

**Original Article:** Hanania, Nicola A et. al. "Lebrikzumab in moderate to severe asthma: pooled data from two randomized placebo controlled studies". *Thorax* 2015;70:748–756

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**Review:**

Several different endophenotypes of asthma have been described based on differing pathophysiologic mechanisms<sup>1</sup>. Separating asthma into different subgroups can not only improve our understanding of the disease, but also provide novel therapeutic targets. A common subtype of asthma involves TH2-polarized inflammation driven, in part, by IL-13. Periostin is a lung protein thought to reflect the amount of Type 2 inflammation, or the inflammation type where Il-13 is suspected to have a role. This article assesses the use of Lebrikizumab, a monoclonal antibody which blocks IL-13 activity, in asthma.

This article is the combination of two trials that were scheduled to become the Phase III trial of Lebrikizumab, but were prematurely terminated as there was a defect in the production of the antibody. The available data before termination of the studies was pooled and reported. The study population was patients with uncontrolled moderate to severe asthma despite appropriate therapy. 463 subjects participated and received injections of placebo or Lebrikizumab at varying doses every 4 weeks for a mean duration of 24 weeks. The primary endpoint was rate of asthma exacerbations. They used a biomarker, periostin, to form periostin-high and periostin-low subgroups for data analysis.

Side effects of the drug were mild and no common safety concerns were identified. Significantly, no episodes of anaphylaxis were reported. There are several limitations of this study. First, the study design was changed in the course of the approved protocol. Second, the studies were stopped earlier than originally planned. Finally, the response to Lebrikizumab was also not dose dependent, as would be expected which raises the concern that the sample size may not have been adequate to evaluate dose response.

Treatment with Lebrikizumab reduced the rate of asthma exacerbations, which was more pronounced in Periostin-high patients (all doses: 60% reduction) than in the periostin-low patients (all doses: 5% reduction). These pooled data support the efficacy of Lebrikizumab at reducing asthma exacerbations in patients with moderate to severe persistent asthma not well controlled with conventional therapy. It also supports the use of periostin as a predictor of response to Lebrikizumab. This drug represents a novel and promising adjunct to current regimens of moderate and severe asthma. As such, awareness of this study is important for the asthma educator as it may represent a future option for patients poorly controlled on present management.

**References:**

1 Song CH, Lee JK. Lebrikizumab treatment in adults with asthma. *N Engl J Med*. 2011 Dec ;365(25):2433; doi:10.1056