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POS0643

ARE BIOLOGIC AND TARGETED SYNTHETIC DMARDS SAFE TO USE IN PATIENTS WITH RENAL IMPAIRMENT?

F. Rees¹, M. Jasim¹. ¹ Cannock Chase Hospital, Rheumatology, Cannock, United Kingdom

Background: Chronic kidney disease (CKD) is defined as a permanent (minimum three month) reduction in glomerular filtration rate.^[1] 10-30% of rheumatoid arthritis (RA) patients have CKD, compared to 5% of the general population.^[1] There are several causes of CKD associated with RA including persistent inflammation, cardiovascular risk factors, frequent use of non-steroidal anti-inflammatory drugs and amyloidosis.^[1] CKD in RA patients is associated with increased mortality.^[2]

The use of biologic and targeted synthetic DMARDs for treating RA has increased significantly in recent years. Studies have shown these therapies might reduce the risk of developing CKD in RA.^[3] However, conversely, biologics have been linked to the development of glomerulonephritis.^[4]

Surprisingly few studies have explored the use of biologics in patients with pre-existing renal disease and whether they contribute to renal impairment themselves.

Objectives: Our objectives were to explore the renal safety profile of biologic and targeted synthetic DMARDs in a real-world cohort of RA patients with and without pre-existing CKD.

Methods: A retrospective observational study was completed using the Biologic Therapy Database at Cannock Chase Hospital. Inclusion criteria were a diagnosis of RA and current treatment with a biologic or targeted synthetic DMARD.

Demographic data, renal function at biologic initiation and any deterioration of renal function were among the recorded information for each patient. Patients with insufficient information available via electronic patient records were excluded.

Results: 998 RA patients on biologics were identified, of whom 213 were excluded. Of the 785 remaining patients, a 3:1 female to male ratio was noted with a mean age of 62. 40% of patients were on an anti-TNF, 22% rituximab, 15% abatacept, 15% JAK inhibitors and 9% anti-IL6 respectively. At biologic initiation 92% of the patients had a GFR of >60 ml/min per 1.73m², 4.8% had a GFR of 30-60 (CKD stage 3a-3b), <1% stage 4 CKD. No patients in the cohort had CKD stage 5 at biologic initiation.

Overall, 13 patients had significant pre-existing CKD (eGFR <45) of these, 6 were treated with abatacept. 7/13 patients had no co-morbid risk factors for CKD – of those remaining, 2 were hypertensive, 2 diabetic and 2 both. None of these 13 patients experienced a drop in renal function by more than 1 stage since initiation of current biologic.

Of those patients without prior CKD at the point of biologic initiation (GFR >45), only 15 patients (2%) developed new renal impairment whilst on biologic treatment. 10 patients' renal function dropped by one stage and five patients by two stages. Crucially, 12 of the 15 patients were aged ≥75yrs and 10 patients had at least one other associated risk factor (e.g. diabetes). Only one patient in the cohort developed renal impairment as a direct result of a biologic – minimal-change disease secondary to etanercept.

Conclusion: Our findings indicate that biologic treatments have a good renal safety profile – even with pre-existing CKD. RA patients most at risk of developing CKD whilst on biologics are likely to have other risk factors such as diabetes or hypertension. As previously stated, there is a very rare association of anti-TNF biologics causing glomerulonephritis.

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AIR POLLUTION IS A PREDICTOR OF POOR RESPONSE TO BIOLOGICAL THERAPIES IN CHRONIC INFLAMMATORY ARTHRITIDES

G. Adami¹, D. Gatti¹, A. Fassio¹, O. Viapiana¹, A. Giollo¹, E. Bertoldo¹, M. Rossini¹. ¹ University of Verona, Rheumatology Unit, Verona, Italy

Background: There is increasingly evidence that environmental air pollution is associated with both development of chronic inflammatory arthritides (CIA). The role of air pollutants on the treatment response of CIA (including psoriatic arthritis [PsA] and ankylosing spondylitis [AS]) is still unclear.

Objectives: The objective of the present study is to determine the association between the concentration of air pollutants and biological drug retention rates in CIA.

Methods: We retrieved longitudinal data of patients affected by CIA on biological therapies and of the daily concentration of air pollutants in the Verona area. We designed a case-crossover study to compare the exposure to pollutants in the 30-day and 60-day periods preceding a drug switch or swap due to disease progression referent to the 30-day and 60-day periods preceding a visit with stable treatment for at least 6 months.

Results: 1,286 patients with CIA (888 with RA, 260 with PsA and 138 with AS) with 5,454 follow-up visits were included in the study. 13,636 daily air pollution records were retrieved. We found an exposure-dependent relationship between exposure to air pollutants and CRP serum levels in CIA. At PM10 exposures of >50 µg/m³ and >40 µg/m³ we found a 150% and 65% higher risk of having CRP above 5 mg/L respectively (OR 2.564, 95% CI 2.114-3.110 and OR 1.659, 95% CI 1.440-1.910, respectively). If the threshold was set at >30 µg/m³ of PM10 (below the European Union health protection limit) we still found a 38% higher risk of having altered CRP (OR 1.383, 95% CI 1.206-1.588). Among CIA patients, 280 patients (21.7%) had at least 2 follow-up visits with at least one drug switch or swap due to drug inefficacy and one visit with stable treatment for at least 6 months, serving as our sample for the case-crossover study. We found that air pollutants concentrations were higher before a switch or swap due to drug inefficacy (Figure 1A). Figure 1B shows the receiver operating characteristic (ROC) curve for the prediction of switch or swap due to drug inefficacy. Discriminatory capacity of disease activity alone was the highest (AUC 0.841) but when the prediction model included the concentrations of air pollutants in the 60 days before the visit the discriminatory capacity increased (AUC 0.879).

Conclusion: We found that environmental air pollution was a determinant of poor response to biological treatment in a cohort of patients with CIA followed over a 5-year period. Intervention aimed to decrease the fossil combustion emissions might have beneficial effects on biologics persistence rate of patients with CIA.

Figure 1. A) Mean concentrations of air pollutants in the 60-day period before switch or swap visit compared to the stable treatment visit. p <0.001 between all groups. B) Receiving operating characteristics (ROC) curves for the prediction of switch or swap due to drug inefficacy

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POS0645

RITUXIMAB THERAPY IN THE INTERSTITIAL LUNG DISEASE OF RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

E. F. Vicente-Rabareda¹, J. De la Macorra¹, J. P. Baldivieso¹, F. Gutiérrez-Rodríguez¹, A. García-Vadillo¹, R. García de Vicuña¹, S. Castañeda¹. ¹ Hospital Universitario de la Princesa, IIS-P, Rheumatology, Madrid, Spain

Background: Interstitial lung disease (ILD) is a severe manifestation of rheumatoid arthritis (RA), linked to increased mortality. There is still no consensus on the best therapeutic strategy as there aren't yet randomized controlled trials.

Objectives: To analyze the available scientific evidence on the efficacy and safety of rituximab (RTX) treatment of interstitial lung disease (ILD) associated with rheumatoid arthritis (RA).

Methods: A systematic search was carried out in PubMed until April 2020 following the PRISMA recommendations. Studies were selected according to the

following inclusion criteria: (1) original research, including case series, case/control studies, cohort studies, and clinical trials; (2) population with RA and associated ILD, either monographically or together with other connective tissue diseases (CTD), provided that individualized data on patients with RA were provided; (3) patients treated with RTX; (4) objective and quantifiable results on the evolution of ILD after treatment with available data of FVC, DLCO and/or HRCT.

Results: Of the 64 papers identified, 9 articles were selected. The studies showed great heterogeneity in design, both in the sample selection criteria and in the objectives of the analysis. Most were observational, retrospective ($n = 6$) or prospective ($n = 2$) studies, with only one open prospective experimental study. Those focused on RA predominated, but 3 of them also included patients with other CTDs. The mean age of the patients in the different studies ranged between 52 and 70 years, predominantly women. 40-79% had a history of smoking and were mostly positive for rheumatoid factor (83-100%) and anti-CCP (82-100%). The most frequent radiological patterns were NSIP, UIP and undefined. The outcome measures were diverse: changes in respiratory function tests (LTF) and HRCT, incidence of pulmonary dysfunction, mortality rates, effect on glucocorticoid deprivation, delay in inclusion in the lung transplant list and/or serious adverse events. The initiation of RTX was motivated by pulmonary and/or joint pathology, in patients with failure to other synthetic or biological DMARDs. A total of 393 treatment cycles were collected in 114 patients, with a mean of 3.45 cycles per patient. The RTX regimen was 2 infusions of 1g 2 weeks apart in all patients, except for 1 who received the lymphoma-like regimen. With regard to the efficacy of the treatment with RTX, improvement and especially stabilization of HRCT and LFT predominated, with numerically greater improvement for DLCO than for FVC. There was also a favorable trend in the evolution of patients treated with RTX compared to controls, although it did not reach statistical significance, and a lower risk of deterioration of lung function in patients treated with RTX versus those who had received other DMARDs. The mortality rate found at 5 years was lower than that previously described for the disease and half for the patients treated with RTX compared to those treated with anti-TNF. The adverse events described in the studies did not show additional safety alerts to those already described for RTX.

Conclusion: RTX seems to be postulated as a promising therapy for patients with ILD associated with RA, showing a stabilizing effect on the lung function, with an acceptable safety profile. However, further research of higher methodological quality prospective studies is needed to confirm these favorable preliminary results.

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Rheumatoid arthritis - non biologic treatment and small molecules

POS0646

RAPID AND CONCURRENT IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES OF RHEUMATOID ARTHRITIS WITH BARICITINIB IN RA-BEAM

Y. Strand¹, A. Sebba², B. Jia³, J. Birt³, A. Quebe³, H. Zhang⁴, P. C. Taylor⁵.

¹Stanford University School of Medicine, Division of Immunology/Rheumatology, Palo Alto, United States of America; ²University of South Florida, Department of Rheumatology, Tampa, United States of America; ³Eli Lilly and Company, Lilly Research Laboratories, Indianapolis, United States of America; ⁴TechData Services, Statistics, King of Prussia, United States of America; ⁵University of Oxford, Nuffield Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences and the Kennedy Institute of Rheumatology, Oxford, United Kingdom

Background: The efficacy and safety of baricitinib (BARI), an oral selective Janus kinase (JAK)1/JAK2 inhibitor, were evaluated in the randomized, controlled trial, RA-BEAM (NCT01710358), in patients (pts) with active rheumatoid arthritis (RA) and inadequate responses (IR) to methotrexate (MTX).^{1,2,3}

Objectives: To compare the time to onset and magnitude of improvement across different patient-reported outcomes (PROs) of BARI, adalimumab (ADA) and placebo (PBO) during the first 12 weeks of treatment in RA-BEAM.

Methods: 1,305 patients on stable background MTX were randomized 3:3:2 to PBO, BARI 4mg, or ADA 40mg. In this intent-to-treat analysis, least-squares mean changes and percentage changes from baseline were assessed up to Week 12 for pain (0-100mm visual analog scale [VAS]), SF-36 physical component summary (PCS, 0-100), morning joint stiffness (MJS) severity (0-10), Health Assessment Questionnaire-Disability Index (HAQ-DI, 0-3), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F, 0-52), and Patient Global Assessment of disease activity (PtGA, 0-100mm VAS) scores. PROs were compared between treatments with ANCOVA; the model included change from baseline as the response variable, baseline of interest, regional baseline, joint erosion status, and treatment as explanatory variables. Last-observation-carried-forward

was applied to impute missing data. Speed of onset and magnitude of PRO improvement are presented in spidergrams.

Results: Statistically significant improvements ($P < 0.05$) with BARI and ADA vs. PBO were reported as early as Week 1 for pain, MJS severity, HAQ-DI, and PtGA and at Week 4 for FACIT-F and SF-36 PCS scores. Statistically significantly larger improvements ($P < 0.05$) with BARI vs. ADA were observed as early as Week 2 for pain, PtGA, Week 3 for MJS severity, and Week 4 for HAQ-DI and SF-36 PCS scores. These improvements were maintained to Week 12.

Conclusion: Among MTX-IR pts, BARI and ADA treatment resulted in improvements across all PROs by Week 4, and as early as Week 1, for all but FACIT-F and SF-36 PCS scores. Statistically significant larger improvements for BARI compared with ADA were reported for all PROs, except FACIT-F, by Week 12.

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Table 1. Change from baseline in patient-reported outcomes at Weeks 4 and 12

LSM Change from Baseline	Week 4			Week 12		
	PBO	ADA	BARI	PBO	ADA	BARI
Pain VAS	-12.6	-22.3***	-27.1***††	-17.1	-26.4***	-31.5***†††
SF-36 PCS	3.0	5.7***	6.9***††	4.2	7.2***	8.7***††
MJS severity	-0.9	-1.5***	-1.9***††	-1.4	-2.0***	-2.5***†††
HAQ-DI	-0.26	-0.47***	-0.54***††	-0.34	-0.56***	-0.66***†††
FACIT-F	5.2	6.9**	7.8***	6.7	8.7***	9.1***
PtGA	-14.2	-23.7***	-26.8***††	-16.7	-26.6***	-31.2***†††

* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$ vs PBO; † $p \leq 0.05$, †† $p \leq 0.01$, ††† $p \leq 0.001$ vs. ADA

ADA: adalimumab; BARI: baricitinib; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI: Health Assessment Questionnaire-Disability Index; MJS: morning joint stiffness; PBO: placebo; PCS: physical component scale; PtGA: Patient Global Assessment; VAS: visual analog scale

Pain VAS = Patient's Assessment of Pain Visual Analog Scale; PCS = Physical Component Score; MJS = Morning Joint Stiffness; HAQ-DI = Health Assessment Questionnaire Disability Index; FACIT-F = Functional Assessment of Chronic Illness Therapy-Fatigue; PtGA = Patient's Global Assessment of Disease Activity.

Figure 1. Percentage improvement from baseline to Week 12 in PROs of patients with RA in RA-BEAM

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POS0647

EFFICACY, SAFETY AND CHARACTERISTICS OF IGURATIMOD-BASED THERAPY IN THE TREATMENT OF UA, ERA AND RA PATIENTS FOR 24 WEEKS: A PROSPECTIVE COHORT STUDY

X. Liu¹, Z. Sun¹, W. Guo¹, F. Wang¹, L. Song¹, J. Li¹, Q. Liu¹, Q. Shu¹. ¹ Qilu Hospital of Shandong University, Department of Rheumatology, Jinan, China