reduce lung volume in emphysema is adequate in quantity and quality to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit.”

In addition, Cochrane Airways Group issued a Cochrane review in 2017,²¹ before the TRANSFORM and LIBERATE data were published. This Health Technology Assessment considers the most recent publications on Zephyr Valve treatment where collateral ventilation was a criterion for inclusion (with the exception of TRANSFORM and LIBERATE data) and was a key reference for the NICE guidance mentioned above.



Zephyr Endobronchial Valves



The Zephyr Valve is the first FDA approved minimally invasive device for the treatment of emphysema.



Zephyr Valves are clinically proven to improve dyspnea, increase exercise, improve lung function, and improve multiple measures of quality of life.



Patients most likely to benefit from Zephyr Valve treatment can be identified with assessment tools also offered by Pulmonx – Chartis Pulmonary Assessment System and StratX Lung Analysis Platform.



Zephyr Valve benefits have been proven in four randomized controlled trials – the most rigorous clinical evidence among endoscopic emphysema treatments.



The Zephyr Valve is included in emphysema treatment guidance from GOLD, NICE and other leading health organizations worldwide.



Zephyr Valve treatment involves placing tiny valves in the airways to occlude a diseased part of the lungs and reduce hyperinflation. This helps the healthier parts of the lungs to expand and lifts pressure off the diaphragm, decreasing shortness of breath and making breathing easier.

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Get more information about the Zephyr Valve treatment for emphysema.

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Brief Statement: The Zephyr® Endobronchial Valve is an implantable bronchial valve intended to control airflow in order to improve lung functions in patients with hyperinflation associated with severe emphysema and/or to reduce air leaks. The Zephyr Valve is contraindicated for: Patients for whom bronchoscopic procedures are contraindicated; Evidence of active pulmonary infection; Patients with known allergies to Nitinol (nickel-titanium) or its constituent metals (nickel or titanium); Patients with known allergies to silicone; Patients who have not quit smoking. Use is restricted to a trained physician. Prior to use, please reference the Zephyr Endobronchial System Instructions for more information on indications, contraindications, warnings, all precautions, and adverse events.

Brief Statement: The Chartis® System is indicated for use by bronchoscopists during a diagnostic bronchoscopy in adult patients with Chronic Obstructive Pulmonary Disease (COPD) and emphysema in a bronchoscopy suite. The system, composed of the Chartis Catheter and Chartis Console, is designed to measure pressure and flow in order to calculate resistance to airflow and quantify collateral ventilation in isolated lung compartments. The Chartis Catheter is used through the working channel of a bronchoscope and connects to the Chartis Console. The Chartis Console is capital equipment that is reusable and displays the patient information. The Chartis System is contraindicated in the presence of active infection or major bleeding diathesis. There are no known interfering substances. Use is restricted to a trained physician. Prior to use, please reference the Chartis System Instructions for Use/ User Manual for more information on indications, contraindications, warnings, all precautions, and adverse events.

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