EMPROVE Clinical Trial

The EMPROVE Trial – a Randomized, Controlled Multicenter Clinical Study to Evaluate the Safety and Effectiveness of the Spiration® Valve System for Single Lobe Treatment of Severe Emphysema

G. Criner[1], A. Delage[2], K. Voelker[3] for the EMPROVE Trial Investigator Group
[1]Temple University Hospital, Philadelphia, PA; [2]Université Laval, Québec, QC;
[3]Sarasota Memorial Hospital, Sarasota, FL.

STUDY OBJECTVES

Current treatments for chronic obstructive pulmonary disease (COPD) fail to reverse the hyperinflation that impairs patients with a predominant emphysematous phenotype. Minimally invasive, bronchoscopic placement of endobronchial one-way valves have been developed to block airflow to targeted hyperinflated, emphysematous lung lobes with the objective to reduce end-expiratory lung volume and improve lung function, quality of life and dyspnea.

METHODS

Key inclusion criteria:

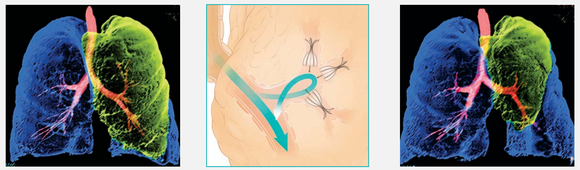
- $FEV_1 \leq 45\%$
- TLC ≥ 100%
- RV ≥ 150% predicted

Randomization was 2:1, Treatment to Control. Both groups received optimal medical management. The treatment group also had target lobe occlusion utilizing the Spiration® Valve System (Olympus Respiratory America).

HRCT ASSESSMENT

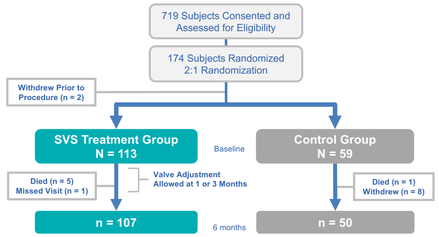
The most diseased lobe was selected based on HRCT assessment. The treated lobe had ≥ 40% emphysema involvement and ≥ 10% difference with the ipsilateral lobe (the right middle lobe was not considered in this analysis). The selected lobe had an intact fissure separation ≥ 90% with the ipsilateral lobe. HRCT analysis was performed by MedQIA (Core Lab) using VIDA Diagnostics software.

SPIRATION VALVE SYSTEM MECHANISM OF ACTION



Pretreatment with hyper-inflated left upper lobe (LUL) ➡ Valves occluding airways ➡ Posttreatment showing left upper lobe (LUL) atelectasis

SUBJECT FLOW



BASELINE CHARACTERISTICS

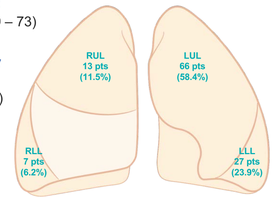
	TREATMENT GROUP (N = 113) Mean ± S.D. or N (%)	CONTROL GROUP (N = 59) Mean ± S.D. or N (%)	DIFFERENCE (T – C) 95% BCI
Sex (male)	54 (47.8%)	38 (64.4%)	(-30.9%, -0.8%)
Age (years)	66.7 ± 6.6	68.1 ± 6.4	(-3.4, 0.7)
FEV_1 (L)	0.825 ± 0.264	0.792 ± 0.260	(-0.051, 0.116)
FEV_1 (% pred, L)	30.8 ± 8.1	28.5 ± 8.5	(-0.4, 5.0)
RV (L)	4.573 ± 1.253	4.848 ± 1.199	(-0.665, 0.115)
RV (% pred, L)	207.5 ± 45.0	213.4 ± 49.3	(-21.3, 9.4)
RV/TLC Ratio	0.632 ± 0.080	0.632 ± 0.086	(-0.028, 0.026)
Dyspnea (mMRC)	2.7 ± 0.7	2.7 ± 0.6	(-0.2, 0.2)
COPD Assessment Test	21.8 ± 6.8	20.0 ± 6.3	(-0.3, 3.9)
SGRQ Total	57.2 ± 14.8	54.6 ± 13.6	(-1.9, 7.1)
Target Lobe Volume (L)	1.843 ± 0.602	1.820 ± 0.456	(-0.140, 0.187)
Emphysema Severity (%)	63.6 ± 10.1	61.6 ± 11.6	(-1.6, 5.5)
Emphysema Heterogeneity (% points)	25.3 ± 12.0	23.3 ± 11.6	(-1.8, 5.8)

PROCEDURAL DATA

Average procedure time:
24.3 ± 11 Minutes (range 9 – 73)

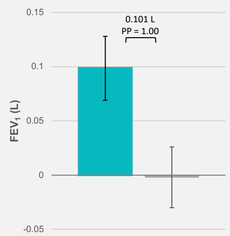
Follow-up bronchoscopy for valve adjustment:
25 of 113 Subjects (22.1%)

Lobes treated:
Upper lobes: 79 (69.9%)
Lower lobes: 34 (30.1%)



RESULTS

CHANGE IN FEV_1
@ 6 MONTHS

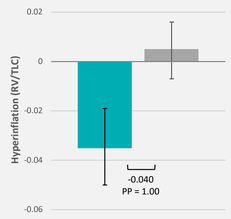


SVS (N = 106) Control (n = 50)
Mean ± 95% Bayesian Credible Interval (BCI); PP = Posterior Probability

FEV_1 RESPONDER RATE

FEV_1 Responders ≥ 15% Improvement	TREATMENT GROUP n/N (%)	CONTROL GROUP n/N (%)
6 Months	39/106 (36.8%)	5/50 (10.0%)
Difference (T–C)	25.7%	
Posterior Probability	0.9998	

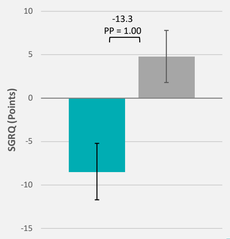
CHANGE IN HYPERINFLATION
@ 6 MONTHS



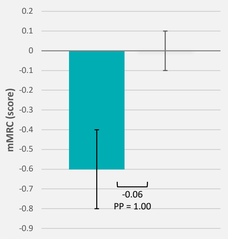
CHANGE IN TARGET LOBE VOLUME
@ 6 MONTHS

SVS (N = 105) Control (n = 50)
Mean ± 95% BCI; PP = Posterior Probability

CHANGE IN SGRQ
@ 6 MONTHS



CHANGE IN mMRC
@ 6 MONTHS



SVS (N = 107) Control (n = 50)
Mean ± 95% BCI; PP = Posterior Probability

SAFETY

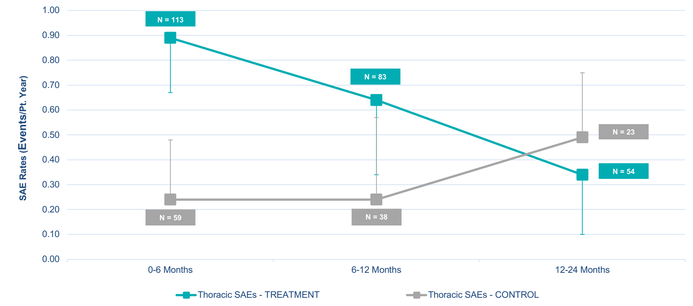
INDIVIDUAL THORACIC SERIOUS ADVERSE EVENTS (THROUGH 6 MONTHS)

	TREATMENT GROUP (N = 113) %	CONTROL GROUP (N = 59) %	DIFFERENCE (T–C) Est	(95% BCI)
Acute exacerbation of COPD requiring hospitalization	15.9	10.2	5.8	(-5.9, 15.1)
Death from procedure or device	0.0	0.0	0.0	(-5.3, 2.3)
Pneumonia in the valve-treated lobe requiring hospitalization	1.8	—	1.8	(-3.9, 5.2)
Pneumonia not in the valve-treated lobe requiring hospitalization	7.1	1.7	5.4	(-2.4, 11.1)
Pneumothorax requiring surgical intervention or prolonged air leak > 7 days	12.4	0.0	12.4	(4.6, 18.6) *
Tension pneumothorax requiring hospitalization	1.8	0.0	1.8	(-3.9, 5.2)
Respiratory failure requiring mechanical ventilatory support	2.7	0.0	2.7	(-3.2, 6.4)
TOTAL	30.1	11.9	18.2	(5.0, 28.8) *

*95% BCI for the difference that excludes "0" = Statistically Significant

- There were no procedure or device-related deaths
- Pneumothorax was the only SAE statistically higher in the Treatment Group as evidenced by a 95% BCI for the difference that excludes "0"
- Early onset pneumothorax due to acute volume reduction in the targeted lobe is a recognized marker of efficacy
- Pneumothorax patients were successfully managed with chest tube drainage and no valve removal was required

LONG TERM THORACIC SERIOUS ADVERSE EVENTS RATES (EVENTS/PATIENT YEAR)



- SAE event rates trend lower in the Treatment Group over time

Mean ± 95% BCI

CONCLUSIONS

The EMPROVE Trial showed that bronchoscopic treatment of severe emphysema patients with the Spiration Valve System provides statistical and clinically meaningful improvements in FEV_1, target lobe volume reduction, dyspnea and quality of life parameters, with a good safety profile. Furthermore, this study demonstrates that HRCT assessment is effective in choosing appropriate patients and the target lobe for treatment.

A7753 / 621 **Contact:** Gerard Criner MD, Gerard.Criner@tuhs.temple.edu

LITC-004695 Rev AA