International Journal of
Rheumatic Diseases

International Journal of Rheumatic Diseases 2018; **21:** 1581–1590

ORIGINAL ARTICLE

A retrospective review of the persistence on bDMARDs prescribed for the treatment of rheumatoid arthritis in the Australian population

Graeme JONES,[1] Stephen HALL,[2] Paul BIRD,[3] Geoff LITTLEJOHN,[4] Kathleen TYMMS,[5] Peter YOUSSEF,[6] Eric CHUNG,[7] Rina BARRETT[8] and Peter BUTTON[8]

[1]*Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania,* [2]*Cabrini Hospital, Malvern, Victoria, ,* [3]*University of New South Wales and Combined Rheumatology Practice, Kogarah, NSW,* [4]*Monash University and Monash Medical Centre, Clayton, Victoria,* [5]*Australian National University and Canberra Rheumatology, Canberra, ACT,* [6]*Royal Prince Alfred Hospital,* [7]*PROSPECTION, Eveleigh, NSW, and* [8]*Roche Products Pty Limited, Sydney, NSW, Australia*

Abstract

Aim: To describe the persistence of biologic disease modifying anti-rheumatic drugs (bDMARDs) in Australian rheumatoid arthritis (RA) patients, and assess the influence of methotrexate and other conventional DMARD (cDMARD) concomitant medications, and treatment line on bDMARD persistence and glucocorticoids usage.

Method: RA patients, from the 10% Australian Medicare random sample, aged ≥18 for whom bDMARDs were dispensed were included. Individual sub-cutaneous (SC) anti-tumor necrosis factor-α (anti-TNFα) agents were combined as they were equivalent.

Results: Data from 1230 patients were analyzed. For all patients the 12-month persistence rates (based on Kaplan–Meier estimates) were 76% for intravenous (IV) tocilizumab, 63% abatacept (SC/IV), 61% SC-anti-TNFs and 36% IV-infliximab. Persistence rates on first-line bDMARDs were 79% (tocilizumab and abatacept), 64% (SC-anti-TNFs) and 13% (infliximab); rates were sustained for tocilizumab but dropped to 49% for abatacept and 51% for SC-anti-TNFs in the second-line setting. Median treatment persistence was 40 months tocilizumab (95% CI: 30-ND), 33 months abatacept (95% CI: 20-ND); 22 months SC-anti-TNF (95% Cl: 18–27), and 4 months infliximab (95% CI: 2–13). Longer persistence was observed for SC-anti-TNFs and abatacept combined with methotrexate or other cDMARDs. For tocilizumab, persistence was robust with or without concomitant medications. The median oral glucocorticoid doses decreased from 4.1 mg/day (min 0, max 21) to 2.0 mg/day (min 0, max 17.3) over 2 years.

Conclusions: Treatment persistence was longer on tocilizumab followed by abatacept then SC-anti-TNF therapy and was influenced by co-therapy. Glucocorticoid dosage decreased with bDMARD use. This real-world data highlights that persistence on bDMARDs differs according to biologics mode of action and co-therapy.

Key words: rheumatoid arthritis, biologics, DMARD, glucocorticoids.

INTRODUCTION

Rheumatoid arthritis (RA) is a heterogeneous disease with no validated predictors for determining optimal choice of therapy in individual patients. Treatment guidelines for RA recommend starting biologic disease

Correspondence: Professor Graeme Jones, Menzies Institute for Medical Research, Private Bag 23, Hobart, 7000, Tasmania, Australia. Email: Graeme.Jones@utas.edu.au

modifying anti-rheumatic drugs (bDMARDs) in combination with methotrexate (MTX) in patients responding insufficiently to MTX and/or other conventional DMARDs (cDMARDs) with or without glucocorticoids.[1]

Persistence on treatment has been suggested as a surrogate for treatment effectiveness.[2–6] There is limited data on treatment persistence by mode of action in the same RA population. Persistence on tumor necrosis factor-α (TNF) inhibitors has been reported in several registries but there are few reports of persistence on tocilizumab in the real-world setting.[7–12] The Danish Rheumatological Database described 48 weeks drug survival rates of 61% (tocilizumab), 41% (infliximab), 56% (etanercept) and 52% (adalimumab).[9] The Japanese Osaka University Biologics Rheumatic Diseases registry reported 1 year drug continuation rates of 89% (tocilizumab), 73% (infliximab), 86% (etanercept) and 78% (adalimumab). In the latter registry, the continuation rates for tocilizumab and etanercept were significantly higher than those for infliximab and adalimumab.[8] The most frequent reasons given for discontinuation are adverse events for tocilizumab and a lack of efficacy for adalimumab and infliximab.[8] In addition data from a Slovenian registry that examined biologic drug survival after first TNF inhibitor failure, found that a second TNF inhibitor was more likely to fail earlier than a bDMARD with a different mode of action, such as tocilizumab and rituximab.[12]

In the Australian landscape, preliminary data on the persistence or survival time on bDMARDs with different modes of action (from the Optimising Patient outcomes in Australian rheumatoLogy-OPAL registry) appear to be consistent with the findings from the Japanese registry.[13]

However, there remain a number of unanswered questions regarding the persistence on bDMARDs in Australia, including the influence of concomitant medications and the effect of changing bDMARD mode of action on bDMARDs persistence.

Glucocorticoids play an important role in the management of RA patients.[14–16] However, long-term use is not without side-effects.[17,18] TNF inhibitors were previously shown to result in significant reduction in glucocorticoid doses[19–21] and recently the effect of tocilizumab on glucocorticoid sparing was reported.[22,23] However, the effects of various bDMARDs on glucocorticoid use in the same patient population has not been investigated. Therefore, this study describes the persistence on bDMARDs in the Australian landscape and assesses the impact on glucocorticoid usage.

METHODS

Study design

This study is a retrospective, observational, non-interventional review of a sample of RA patients in the Australian Medicare database (dating from 1 August, 2010 to 30 June, 2014).

Approval for this study and publication of the results were obtained from the External Request Evaluation Committee for the Department of Human Services; no approval from an independent ethics committee was required for this aggregate data.

The primary objective was to describe the persistence on bDMARDs in the Australian landscape. The secondary objectives were to investigate the influence of MTX and other cDMARDs concomitant medications, patient age at initiation and treatment line on bDMARDs persistence. The average annual glucocorticoid consumption before and after patients take bDMARDs for the management of their RA and the influence of MTX and other cDMARDs concomitant medications on the glucocorticoid consumption over the time were also assessed.

Patient population

Adult patients aged 18 years or older who met the Australian Pharmaceutical Benefit Scheme (PBS) reimbursement criteria[24,25] for a bDMARD for the treatment of RA and who had bDMARDs dispensed for the treatment of RA from 1 August, 2010 until 30 June, 2014, were selected for inclusion in the analyses. The PBS eligibility criteria mandate that a patient must fail a 6 month intensive course of DMARDs and have active disease (20 affected small joints or four large joints, erythrocyte sedimentation rate [ESR] >25 or C-reactive protein [CRP] >15 mg/dL). Patients are eligible for PBS subsidized treatment for only one bDMARD at a time and the response must be document after 3 months and then every 6 months thereafter (joint count and blood tests) to stay eligible on treatment. They are eligible to swap between bDMARDs within a treatment cycle (while documenting a response).

The glucocorticoid analysis included concessional (government subsidized) RA patients aged 18 years or older, who had bDMARDs dispensed for the treatment of RA from 1 August, 2010 until 31 July, 2013 and who had persisted on bDMARDs for 2 years. We had

performed a sensitivity analysis which showed that when considering concessional patients only, the rate of co-medication with methotrexate is similar to that for all patients, with only around 2% difference in total patients co-medicating (data not shown).

Data source

Data were provided by the Australian Department of Health and Aging (DoHA) through PROSPECTION, an Australian healthcare consulting company. Ten percent of the patients were taken as a random representation of the living RA population in Australia. Data collection included summary data that allowed for identification and description of dispensing patterns only (demographic and RA biologic dispensing data).

The RA patient population was identified based on the required specific PBS item codes for each bDMARD script, which are specific to disease indication and medication dose. Initial dose and repeat doses have separate item codes.

Treatments

Data were collected for intravenous (IV) and sub-cutaneous (SC) abatacept, SC adalimumab, SC certolizumab pegol, SC etanercept, SC golimumab, IV infliximab and IV tocilizumab. Rituximab was excluded from the analysis due to the broad variability in time to next treatment. All formulations of MTX, sulfasalazine, leflunomide were included in the analyses. Only oral glucocorticoids were analyzed.

The start date of 2010 was chosen as it was the date from which all of the above bDMARDs were available through the PBS.

Definition of persistence

Persistence was defined as the time from when the first dose of a particular bDMARD (regardless of route of administration) was dispensed until the date of the last dose when there had not been a script dispensed for 6 months; except for infliximab, where an 8-month gap was applied. This window was selected because the subsidized prescription frequency was 7-monthly for infliximab and 6-monthly for the other assessed bDMRADs. For abatacept, a new SC formulation became available during the data collection period; however, patients who moved from an IV to SC were considered persistent. Patients were considered not persistent at the time they switched to another bDMARD. Patients with one dispensing of a bDMARD were considered persistent for 1 month.

Statistics

Analyses were performed for all patients by concomitant medication, with the following sub-groups: (a) monotherapy (bDMARDs prescribed in the absence of cDMARDs and MTX); (b) combination MTX (bDMARD prescribed with MTX at initiation, with or without other cDMARDs and excludes patients taking other cDMARDs only); and (c) combination cDMARDs (bDMARD prescribed with a cDMARD at initiation, with or without MTX and excludes patients taking MTX only). Patients taking cDMARDs and MTX were counted in both groups (b) and (c) and therefore the combined total of the sub-groups does not equal the total number of patients included in the 'All bDMARD population' analysis. Analyses were also performed by line of bDMARD treatment (first, second or third line bDMARDs).

Data were summarized using descriptive statistics for continuous variables and frequency counts and percentages for categorical variables. The time-to-endpoints were summarized using Kaplan–Meier (K-M) methodology; persistence times for patients were censored if they were ongoing at the time of data transfer. Comparisons between groups were made using the log rank test which used the length of time a patient remained on a particular prescription of a bDMARD treatment for RA; however, no adjustments were made to account for the multiple tests (as is standard in epidemiological research). The K-M estimates for the probability of persisting on a medication have been represented as percentage in the results. Individual SC-anti-TNFs were equivalent in all analyses and therefore they were combined for simplicity; and since patients could have taken more than one medication in this category during the observation period, the number of patients in the SC-anti-TNF group is greater than the number of patients in the study.

Change in glucocorticoid use, within a group, was assessed using the Wilcoxon Signed Rank test.

RESULTS

Treatment persistence

A total of 1230 patients met the inclusion criteria for the treatment persistence analyses. The majority were female (n = 895, 73%) in the age range 18–64 years (n = 903; 73%). Basic demographics at the time of starting bDMARD are presented in Table 1. All were similar with the exception of abatacept which was more commonly used in those aged over 65 years.

Table 1 Demographics at the time of bDMARD initiation

bDMARD†	Age			Gender		
	Years	*n*	%		*n*	%
Adalimumab (*N* = 593)	18–64	454	77	F	444	75
	65+	139	23	M	149	25
Etanercept (*N* = 459)	18–64	339	74	F	344	75
	65+	120	26	M	115	25
Tocilizumab (*N* = 308)	18–64	219	71	F	234	76
	65+	89	29	M	74	24
Abatacept (*N* = 284)	18–64	188	66	F	225	79
	65+	96	34	M	59	21
Golimimab (*N* = 267)	18–64	199	75	F	207	78
	65+	68	26	M	60	22
Certolizumab (*N* = 171)	18–64	130	76	F	136	80
	65+	41	24	M	35	20
Infliximab (*N* = 40)	18–64	32	80	F	27	68
	65+	8	20	M	13	32

bDMARD, biologic disease-modifying antirheumatic drugs.
†Patients might have received more than one bDMARD therefore the *n* value does not add up to 1230.

Table 2 Concomitant medications and bDMARD persistence rates at 12 months post-treatment initiation, percentage based on Kaplan–Meier estimates of persistence

	All		Combination methotrexate†		Combination cDMARD‡		Monotherapy	
	n	12 months	*n*	12 months	*n*	12 months	*n*	12 months
SC-anti-TNFs	1490	61%	864	63%*	570	66%**	420	53%***
Tocilizumab	308	76%	139	71%	97	77%	118	77%*****
Abatacept	284	63%	197	65%	90	66%	63	58%
Infliximab	40	36%	14	62%****	7	43%	22	13%

bDMARD, biologic disease-modifying antirheumatic drugs; cDMARD, conventional disease-modifying antirheumatic drugs; SC-anti-TNF, subcutaneous anti-tumor necrosis factor.
†bDMARD prescribed with methotrexate at initiation, with or without other cDMARDs and excludes patients taking other cDMARDs only.
‡bDMARD prescribed with cDMARDS other than methotrexate at initiation, with or without methotrexate and excludes patients taking methotrexate only.
**P* = 0.0004 for SC-anti-TNFs with combination methotrexate at initiation versus SC-anti-TNFs monotherapy.
***P* = 0.0001 for SC-anti-TNFs with combination cDMARD at initiation versus SC-anti-TNFs monotherapy.
****P* < 0.0001 SC-anti-TNF monotherapy versus tocilizumab monotherapy.
*****P* = 0.007 infliximab with combination methotrexate versus infliximab monotherapy.
******P* = 0.013 tocilizumab monotherapy versus abatacept monotherapy.

Overall, at 12 months post-initiation of bDMARDs, the rate of persistence on treatment based on K-M estimates of persistence was 76% for tocilizumab, 63% for abatacept, 61% for SC-anti-TNFs and 36% for infliximab (Table 2).

Persistence rates were higher when comparing SC-anti-TNFs in combination with MTX and in combination with other cDMARDs to monotherapy SC-anti-TNFs (63% [$P = 0.0004$] and 66% [$P = 0.0001$] *vs.* 53%); infliximab in combination with MTX to monotherapy infliximab (62% *vs.* 13%; $P = 0.0069$); monotherapy tocilizumab to monotherapy anti-TNFs (77% *vs.* 53%; $P < 0.0001$) and monotherapy tocilizumab to monotherapy abatacept (77% *vs.* 58%; $P = 0.013$). Persistence rates on abatacept were higher in combination with MTX and in combination with other cDMARDs to monotherapy abatacept (65% and 66% *vs.* 58%; $P = 0.013$). No differences in the 12-months persistence rates were observed across concomitant treatment groups for tocilizumab (Table 2).

The median time to stopping treatment in the overall population (Fig. 1a) was the longest for tocilizumab

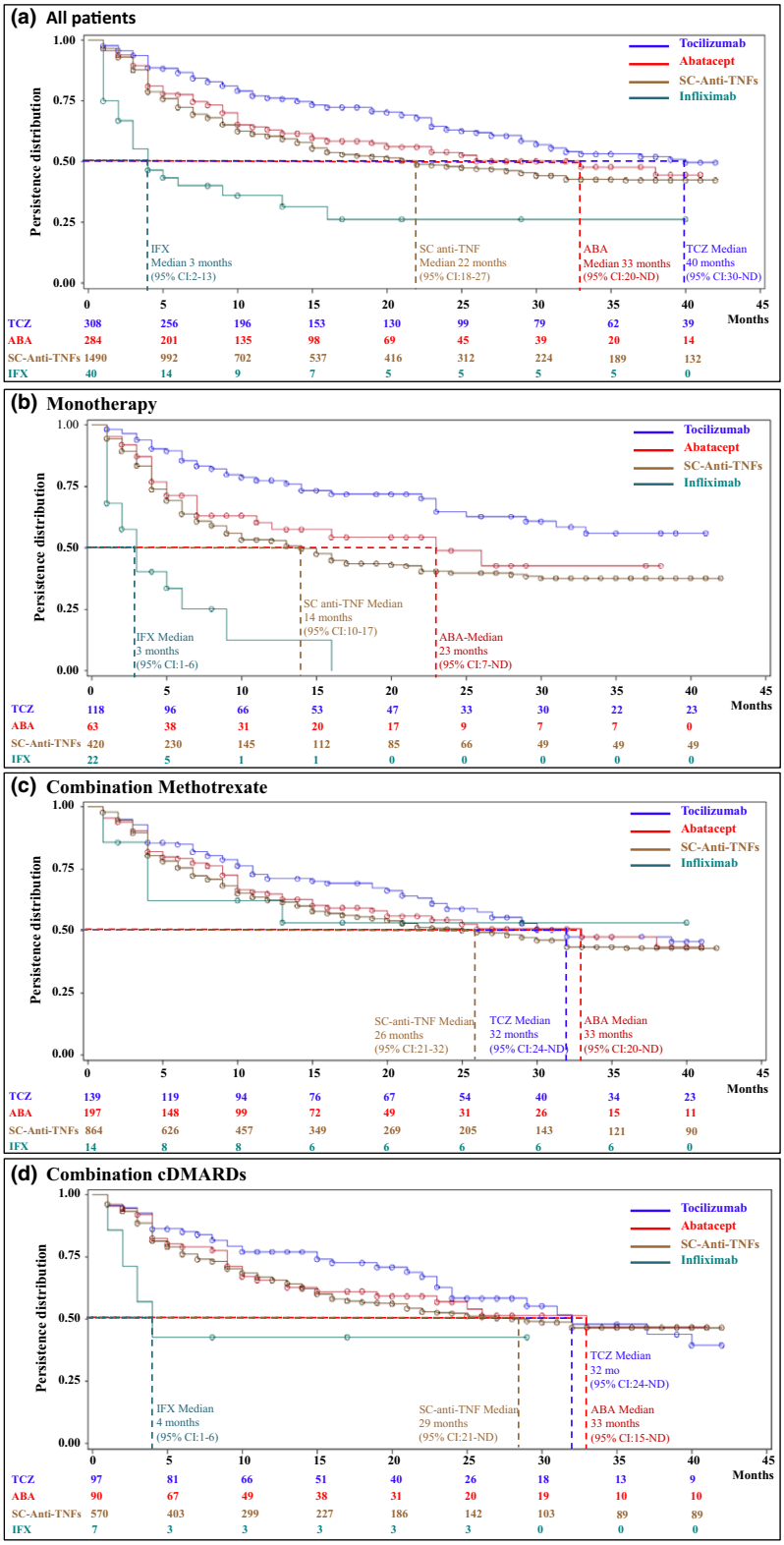

Figure 1 Kaplan–Meier estimates of treatment persistence by concomitant medication.

Table 3 Line of treatment and bDMARDs persistence rates at 12 months post treatment initiation, percentage based on Kaplan–Meier estimates of persistence

	First line		Second line		Third line	
	n	12 months	*n*	12 months	*n*	12 months
SC-anti-TNFs	1011	64%	358	51%	95	56%
Tocilizumab	83	79%*	90	81%***	93	72%
Abatacept	82	79%*,**	101	49%	77	60%
Infliximab	26	13%	-	-	5	50%

bDMARD, biologic disease-modifying antirheumatic drugs; SC-anti-TNF, subcutaneous anti-tumor necrosis factor.
*$P < 0.0001$ versus infliximab first line.
**$P < 0.05$ versus SC-anti-TNFs first line.
***$P < 0.0001$ versus SC-anti-TNF and abatacept second line.

(40 months, 95% CI: 30 to not determined [ND]) (Fig. 1a). As monotherapy, the median time to stopping tocilizumab was not reached (Fig. 1b); abatacept had a longer median time to stopping treatment (23 months; 95% CI: 7 to ND) than SC-anti-TNFs and infliximab. In combination therapy with MTX, or in combination with cDMARDs at initiation, the median time to stopping treatment was longest for abatacept (Fig. 1c, d). Persistence rates at 12 months by line of treatment were also assessed; differences were observed for treatment lines across the bDMARDs analyzed (Table 3). Overall, the persistence rates decreased with the line of treatment for the assessed bDMARDs, with the exception of infliximab; however, there were only five patients receiving the treatment in the third-line setting. As first line treatment, both abatacept and tocilizumab had higher persistence on treatment than SC-anti-TNFs. As second line treatment, tocilizumab had higher persistence at 12 months than abatacept and SC-anti-TNFs.

The median time to stopping treatment when administered as a first-line bDMARD was 39 months (95% CI: 27 to ND) for tocilizumab, 29 months (95% CI: 22–36) for SC-anti-TNFs and 2 months (95% Cl: 1–3) for infliximab. The median time to stopping abatacept was not reached. As second-line therapy, the median time to stopping treatment was 12 months (95% CI: 10 to ND) for abatacept and 13 months (95% CI: 10–20) for SC-anti-TNFs. The median time to stopping tocilizumab was not reached. As third-line therapy, the median time to stopping treatment was 29 months (95% CI: 19 to ND) for tocilizumab, 26 months (95% CI: 10 to ND) for abatacept and 17 months (95% CI: 9 to ND) for SC anti-TNFs. The median was not assessed for infliximab in the second and third line of treatment due to low patient numbers.

The persistence on treatment relative to age groups was assessed and no differences were observed (data not shown).

Glucocorticoid usage

A total of 230 patients met the criteria for inclusion in the glucocorticoid analysis, of whom 112 (49%) patients were aged ≥ 65 years and the majority were female ($n = 186$; 81%). For all patients ($n = 230$), the median dose of oral glucocorticoids was 4.1 mg/day (min 0, max 21) at 1 year prior to initiation of a bDMARD, 2.9 mg/day (min 0, max 22.2) and 2.0 mg/day (min 0, max 17.3) at 1 and 2 years, respectively, post-bDMARD initiation. The average daily glucocorticoids consumption by bDMARD in any setting (in combination with cDMARDs and as monotherapy) is presented in Figure 2. Daily dose changes at 1–2 years post-initiation of bDMARD from 1 year before initiation of bDMARD were statistically significant for all bDMARDs ($P < 0.0001$), all anti-TNFs ($P < 0.0001$) and tocilizumab ($P = 0.0002$).

The percentage of patients who stopped glucocorticoids 1–2 years post-initiation of bDMARDs was 34% for all RA bDMARDs, 36% for all anti-TNFs, 18% for abatacept and 36% for tocilizumab. Thirty-one percent of the patients who remained on biologics for the observation period in the 'all RA bDMARDs' group had an increase in glucocorticoids dose and 60% had a decrease after 1 year and 65% after 2 years. The percentage increase and decrease in glucocorticoids doses for all groups are listed in Table 4.

DISCUSSION

This study used Australian dispensing data to assess bDMARD treatment persistence rates and

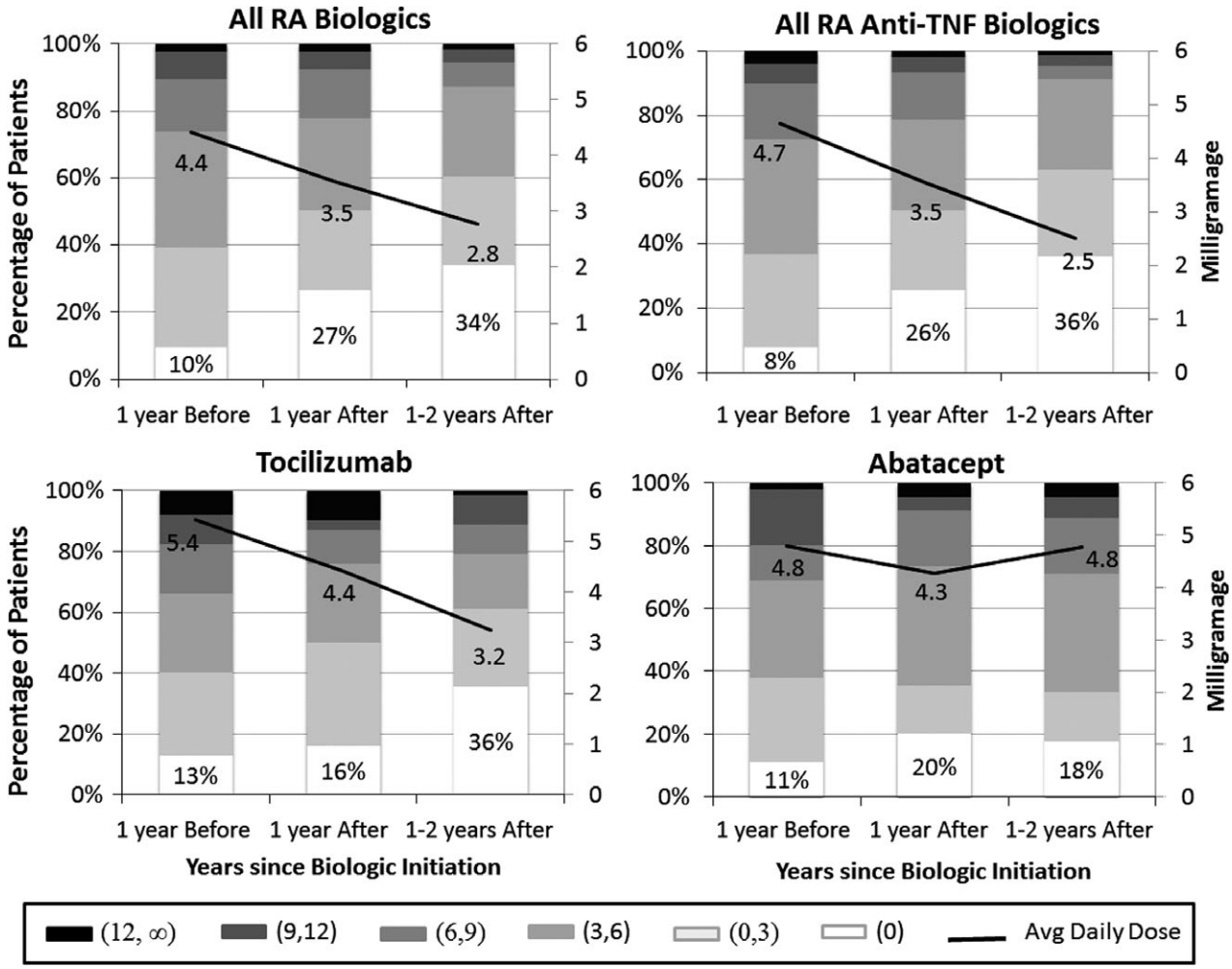

Figure 2 Average daily glucocorticoid consumption in patients taking a bDMARD in any setting (combination and as monotherapy). bDMARD, biologic disease-modifying antirheumatic drugs.

glucocorticoid usage over time in Australian RA patients. Our results have shown that, in the real-world clinical practice setting, Australian RA patients have high persistence rates on bDMARDs, with tocilizumab having the highest persistence rates at 12 months post-treatment initiation, followed by abatacept then SC-anti-TNFs therapy. Persistence on tocilizumab was consistent and independent of co-medication status and the line of treatment. Superior persistence for both abatacept and tocilizumab over SC-anti-TNFs was observed in the first-line setting. The persistence on abatacept and SC-anti-TNFs decreased in the second- and third-line settings, whereas the persistence on tocilizumab remained relatively stable.

Persistence on treatment has been identified as a surrogate for treatment effectiveness;[2–6] however, in the absence of patient level data in our study, it is not possible to determine whether these results are consistent with the published data reflecting real-world efficacy or representative of the underlying characteristics of specific patient populations receiving specific treatments as restricted under the Australian funding rules for bDMARDs.[24,25]

Our results are consistent with a recent study by Johnston *et al.*, although their investigated population was limited to patients who had received at least one previous bDMARD.[26] The persistence rates on SC-anti-TNFs were lower in Australian RA patient than previously reported.[10, 27] The observed persistence rates for abatacept at 12 months are higher than those reported for the German RA patients (Australia 63% *vs.* Germany 50%), while persistence rates on infliximab were lower

Table 4 Proportion of patients with glucocorticoids dose changes from 1 year before to 1 and 1–2 years after initiation of bDMARDs.

	Time period	*n*	Increased *n* (%)	Decreased *n* (%)	No change *n* (%)
All RA bDMARDs	1 year after	230	72 (31)	137 (60)	21 (9)
	>1–2 years after	230	63 (27)	149 (65)	18 (8)
All RA anti-TNF	1 year after	145	46 (32)	90 (62)	9 (6)
	>1–2 years after	145	34 (23)	101 (70)	10 (7)
Abatacept	1 year after	45	19 (42)	21 (47)	5 (11)
	>1–2 years after	45	18 (40)	23 (51)	4 (9)
Tocilizumab	1 year after	62	23 (37)	34 (55)	5 (8)
	>1–2 years after	62	14 (23)	43 (69)	5 (8)

bDMARD, biologic disease-modifying antirheumatic drugs; RA, rheumatoid arthritis; anti-TNF, anti-tumor necrosis factor.

for the Australian RA patients (Australia 36% *vs*. Germany 48%).[28] The pattern for lower persistence rates on infliximab versus SC-anti-TNFs is consistent with that reported for Swedish RA patients.[10] The persistence rates appear to decrease in our study with the line of treatment for abatacept and SC-anti-TNFs, which is in contrast with the recently published Danish registry data.[29] Persistence rates on tocilizumab were higher regardless of the line of treatment or concomitant medications status, unlike the study by Gabay *et al.*,[7] which showed that persistence on tocilizumab was higher when administered in combination with cDMARDs. The 12-month persistence rates were slightly lower than what was reported in the Japanese registry data.[8]

Of the patients taking abatacept, a higher proportion was in the over 65 years age group, compared to other bDMARDs. This might be due to a perception that it is safer than other bDMARDs, although available data do not support this.[30,31] Despite the fact that it is not reimbursed in Australia as monotherapy, abatacept appears to be used as a monotherapy in approximately 22% of the abatacept-treated patients. Similar results were seen for infliximab.

In the Australian setting, the mean dose of glucocorticoids decreases in the 2 years after commencing a bDMARD. This was most obvious for tocilizumab and SC-anti-TNFs. While the majority of patients decrease their dose of glucocorticoid, a proportion (31%) had an increase in dose over time. It is not possible to determine the reasons for this due to the nature of the study as the medical histories of the patients are absent. It is also noteworthy that the only patients included in these analyses were concession card holders. To qualify for a concession card the patient must meet specific socioeconomic criteria which in itself may define a population of patients with higher social stress and comorbidity than those with greater economic resources. These findings regarding corticosteroids therefore may not be generalizable to the overall population.

Strengths of this study include the population-based Australia-wide data with random sample of both public and private use. In addition, results seemed robust if we varied the year of observation (data not shown).

The study has some limitations, being retrospective and observational. The data represents a sample population of prescribing patterns with no individual level patient medical history to confirm derived comparative effectiveness of the assessed therapies or the role of any associated toxicities. We acknowledge that there may be a greater likelihood of a switch between TNF agents due to intolerance, whereas it is less likely to switch patients from a novel drug class (tocilizumab, abatacept) due to minor toxicities or patient preference. The analyzed data were only available for scripts filled and not confirmed to be taken by the patients. Finally, there were small numbers of patients on infliximab, leading to some uncertainty around its short persistence.

CONCLUSION

In the Australian clinical practice setting treatment persistence was longer on tocilizumab followed by abatacept, then SC-anti-TNFs therapy and was influenced by co-therapy. Glucocorticoid dosage decreased with bDMARD use.

AUTHOR CONTRIBUTIONS

All authors were involved in the study design and interpreting the data, drafting the article and revising it critically for important intellectual content and gave final approval of the version to be published. All authors agree to be accountable for all aspects of the work.

ACKNOWLEDGMENTS

Medical writing assistance was provided by Dr Joseline Ojaimi from Roche.

Funding: the study was supported by Roche Products Pty Ltd (Australia).

CONFLICT OF INTEREST DISCLOSURES

G. Jones: receives funds from the National Health and Medical Research Council and is a speaker, consultant or clinical triallist for the following companies that make biological agents: Sanofi-Aventis, AbbVie, Janssen, Pfizer, Roche, Eli-Lilly, Amgen, Bristol–Myers Squibb and UCB; S. Hall: none declared; P. Bird: has received consultancy fees, outside the submitted work, from AbbVie, Eli-Lilly, Roche, UCB, Wyeth, Bristol-Myers Squibb and MSD; G. Littlejohn: reports consulting fees for activities outside the submitted work from AbbVie, Bristol-Myers Squibb, Celgene, Pfizer, Roche and UCB; K. Tymms: none declared; P. Youssef: none declared; E. Chung: consultant for: Roche Products Pty Limited; R. Barrett and P. Button: employees of Roche Products Pty Limited.

REFERENCES

1 Smolen JS, Landewe R, Breedveld FC *et al.* (2014) EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. *Ann Rheum Dis* **73**, 492–509.

2 Greenberg JD, Reed G, Decktor D *et al.* (2012) A comparative effectiveness study of adalimumab, etanercept and infliximab in biologically naive and switched rheumatoid arthritis patients: results from the US CORRONA registry. *Ann Rheum Dis* **71**, 1134–42.

3 Choy EH, Smith C, Dore CJ, Scott DL (2005) A meta-analysis of the efficacy and toxicity of combining disease-modifying anti-rheumatic drugs in rheumatoid arthritis based on patient withdrawal. *Rheumatology (Oxford)* **44**, 1414–21.

4 Geborek P, Crnkic M, Petersson IF, Saxne T (2002) Etanercept, infliximab, and leflunomide in established rheumatoid arthritis: clinical experience using a structured follow up programme in southern Sweden. *Ann Rheum Dis* **61**, 793–8.

5 Hetland ML, Christensen IJ, Tarp U *et al.* (2010) Direct comparison of treatment responses, remission rates, and drug adherence in patients with rheumatoid arthritis treated with adalimumab, etanercept, or infliximab: results from eight years of surveillance of clinical practice in the nationwide Danish DANBIO registry. *Arthritis Rheum* **62**, 22–32.

6 Salaffi F, Carotti M, Di Carlo M, Farah S (2015) Adherence to anti-tumor necrosis factor therapy administered subcutaneously and associated factors in patients with rheumatoid arthritis. *J Clin Rheumatol* **21**, 419–25.

7 Gabay C, Riek M, Hetland ML *et al.* (2016) Effectiveness of tocilizumab with and without synthetic disease-modifying antirheumatic drugs in rheumatoid arthritis: results from a European collaborative study. *Ann Rheum Dis* **75**, 1336–42.

8 Hishitani Y, Ogata A, Shima Y *et al.* (2013) Retention of tocilizumab and anti-tumour necrosis factor drugs in the treatment of rheumatoid arthritis. *Scand J Rheumatol* **42**, 253–9.

9 Leffers HC, Ostergaard M, Glintborg B *et al.* (2011) Efficacy of abatacept and tocilizumab in patients with rheumatoid arthritis treated in clinical practice: results from the nationwide Danish DANBIO registry. *Ann Rheum Dis* **70**, 1216–22.

10 Neovius M, Arkema EV, Olsson H *et al.* (2015) Drug survival on TNF inhibitors in patients with rheumatoid arthritis comparison of adalimumab, etanercept and infliximab. *Ann Rheum Dis* **74**, 354–60.

11 Tanaka T, Hishitani Y, Ogata A (2014) Monoclonal antibodies in rheumatoid arthritis: comparative effectiveness of tocilizumab with tumor necrosis factor inhibitors. *Biologics* **8**, 141–53.

12 Rotar Z, Hocevar A, Rebolj Kodre A, Praprotnik S, Tomsic M (2015) Retention of the second-line biologic disease-modifying antirheumatic drugs in patients with rheumatoid arthritis failing one tumor necrosis factor alpha inhibitor: data from the BioRx.si registry. *Clin Rheumatol* **34**, 1787–93.

13 Roberts L, Tymms K, de Jager J *et al.* (2013) A longitudinal study of the clinical effects of conventional and biologic disease modifying anti-rheumatic drugs in Australian rheumatology practice. Australian Rheumatology Association, 54th Annual Scientific Meeting; 18–22 May Perth, WA, Australia.

14 Gorter SL, Bijlsma JW, Cutolo M *et al.* (2010) Current evidence for the management of rheumatoid arthritis with glucocorticoids: a systematic literature review informing the EULAR recommendations for the management of rheumatoid arthritis. *Ann Rheum Dis [Review]* **69**, 1010–4.

15 Smolen JS, Landewe R, Breedveld FC *et al.* (2010) EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs. *Ann Rheum Dis* **69**, 964–75.

16 Duru N, van der Goes MC, Jacobs JW *et al.* (2013) EULAR evidence-based and consensus-based recommendations on the management of medium to high-dose glucocorticoid therapy in rheumatic diseases. *Ann Rheum Dis* **72**, 1905–13.

17 Hoes JN, Jacobs JW, Verstappen SM, Bijlsma JW, Van der Heijden GJ (2009) Adverse events of low- to medium-dose

oral glucocorticoids in inflammatory diseases: a meta-analysis. *Ann Rheum Dis* **68**, 1833–8.
18 Grijalva CG, Kaltenbach L, Arbogast PG, Mitchel EF Jr, Griffin MR (2010) Initiation of rheumatoid arthritis treatments and the risk of serious infections. *Rheumatology (Oxford)* **49**, 82–90.
19 Seror R, Dougados M, Gossec L (2009) Glucocorticoid sparing effect of tumour necrosis factor alpha inhibitors in rheumatoid arthritis in real life practice. *Clin Exp Rheumatol* **27**, 807–13.
20 Naumann L, Huscher D, Detert J, Spengler M, Burmester GR, Buttgereit F (2009) Anti-tumour necrosis factor alpha therapy in patients with rheumatoid arthritis results in a significant and long-lasting decrease of concomitant glucocorticoid treatment. *Ann Rheum Dis* **68**, 1934–6.
21 Nilsson AC, Christensen AF, Junker P, Lindegaard HM (2011) Tumour necrosis factor-alpha inhibitors are glucocorticoid-sparing in rheumatoid arthritis. *Dan Med Bull* **58**, A4257.
22 Fortunet C, Pers YM, Lambert J *et al.* (2015) Tocilizumab induces corticosteroid sparing in rheumatoid arthritis patients in clinical practice. *Rheumatology (Oxford)* **54**, 672–7.
23 Saraux A, Rouanet S, Flipo RM *et al.* (2016) Glucocorticoid-sparing in patients suffering from rheumatoid arthritis and treated with tocilizumab: the SPARE-1 study. *Clin Exp Rheumatol* **34**, 303–10.
24 Australian Government. Rheumatoid arthritis. [Web Page] [cited December 2016]; Available from: https://www.humanservices.gov.au/health-professionals/enablers/rheumatoid-arthritis#a2. Accessed September 2017.
25 Australian Government. Schedule of Pharmaceutical Benefits[Cited December 2014]. Available from http://www.pbs.gov.au/publication/schedule/2014/12/2014–12–01-general-schedule.pdf. In: Department of Health, editor. Accessed September 2017
26 Johnston SS, McMorrow D, Farr AM, Juneau P (2015) Comparison of biologic disease-modifying antirheumatic drug therapy persistence between biologics among rheumatoid arthritis patients switching from another biologic. *Rheumatol Ther* **2**, 59–71.
27 Soliman MM, Ashcroft DM, Watson KD, Lunt M, Symmons DP, Hyrich KL (2011) Impact of concomitant use of DMARDs on the persistence with anti-TNF therapies in patients with rheumatoid arthritis: results from the British Society for Rheumatology Biologics Register. *Ann Rheum Dis* **70**, 583–9.
28 Neubauer S, Cifaldi M, Mittendorf T, Ganguli A, Wolff M, Zeidler J (2014) Biologic TNF inhibiting agents for treatment of rheumatoid arthritis: persistence and dosing patterns in Germany. *Health Econ Rev* **4**, 32.
29 Jorgensen TS, Kristensen LE, Christensen R *et al.* (2015) Effectiveness and drug adherence of biologic monotherapy in routine care of patients with rheumatoid arthritis: a cohort study of patients registered in the Danish biologics registry. *Rheumatology (Oxford)* **54**, 2156–65.
30 Singh JA, Hossain A, Tanjong Ghogomu E, Mudano AS, Tugwell P, Wells GA (2016) Biologic or tofacitinib monotherapy for rheumatoid arthritis in people with traditional disease-modifying anti-rheumatic drug (DMARD) failure: a Cochrane Systematic Review and network meta-analysis (NMA). *Cochrane Database Syst Rev* **11**, CD012437.
31 Weinblatt ME, Schiff M, Valente R *et al.* (2013) Head-to-head comparison of subcutaneous abatacept versus adalimumab for rheumatoid arthritis: findings of a phase IIIb, multinational, prospective, randomized study. *Arthritis Rheum* **65**, 28–38.