Mast Cells Are Significantly Activated In Patients with Ulcerative Colitis and Are Inhibited by an Anti-Siglec-8 Antibody, Antolimab (AK002)

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**BACKGROUND**

- Accumulation and activation of mast cells and eosinophils have been implicated in the pathogenesis of several chronic inflammatory gastrointestinal (GI) diseases, including eosinophilic gastrointestinal diseases (EGIDs) and inflammatory bowel disease (IBD).
- Despite the strong association of mast cells and eosinophils in IBD, no further characterization of these cells has been performed.
- Here, we evaluated the activation state of mast cells and eosinophils and quantified the production of cytokines from mast cells in colon tissue from IBD or non-diseased control patients.

**METHODS**

- Single-cell suspensions were prepared by enzymatic digestion of fresh colon biopsies from patients with IBD or non-diseased control colon tissue.
- Multi-color flow cytometry was performed to identify and evaluate the activation state of mast cells and eosinophils.
- The expression of the mast cell degranulation marker CD107a was significantly increased in mast cells from UC tissue compared to CD and non-diseased colon tissue mast cells.
- In addition, percentage of CD45+ viable cells from individual patients +/− SEM. * p=<0.05, ** p=<0.01, *** p=<0.001 determined by paired t-test.

**RESULTS**

- **Figure 1.** Mast Cells and Eosinophils are Key Drivers of Acute and Chronic Inflammation
- **Figure 2.** Antolimab (AK002) Mechanism of Action
- **Figure 3.** Study Design
- **Figure 4.** Flow Cytometry Gating Strategy for Mast Cells and Eosinophils in IBD Biopsy Tissue
- **Figure 5.** Mast Cells and Eosinophils are Significantly Elevated in Ulcerative Colitis Biopsies
- **Figure 6.** Mast Cells in Ulcerative Colitis Tissue Display an Increased Degranulation and Activation State
- **Figure 7.** Eosinophils in Ulcerative Colitis and Crohn’s Disease Tissue Display an Increased Activation State
- **Figure 8.** Mast Cells from Ulcerative Colitis Tissue Produce Higher Levels of TNF, IL-5, and CCL3 Compared to Normal Colon Tissue Mast Cells
- **Figure 9.** Antolimab (AK002) Suppresses Cytokine Production from Human GI Tissue Mast Cells

**CONCLUSIONS/DISCUSSION**

- Mast cells and eosinophils may play a significant role in driving the pathogenesis of ulcerative colitis.
- Ulcerative colitis tissue mast cells produce increased levels of disease-driving mediators, including TNFα that are inhibited by antolimab (AK002).
- Antolimab may represent a potential targeted therapy in IBD.


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