

Multicentre, randomised, double-blind, parallel group, placebo-controlled trial phase 2a/b.

GSK2831781 is a humanised monoclonal antibody that is specific to the LAG-3 protein*

Patients with moderate to severe UC were randomised to GSK2831781 (450mg IV) or placebo.

Primary endpoint: Change in complete Mayo score at week 10.

Results: N=104 (including all dose levels); double-blind induction with 450mgIV GSK2831781 vs placebo n=75)

- Median change in complete Mayo score change was similar between groups GSK2831781 (450mg IV) and placebo.
- Response rates for endoscopic improvement favoured placebo.
- Clinical remission rates were similar between groups.
- Adverse events GSK2831781 (450mg) vs placebo, 56% vs 37%.
- LAG-3+ cells were depleted to 51% in blood but not in the colonic mucosa.

Conclusion:

Despite evidence of target cell depletion in blood, GSK2831781 failed to reduce inflammation in the colonic mucosa suggesting no pharmacological effect. The study was terminated early.

*Lymphocyte-activating gene 3 (LAG-3) is an inhibitory transmembrane receptor that is upregulated as an immune checkpoint on recently activated pathogenic Tcells

A randomised, double-blind, placebo-controlled study of the LAG-3-depleting monoclonal antibody GSK2831781 in patients with active ulcerative colitis

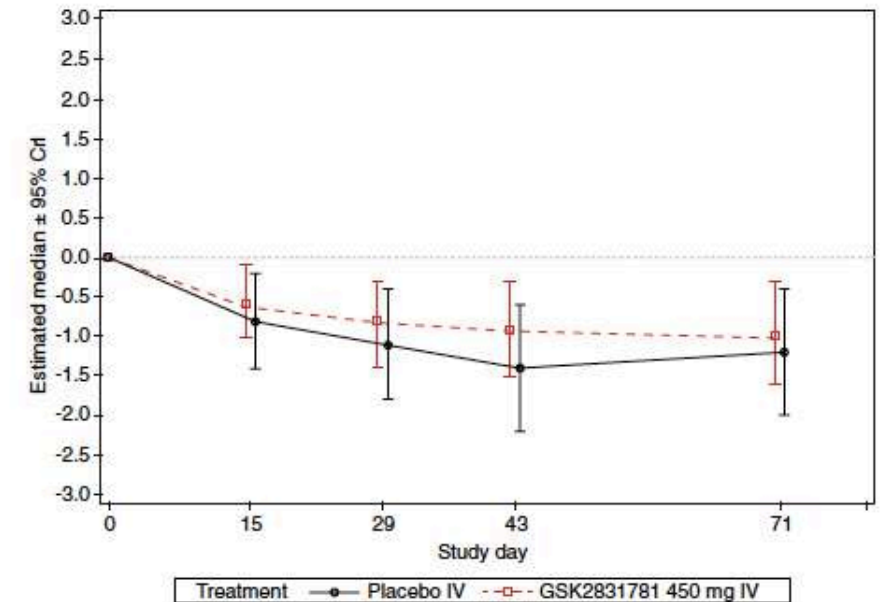


FIGURE 3 Change from baseline in partial Mayo score. CrI, credible interval; IV, intravenously.