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Summary

CD122 ANTAGONISM PREVENTED INFLAMMATION IN A MURINE MODEL OF CELIAC DISEASE AND INHIBITED THE ACTIVITY OF CYTOTOXIC CD8+ AND ACTIVATED CD4+ T CELLS FROM CELIAC PATIENTS IN VITRO, SUPPORTING THE EVALUATION OF ANB033 IN AN ONGOING PHASE 1B STUDY IN CELIAC D

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ANB033, a novel CD122 antagonist monoclonal antibody targeting both IL-15 and IL-2 signaling, prevented villous atrophy and reduced gluten-driven inflammation in a murine celiac disease model and suppressed T cell proliferation and inflammatory cytokine secretion in patient-derived cells in vitro.

KEY POINTS

- ANB033 is engineered to bind CD122 with high affinity, resulting in potent inhibition of both IL-15 and IL-2 signaling on cytotoxic CD8+ and memory CD4+ T cells that mediate celiac disease pathology.
- In a murine celiac disease model, an ANB033 surrogate antibody prevented gluten-dependent expansion of cytotoxic CD8+ intraepithelial lymphocytes, prevented expansion of IFNγ+ CD4+ T cells in the lamina propria, and preserved the villus height-to-crypt depth ratio compared to isotype control.
- In celiac disease patient-derived peripheral blood mononuclear cells, ANB033 reduced proliferation, secretion of inflammatory cytokines including IFN-γ, and mediators of cytotoxicity in CD8+ and CD4+ T cells in vitro.
- Secondary analyses of single-cell RNA sequencing data from duodenal biopsies demonstrated significant infiltration of CD4+ and CD8+ T cells that overlapped with expression of CD122, IFNG, and GZMB, along with prominent IL-15 expression.

– ANB033 is being evaluated in an ongoing Phase 1b study in celiac disease, supported by these preclinical data demonstrating dual inhibition of the IL-15 and IL-2 pathways implicated in disease pathology.

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