The efficacy of Tofacitinib and a selective Janus Kinase 1 inhibitor in Dextran Sulphate Sodium colitis models

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Background

Non-selective Janus Kinase (JAK) inhibitors such as tofacitinib have shown efficacy in treatment of ulcerative colitis. Side effects such as challenges the clinical application of tofacitinib.

Aim: to investigate the potency of a selective JAK1 inhibitor (JAK1i, GSK2276186) vs tofacitinib (CP-690,550, Pfizer) in acute and chronic DSS colitis models.

Methods

Female C57/B16 mice (8-12 weeks)

DSS 2% in drinking water ad libitum

Fig.1 | Schematic overview of acute and chronic DSS-induced colitis experiments: JAK1i vs tofacitinib

Assessments:

Clinical scoring

- colon weight-length ratio
- diarrhea score
- histology and endoscopy score

Other

- qPCR colon
- ELISA homogenates

Results

In vivo, 3, 10 or 30 mg/kg JAK1i and tofacitinib did not protect mice from acute DSS colitis.

Tofacitinib but not JAK1i ameliorated some aspects of the course of a chronic DSS colitis at the highest dose given.

Data on a different selective JAK1 inhibitor molecule GLPG0634 reported efficacy in a mouse DSS-induced colitis model1.

1. http://dx.doi.org/10.1016/S1873-9946(14)60194-X