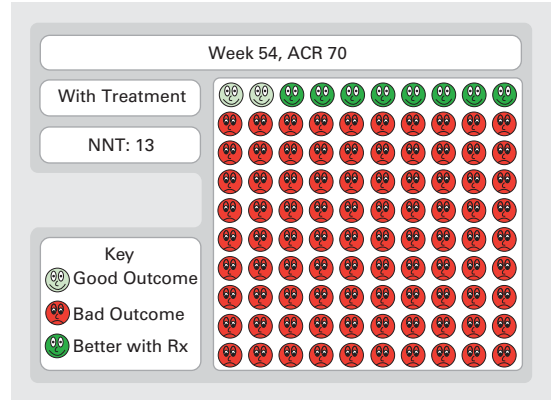
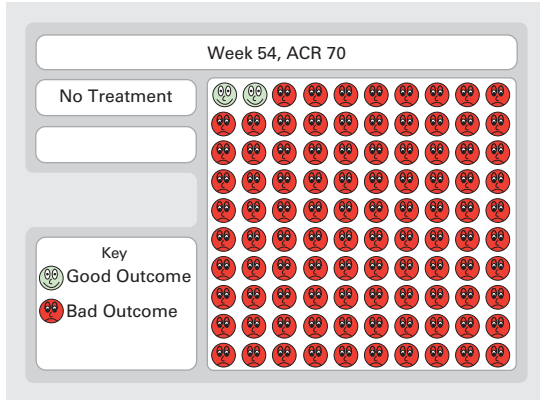
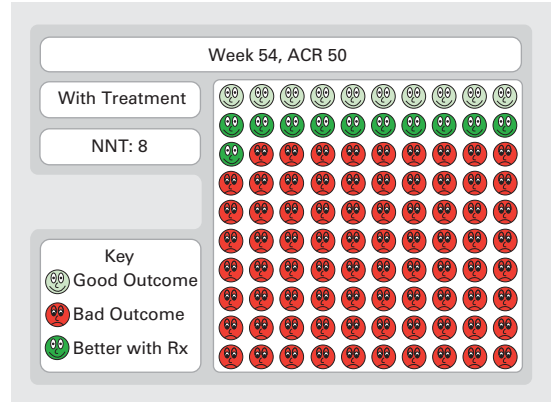
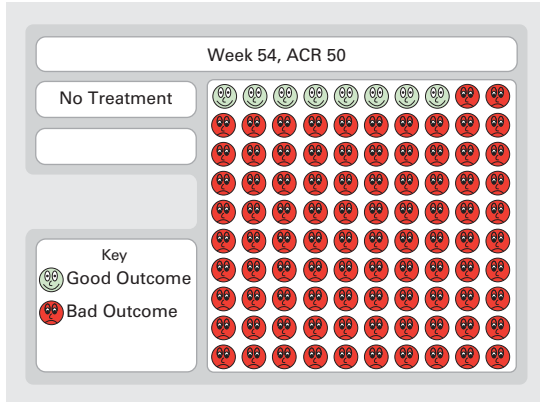
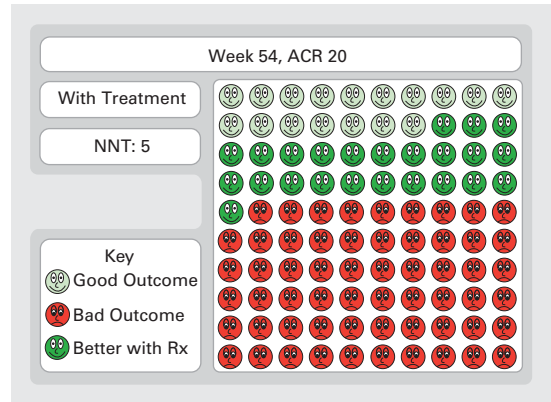
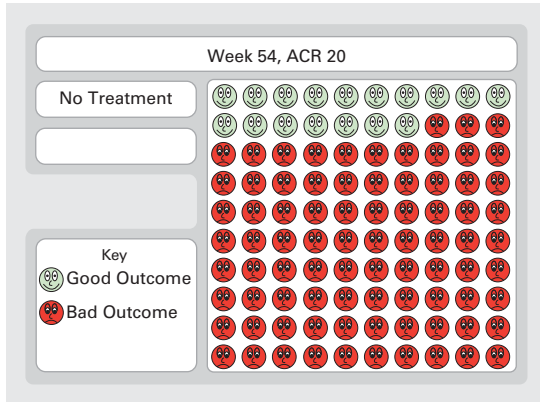


Visual Rx Faces 9.3 NNT for infliximab + MTX compared to MTX



Rheumatoid arthritis and infliximab Summaries and decision aid

How well does infliximab (Remicade) work when methotrexate alone is not controlling rheumatoid arthritis and how safe is it?

To answer this question, scientists found and analyzed 2 high quality studies in a Cochrane Review. The studies tested over 400 people who had rheumatoid arthritis for 7 to 9 years. People had either injections of infliximab at 3 mg/kg or 10 mg/kg every 4 or 8 weeks plus methotrexate (MTX) or MTX plus placebo injections. This Cochrane Review provides the best evidence today.

What is infliximab (Remicade) and why is it prescribed?

Rheumatoid arthritis is a disease in which the body's immune system attacks its own healthy tissues. The attack happens mostly in the joints of the feet and hands and causes redness, pain, swelling, and heat around the joint. Infliximab (Remicade) is a "biologic" used to decrease pain and swelling and slow the progress of rheumatoid arthritis. It is usually prescribed when other DMARDs (disease modifying antirheumatic drugs) do not work well.

How well does it work?

After 1 year of treatment, more people who had infliximab plus MTX improved compared to people who had injections of MTX alone. These people showed a 20%, 50% or 70% improvement in the number of tender and swollen joints and improvement in pain, disease activity, ability to do everyday activities, physical check-ups or blood tests.

According to x-rays taken after 1 year of treatment, more people who had infliximab plus MTX improved and fewer worsened compared to people who had MTX alone.

How safe is it?

In these studies, common side effects were upper respiratory infections (colds), headache, diarrhoea, and stomach pain. Headache, nausea, and hives, occurred during or immediately after the injection of infliximab. The levels of anti-nuclear antibodies (ANA) and anti-double stranded DNA antibodies (ds-DNA) were higher in more people who received infliximab plus MTX than in people with MTX alone. But the number of people who stopped taking infliximab due to side effects was the same as the number of people who stopped taking a placebo. Other studies have found that tuberculosis and other serious infections that sometimes cause death have occurred in people taking infliximab.

What is the bottom line?

There is "Gold" level evidence that when methotrexate is not controlling rheumatoid arthritis, infliximab up to 1 year decreases pain and swelling and slows the progress of rheumatoid arthritis. Infliximab also works within weeks rather than months.

More cases of infections, such as tuberculosis, have occurred when receiving infliximab. More time is needed before rare and late side effects are known.

Based on Suarez-Almazor M, Osiri M, Emery P, Ottawa Methods Group. Rheumatoid arthritis. In: *Evidence-based Rheumatology*. London: BMJ Books, 2003.

How well does infliximab (Remicade) work when methotrexate alone is not controlling rheumatoid arthritis?

What is infliximab and how does it work?

Rheumatoid arthritis is a disease in which the body's immune system attacks its own healthy tissues. The attack happens mostly in the joints of the feet and hands and causes redness, pain, swelling, and heat around the joint. Medications known as DMARDs (disease modifying antirheumatic drugs) are often prescribed to decrease pain and swelling and slow the progress of rheumatoid arthritis. In some people, these drugs do not work well and they may even cause side effects that people cannot tolerate. In cases when DMARDs do not work well, new and more expensive agents called "biologics" are often prescribed.

Infliximab (Remicade) is one "biologic agent" or "biological response modifier" that was recently approved in Canada to treat rheumatoid arthritis. These new biologic agents are injected into the body and work by clamping onto a substance in the body called the tumour necrosis factor-alpha (TNF-alpha). TNF-alpha may start a chain reaction in the body that causes swelling, pain, and damage in the body's joints. When clamping onto TNF-alpha, the biologic agents stop the chain reaction, which may decrease the pain and swelling in the joints. And since biologics work in a different way than DMARDs, they may help people in whom DMARDs did not work. But there are concerns that infliximab may increase the chances of infections such as tuberculosis or the chances of cancer. Up to June 2001, approximately 170 000 patients have been treated worldwide with infliximab.

How did the scientists find the information and analyse it?

The scientists searched for studies testing infliximab. Not all studies found were of a high quality and so only those studies that met high standards were selected.

The studies selected to include in this summary were reported in a Cochrane Review and had to be randomised controlled trials or controlled clinical trials – where a group of patients receiving infliximab was compared to patients receiving a different treatment or a placebo (or sugar pill). The studies also had to show how well infliximab works and its safety by using internationally accepted measurements.

Which high quality studies were included in the summary?

One study and a report that was a follow-up of the study were included in a Cochrane Review. The study tested 428 rheumatoid arthritis patients, aged 16 years or more, who did not improve with methotrexate (MTX) after 3 or 6 months. Most of the patients were women and had rheumatoid arthritis for about 7 to 9 years. The study tested different doses of infliximab with MTX:

- a 30 week (7 month) study with 428 patients compared injections of infliximab at 3 mg/kg every 4 or 8 weeks or 10 mg/kg every 4 or 8 weeks to placebo every 4 weeks. Patients stayed on the same dose of MTX they were on before they started the study. This study was called the ATTRACT study; and,
- a 54 week (1 year) report that was a follow-up of the ATTRACT study above.

How well did infliximab work?

In both the 7 month and 1 year studies, more patients improved with all doses of infliximab than patients who had injections of MTX and placebo. In all of the studies improvement was measured by using ACR

20, ACR 50, and ACR 70 responses. These responses mean that patients experienced either a 20%, 50% or 70% improvement in the number and tenderness of inflamed joints. They also had either a 20%, 50% or 70% improvement in at least three of the following five measures: the level of pain they reported, the level of disease activity they described, their ability to do everyday activities, their physical check-up, and their results on blood tests.

After 1 year, the study showed:

ACR 20 response: 42 out of 100 patients with infliximab plus MTX had a 20% improvement compared to 17 out of 100 patients with MTX alone. *This means that after 1 year 25 more patients out of 100 benefited from receiving infliximab.*

ACR 50 response: 41 out of 100 patients with infliximab plus MTX had a 50% improvement compared to 8 out of 100 patients with MTX alone. *This means that after 1 year 13 more patients out of 100 benefited from receiving infliximab.*

ACR 70 response: 10 out of 100 patients with infliximab plus MTX had a 70% improvement compared to 2 out of 100 patients with MTX alone. *This means that after 1 year 9 more patients out of 100 benefited from receiving infliximab.*

The progress of the disease shown in x-rays was tested in the 1 year study. More patients improved and fewer patients worsened when they received infliximab compared to MTX and placebo injections:

- 47 out of 100 patients improved with infliximab plus MTX compared to 14 out of 100 patients with MTX injections alone. *This means that about 33 more patients out of 100 benefited from receiving infliximab*
- 11 out of 100 patients worsened with infliximab plus MTX compared to 31 out of 100 patients with MTX and placebo injections. *This means that about 20 more patients out of 100 benefited from receiving infliximab.*

What side effects occurred with infliximab?

Common side effects in these studies were upper respiratory infections (colds), headache diarrhoea, and stomach pain. Other side effects, such as headache, nausea and hives, occurred during or immediately after the injection of infliximab.

In these studies, people tested after receiving infliximab plus MTX for 6 months or 1 year had infections or developed cancer just as often as people who had MTX alone. And, the number of patients (5 out of 100) who stopped infliximab injections due to side effects was about equal to the number (7 out of 100) who stopped methotrexate.

At 1 year, blood tests that measure antibodies such as anti-nuclear antibodies (ANA) and anti-double stranded DNA antibodies (ds-DNA) were higher in more patients who received infliximab plus MTX than in patients who received MTX alone. These high levels may have occurred due to chance or they may mean a reaction in disease activity of rheumatoid arthritis. It is not known whether those patients with high levels will have health problems in the future. But it is known that patients with uncontrolled rheumatoid arthritis have a higher risk of death and disability than patients with controlled rheumatoid arthritis.

Other studies have found that serious harms such as tuberculosis and other infections occurred in patients receiving infliximab. Some of the infections have caused death. Before starting infliximab, patients should be tested for tuberculosis and patients who have tuberculosis should be treated.

What is the bottom line?

There is “Gold” level evidence that when methotrexate is not controlling rheumatoid arthritis, infliximab up to 1 year decreases pain and swelling and slows the progress of rheumatoid arthritis. Infliximab also works within weeks rather than months.

More cases of infections, such as tuberculosis, have occurred when receiving infliximab. More time is needed before rare and late side effects are known.

Based on Suarez-Almazor M, Osiri M, Emery P, Ottawa Methods Group. Rheumatoid arthritis. In: *Evidence-based Rheumatology*. London: BMJ Books, 2003.

Information about rheumatoid arthritis and treatment

What is rheumatoid arthritis?

Rheumatoid arthritis is a disease in which the body's immune system attacks its own healthy tissues. The attack happens mostly in the joints of the feet and hands, causing redness, pain, swelling, and heat around the joint. There also can be damage to cartilage, bone, tendons, and ligaments. The pain and damage from rheumatoid arthritis limits people's ability to do daily activities at home and work and affects their wellbeing.

The pain and swelling sometimes gets worse and then gets better on its own. However, if the disease progresses or if it is moderate or severe rheumatoid arthritis and is not treated, it may result in:

- limited daily activities
- permanent damage to joints
- deformed joints
- need for surgery.

What can I do on my own to manage my disease?

✓ exercise ✓ hot/cold packs ✓ relaxation ✓ activity with less stress on joints

What treatments are used for rheumatoid arthritis?

Four kinds of treatment may be used alone or together. The common (generic) names of treatment are shown below:

1. *Pain medicine, aspirin, and non-steroidal anti-inflammatory drugs (NSAIDs)*
 - Acetylsalicylic acid
 - Acetaminophen
 - Celecoxib
 - Diclofenac
 - Etodolac
 - Ibuprofen
 - Indomethacin
 - Ketoprofen
 - Naproxen
 - Piroxicam
 - Rofecoxib
 - Sulindac
 - Tenoxicam
2. *Disease modifying antirheumatic drugs (DMARDs)*
 - Antimalarials
 - Auranofin
 - Azathioprine
 - Chloroquine
 - Cyclophosphamide
 - Ciclosporin
 - Leflunomide
 - Methotrexate
 - Minocycline
 - Parenteral gold
 - Penicillamine
 - Sulphasalazine
3. *Biologic agents*
 - Etanercept
 - Infliximab
 - Adalimumab
 - Anakinra
4. *Oral corticosteroids*
 - Prednisolone
 - Prednisone

What about other treatments I have heard about?

There is not enough evidence about the effects of some treatments. Other treatments do not work. For example:

- Acupuncture
- Electropuncture
- Ultrasound
- Electrical stimulation.
- Thermotherapy

What are my choices? How can I decide?

Treatment for your disease will depend on your condition. You need to know the good points (pros) and the bad points (cons) about each treatment before you can decide.

Rheumatoid arthritis (RA) decision aid

Should I take infliximab?

This guide can help you make decisions about the treatment your doctor is asking you to consider.

It will help you to:

1. Clarify what you need to decide.
2. Consider the pros and cons of different choices.
3. Decide what role you want to have in choosing your treatment.
4. Identify what you need to help you make the decision.
5. Plan the next steps.
6. Share your thinking with your doctor.

Step 1: Clarify what you need to decide

What is the decision?

Should I start taking infliximab when methotrexate alone is not working to control rheumatoid arthritis?

Infliximab is an intravenous (IV) injection given at set times every few weeks.

When does this decision have to be made? Check one

within days within weeks within months

How far along are you with this decision? Check one

- I have not thought about it yet
- I am considering the choices
- I am close to making a choice
- I have already made a choice

Step 2: Consider the pros and cons of different choices

What does the research show?

Infliximab is classified as: **Trade-off between benefits and harms**

There is “Gold” level evidence from 2 studies of 428 people with rheumatoid arthritis. The studies tested infliximab and lasted 6 months to 1 year. These studies found pros and cons that are listed in the chart below.

What do I think of the pros and cons of infliximab?

1. Review the common pros and cons.
2. Add any other pros and cons that are important to you.
3. Show how important each pro and con is to you by circling from one (*) star if it is a little important to you, to up to five (*****) stars if it is very important to you.

PROS AND CONS OF INFLIXIMAB TREATMENT	
PROS (number of people affected)	How important is it to you?
Improves pain and function 41 out of 100 people are helped at least a little 31 out of 100 people are helped a lot	* * * * *
Slows progress of disease X-rays are better in 47 out of 100 people	* * * * *
Works within weeks rather than months	* * * * *
Other pros:	* * * * *
CONS (number of people affected)	How important is it to you?
Side effects: colds, headache, diarrhoea, abdominal pain 5 out of 100 people stopped taking infliximab because of the side effects 7 out of 100 people stopped taking methotrexate because of side effects	* * * * *
Reactions during or immediately after the injection headache, nausea, and hives	* * * * *
Serious harms: tuberculosis and other serious infections (some have caused death)	* * * * *
Unsure if can travel with this medicine	* * * * *
Extra clinic visits and blood tests needed	* * * * *
Cost of medicine	* * * * *
Other cons:	* * * * *

What do you think about taking infliximab? Check one

Willing to consider this treatment
 Pros are more important to me than the Cons

Unsure

Not willing to consider this treatment
 Cons are more important to me than the Pros

Step 3: Choose the role you want to have in choosing your treatment

Check ✓ one.

- I prefer to decide on my own after listening to the opinions of others
- I prefer to share the decision with: _____
- I prefer someone else to decide for me, namely: _____

Step 4: Identify what you need to help you make the decision

What I know	Do you know enough about your condition to make a choice?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you know which options are available to you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you know the good points (pros) of each option?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you know the bad points (cons) of each option?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
What's important	Are you clear about which pros are most <i>important to you</i> ?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Are you clear about which cons are most <i>important to you</i> ?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
How others help	Do you have enough support from others to make a choice?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Are you choosing without pressure from others?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you have enough advice to make a choice?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
How sure I feel	Are you clear about the best choice for you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure
	Do you feel sure about what to choose?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unsure

If you answered No or Unsure to many of these questions, you should talk to your doctor.

Step 5: Plan the next steps

What do you need to do before you make this decision?

For example – talk to your doctor, read more about this treatment or other treatments for rheumatoid arthritis.

Step 6: Share the information on this form with your doctor

It will help your doctor understand what you think about this treatment.

Decisional Conflict Scale © A O'Connor 1993, Revised 1999.

Format based on the Ottawa Personal Decision Guide © 2000, A O'Connor, D Stacey, University of Ottawa, Ottawa Health Research Institute.