

## Research in Severe Asthma (RISA) Trial—5 Year Results

Pavord ID, Cox G, Thomson NC, Rubin AS, Corris PA, Niven RM, Chung KF, Lavolette M; RISA Trial Study Group

**Safety and efficacy of bronchial thermoplasty in symptomatic, severe asthma.**  
*American Journal of Respiratory and Critical Care Medicine.* 2007;176:1185-1191.

Pavord ID, Thomson NC, Niven RM, Corris PA, Chung KF, Cox G, Armstrong B, Shargill NS, Lavolette M, for the RISA Trial Study Group

**Safety of bronchial thermoplasty in patients with severe refractory asthma.**  
*Annals of Allergy, Asthma & Immunology.* 2013;111(5):402-407.

### Objective

The Research in Severe Asthma (RISA) Trial was a multicenter, randomized, controlled clinical trial (randomized 1:1), designed to evaluate the safety of Bronchial Thermoplasty (BT), delivered by the Alair™ System, in symptomatic, severe, persistent asthma patients who were symptomatic despite treatment with high dose medication, including ICS (>750 µg/day of fluticasone or equivalent), LABA (at least 100 µg salmeterol per day or equivalent) and OCS (up to 30 mg oral prednisone/day). Secondary objectives were to evaluate whether asthma symptoms or medication levels could be reduced in this population.

### Methods

The treated group received bronchial thermoplasty in addition to these standard medications. Both groups remained on baseline medications through 22 weeks (Steroid Stable Phase), before attempting to wean off oral and inhaled corticosteroids in a pre-specified 14-week (Steroid Wean) period. Patients were then followed an additional 4 months (through a total of 1 year follow-up from treatment) to determine stability following any change in medications that resulted from the Steroid Wean (Reduced Steroid Phase).

The clinical trial was conducted at 8 Investigational Sites in 3 countries (Canada, United Kingdom, and Brazil) with a total of 34 randomized patients, 32 of whom completed the study (15 BT and 17 Control).

To assess long-term safety of BT in this group of patients, BT-group patients were followed out to 5 years. Fourteen (14) patients participated in the long-term follow-up. Patients were evaluated annually during office visits to assess lung function, undergo a physical examination and chest x-ray, and were questioned on respiratory-related adverse events and healthcare utilization events.

### Key Effectiveness Results

In the **Steroid Stable Phase**, clinically and statistically significant changes compared to control were observed in:

- Use of rescue medication (25 fewer puffs/7 days, or **1300 fewer puffs per year** or 6.5 canisters/yr)
- FEV<sub>1</sub>, % predicted (**15.8% improvement in lung function**, with 12% considered clinically significant)
- **Quality of Life** (+1.1 in AQLQ scores, on scale of 1 to 7 with higher numbers indicating better quality of life)
- **Asthma Control** (-0.9 in ACQ scores, on scale of 0 to 6 with lower numbers indicating better asthma control)

In the **Steroid Wean Phase**, three patients in the Control group did not attempt steroid reduction due to unstable asthma. All patients in the BT group were able to initiate steroid reduction.

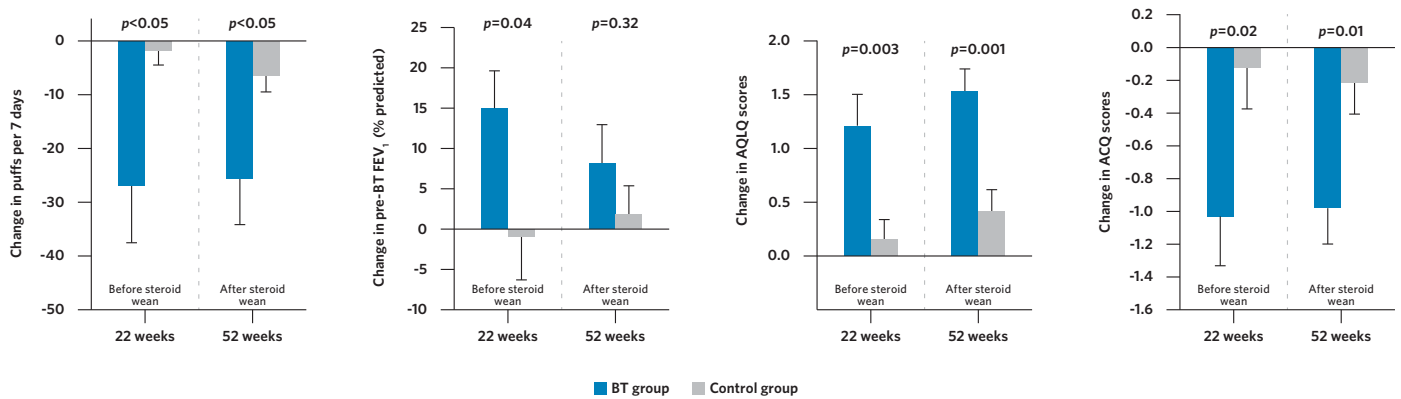
In the **Reduced Steroid Phase** (Weeks 36-52), highlights include:

- 4 of 8 BT patients were able to completely wean off oral corticosteroids (OCS) and stay off through 52 weeks, compared to 1 of 7 Control patients.
- A greater overall reduction in OCS dose was observed in the BT group compared with the Control group at 52 weeks (63.5% reduction versus 26.2%); (*P* = 0.12).
- Despite this difference in corticosteroid use, statistically significant improvements over baseline for BT compared to control were still observed in rescue medication use, and quality of life and asthma control scores 16 weeks after the Steroid Wean Phase was complete (see **Figure 1** inside).

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**Figure 1: Change in efficacy outcomes at Week 22 (Steroid Stable Phase) and at Week 52 (Reduced Steroid Phase) compared to baseline**



Results for the Steroid Stable Phase and Reduced Steroid Phase compared to baseline are shown in Figure 1.

## Key Safety Results

- Most common respiratory adverse events during treatment period were: wheeze, chest discomfort, dyspnea, productive cough, chest pain, and discolored sputum
  - Median time to onset within 1 day of the procedure
  - Resolved on average within 7 days after the onset of the event
- There was a higher rate of hospitalization in the BT group during the treatment period. However, subsequently during the post-treatment period, the BT group had a similar number of hospitalizations compared to the control group, and a lower number of hospitalizations compared to baseline (**Table 1** below).

**Table 1: Hospitalization summary for respiratory adverse events**

	BT (n=15)	Control (n=17)
	Number of hospitalizations (No. of patients)	Number of hospitalizations (No. of patients)
Before study entry (52 weeks)	10 (6)	5 (2)
Treatment period (12 weeks)	7 (4)	0 (0)
Post-treatment period (40 weeks)	5 (3)	4 (1)

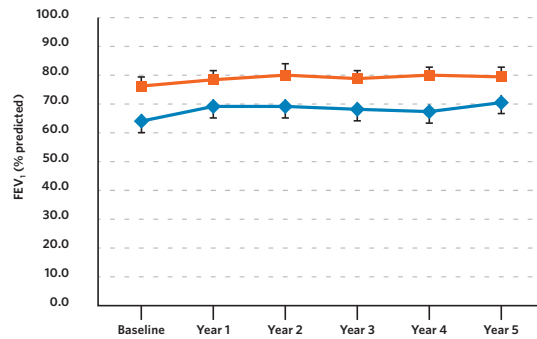
## Long-term Safety

- No deterioration of pre-bronchodilator or post-bronchodilator FEV<sub>1</sub> over the 5 years of follow-up (**Figure 2A**)
- No increase in the rate of respiratory adverse events between year 2 and year 5; reported adverse events were of the type typically seen in patients with severe asthma
- Trend for a reduction in respiratory related emergency department visits (**Figure 2B**) and hospitalizations (**Figure 2C**)

## Conclusions

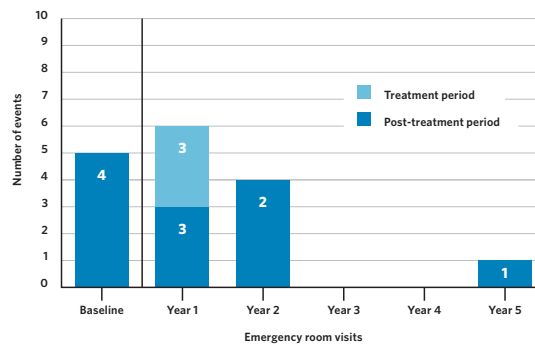
The results of this study show that patients with severe refractory asthma can safely undergo BT delivered by the Alair™ System. A stable long-term safety profile of BT has been demonstrated for at least 5 years in patients with severe asthma refractory to the current standard of care.

**Figure 2A: Mean prebronchodilator and postbronchodilator FEV<sub>1</sub> values over 5 years**

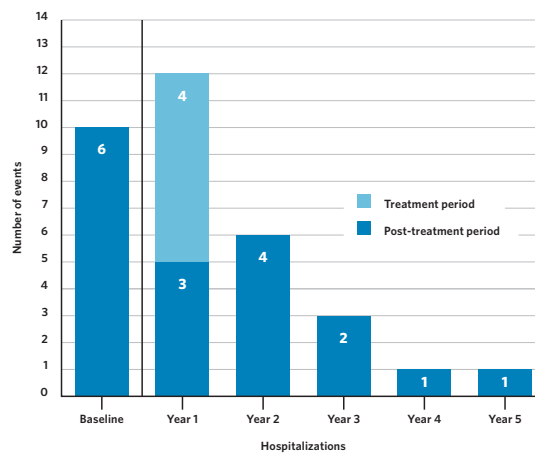


Prebronchodilator (◆) and postbronchodilator (■) forced expiratory volume in 1 second (FEV<sub>1</sub>) over time (percent predicted). Values represent mean ±SEM.

**Figure 2B: Reduction in respiratory-related emergency department visits over 5 years**



**Figure 2C: Reduction in respiratory-related hospitalizations over 5 years**




Bars represent number of events. Numbers within bars represent the number of patients contributing to the events. Year 1 data represent events occurring in the treatment period (day of first BT procedure until 6 weeks after the third BT procedure) and the posttreatment period (46-week period beginning 6 weeks after the last BT procedure to 12 months).  $P = .16$  for the trend in the percentage of patients with hospitalizations for respiratory symptoms and  $P = .22$  for the trend in the percentage of patients with emergency department visits for respiratory symptoms across years 1 to 5 (posttreatment period) using a repeated-measures logistic regression (generalized estimating equation), modeling the percentage of patients reporting an event.

## View the 5-year clinical trial results at [BTat5years.com](http://BTat5years.com)

**Brief Statement of Relevant Indications for Use, Contraindications, Warnings, and Adverse Events:** The Alair™ Bronchial Thermoplasty System is indicated for the treatment of severe persistent asthma in patients 18 years and older whose asthma is not well controlled with inhaled corticosteroids and long-acting beta-agonists. The Alair System is not for use in patients with an active implantable electronic device or known sensitivity to medications used in bronchoscopy. Previously treated airways of the lung should not be retreated with the Alair System. Patients should be stable and suitable to undergo bronchoscopy. The most common adverse event of BT is an expected transient increase in the frequency and worsening of respiratory-related symptoms. Rx only.

**CAUTION:** Law restricts this device to sale by or on the order of a physician. Indications, contraindications, precautions, and warnings can be found with product labeling.



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