



# Rituximab for Rheumatoid Arthritis: A Systematic Review to Inform Knowledge Users

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## Background

While **rituximab (RTX)** is used in combination with **methotrexate (MTX)** to treat refractory rheumatoid arthritis (RA), reimbursement is criteria-based. Evidence was systematically reviewed to inform clinicians, consumers and policy makers regarding the safety and efficacy of RTX.

## Objective

To assess whether **RTX** alone or in combination with disease modifying anti-rheumatic drugs (DMARDs) is a safe, effective RA treatment.

## Methods

Published literature was identified by searching electronic databases (MEDLINE, EMBASE, CINAHL, The Cochrane Library, Web of Science) and reference lists from comprehensive reviews. Two reviewers independently selected studies and assessed trial quality. Safety and efficacy data were extracted independently by two reviewers and dichotomous data were pooled as relative risk (RR). Number needed to treat (NNT) and 95% confidence intervals were calculated using the Visual Rx 3.0 NNT calculator at <http://www.nntonline.net/>.

## Results

Of 2,100 citations identified, five studies comparing RTX (2 x 1000mg) with MTX versus MTX, provided data for quantitative meta-analyses. Four of five studies did not report the randomization method or allocation concealment. While sample sizes ranged from 16 to 755, a total of 2,412 patients were included for this comparison.

American College of Rheumatology (ACR) clinical response rates, Disease Activity Scores (DAS) and radiographic disease progression improved significantly among RTX plus MTX recipients versus MTX alone, with no differences in the rates of severe adverse events (SAEs). Acute infusion reactions were reported in 26% of RTX plus MTX patients and 16% of MTX recipients (Absolute Risk Difference (ARD) 9% (95% CI 5%, 13%).

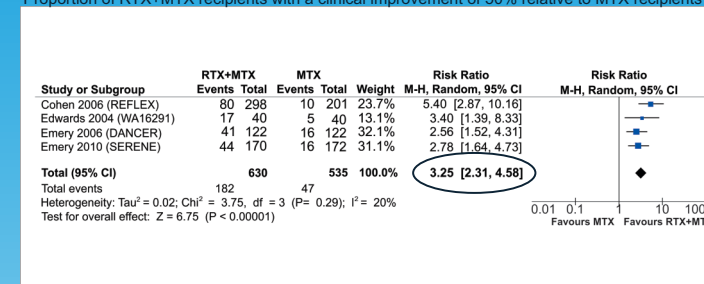
- Pooling of 24-week data showed 29% and 14% of RTX+MTX users achieved ACR response rates of 50 and 70, respectively versus 9% and 4% of MTX recipients.
- Relative risk (RR) of achieving an ACR 50 or 70 response was 3.3 (95% CI 2.3, 4.6) and 3.9 (95% CI 1.8, 8.3), respectively (Figures 1 and 2)
- At 52 weeks, 62% of RTX+MTX users showed no radiographic disease progression compared to 50% of MTX users (Figure 3)
- At 52 weeks, the RR of achieving clinical remission (DAS 28<2.6) with RTX+MTX was 2.4 (95% CI 1.7, 3.5). (Figure 4)
- To achieve ACR response rates of 50 and 70 at 24 weeks, 5 (95% CI 4, 9) and 9 (95% CI 4, 30) people need to be treated with RTX (2 x 1000 mg) plus MTX.
- Out of 100 RTX plus MTX recipients, 29 and 14 would achieve ACR response rates of 50 and 70, respectively (Figures 5 and 6)
- To prevent radiographic disease progression or achieve clinical remission at 52 weeks, 8 (95% CI 5, 19) and 7 (95% CI 4, 13) people need to be treated with RTX (2 x 100 mg) plus MTX, respectively
- Out of 100 RTX plus MTX recipients, 62 would achieve no radiographic disease progression and 22% would achieve clinical remission (DAS 28<2.6) at 52 weeks. (Figures 7 and 8)

## Discussion

RTX with MTX improves RA symptoms and prevents disease progression compared to MTX monotherapy. While no differences in the rates of SAEs were noted between groups, RTX recipients experienced higher rates of infusion reactions, vascular events, and cough compared to controls. Knowledge users must consider limitations in the evidence, as all trials were industry sponsored and of moderate quality. Evidence regarding radiographic disease progression is based on few studies, and small sample sizes with few events that may lead to wide confidence intervals.

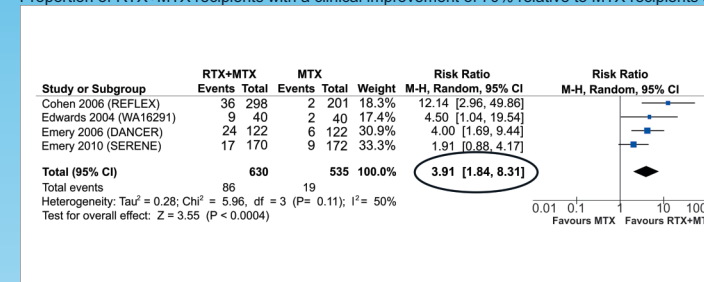
**Figure 1. ACR 50**

Proportion of RTX+MTX recipients with a clinical improvement of 50% relative to MTX recipients at 24 weeks.



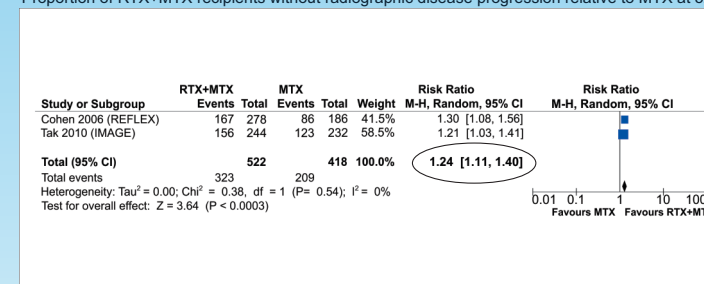
**Figure 2. ACR 70**

Proportion of RTX+MTX recipients with a clinical improvement of 70% relative to MTX recipients at 24 weeks.



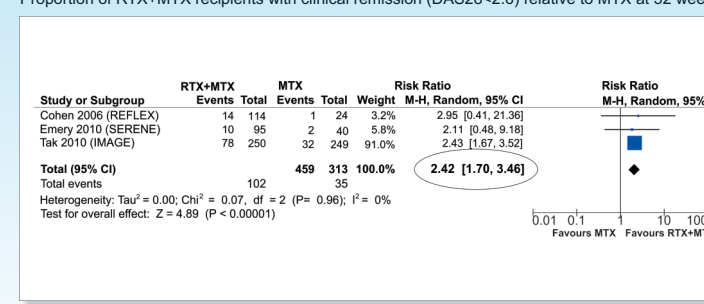
**Figure 3. No Radiographic Progression**

Proportion of RTX+MTX recipients without radiographic disease progression relative to MTX at 52 weeks.



**Figure 4. Clinical Remission (DAS28<2.6)**

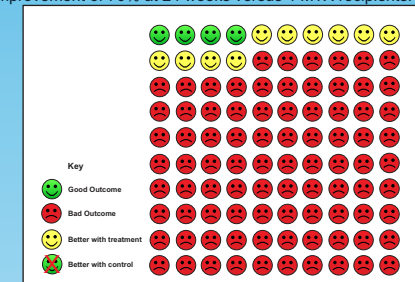
Proportion of RTX+MTX recipients with clinical remission (DAS28<2.6) relative to MTX at 52 weeks.



**Figure 5. NNT: 5 (95% CI 4, 9).** Twenty-nine out of every 100 RTX+MTX recipients experience a clinical improvement of 50% at 24 weeks versus 9 MTX recipients.



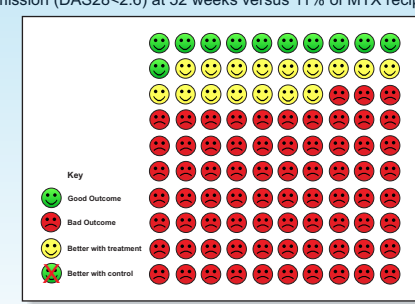
**Figure 6. NNT: 9 (95% CI 4, 30).** Fourteen out of every 100 RTX+MTX recipients experience a clinical improvement of 70% at 24 weeks versus 4 MTX recipients.



**Figure 7. NNT: 8 (95% CI 5, 19).** Sixty-two out of every 100 RTX+MTX recipients experience no radiographic disease progression at 52 weeks versus 50% of MTX recipients.



**Figure 8. NNT: 7 (95% CI 4, 13).** Twenty-seven out of every 100 RTX+MTX recipients experience clinical remission (DAS28<2.6) at 52 weeks versus 11% of MTX recipients at 52 weeks.



Dr. Suarez-Almazor is the recipient of a K24 career award from the National Institute for Musculoskeletal and Skin Disorders.



## References

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