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Summary

AZD7798: A NEW CCR9 DEPLETING ANTIBODY TO TREAT CROHN'S DISEASE

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AZD7798, a humanized anti-CCR9 monoclonal antibody with enhanced effector function, demonstrated potent depletion of CCR9-expressing immune cells in blood and ileal tissue in non-human primate studies.

KEY POINTS

- AZD7798 was developed through screening of 8,448 hybridomas and optimization via CDR mutagenesis, resulting in 40-fold potency improvement over the parent antibody.
- The antibody showed specific binding to human and cynomolgus CCR9, prevented CCL25 binding to CCR9, and induced potent antibody-dependent cell-mediated cytotoxicity in the presence of NK cells.
- CCR9 is highly expressed in human ileum, predominantly on memory T cells, B cells, and T regulatory cells, with CCR9-expressing CD4+ and CD8+ T cells showing increased pro-inflammatory cytokine production compared to CCR9-negative T cells.
- In cynomolgus monkeys treated with 10 mg/kg AZD7798, complete depletion of circulating CCR9-expressing T cells was achieved within 2 days, with depletion also observed in ileal tissue.
- Safety of AZD7798 is being assessed in a Phase 1 clinical trial (NCT05452304); all authors are AstraZeneca employees or shareholders.

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