Lirentelimab (AK002), an Anti-Siglec-8 Antibody, Suppresses Acute IL-33-induced Neutrophil Infiltration and Attenuates Tissue Damage in a Chronic Experimental COPD Model Through Mast Cell Inhibition
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- IL-33 stimulation of mast cells is believed to play a role in driving allergic and non-allergic inflammation in many diseases including asthma, chronic obstructive pulmonary disease (COPD), atopic dermatitis (AD), and inflammatory bowel disease (IBD) (Figure 1)
- Siglec-8 monomeric antibodies (mAbs) previously have been shown to inhibit mast cell activation and selectively deplete eosinophils in atopic diseases
- However, the effect of an anti-Siglec-8 antibody has not been evaluated in non-allergic models of inflammation

**METHODS**

**BACKGROUND**
Lirentelimab (AK002), an Anti-Siglec-8 Antibody, Suppresses Acute IL-33-induced Neutrophil Infiltration and Attenuates Tissue Damage in a Chronic Experimental COPD Model Through Mast Cell Inhibition

**RESULTS**

- IL-33 directly activates mast cells and lirentelimab treatment substantially modulates the mast cell transcriptome
  - These data suggest that lirentelimab reduces IL-33-driven non-allergic inflammation by inhibiting mast cells

**CONCLUSIONS**

- These data support the clinical evaluation of anti-Siglec-8 mAbs, such as lirentelimab, as a therapeutic approach in both allergic and non-allergic diseases, such as IBD, COPD, and AD

**REFERENCES**

**ACKNOWLEDGMENTS**

- In addition to the demonstrated anti-inflammatory activity in allergic diseases, lirentelimab, an anti-Siglec-8 mAb, also reduces non-allergic inflammation by inhibiting non-IgE-mediated mast cell activation
- These data support the clinical evaluation of anti-Siglec-8 mAbs, such as lirentelimab, as a therapeutic approach in both allergic and non-allergic diseases, such as IBD, COPD, and AD

**FIGURE 1: Mouse Model of IL-33-Induced Neutrophil Infiltration**

- Acute MC-dependent neutrophil recruitment was induced in Siglec-8-Transgenic (TG) mice by intraperitoneal injection of IL-33 (Figure 3)
- Peripheral lavage was collected and analyzed 3 hours later
- Experimental COPD was induced by exposing TG mice to chronic cigarette smoke (CS) for 12 weeks followed by analysis of lung function and injury. Mice were dosed therapeutically on week 8 with lirentelimab or isotype control mAb

- Figure 4: Lirentelimab Reduces IL-33-driven Non-allergic Inflammation
  - IL-33 directly activates mast cells and lirentelimab treatment substantially modulates the mast cell transcriptome
  - These data suggest that lirentelimab reduces IL-33-driven non-allergic inflammation by inhibiting mast cells