

DISCRIMINATION OF THE DIFFERENTIAL EFFECTS OF SELECTIVE SUPPRESSION OF IL-6 TRANS-SIGNALING BY OLAMKICEPT IN MODERATE-TO-SEVERE ULCERATIVE COLITIS

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An in silico computational model of ulcerative colitis inflammation suggests that selective IL-6 trans-signaling inhibition with olamkicept reduces Th17-mediated inflammation while preserving tissue healing pathways, unlike pan-IL-6 inhibition.

KEY POINTS

- A hybrid mechanistic-statistical computational model of colonic inflammation in UC was developed and tested against clinical trial data from a phase II olamkicept study (NCT03235752).
- Simulations showed that olamkicept suppression of IL-6 trans-signaling caused a transition away from a Th17-rich state in gut tissue and attenuated inflammatory chemotactic signals in a dose-dependent manner.
- In gut tissue, IL-6 concentrations decreased by approximately 10% at the highest olamkicept dose tested and returned to pre-treatment levels within a day post dose.
- Pan-inhibition of IL-6 signaling reduced Th17-mediated inflammatory activity but also suppressed tissue healing pathways dependent on IL-6 cis-signaling, whereas olamkicept preserved homeostatic classical IL-6 signaling.
- This modeling study may be relevant to researchers and clinicians interested in IL-6-targeted therapeutic strategies for ulcerative colitis.

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