Zephyr Valve Benefits Previously Ineligible Patients Following Blocking of Collateral Channels with AeriSeal: CONVERT Trial

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BACKGROUND

Bronchoscopic Lung Volume Reduction with one-way endobronchial valves is an established guideline-based treatment option for patients with hyperinflation associated with severe COPD/emphysema. However, this treatment is ineffective when there is collateral ventilation in the target lobe. Recent data has shown that collateral ventilation status can be reversed with the use of AeriSeal® Foam (Figure 1), making the patient eligible for BLVR with Zephyr Valves (Ing A et al. Respirology. 2022: 27(12):1064-72; Bezzi M et al. Eur Respir J. 2022; 60: Suppl. 66, 1231).

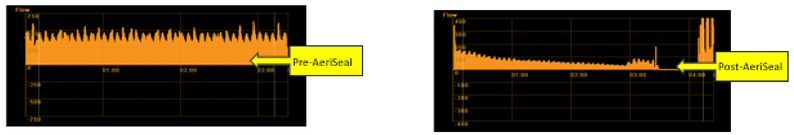
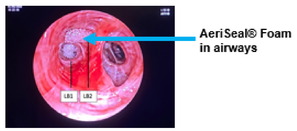
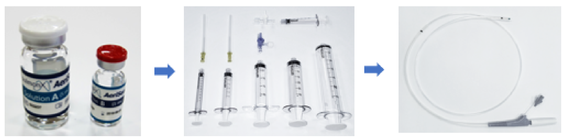


Figure 1: AeriSeal® System

The AeriSeal® Foam is a polymerizing sealant (composed of aminated polyvinyl alcohol and glutaraldehyde) that functions by blocking both small airways and collateral channels which limits the collateral ventilation of a target lobe.





AeriSeal is delivered as a foam that polymerizes at time of delivery via a balloon catheter through a therapeutic bronchoscope (2.8mm working channel) to segmental or subsegmental bronchi.

METHODS

CONVERT Study Design: Prospective, open-label, multi-center, single-arm study conducted at 14 sites. The study flow diagram is shown in Figure 2.

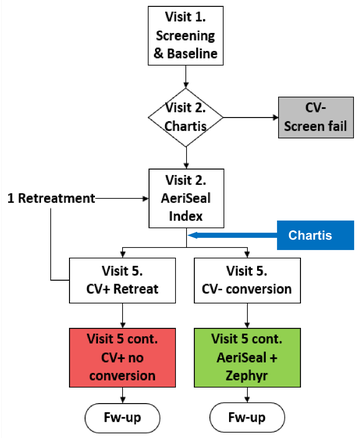
Study Objective: Evaluate utility of the AeriSeal System to occlude collateral air channels in a target lung lobe of severe emphysema patients with collateral ventilation (CV+) and convert the target lung lobe to having little to no collateral ventilation (CV-).

Endpoints:

AeriSeal Endpoint: Percentage of subjects converted from CV+ to CV- measured by Chartis® at 6 weeks post-AeriSeal.

Zephyr Valve Endpoint: Percentage of subjects achieving Treated Lobar Volume Reduction (TLVR) ≥350 mL at 45-days post-lobar occlusion with Zephyr Valves.

Figure 2: Study Flow



METHODS

The AeriSeal target lobe is the same as the Zephyr Valve target lobe.

Target lobe selection

- Fissure integrity ≥ 80%
- Maximum 3 segments feeding fissure defect
- CV+ by Chartis

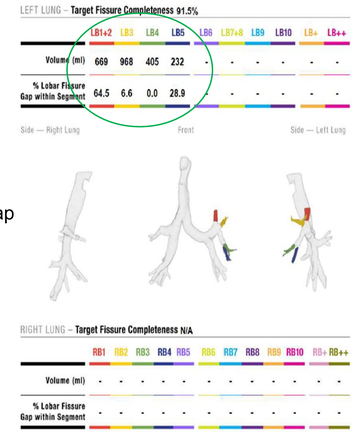
Unique QCT report detailing

- Percent lobar fissure gap within segment
- Number of segments involved with lobar fissure gap
- Segmental volume

Treatment algorithm

- 40mL maximum AeriSeal Foam unilaterally
- Assess CV status by Chartis at 6-weeks
- One re-treatment if needed; total AeriSeal Foam limited to 40mL
- CV-converted patients treated with Zephyr Valves

Figure 3: Target Lobe Selection and Fissure Targeting Report



RESULTS

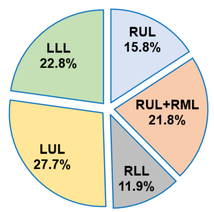
One-hundred and one (101) patients (57 males/44 females) with severe emphysema (43 heterogeneous and 58 homogeneous) were enrolled in the intent-to-treat population; baseline demographics were: age, 65.1± 6.9 yrs; smoking history, 45.1±24.3 pack/yrs; Post-BD FEV1, 30.7±9.2% pred.; TLC, 136.9±17.5% pred.; RV, 235.7±46.5% pred.: 6MWD, 347±75meters; and SGRQ, 58.9±15.3 points.

Table 1 shows the lobes treated, their respective fissure completeness scores and emphysema destruction scores at -910 HU.

Lobe Status				
	Fissure Completeness (%)*	Emphysema Destruction at -910 HU*	AeriSeal Treated (n=101)	Zephyr Valve Treated (n=76)
RUL	68.2 ± 16.26	66.6 ± 12.40	16 (15.8%)	12 (15.8%)
RML	75.3 ± 15.76	59.2 ± 15.70	0	0
RUL + RML	87.0 ± 7.91	65.7 ± 11.12	22 (21.8%)	15 (19.7%)
RLL	87.0 ± 7.91	57.7 ± 13.97	12 (11.9%)	8 (10.5%)
LUL	87.6 ± 11.25	63.6 ± 11.28	28 (27.7%)	22 (27.6%)
LLL	87.6 ± 11.25	56.9 ± 14.25	23 (22.8%)	20 (26.3%)
Treated Lobe	**88.3 ± 5.94**	**70.6 ± 8.12**		

*: mean ± SD

Treated Lobes



88% of the procedures were performed under general anesthesia and 12% under conscious sedation. A median volume of 30mL AeriSeal® Foam was administered.

Primary Endpoint: At 45-days after final administration of AeriSeal, the Chartis confirmed CONVERSION from CV+ to CV– was achieved in 77.6% of patients (95% CI: 68.0%, 85.4%). 89% of CV-converted patients achieved a Treated Lobar Volume Reduction (TLVR) of ≥350 mL. Mean TLVR was 1080±671 mL at Day 45 and 1062±649 mL at 6 months.

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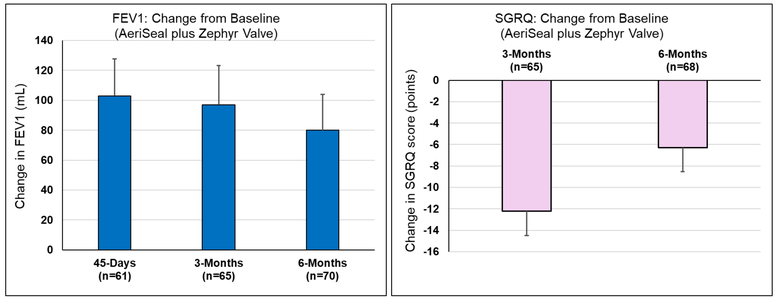
RESULTS

CV-converted patients treated with Zephyr Valves experienced improvement in clinical outcomes as shown in Figure 4.

Figure 4: FEV1 and SGRQ following BLVR with Zephyr Valves in CV-converted Patients.



Serious Adverse Events (SAEs) occurring after AeriSeal Foam treatment and after Zephyr Valve placement in CV-converted patients are summarized in Table 2.

Table 2: Serious Adverse Events

Event	AeriSeal Only	AeriSeal + Zephyr Valves	
	Stage 1† Post-AeriSeal only	Short-term (45-days post-Zephyr Valve)	Long-term (≥46-days post-Zephyr Valve)
	N=102	N=77	N=65
PAIR*	16 (15.7%)	0	0
Pneumonia	7 (6.9%)	1 (1.3%)	7 (10.8%)
Pneumonitis	6 (5.9%)	0	1 (1.5%)
COPD Exacerbation	6 (5.9%)	0	9 (13.8%)
Hemoptysis	1 (1.0%)	0	2 (3.1%)
Lung consolidation	1 (1.0%)	0	0
Pneumothorax	0	15 (19.5%)	4 (6.2%)
Respiratory failure	1 (1.0%)	0	1 (1.5%)

† Stage 1: Period from first AeriSeal treatment to final CV determination at 45 days (single AeriSeal treatment) or 90 days (repeat AeriSeal treatment) post-procedure.
* PAIR (Post-Treatment Acute Inflammatory Response)

CONCLUSIONS

BLVR with endobronchial valves is feasible in emphysema patients with collateral ventilation.

- AeriSeal® Foam can safely and effectively occlude collateral channels and convert a CV+ lobe to having little-to-no collateral ventilation.
- Zephyr Valves are effective in reducing treated lobar volume in CV- converted lobes and in improving clinical outcomes (lung function and Quality of Life).
- AeriSeal has an acceptable safety profile: most common SAE after AeriSeal was transient PAIR, which resolved with standard medical management.
- SAEs after Zephyr Valves in CV-converted subjects were of the type seen in other Zephyr Valve trials, primarily pneumothorax.
- Emphysema patients with a defined fissure gap in the target lobe may have an option for BLVR with Zephyr Valves after closure of the fissure gap with AeriSeal Foam.