Evolution of radiographic joint damage in rituximab-treated versus TNF-treated rheumatoid arthritis cases with inadequate response to TNF antagonists

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ABSTRACT

Background Observational studies have suggested that patients with rheumatoid arthritis (RA) who experience inadequate response to anti-tumour necrosis factor (anti-TNF) agents respond more favourably to rituximab (RTX) than to an alternative anti-TNF agent. However, the relative effectiveness of these agents on long-term outcomes, particularly in radiographic damage, remains unclear.

Objective To compare the effectiveness of RTX against anti-TNF agents in preventing joint damage in patients with RA who have experienced inadequate response to at least one prior anti-TNF agent.

Methods This is a prospective cohort study within the Swiss registry of patients with RA who discontinued at least one prior anti-TNF agent and subsequently received either RTX or an alternative anti-TNF agent. The primary outcome, progression of radiographic joint erosions (Ratering erosion score) over time, and the secondary outcome, functional disability (Health Assessment Questionnaire Disability Index), were analysed using regression models for longitudinal data and adjusted for potential confounders.

Results Of the 371 patients included, 104 received RTX and 267 received an alternative anti-TNF agent. During the 2.6-year median follow-up period, the rates of Ratering erosion score progression were similar between patients taking RTX and patients taking an alternative anti-TNF agent (p = 0.67). The evolution of the Health Assessment Questionnaire score was statistically significantly better in the RTX group (p = 0.016), but the magnitude of the effect was probably not clinically relevant.

Conclusion This observational study suggests that RTX is as effective as an alternative anti-TNF agent in preventing erosions in patients with RA who have previously experienced inadequate response to anti-TNF agents.

INTRODUCTION

Over the last decade, remarkable advances in the treatment of rheumatoid arthritis (RA) have been achieved, mostly owing to new anti-rheumatic treatments. The current anti-rheumatic armamentarium in RA includes several synthetic disease-modifying anti-rheumatic drugs (DMARDs) and nine approved biological agents. However, more choices also lead to new challenges. One of these challenges is selecting the best treatment for an individual patient and pondering the potential benefits against the possible harms of a particular intervention in a given clinical setting. A recent conference aimed to identify major gaps in our current clinical knowledge of RA management and listed ‘the comparison of active anti-rheumatic treatment options in patients whom at least one tumour necrosis factor (TNF) inhibitor has failed’ as one of the key areas for clinical investigation.

Comparative effectiveness research in RA is still in its infancy; the positioning of newer biological agents, in particular, has not been fully established. The only published randomised controlled trial (RCT) to indirectly compare two biological agents has been the ATTEST trial (‘Abatacept or infliximab versus placebo, a Trial for Tolerability, Efficacy and Safety in Treating RA’), which evaluated a T cell costimulation blocker against a TNF inhibitor (anti-TNF) in patients who have failed methotrexate treatment. Lacking head-to-head trials comparing biological agents, we have used observational studies to examine comparative effectiveness despite their susceptibility to selection biases and confounding factors. In particular, several cohort studies have analysed the effectiveness of switching to a second anti-TNF agent, compared to switching to a biological agent with a different mechanism of action, in patients who have experienced inadequate response to previous anti-TNF agents. A meta-analysis concluded that switching to rituximab (RTX) was slightly more effective than maintaining drug class by switching to a second anti-TNF agent in reaching American College of Rheumatology 70% improvement criteria or a disease activity score remission response. Some studies have suggested that the relative benefit of RTX over an anti-TNF agent was restricted to patients switching due to the ineffectiveness of prior anti-TNF agents, but published results are essentially limited to only short-term outcomes such as RA disease activity. Long-term outcomes, such as structural joint damage or disability, may however be more relevant to chronic conditions such as RA and remain a concern. Prevention of structural damage has been suggested as the gold standard for drug studies in RA. Anti-TNF agents have demonstrated outstanding efficacy in preventing radiographic joint damage even when
The clinical response was not satisfactory, while inhibition of structural joint damage by RTX was initially perceived as less impressive, probably owing to different patient populations. The aim of this analysis was to examine the effectiveness of switching to an alternative anti-TNF agent versus initiating RTX on long-term outcomes such as radiographic damage progression and functional disability. Both biological agents have established efficacy in preventing radiographic damage in placebo-controlled RCTs but have never been compared directly for their efficacy in this key outcome.

**METHODS**

**Study design**

We performed a nested cohort study to examine the impact of switching to an alternative anti-TNF agent versus initiating RTX on long-term outcomes such as radiographic damage progression and functional disability. Both biological agents have established efficacy in preventing radiographic damage in placebo-controlled RCTs but have never been compared directly for their efficacy in this key outcome.

**Study population**

SCQM-RA is a Swiss cohort of patients with RA that has been described in detail elsewhere. Patients are assessed at regular intervals for disease activity, radiographic erosions, past and current anti-rheumatic treatments, reasons for changes in treatment, adverse events and RA symptoms. The Swiss regulatory authorities perform continuous monitoring of all patients with arthritis who are taking biological agents within the SCQM programme; therefore, the cohort can be considered a representative population-based sample of Swiss patients with RA having biotreatment. SCQM patients come from a range of clinical settings, with more than 50% enrolled by private practices, 30% from non-academic centres and 20% from academic centres. The analysis included data collected from March 1996 through November 2010. The estimated proportion of Swiss patients with RA having biotreatment was around 13% in 2008, in line with other western European countries.

RTX has been approved for the treatment of moderate to severe cases of RA only after the failure of anti-TNF agents. We therefore restricted the eligibility criteria for this analysis to patients who discontinued at least one anti-TNF agent (infliximab, etanercept, adalimumab, golimumab or certolizumab) and subsequently initiated either an alternative anti-TNF agent or a first course of RTX. Thus, patients receiving anti-TNF or RTX treatment as their first biotreatment were excluded from the analysis. Other inclusion criteria were a diagnosis of RA by a board-certified rheumatologist and the availability of at least two consecutive sets of radiographs. Because radiographs should reflect structural joint damage occurring during the treatment of interest, we excluded radiographs that preceded the initiation of treatment by more than 6 months. The only exclusion criterion was RTX treatment for lymphoma.

The duration of drug exposure is not always clear-cut for biotreatments, particularly for RTX, and patients can be lost to follow-up after varying durations, affecting the period of drug exposure. Performing an ‘on-drug-only’ analysis or a ‘completers-only’ analysis (ie, including only the patients with at least two consecutive sets of radiographs) carries the risk of overestimating the true treatment effect, as only patients with satisfactory responses to treatment will remain on treatment long enough to have two radiographic assessments. To avoid this bias, we operationally defined drug exposure at the initiation of the new treatment, whether or not patients continued to receive their initial treatment. This is a conservative approach comparable to an intent-to-treat analysis in randomised trials. In sensitivity analysis, we considered an alternative definition for drug exposure (‘on drug only’, with observations censored after treatment interruption) according to recently published recommendations.

**Table 1** Baseline patient and treatment characteristics

<table>
<thead>
<tr>
<th>Disease characteristics</th>
<th>RTX (n=155)</th>
<th>Alternative anti-TNF agent (n=163)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years, median IQR)</td>
<td>58 (47–66)</td>
<td>56 (44–64)</td>
<td>0.15</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>25</td>
<td>19</td>
<td>0.18</td>
</tr>
<tr>
<td>ACPA (%)</td>
<td>81</td>
<td>74</td>
<td>0.30</td>
</tr>
<tr>
<td>RF (%)</td>
<td>92</td>
<td>82</td>
<td>0.01</td>
</tr>
<tr>
<td>Disease duration (years, mean SEM)</td>
<td>12 (0.8)</td>
<td>11 (0.5)</td>
<td>0.13</td>
</tr>
<tr>
<td>Disease activity (DAS28, mean SEM)</td>
<td>4.7 (0.14)</td>
<td>4.2 (0.08)</td>
<td>0.003</td>
</tr>
<tr>
<td>Radiographic erosion score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ratingen erosion score (0–190), mean (SEM)</td>
<td>34.9 (3.2)</td>
<td>32.5 (2.3)</td>
<td>0.64</td>
</tr>
<tr>
<td>ERO', mean (SEM)</td>
<td>18.1 (1.7)</td>
<td>17.1 (1.2)</td>
<td>0.64</td>
</tr>
<tr>
<td>Health Assessment Questionnaire (0–3), mean (SEM)</td>
<td>1.27 (0.07)</td>
<td>1.13 (0.04)</td>
<td>0.07</td>
</tr>
<tr>
<td>Concomitant use of DMARDs (%)</td>
<td>74</td>
<td>79</td>
<td>0.30</td>
</tr>
<tr>
<td>Methotrexate (%)</td>
<td>34</td>
<td>46</td>
<td>0.03</td>
</tr>
<tr>
<td>Leflunomide (%)</td>
<td>14</td>
<td>20</td>
<td>0.15</td>
</tr>
<tr>
<td>Other DMARDs (%)†</td>
<td>8</td>
<td>9</td>
<td>0.61</td>
</tr>
<tr>
<td>Glucocorticoids (%)</td>
<td>56</td>
<td>48</td>
<td>0.16</td>
</tr>
<tr>
<td>Previous anti-TNF agents (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>1 (1–2)</td>
<td>1 (1–1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1.43 (0.6)</td>
<td>1.01 (0.12)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time since the discontinuation of previous anti-TNF agent (months, median IQR)</td>
<td>1 (0.1–4.3)</td>
<td>1.8 (0.5–13.8)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Percentages indicate the use of each cotreatment at baseline. Patients could receive more than one DMARD cotreatment, explaining why the sum of individual DMARDs may exceed 100%.

†Other DMARDs included synthetic DMARDs such as hydroxychloroquine, sulfasalazine and azathioprine.

*Available for only half of all patients.

**ACPA, anti-citrullinated protein antibody; DAS28, Disease Activity Score based on 28 joints; DMARDs, disease-modifying anti-rheumatic drugs (including oral glucocorticoids); ERO', Ratingen erosion score expressed in per cent maximum erosion score; RF, rheumatoid factor; RTX, rituximab; TNF, tumour necrosis factor; IQR, interquartile ranges; SEM, standard error of the mean.
Outcomes
The primary end point of this analysis was radiographic erosion progression as measured by the change in radiographic scores from baseline. A validated scoring method (Ratingen erosion score) was used to grade serial radiographs according to the number and size of bone erosions. The Ratingen scoring method has good reliability, with an intrarater intraclass correlation coefficient (ICC) of 0.8–0.9 and an inter-rater ICC of 0.7–0.9, and is less susceptible to ceiling effects in advanced disease because of a true ordinal rating system. The minimal detectable radiographic change for this method has been determined to be around 3.3% of the maximum score. Radiographic damage was assessed prospectively by two independent assessors who were blinded to clinical information. Their reliability was good, with an intrarader ICC of 0.83 and an inter-rater ICC of between 0.83 and 0.96. The average of the two assessors’ change scores was used for the analysis. Ratingen erosion score can be expressed both in the original unit (Ratingen, range 0–190) and in per cent maximum damage score (ERO%).

A secondary study end point was the evolution of functional disability, measured as a change in the Health Assessment Questionnaire Disability Index (HAQ-DI) from baseline. The Health Assessment Questionnaire (HAQ) score ranges from 0 to 2, with 3 representing the maximum possible disability. Furthermore, important baseline predictors of RA disease progression, such as demographic characteristics, various disease characteristics, concomitant treatment with DMARD and self-assessed questionnaires, were extracted from the SCQM-RA database and used to assess the comparability of the patient groups and to adjust the analysis.

Analysis
Based on a previous analysis, we calculated that 320 patients (with a 2:1 ratio of anti-TNF-agent-treated patients to RTX-treated patients) would be required to demonstrate a similar difference in radiographic progression, a type I error probability of 0.05 and a statistical power of 80%. Baseline disease and treatment characteristics were compared using conventional descriptive statistics. The significance of differences in baseline disease characteristics was assessed with Student t test for normally distributed mean values of continuous variables and with Kruskal–Wallis test for non-normally distributed variables. For dichotomous variables, Pearson’s chi-square test was used to evaluate the statistical significance of differences in proportions. Drug retention was examined using survival analysis, and differences in drug survival were explored with a Cox proportional hazard model. In order to minimise potential biases induced by sporadically missing covariates (≤5%), we used the population average as substitute. Statistical tests were two-sided and were evaluated at the 0.05 significance level. The analysis was performed with STATA V.11 (Stata Statistical Software, College Station, Texas, USA).

In observational studies, selection bias is always of concern because assignment to RTX versus alternative TNFs is not performed randomly. Because differences in disease characteristics may substantially influence subsequent radiographic progression, we used multivariate regression models to adjust for potential confounding factors. The final adjusted model was adjusted for age, sex, rheumatoid factor (RF) positivity, disease duration, functional disability (HAQ), disease activity (Disease Activity Score based on 28 joints (DAS28)), time since discontinuation of previous anti-TNF agent, radiographic damage at baseline, use of low-dose glucocorticoid, concomitant use of synthetic DMARD, number of prior anti-TNF agent failures and primary failure of the previous anti-TNF agent (defined as discontinuation within the first 6 months). The evolution of radiographic erosions or functional disability outcomes was analysed using generalised mixed models for longitudinal data. We first selected the best-fitting model without controlling for potential confounders. We then adjusted the analysis for differences in baseline disease characteristics using a multivariate model (adjusted model). We explored potential effect modification by concomitant DMARD treatment, concomitant glucocorticoid treatment, RF positivity and primary failure of the previous anti-TNF agent.
and 8% received either golimumab or certulizumab. Ten percent (25 mg subcutaneously every 2 weeks), 25% received etanercept (50 mg intravenously every 2 weeks), and 52% received an alternative anti-TNF agent. The patients excluded from the analysis initiated their biotreatment significantly later (1.9 years, p<0.001) but had otherwise mostly similar disease characteristics (supplemental file), suggesting that missing follow-up time was the main reason for the absence of subsequent radiographs in these patients. The 371 patients taking an alternative anti-TNF agent and the 267 patients taking RTX were more often positive for RF or anti-citrullinated protein antibody, had higher baseline DAS28 levels (4.7 vs 4.2), had a shorter interval between discontinuing the prior anti-TNF agent and starting the new biotreatment (1 vs 1.8 months) and failed more prior anti-TNF agents (1.4 vs 1). RTX was the second biological agent in 52% of patients, the third biological agent in 39% of patients and the fourth biological agent in 9% of patients; anti-TNF agent was the second biological agent in 80% of patients, the third biological agent in 18% of patients and the fourth or fifth biological agent in 2% of patients. Other important prognostic markers for radiographic progression, in particular baseline radiographic erosion scores and functional disability (HAQ) scores, were similar.

While the evolution of disease activity (DAS28) was significantly better in the RTX-treated group (at 1 year, incremental DAS28 improvement −0.34 (95% CI −0.14 to −0.53)) as previously demonstrated,4 the longitudinal evolution of radiographic erosions was similar between the RTX group and the alternative anti-TNF group (p=0.67; figure 1). Overall, ERO% progressed, on average, by 0.23% (95% CI −0.22 to +0.69; Ratingen +0.44 (95% CI −0.42 to +1.51)) during the first year, representing approximately one new erosion in 2 years of follow-up or a low level of damage progression.20 ERO% progression with an alternative anti-TNF agent was 0.25% (95% CI −0.06 to +0.57; Ratingen +0.48 (95% CI −0.11 to +1.08)) during the first year after the switch, compared to 0.23% (95% CI −0.41 to +0.88; Ratingen +0.44 (95% CI −0.76 to +1.67)) with RTX. This means that 33% (34/104) of all patients taking RTX have presented at least one new erosion over a period of 1 year compared to 30% (81/266) of patients taking an alternative anti-TNF agent (p=0.69; figure 2). Significant predictors of subsequent radiographic progression were baseline ERO% level and high disease activity. We found no effect modification by concomitant use of DMARD (p=0.18), use of low-dose oral glucocorticoid use (p=0.26), RF seropositivity (p=0.79) or a personal history of primary anti-TNF agent failure (p=0.20). A sensitivity analysis with an alternative definition of drug exposure (‘on drug only’ did not qualitatively change the conclusions (supplemental file).

The longitudinal evolution of functional disability was statistically significantly better in the RTX group compared to the alternative anti-TNF group (p=0.015; figure 3); however, the difference was far from reaching a minimally clinically important difference, estimated to be at least 0.22 HAQ-DI units.25 The HAQ-DI score improved by 0.05 HAQ units (95% CI −0.017 to +0.11) more on RTX 1 year after the switch and by 0.14 HAQ units (95% CI 0.04 to 0.25) 3 years after the switch. Significant predictors for functional deterioration were high baseline levels of functional disability (p=0.001), older age (p=0.03), high disease activity (p=0.03) and a trend for a more favourable evolution with concomitant use of steroid (p=0.07).

**DISCUSSION**

In the absence of any trial directly comparing the efficacy of RTX and an alternative anti-TNF agent,26 we analysed the effectiveness of switching to an alternative anti-TNF agent versus RTX on long-term outcomes in a longitudinal cohort study. After adjusting for potential confounders, we found no significant differences in the rates of erosion progression between patients taking an alternative anti-TNF agent and patients taking RTX. The longitudinal progression of functional disability (HAQ) suggested an advantage for patients treated with RTX compared to patients treated with an alternative anti-TNF agent.

Previous observational studies have generally suggested that biological agents with a different mechanism of action, such as...
RTX, are more effective on disease activity than an alternative anti-TNF agent in patients with RA who experienced inadequate response to a previous anti-TNF agent.3–6 However, there has been a concern that RTX might not be as effective in preventing radiographic damage as anti-TNF agents. While we could confirm the relative benefit of RTX over alternative anti-TNF agents on disease activity, we found a similar rate of radiographic erosion progression between these two treatments. Given the established disconnect between inflammation control and radiographic damage progression with biological agents,37 this is not surprising. However, because of the limited sample size and follow-up, we cannot exclude the possibility that minor differences could appear over time, yet large differences in radiographic erosion progression between these agents appear very unlikely. We found no evidence for an effect modification by RF seropositivity, in contrast with what has been suggested for RTX.27 The improved effectiveness of RTX in seropositive patients has been established only for disease activity but not for radiographic progression or compared to other biological agents. Comparing our results to those of RCTs is difficult, as they involve very different patient populations, treatment designs and scoring methods. Nevertheless, our results confirm the effectiveness of these biological agents in halting radiographic disease progression, independently of their impact on disease activity.

The difference in the evolution of functional disability was unexpected, as functional disability in RA is thought to be related to underlying structural joint damage. However, disease activity may greatly influence the assessment of functional capacity particularly in early disease,38 which would explain the beneficial trend in the RTX group, as this agent has a more favourable impact on RA disease activity in this setting.4,11

Observational studies have inherent limitations when comparing the effectiveness of different treatment options. Selection bias may arise because assignment to these agents is not performed randomly. In fact, patients taking RTX were more often RF ‘seropositive’, had higher DAS28 levels at baseline and had failed more biotreatments before switching. While we could adjust for these differences using multivariate regression models, we cannot exclude some degree of residual confounding or confounding by unmeasured factors such as a carryover effect of the previous anti-TNF agent. However, major selection bias is unlikely, as the choice of an alternative biotreatment is currently still essentially a matter of the physician’s personal preference (there are no ‘treatment guidelines’ for Swiss rheumatologists) and can thus be considered largely at random. The primary end point of this analysis was radiographic erosion progression as measured by the Ratingen scoring method,37 which implies that we could not assess the relative benefit of these treatments on joint space narrowing or cartilage degradation. Having incomplete data is another limitation of observational studies (ie, anti-citrullinated protein antibody status was available for only 50% of patients). Of all patients receiving an alternative biological agent after a prior inadequate response to an anti-TNF agent in the SCQM-RA cohort, 43% did not have at least two sets of consecutive radiographs. The SCQM received grants from the Swiss health authorities (Bundesamt für Gesundheit), the Swiss Academy for Medical Sciences, the J. W. Warren Foundation, the Swiss Society of Polyarthritis Patients and various pharmaceutical companies (Abbott, Pfizer, MSD, Roche, Bristol-Myers Squibb, Mepha, Novartis, Sanofi-Aventis and UCB). The authors specifically thank those rheumatologists who enrolled these patients (n=10): Aeilen, Nyor; Badaracco, Lugano; Bosia, Locarno; Blesch, Lausanne; Boitsch, Romanshorn; Careby-Bemer, Lausanne; Chamot A-M, Morges; Eigenmann, Zurich; Exer P, Basel; Forster A, Diessenhofen; Elmiger, Bern; Gämmin, Murten; Gerni, Thun; Gratz, Basel; Häfelin, Schlieren; Gut, Reinach; Jaccard, Genolier; Kaiser, Thun; Kolb R, Brugg; Kowskali, Solothurn; Leuba-Mansuelli, Neuchâtel; Lehmann T, Bern; Maier, Aarau; Muschlan, Heiden; Mathieu, Solothurn; Martin, Liestal; Masina, Lugano; Meder, Zofingen; Meierhofer, Zurich; Morell, Schaffhausen; Muff, Affoltern a. Albis; Müller-Werth, Samer; Marbet Grierson, Otten; Messikommer, Visp; Pancald, Muralto; Pfister, Bulach; Racaud, Lausanne; Schönbächler, Zurich; Schönenberger, Martigny; Schwarz, Carouge; Schuch, Lausanne; Suter, Bern; von Mühlenen I, Basel; Wicht, Solothurn; Rheumatologie im Silberturm, St Gallen; Rheumazentrum Kreuzlingen; Rheumapraxis Männedorf; Rösler, Bern; Suvain, Frickhof, Täuffe, Vevey; Tinner, Weinfelden; Volken, Sienna; Widing-Bernhardt, St Gallen; Wuest, Wädenswil; Zichmann, Zurich, Zuff, Estavayer Le Lac. The authors also especially thank the participating rheumatology clinics that registered these cases (n=20): the rheumatology divisions of the University Hospital of Zurich; the University Hospitals of Geneva; the University Hospital of Vaud; the University Hospital of Bern; Bethesda Spital, Basel; Felix Platter Spital, Basel; Cantonal Hospital Aarau; Cantonspital St Gallen; Cantonal Hospital Luzern; Cantonal Hospital Winterthur; Burgerspital Solothurn; Schulthess Klinik, Zurich; Hirslunden Klinik St Ana, Luzern; Stadtspital Triemli, Zurich; Clinic Impuls, Wettingen; Kantonspital Schaffhausen; Immunologie-Zentrum, Zurich; Rehaclin Zuzich; Aale Rehaclin Schinznach, Cantonal Hospital Zug: Hirslunden Clinic Binhof, Münchinnen; Cantonal Hospital Fribourg.

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Ethics approval Swiss Academy of Medical Sciences review board.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The original data for this research are kept in the SCQM registry.
REFERENCES
Supplemental File

Results

Excluded patient population: Patients corresponding to the study inclusion criteria initiated their alternative biotherapy on average in January 2006, while patients excluded started their biotherapy on average beginning of 2008 (p < 0.0001). The gender distribution (20.5% versus 23% of male sex, p = 0.45), rheumatoid-factor positivity (85% versus 79%, p = 0.06), mean age (55 versus 55, p = 0.55) and RA disease duration (11 versus 11, p = 0.52) were similar between the two groups. Some differences existed in the proportion of patients on concomitant DMARD or low dose oral glucocorticoids (74% versus 48%, p < 0.01) and radiographic damage at baseline (17% versus 12%, p < 0.01). The proportion of RTX prescription has become more prevalent in recent years, which resulted in a slightly higher proportion of RTX usage in the excluded population (42% versus 28%, p < 0.01).

X-ray assessment in the two treatment groups: The median time interval between switching and the first X-ray was 0 [IQR: 0 ; 6. 8] months and the mean time interval was 3 months. The mean time interval was not different between the two treatment groups (t-test, p = 0.25). The median duration between the first and second X-ray was 1.05 (IQR: 0.96 ; 1.63) years, similar in the two treatment groups (1.05 versus 1.06, p = 0.96).

Longitudinal evolution of radiographic damage with an ‘on drug only’ definition of drug exposure (sensitivity analysis): Longitudinal evolution of radiographic damage was similar between the RTX group and the alternative aTNF group (p = 0.35). Radiographic progression was of 0.19% (95% CI: -.14 ; +0.51) with alternative aTNF during the first year after the switch, compared to 0.21% (95% CI: -.43 ; +0.86) with RTX.