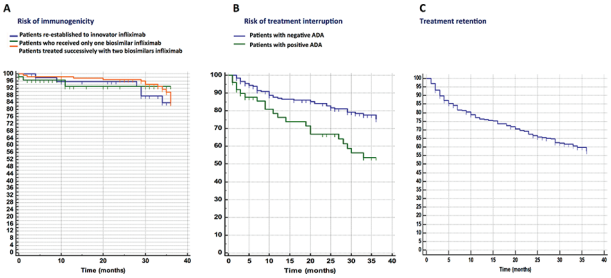


**Figure 1**. Kaplan Meyer Survival Analyses. A, risk of immunogenicity according to the number of biosimilars infliximab received; B, risk of treatment interruption according to the presence of anti-drug antibodies (ADA); and C, treatment retention within the observation period

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OP0228

## GSK3196165 AN INVESTIGATIONAL ANTI-GM-CSF MONOCLONAL ANTIBODY, IMPROVES PATIENT REPORTED OUTCOMES IN A PHASE IIB STUDY OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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**Background:** GSK3196165 is a human mAb that inhibits GM-CSF, a key driver in a broad range of immune-mediated conditions (Hamilton, 2016). In trials of patients with RA, inhibition of GM-CSF signaling has resulted in clinical benefit. GM-CSF is not only a key mediator of inflammation, but emerging science suggests it is also an important regulator of pain.
**Objectives:** To evaluate the treatment effect of GSK3196165 on pain, fatigue, physical functioning, mental functioning and global assessment of disease, in patients with moderate-to-severely active RA.
**Methods:** 222 adult patients with active, moderate-severe RA (ACR 2010 criteria), ≥4 each of swollen and tender joints, DAS28(CRP) ≥3.2 and CRP ≥5.0 mg/L, were randomized equally to placebo or GSK3196165 22.5mg, 45mg, 90mg, 135mg or 180mg SC weekly for 5 injections, then every other week until Week 50. The Patient Reported Outcomes (PROs) measured throughout the study included, pain Visual Analogue Scale (VAS), Patient's Global Assessment of Arthritis (PtGA), Health Assessment Questionnaire - Disability Index (HAQ-DI), Brief Fatigue Inventory (BFI) Question 3, the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F), and the 36-item short form health survey (SF-36). The primary outcome was the proportion of patients who achieved remission (DAS28(CRP) <2.6) at Week 24 and the data has been previously reported (Buckley, 2018).
**Results:** 37 patients were randomised to each treatment group. The observed GSK3196165 pharmacokinetic exposures were lower than anticipated but despite this, there was a rapid and substantial improvement in RA symptoms in patients treated with GSK3196165 compared with placebo.
The table below summarizes the change from baseline data for the GSK3196165 180 mg dose and placebo at Week 12. An increase in the FACIT-F and SF-36 scores and a decrease in all other scores indicate an improvement in RA symptoms.

| PRO endpoint at Week 12 | Placebo (N=37) | GSK3196165 180mg (N=37) | |
|---|---|---|---|
| | Least squares mean change from baseline (SE) | | Difference from placebo (95% CI, p Value) |
| Pain VAS | -7.07 (3.705) | -25.01 (3.650) | -17.94 (-28.18, -7.70, p<0.001) |
| PtGA | -6.72 (3.660) | -23.90 (3.606) | -17.18 (-27.27, -7.10, p<0.001) |
| HAQ-DI | -0.26 (0.091) | -0.50 (0.090) | -0.24 (-0.49, 0.01, p=0.059) |
| BFI Question 3 | -0.63 (0.346) | -2.20 (0.339) | -1.57 (-2.53, -0.62, p=0.001) |
| FACIT-F | 3.37 (1.291) | 8.70 (1.262) | 5.33 (1.77, 8.89, p=0.004) |
| SF-36 Physical Component | 3.42 (1.203) | 6.97 (1.182) | 3.55 (0.22, 6.88, p=0.037) |
| SF-36 Mental Component | 3.54 (1.558) | 6.79 (1.521) | 3.25 (-1.05, 7.54, p=0.138 |

**Conclusion:** The results of this Phase IIb study showed that GSK3196165 substantially improved the scores of a range of PRO measures among RA patients. In particular, there was a highly significant improvement in pain; a key symptom of RA. These effects were observed despite achieving much lower drug exposure than predicted. Further studies are required to confirm the additional patient relevant benefits that are expected to arise from increased exposure to GSK3196165.

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OP0229

## PHASEII CLINICAL TRIALS SYSTEMATICALLY OVERESTIMATE TREATMENT EFFECTS OF SUBSEQUENT PHASE III TRIALS IN RHEUMATOID ARTHRITIS

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**Background:** Phase 3 (P3) clinical trials are the mainstay of drug development in all areas of medicine, including rheumatology, allowing to determine safety and efficacy of new drugs on their way to approval. Historically, efficacy results of P3 trials have often been disappointing with respect to the expectations set by phase 2 (P2) trials. It is unclear whether these observations are reflection of a true bias or merely a play of chance.
**Objectives:** To systematically compare efficacy results of P2 versus P3 trials in RA and investigate potential determinants of efficacy differences.
**Methods:** We performed a systematic review of disease modifying anti-rheumatic drugs (DMARDs) tested in P2 trials in rheumatoid arthritis (RA) over the last 20 years for which also P3 trials exist. We searched Medline, EMBASE, and the