AB0397 ABATACEPT SHOWS BETTER SUSTAINABILITY THAN TNF INHIBITORS WHEN USED FOLLOWING INITIAL BIOLOGIC DMARD FAILURE IN THE TREATMENT OF RHEUMATOID ARTHRITIS: 8 YEARS OF REAL-WORLD OBSERVATIONS FROM THE RHUMADATA® CLINICAL DATABASE AND REGISTRY

D. Choquette[1], L. Bessette[2], E. Alemao[3], B. Haraoui[1], F. Massicotte[1], M. Mtibaa[4], E. Muratti[4], J.-P. Pelletier[1], R. Postema[5], J.-P. Raynauld[1], M.-A. Rémillard[1], D. Sauvageau[1], A. Turcotte[2], É. Villeneuve[1], L. Coupal[1]. *[1]Rheumatology, Institut de recherche en rhumatologie de Montréal (IRRM), Montréal; [2]Rheumatology, Centre d'ostéoporose et de rhumatologie de Québec (CORQ), Québec, Canada; [3]Bristol-Myers Squibb, Princeton, United States; [4]Bristol-Myers Squibb, Montréal, Canada; [5]Bristol-Myers Squibb, Uxbridge, United Kingdom*

Background: In the absence of biomarkers predicting response to a specific therapy, the choice of second biologic is based mostly on habit and availability of an alternative agent. Traditionally, a second anti-TNF was the preferred option, but recent registry data point to better responses and retention if a drug with a different mode of action is prescribed.
Objectives: Assess the long-term retention of abatacept (ABA) and TNFi following first biologic (b)DMARD inadequate response in RHUMADATA® registry patients (pts) with RA.
Methods: Data from RHUMADATA® pts with RA prescribed either ABA or TNFi as the second bDMARD after 1 January 2006 were analysed. Pts were followed until treatment discontinuation or 9 January 2017 cut-off. Pt characteristics were compared using descriptive statistics, bDMARD discontinuation rates using Kaplan-Meier methods, and proportional hazard models were used to identify predictors of treatment discontinuation.
Results: Data for 92 and 194 pts prescribed ABA or a TNFi, respectively, as second-line treatment were extracted. No clinically significant differences in baseline characteristics were noted between treatment groups. Most pts were women (76.2%), average age (SD) was 45.1 (13.3) years at diagnosis and disease duration 10.8 (9.0) years. Most pts were stopping an anti-TNF agent: 97% of those who were switched to ABA and 83% of those who were prescribed a second anti-TNF. Overall, 77.6% of pts stopped their first bDMARD after >6 months of treatment (secondary failure). Significant differences in retention between ABA and TNFi groups (log-rank p=0.0002) were observed (Table, Figure). Results remained unchanged for pts treated with TNFi only in first line, and primary/secondary failure of the first bDMARD did not affect sustainability of the second agent. Lack of efficacy (57.7%) and AEs (16.5%) were the most commonly cited reasons for treatment discontinuation.
Conclusions: Abatacept has better sustainability over a second line TNFi in RA patients having failed one prior bDMARD.
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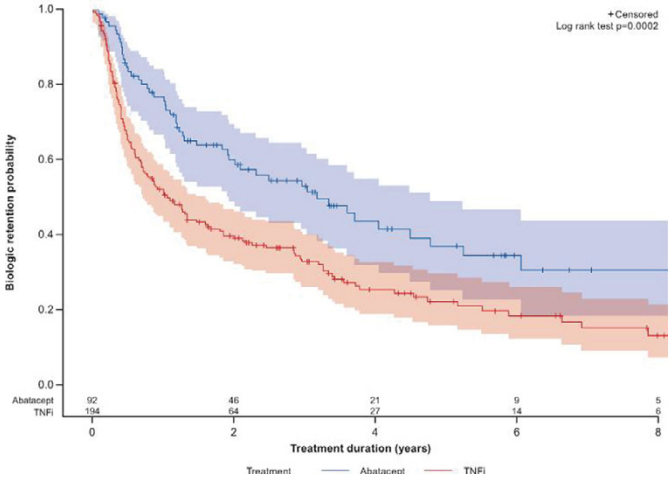
Table 1. First bDMARD failure and retention characteristics of the second bDMARD

First bDMARD Failed	Second bDMARD					
	TNFi			Abatacept		
	Failure type		All	Failure type		All
	Primary	Secondary		Primary	Secondary	
TNF inhibitor, n, %	41, 25.5%	120, 74.5%	161, 100%	17, 19.1%	72, 80.9%	89, 100%
Other mode of action	6, 18.2%	27, 81.8%	33, 100%	0, 0%	3, 100%	3, 100%
Total	47, 24.2%	147, 75.8%	194, 100%	17, 18.5%	75, 81.5%	92, 100%
Second bDMARD Retention Probability at[1]:						
6 Months	64.68% (3.45%)			83.51% (3.89%)		
12 Months	50.54% (3.61%)			76.73% (4.45%)		
24 Months	39.77% (3.59%)			59.97% (5.29%)		
60 Months	22.26% (3.53%)			36.95% (6.17%)		
96 Months	13.22% (3.62%)			30.66% (6.61%)		
Biologic Retention Time (years)						
Mean, mean (SE)	2.71 (0.25)			3.33 (0.26)		
Lower Quartile (95% CI)	0.36 (0.28–0.44)			1.02 (0.49–1.29)		
Median (95% CI)	1.08 (0.71–1.60)			3.17 (1.92–4.78)		
Upper Quartile (95% CI)	4.26 (3.25–6.64)			++ (5.24-++)		

[1]% survival (standard error of % survival).

Figure. Retention Rates of Abatacept and TNFi Groups



AB0398 IMPACT OF BODY COMPOSITION ON RESPONSE TO BIOTHERAPY IN RHEUMATOID ARTHRITIS

S. Bouden, D. Kaffel, W. Hamdi[1,1], M.M. Kchir. *Rheumatology, Institut kassab, tunis, Tunisia*

Background: Biological therapies had greatly improved the treatment of rheumatoid arthritis (RA). The response to biologics may be influenced by many factors. Little is known about the impact of body composition inRA biologics.
Objectives: We aimed to investigate the impact of obesity (BMI≥30) andbody composition (lean mass/ fat mass)on response to biotherapy in RA.
Methods: A retrospective study was performed over a period of 11 years (2006–2016). Patients diagnosed RA (according to the ACR 1987 criteria) and treated by biologics were enrolled. Body composition (lean mass/ fat mass) was measured by X-ray biphotonic absorption (DXA). The threshold of signification was set for a value of $p<0.05$.
Results: Fifty patients were enrolled, including 5 men and 45 women (sex ratio=0.11). The mean age was 66 years [38–79]. The mean duration of RA was 5 years [1–30]. The mean duration of treatment with biologics was 38 months [6–120]. Thirty nine patients were treated by TNF alpha inhibitors (25 etanercept, 7 adalimumab, 6 infliximab and 1 certolizumabpegol), 6 rituximab and 5 tocilizumab. Nine patients had a normal weight (18%), 17 had overweight (34%) and 24 had obesity (49%). The average percentage of fat mass was 44.8 [23–54], with a median of 46. While comparing obese patients with others, we did not notice a significant difference in the mean variation of the DAS28 at 6 months for TNF alpha inhibitors nor for all biotherapies combined (respectively p=0.6 and p=0.9). The same result was observed while comparing the DAS28 according to the body composition (relative to the median of the percentage of the fat mass: for TNF alpha inhibitors (p=0,6) and for all biotherapies combined (p=0,09)).
Conclusions: In our study, there was no change in response to biologics in patients with RA. Further prospective studies with a larger size will be required to confirm or reverse these results.
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AB0399 RITUXIMAB TREATMENT AND IMMUNOGLOBULIN LEVELS MONITORING

G. Kasavkar, S. Kamath. *Rheumatology, Haywood hospital, Stoke on Trent, United Kingdom*

Background: Rheumatoid arthritis is a well-known inflammatory condition with a prevalence around 1% in females and 0.5% in males in UK (as per NOAR study). In the past decade use of biologic therapy has helped clinicians to treat rheumatoid arthritis more effectively. Rituximab is one of the biologics which is used commonly for treating rheumatoid arthritis. Rituximab is chimeric monoclonal antibody targeting CD20 molecule of B cells. First trial of rituximab in treating rheumatoid arthritis was published in 2004 and since then it has shown promising results in trials. In order to guide clinicians British society of rheumatology proposed recommendations in March 2010. An audit is required to ensure adherence to clinical guidelines at Haywood hospital.
Objectives: To assess whether patients receiving Rituximab are appropriately monitored with pretherapy evaluation of immunoglobulin levels

To assess the effects of rituximab on immunoglobulin levels and incidence of infection among patients on rituximab
Methods: Data was collected of all (N=105) patients who received Rituximab between May 2014 until April 2015 at the Haywood Hospital where patients attend for Rituximab injections.
Data was collected retrospectively from the Diamond System, Medisec system and Clinical Information System and entered onto an excel spread sheet which included following details
- Start date of Rituximab
- IgG levels prior to Rituximab and current IgG levels
- Total doses of rituximab and frequency of IgG monitoring
- Intermittent infections and type of infections.

Results: We observed that 82 out of 105 patients were started on rituximab after February 2011 when the BSR guidance was published and 53 out of 105 patients had their immunoglobulin levels checked prior to commencing rituximab
35/76 (46%) patients had 1 or more episodes of infections whilst on Rituximab which required treatment. Of these, 16 (46%) had recurrent infections.
39 patients had dropped their IgG levels after starting rituximab 18 (46%) of these suffered from infections.
17 patients had a drop in IgG ≥20% and 6 of these (36%) had recurrent infections and 1 patient had 1 episode of infection.
None of the patients had dropped their IgG levels below 5
Conclusions: A significant number of patients (35/76 =46%) had 1 or more episodes of infections despite IgG levels being above lower normal limit
Among patients who dropped their IgG levels had increased number infections. Also they had more than 1 episodes of infection
Patients who dropped IgG levels ≥20% suffered with recurrent infections
References:
[1] BSR and BHPR guidelines on the use of rituximab in rheumatoid arthritis doi:10.1093/rheumatology/ker106b.
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AB0400 EFFICACY AND SAFETY OF INTRAVENOUS AND SUBCUTANEOUS TOCILIZUMAB IN A COHORT OF PATIENTS AFFECTED BY RHEUMATOID ARTHRITIS IN REAL-LIFE

G. Pomponio, C. Tontini, A. Angeletti, D. Olivari, D. Benfaremo, L. Manfredi, M.G. Danieli, P. Fraticelli, M.M. Luchetti, G. Moroncini, A. Gabrielli. *Department of Internal Medicine, Azienda Ospedaliero-universitaria 'Ospedali Riuniti', Ancona, Italy*

Background: Tocilizumab (TCZ) is a humanized monoclonal anti-interleukin-6 receptor antibody, used for the treatment of moderate to severe rheumatoid arthritis (RA). Although TCZ has been proved to be highly effective and safe in RA patients in large clinical trials, few data are available from real-life practice [1].
Objectives: To evaluate efficacy, safety and retention rate of intravenous (IV) and subcutaneous (SC) TCZ in a real-world setting.
Methods: We evaluated patients affected by moderate-to-severe RA and treated with TCZ from April 2010 to January 2017. Data of patients treated with IV-TCZ until January 2017 were collected retrospectively, while patients treated with either IV or SC-TCZ from January 2015 were included in a prospective cohort and assessed for disease activity, treatment discontinuation and/or onset of adverse events (AEs). DAS28-CRP, CDAI and SDAI scores were used for disease activity assessment and paired t test was used for statistical analysis. Treatment retention rate was estimated by Kaplan-Meier method.
Results: We evaluated 100 patients, 58 treated with IV-TCZ (8 mg/kg every 4w), 16 with SC-TCZ (162 mg every week), 26 switched from IV to SC during followup and 6 of these returned to IV-TCZ for cutaneous intolerance (80 females, median age 63 y, median duration of disease 11 y, median follow-up 16 months). Seventy-eight patients (78%) were treated with monotherapy and twenty-two (22%) in combination with methotrexate. At baseline, disease activity was severe in 87% of patients, moderate in 6% and mild or inactive in 7%; at the latest follow-up 60% of patients are in clinical remission. The mean DAS28-CRP in IV-TCZ and SW-TCZ groups considered as a whole was 4.34 at baseline and 2.71 at the latest follow-up available ($p<0.0001$). In the SC-TCZ group, mean basal DAS28-CRP was 3.70 vs 1.89 measured at the latest follow-up ($p<0.0001$). Fifty-three patients (53%) discontinued TCZ because of inefficacy (19), AEs (13) or other reasons (21, mostly lost to follow-up). Infections were the most frequent AE (45.1/100 person-years), 3 cases of severe pneumonia, one required treatment discontinuation. Infusion reactions were reported in 6/58 IV-TCZ patients, while injection site reactions in 14/42 SC-TCZ patients. Six of these intolerant patients were subsequently treated with i.v. tocilizumab without reactions. We observed an overall high retention rate of IV-TCZ and SW-TCZ (91.1%, 81.2%, 70.6%, 61.3%, 57.1% and 50% at 1, 2, 3, 4, 5, and 6 years respectively). The retention rate of SC-TCZ patients at 3 years was about 77%. The difference between IV/SW-TCZ and SC-TCZ groups was not significant (Fig. 2).
Conclusions: TCZ is effective, well tolerated and safe in a population of RA patients followed in a real-life setting.
No unexpected AE was observed in this large population followed for a long period. Interestingly retention rate was not affected by the administration route and in real life many patients can safely shift across different administration modalities.
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AB0401 THE EFFICENT REGULATION OF TOCILIZUMAB FOR THE EXPRESSION OF CD4+/CD8+ T/CD19 + B CELLS AND THE IMMUNOGLOBULIN IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

H. Li[1], H. Zeng[2]. *[1]Department of Pediatric Allergy, Immunology and Rheumatolog; [2]Department of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Objectives: To study the influence of tocilizumab on lymphocyte subsets, immunoglobulin and biochemical indicators of Systemic juvenile idiopathic arthritis.
Methods: DMARDs poor efficacy in children with severe SJIA 18 patients were divided into two groups, of which eight patients tocilizumab + DMARDs group (in cluding a case of refractory MAS), 10 patients in the placebo + DMARDs control group, according to the weight>30kg, 8mg/kg, <30kg, 12mg/kg, injected once every two weeks in hospital.Symptoms and CD3 +, CD4 +, CD8 + T, CD19 + B, CD16 + 56-NK cell ratio in two groups were observed by the flow cytometry before or after 12 weeks treatment. Comparing immunoglobulin IgG, IgM, IgA, IgE with baseline after the therepy in two group, and continuous observe inflammatory markers (CRP, ESR, FER, WBC) and ALT/AST changes, adverse reactions and reduce stopping hormone case inductive analysis in following 12 weeks.
Results: After 12 weeks, tocilizumab + DMARDs group, CRP, ESR, FER were significantly decreased, the most frequently occurring adverse reaction was infection, mostly upper respiratory tract infection, followed by elevated transaminase, cholesterol, low-density lipoprotein High-density lipoprotein and triglyceride levels increased; two groups no serious adverse events (three-line reduction, severe infections, etc.). the proportion of CD4 + T, CD19 + B cells in Tocilizumab group were lower than baseline ($P<0.05$), CD8, CD3 + T cells were increased in comparing with baseline, however,no significant change with CD16 + 56-NK cells ($P>0.05$), and immunoglobulins IgG, IgM, IgA lower than baseline ($P<0.05$). The control group had no significant difference ($P>0.05$).
Conclusions: Tocilizumab can significantly reduce inflammatory markers (CRP, ESR, FER), but affect lipid metabolism and ALT/AST.Blocking IL-6 can be adjusted hyperthyroidism humoral and regulate CD4 + T, CD19 + B cells, reduce joint destruction. Tocilizumab can effectively control the development of DMARDs poor efficacy SJIA.
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AB0402 RITUXIMAB MAY DELAY THE MOVEMENT OF RHEUMATOID ARTHRITIS PATIENTS ON CARDIORENAL CONTINUUM: RESULTS FROM A PROSPECTIVE OBSERVATIONAL SINGLE-CENTRE COHORT STUDY

I.R. Gaisin[1], L.V. Ivanova[2], A.A. Trukchina[2], A.A. Tukmacheva[2], Y.A. Volkova[1], A.A. Tebenkova[1], N.I. Maximov[1]. *[1]Izhevsk State Medical Academy; [2]Clinical Diagnostic Centre of the Udmurt Republic, Izhevsk, Russian Federation*

Background: Similarities in risk factors, initial stages, progression and final stage of both atherosclerotic cardiovascular disease (CVD) and chronic kidney disease (CKD) allowed formulating a concept of cardiorenal continuum.[1] CVD and CKD remain the main causes of mortality in rheumatoid arthritis (RA) patients.[2,3]
Objectives: We aimed to evaluate the effects of rituximab biologic therapy on cardiorenal continuum of RA patients.
Methods: Biologics-naïve RA patients (n=50; age 55.1±10.3) were followed up for 72 months after commencing and continuing rituximab therapy (1–10 standard courses) compared with 30 control RA patients (age 53.2±9.8).
Results: At year 6, rituximab patients have fewer incidences of hypertension, anxiety/depression, atherosclerosis and diastolic dysfunction than control patients (Table).
There were no significant differences in frequencies of other risk factors, signs of asymptomatic multiorgan damage and cases of established heart, cerebrovascular and renal diseases/complications.
Conclusions: Rituximab may be effective in delay of the movement of RA patients on cardiorenal continuum. The clinical implications of rituximab for cardiorenal correlations in RA patients need to be confirmed in large-scale clinical outcome trials.
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