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Title: Lebrikizumab reduces serum periostin in asthma patients with elevated baseline periostin

Heleen 6979 Scheerens scheerens.heleen@gene.com [1], Joseph 6988 Arron arron.joseph@gene.com MD [2], David 6990 Choy choy.david@gene.com [2], Sofia 7005 Mosesova mosesova.sofia@gene.com [3], Preeti 7006 Lal lal.preeti@gene.com [4] and John 7010 Matthews matthews.john@gene.com MD [4]. [1] PD Biomarkers, Genentech Inc, South San Francisco, CA, United States, CA 94080 ; [2] Research and Early Development, Genentech Inc, South San Francisco, CA, United States, CA 94080 ; [3] Inflammation & Opthalmology Biostatistics, Genentech Inc, South San Francisco, CA, United States, CA 94080 and [4] Product Development - Immunology, Genentech Inc, South San Francisco, CA, United States, CA 94080 .

Body: Background: Periostin is a matricellular protein induced in airway epithelia by interleukin-13 (IL13) and a good systemic biomarker for IL13 activity. Lebrikizumab, a humanized monoclonal antibody, binds IL13 and improved lung function in moderate-to-severe asthma patients (pts) with elevated baseline serum periostin in a Phase II study. Aims: To examine the effect of blocking IL13 on systemic periostin levels in pts with uncontrolled asthma, despite inhaled corticosteriods. Methods: Pts (n=218) were randomized to lebrikizumab 250 mg (n=106) or placebo (PB) (n=112) SC every 4 weeks for 6 doses, with 12 weeks follow-up (NCT00930163). Serum periostin was measured at baseline and throughout the study. Pts were classified as periostin-high (≥median) or periostin-low (<median) based on baseline serum levels. Results: PB-corrected reductions in periostin were evident after 1 week of lebrikizumab treatment: 5.4% baseline reduction across all pts and 7.3% baseline reduction in periostin-high pts ($p<0.001$). At 12 weeks, periostin reductions were 9.7% ($p<0.001$) for all lebrikizumab-treated pts vs PB and 14.4% ($p<0.001$) in periostin-high pts. Periostin-low pts had no significant reduction in periostin (2.9%; $p=0.3$). This effect was sustained at Week 32. Most pts (>90%) who were periostin-low at baseline maintained the periostin levels <median, whereas 72% of periostin-high pts treated with PB and only 40% treated with lebrikizumab maintained periostin levels ≥median at Week 12. Conclusions: Lebrikizumab reduced serum periostin in periostin-high, but not periostin-low pts, vs placebo. These data suggest that in asthma pts, elevated serum periostin levels are dependent on IL13 activity.