Editorial

Bronchial thermoplasty: Quo vadis?

Introduction: In recent years a number of emerging new therapies have become available for the treatment of severe asthma among which bronchial thermoplasty is the only nonpharmacologic intervention that has been approved by the United States Food and Drug Administration in 2010.[1] Although bronchial thermoplasty has great promise for the patient with severe asthma and is now within the therapeutic armamentarium of the allergist-immunologist, the modality has paradoxically raised both excitement and curiosity but also questions as to when and how to recommend its use[2] as well as concerns relating to any potential harm that may be associated with the procedure.[3–5] In the interest of assisting the allergist-immunologist in the decision-making process for the use of this new treatment modality, two separate articles by Dunn and Wechsler ME[6] and Iyler and Lim[7] are presented in this issue of the ***Proceedings*** that offer opposing viewpoints on the role of bronchial thermoplasty in a pro/con debate format. In addition, employing a novel publication format, each author was given an opportunity to make rebuttal comments to each other's presentation which are printed below in this editorial. It is our hope that this information will be useful and will assist the allergist-immunologist in making the best therapeutic decisions for the patient with severe asthma.

Joseph A. Bellanti, M.D.
Russell A. Settipane, M.D.

Rebuttal Comments from Dr. Iyer and Dr. Lim

Response to Dunn and Wechsler[6]:

"Facts are stubborn things; and whatever may be our wishes, our inclinations, or the dictates of our passion, they cannot alter the state of facts and evidence"- John Adams, 1770.

Unfortunately, the 'pro' article on Bronchial thermoplasty (BT) by Dunn and Wechsler skillfully avoids dealing with the facts and truth about bronchial thermoplasty.

The first (and most important) fact is that the primary end point in the AIR-2 trial was negative (posterior probability of superiority [PPS] of 96% rather than the prespecified value of 96.4% in the AIR-2 trial). The 2nd most important fact is the lack of follow up in the sham controlled arm of the AIR-2 trial. These two facts alone would be a reason to pause and question any further claims regarding the efficacy of BT.

We must accept only the highest and most robust standards for medical evidence before changing clinical practice. The available evidence for BT does not meet these standards. In fact, the very approval of BT by the FDA is both troubling and puzzling. We cannot think of a single approved device (or drug) that failed to meet any of its primary or secondary end points in a pivotal trial.

We wish to sincerely thank the editors of ***Allergy and Asthma Proceedings*** for putting together this very thoughtful and timely pro-con debate regarding BT. Clever marketing and glossy brochures should not distract us from the shaky evidence underpinning BT. We urge patients, providers and others to carefully review every point in our article and then decide whether BT would still be something they would consider for themselves or their loved ones. Dr. William. J. Mayo's timeless words at the 1910 Rush Medical College commencement address in Chicago sums up our argument; *"the best interest of the patient is the only interest to be considered"*.

Vivek Iyer, M.D.
Kaiser G. Lim, M.D.

Rebuttal Comments from Dr. Dunn and Dr. Wechsler

Response to Iyer and Lim[7]:

As with any novel therapy, we believe that critical review of clinical trials is vital to advancing science and thus we appreciate the comments of Dr. Iyer and Lim who have thoroughly reviewed the literature on bronchial thermoplasty. However, we are concerned that misinterpretation of data can lead to incorrect conclusions and potentially result in misuse or nonuse of beneficial therapies such as bronchial thermoplasty.

For example, Drs. Iyer and Lim deemphasize the beneficial effects of BT on hospitalizations, emergency room visits, and exacerbations, and neglect to report on the long term benefits on these outcomes lasting up to 5 years and they incorrectly note that the AIR2 study excluded individuals with these outcomes. Indeed, while patients with greater than four asthma exacerbations/year, three or more asthma-related hospitalizations or an FEV1 less than 60% were excluded for safety concerns, over 85% patients in both treatment and sham arm met American Thoracic Society criteria

for severe refractory asthma. Further, while they suggest that an outlier with several exacerbations may have skewed the data, analyses without that subject did not significantly change study findings.

In addition, Drs. Iyer and Lim are critical of the AIR2 study's primary end point, but fail to recognize that the minimally clinically significant important difference (MCID) is a measure relevant to an *individual* and is used to show a significant change in an *individual's* asthma QOL at different time points. Thus, the conclusion that a mean change of 0.19 does not reflect a clinically significant change in a *group* is invalid. It is very relevant that there were both a statistically significant change in mean AQLQ scores in the group and a significantly higher number of subjects in the treatment group who, *individually*, achieved an MCID of 0.5. Statistically, the change in AQLQ scores was significant as the adjusted posterior probability (PPS) of superiority cut-off was 95.2% and the improvement in AQLQ PPS was 96%.

BT has performed well in multiple published studies to date, and thus we disagree with their conclusion that "BT does not meet the burden of proof required to incorporate this procedure into routine clinical practice." Indeed, while we agree that BT requires further study so that we can identify specific responders and better understand the mechanisms by which BT works, we are supportive of recommendations to include BT as part of treatment strategies recommended by the Global Initiative for Asthma, the American College of Chest Physicians, and the British Thoracic Society. We feel that the demonstrated efficacy and safety of BT, coupled with the significant unmet needs in this patient population, warrant increased use of this exciting and novel therapy.

Ryan Dunn, M.D.,
Michael E. Wechsler, M.D., M.M.Sc.

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