

# Biologics for rheumatoid arthritis: an overview of Cochrane reviews (Review)

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[Overview of Reviews]

## Biologics for rheumatoid arthritis: an overview of Cochrane reviews

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### ABSTRACT

#### Background

The biologic disease-modifying anti-rheumatic drugs (DMARDs) are very effective in treating rheumatoid arthritis (RA), however there is a lack of head-to-head comparison studies.

#### Objectives

To compare the efficacy and safety of abatacept, adalimumab, anakinra, etanercept, infliximab, and rituximab in patients with RA.

#### Methods

This 'Overview of Reviews' was done by including all Cochrane Reviews on Biologics for RA available in *The Cochrane Library*. We included only data on standard dosing regimens for these biologic DMARDs from placebo-controlled trials. The primary efficacy and safety outcomes were ACR50 and withdrawals due to adverse events. We calculated Risk Ratios (RR) for efficacy, Odds Ratio (OR) for safety and combined estimates of events across the placebo groups as the expected Control Event Rate (CER). Indirect comparisons of biologics were performed for efficacy and safety using a hierarchical linear mixed model incorporating the most important study-level characteristic (i.e. type of biologic) as a fixed factor and study as a random factor; reducing the between study heterogeneity by adjusting for the interaction between the proportion of patients responding on placebo and the duration of the trial.

#### Main results

From the six available Cochrane reviews, we obtained data from seven studies on abatacept, eight on adalimumab, five on anakinra, four on etanercept, four on infliximab, and three on rituximab.

The indirect comparison estimates showed similar efficacy for the primary efficacy outcome for all biologics with three exceptions. Anakinra was less efficacious than etanercept with a ratio of RRs (95% CI; P value) of 0.44 (0.23 to 0.85; P = 0.014); anakinra was less

efficacious than rituximab, 0.45 (0.22 to 0.90; P = 0.023); and likewise adalimumab was more efficacious than anakinra, 2.34 (1.32 to 4.13; P = 0.003).

In terms of safety, adalimumab was more likely to lead to withdrawals compared to etanercept, with a ratio of ORs of 1.89 (1.18 to 3.04; P = 0.009); anakinra more likely than etanercept, 2.05 (1.27 to 3.29; P = 0.003); and likewise etanercept less likely than infliximab, 0.37 (0.19 to 0.70; P = 0.002).

### **Authors' conclusions**

Based upon indirect comparisons, anakinra seemed less efficacious than etanercept, adalimumab and rituximab and etanercept seemed to cause fewer withdrawals due to adverse events than adalimumab, anakinra and infliximab. Significant heterogeneity in characteristics of trial populations imply that these findings must be interpreted with caution. These findings can inform physicians and patients regarding their choice of biologic for treatment of RA.

## **PLAIN LANGUAGE SUMMARY**

### **Biologics for rheumatoid arthritis: an overview of Cochrane reviews**

This summary of a Cochrane review presents what we know from research about the effect of biologics on Rheumatoid Arthritis (RA).

#### **The review shows that in people with RA;**

- abatacept, adalimumab, etanercept, infliximab, and rituximab probably improve signs of rheumatoid arthritis such as the number of tender or swollen joints and other outcomes such as pain and disability.

- anakinra probably improve signs of rheumatoid arthritis such as the number of tender or swollen joints and other outcomes such as pain and disability (but not as well as the others).

We do not have precise information about possible side effects and complications. This is particularly true for rare but serious side effects. Possible side effects may include a serious infection or upper respiratory infection. Rare complications may include certain types of cancer.

#### **What is Rheumatoid arthritis (RA) and what are biologics?**

When you have rheumatoid arthritis, your immune system, which normally fights infection, attacks the lining of your joints making them inflamed. This inflammation causes your joints to be hot, swollen, stiff, and painful. The small joints of your hands and feet are usually affected first. If the inflammation goes on without treatment, it can lead to damaged joints. Once the joint is damaged it cannot be repaired, so treating rheumatoid arthritis early is important.

Biologics are a group of medications that suppress the immune system and reduce the inflammation in the joints. Even though suppressing the immune system can make it slightly harder to fight off infections, it also helps to stabilize an overactive immune system. By reducing the inflammation, the aim is to help prevent damage to the joints.

#### **Best estimate of what happens to people with rheumatoid arthritis who take biologics:**

##### **ACR 50 (number of tender or swollen joints and other doctor or patient assessed aspects of rheumatoid arthritis)**

Among people who took abatacept, 47 people out of 100 experienced improvement in the signs of their rheumatoid arthritis compared to 21 people out of 100 who took a placebo (26% absolute improvement).

Among people who took adalimumab 63 people out of 100 experienced improvement in the signs of their rheumatoid arthritis compared to 21 people out of 100 who took a placebo (42% absolute improvement).

Among people who took anakinra 27 people out of 100 experienced improvement in the signs of their rheumatoid arthritis compared to 21 people out of 100 who took a placebo (6% absolute improvement).

Among people who took etanercept 61 people out of 100 experienced improvement in the signs of their rheumatoid arthritis compared to 21 people out of 100 who took a placebo (40% absolute improvement).

Among people who took infliximab 45 people out of 100 experienced improvement in the signs of their rheumatoid arthritis compared to 21 people out of 100 who took a placebo (24% improvement).

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Among people who took rituximab 60 people out of 100 experienced improvement in the signs of their rheumatoid arthritis compared to 9 people out of 100 who took a placebo (51% improvement).

#### **Side effects**

Among people who took adalimumab 8 people out of 100 dropped out of the study because of the side effects compared to 5 people out of 100 who took a placebo (3% absolute difference).

Among people who took anakinra 9 people out of 100 dropped out of the study because of the side effects compared to 5 people out of 100 who took a placebo (4% absolute difference).

Among people who took infliximab 11 people out of 100 dropped out of the study because of the side effects compared to 5 people out of 100 who took a placebo (6% absolute difference).

There may be little or no difference in people who dropped out because of side effects with abatacept, etanercept, and infliximab compared to people who took a placebo (fake pill).