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POS0207

REAL-WORLD RETENTION OF JAK INHIBITORS IS LONGER THAN bDMARDs IN RHEUMATOID ARTHRITIS

K. Machlab¹, S. M. Iskandar¹, T. Nevskaya¹, L. Vanderhoek¹, J. Bylsma¹, S. Hewitt¹, J. Pope¹. ¹University of Western Ontario, Schulich School of Medicine & Dentistry, London, Canada

Background: Biological disease modifying anti-rheumatic drugs (bDMARDs) and Janus Kinase inhibitors (JAKi) are both recommended post conventional synthetic disease modifying anti-rheumatic drug (csDMARD) therapy failure in active rheumatoid arthritis (RA), but the data on long-term durability are limited. **Objectives:** The objective of this study is to analyze a database of patients at the Western University, Rheumatology Center who initiated a bDMARD or JAKi and compare the proportion and characteristics of patients associated with retention of a drug class.

Methods: This was a single-center study of 215 adult RA patients (82.76 % females, age 59.8 ± 12.0 years, disease duration 15.5 ± 10.0 years; table 1) failing multiple csDMARDs prior to initiating either bDMARDs (TNF inhibitors, abatacept, rituximab, tocilizumab) or JAKi, between June 2014 (when tofacitinib was approved in Canada) and April 2020. All patients enrolled had failed traditional DMARDs, including methotrexate, hydroxychloroquine, sulfasalazine and/or leflunomide. Durability and predictors of discontinuation were analyzed by Kaplan-Meier and Cox regression analyses for all treatment trials, and for patients receiving bDMARDs/JAKi as a first line after csDMARDs failure.

Results: In 215 patients, there were 320 treatment events (148 bDMARDs, 172 JAKi) and 142 discontinuations (53.5% bDMARDs, 46.5% JAKi). Figure 1 represents the Kaplan-Meier survival curve for time to therapy discontinuation in 215 patients receiving bDMARDs vs JAKi. The Cox proportional hazards model was significant with better retention for JAKi, with a hazard ratio (HR) for treatment discontinuation of JAKi compared with bDMARDs of 0.676 (95% CI 0.47-0.97, p=0.034), adjusted for gender, age, disease duration, and line of therapy (Table 1). Moreover, the analysis revealed better retention for both groups as first line advanced therapy compared to later lines of therapy; 57.6% of JAKi and 31.1% of bDMARDs were used as first line advanced therapy. HR for treatment discontinuation for first line vs later lines of therapy was 0.593 (95% CI 0.40-0.88, p=0.01), adjusted for drug class, gender, age, and disease duration (Table 1). The most common reasons for discontinuations were inefficacy (60%), side effects (22%), or other reasons (18%). Inefficacy (58% vs 62%, p=0.8) and side-effects (16% vs 27%, p=0.4) were equally common for bDMARDs and JAKi. Sex, age at treatment onset, and RA duration did not predict discontinuation by Cox regression analyses, and after sub-grouping into bDMARDs and JAKi.

Conclusion: EULAR guidelines have placed bDMARDs equal to JAKi as post csDMARD failure therapy in active RA. However, this study demonstrates that JAKi has a greater durability than biologics regardless of gender, age, disease duration, and line of therapy. Therefore, JAKi may be considered as a preferable method of treatment post csDMARD failure in active RA.

Figure 1. Kaplan-Meier survival curves for (A) time to discontinuation of therapy in all RA patients receiving bDMARDs versus JAKi; P-value represents Cox regression adjusted for gender, age, disease duration, and line of therapy (B) time to discontinuation of therapy in patients using bDMARDs/JAKi as first line of advanced therapy; P-value represents Cox regression adjusted for drug class, gender, age, and disease duration

Table 1. Patient demographics and hazard ratios for discontinuation of bDMARDs versus JAKi by Cox regression model

Characteristic	JAKi (N=172)	bDMARD (N=148)	Mean
Age (years)	60.9	58.5	59.8
Sex (% F)	77.8	88.5	82.8
Disease duration (years)	15.3	15.8	15.5
Line of advanced therapy (% first line)	57.6	31.1	45.3
Drug used (%)	Tofacitinib: 93.5	Rituximab: 26.4 Etanercept: 19.6 Adalimumab: 17.6	
Predictors of Drug Discontinuation			
Crude Model	JAKi vs bDMARDs	0.60 (0.43, 0.84)	0.003
Adjusted model	JAKi vs bDMARDs	0.68 (0.47, 0.97)	0.034
	Male vs female	0.77 (0.46, 1.31)	0.342
	Age	1.01 (0.99, 1.03)	0.123
	RA duration	0.99 (0.97, 1.01)	0.500
	Treatment line 1 vs >1	0.59 (0.40, 0.88)	0.010

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POS0208

GENDER DIFFERENCES IN RESPONSE TO BIOLOGICALS. WOMEN FARE WORSE ACROSS INFLAMMATORY ARTHRITIS DISEASES - DATA FROM THE BIOREG

E. Loibner¹, V. Ritschl², B. Leeb^{3,4}, P. Spellitz^{5,6}, G. Eichbauer-Sturm⁵, J. Zwerina^{5,7,8}, M. Herold^{5,9}, M. Stetter⁵, R. Puchner⁵, F. Singer⁵, B. Fritsch-Stork^{1,7,8}. ¹Sigmund Freud Private University, Medical Faculty, Vienna, Austria; ²Medical University of Vienna, Center for Medical Statistics, Informatics and Intelligent Systems; Section for Outcomes Research, Vienna, Austria; ³BioReg, BioReg, Vienna, Austria; ⁴Karl Landsteiner Private University of Health Science, Rheumatology, Krems, Austria; ⁵BioReg, BioReg, Vienna, Austria; ⁶Rheumazentrum Wien Oberlaa, rheumatology, Vienna, Austria; ⁷Ludwig Boltzmann Institute of Osteology, Hanusch Hospital of Oesterreichische Gesundheitskassa and Allgemeine Unfallversicherungsanstalt, Vienna, Austria; ⁸Hanusch Hospital, 1st Internal Medicine, wien, Austria; ⁹Medical University- Innsbruck, Autoimmune Laboratory, Innsbruck, Austria

Background: Gender differences in prevalence and disease course are known in various rheumatic diseases; however, investigations of gender difference concerning therapeutic response have yielded variable results.

Objectives: The aim of this retrospective study was to investigate, whether a gender difference in response rate to biological disease-modifying antirheumatic drugs (bDMARDs) and apremilast in bDMARD-naïve patients could be observed across the three most prevalent inflammatory arthritis diseases: rheumatoid arthritis (RA), spondylarthritis (SpA) and psoriatic arthritis (PsA). Additionally, a response to individual TNF blockers was investigated in this respect.

Methods: Data from bDMARD-naïve RA-, SpA- and PsA-patients from Bioreg, the Austrian registry for biological DMARDs in rheumatic diseases, were used. Patients with a baseline (Visit 1=V1) and follow-up visits at 6 months (Visit 2=V2) and 12 months (Visit 3=V3) were included and response to therapy with TNF-inhibitors (TNFi), furthermore to therapy with rituximab, tocilizumab and apremilast was analyzed according to gender. The remaining bDMARDs were not analyzed due to small numbers. Key response-parameter for RA was disease activity score (DAS28), whereas for PsA the Stocker Activity Score for Psoriatic Arthritis (SASPA) and for SpA the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) were employed; in addition, the Health assessment Questionnaire

(HAQ) was used. Data were analyzed in R Statistic stratified by gender using Kruskal-Wallis and Wilcoxon tests.

Results: 354 women and 123 men with RA (n=477), 81 women and 69 men with PsA (n=150), 121 women and 191 men with SpA (n=312) were included. No significant differences in biometrics was seen between female and male patients at baseline in all diseases.

In RA patients overall DAS28 decreased from baseline (V1) to V2 and V3 (DAS28: V1: male: 4.38 [3.66, 5.11], female: 4.30 [3.68, 5.03], p(m/f) = 0.905; V2: male: 2.66 [1.73, 3.63], female: 3.10 [2.17, 3.98], p(m/f) = 0.015; V3: male: 2.25 [1.39, 3.36], female: 3.01 [1.87, 3.87], p(m/f) = 0.002). For TNF inhibitors (n=311), there was a significant difference between genders at V2 (Fig.1a). Patients receiving Rituximab (n=41) displayed a significantly higher DAS28 at baseline in females, which diminished in the follow up: V1: (p(m/f) p=0.002; V2: p=0.019; V3: p=0.13); response to tocilizumab (n=63) did not show any gender differences.

In PsA patients overall SASPA decreased from baseline (V1) to V2 and V3 (SASPA: V1: male: 4.00 [2.80, 5.20], female: 4.40 [2.80, 5.80], p(m/f) = 0.399; V2: male: 2.20 [1.20, 3.50], female: 3.40 [2.00, 5.00], p(m/f) = 0.071; V3: male: 1.80 [0.80, 2.70], female: 3.01 [2.35, 4.80], p(m/f) = 0.001). For TNF inhibitors (n=79), there was a significant difference between genders at V3 (Fig. 1a). For Apremilast (n=39), there was a significant difference between genders at V2 (Fig.1c).

In SpA patients overall BASDAI decreased from baseline (V1) to V2 and V3 (BASDAI: V1: male: 4.70 [2.88, 6.18], female: 4.80 [3.30, 6.20], p(m/f) = 0.463; V2: male: 3.05 [2.00, 4.60], female: 3.64 [2.62, 5.41], p(m/f) = 0.039; V3: male: 3.02 [1.67, 4.20], female: 3.65 [2.18, 5.47], p(m/f) = 0.016). In V3 a differential BASDAI in response to TNFi (n=299) was observed (Fig.1a).

Possible differences of response to individual TNFi (etanercept, infliximab, other TNFi) measured by HAQ were investigated in all diseases together. The difference between male and females was significant at baseline for all 3 TNFi; whereas with the use of ETA the significant difference was carried through to V2 and V3, it was lost with the use of IFX and was variable with the other TNFi (Fig.1b)

Figure 1a

Figure 1b

Figure 1c

Figure 1.

Conclusion: Female patients showed a statistically lower response to TNFi in all three disease entities (RA, SpA and PsA) to a variable degree in our homogeneous central european population. Interestingly, the difference was not uniform across individual TNFi when measured by HAQ. Gender differences were also seen in response to Apremilast.

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POS0209

ASSOCIATION OF FIRST, SECOND, AND THIRD-LINE BDMARDS AND TSDMARD WITH DRUG SURVIVAL AMONG RHEUMATOID ARTHRITIS PATIENTS: A COHORT STUDY

B. Ghang¹, S. Choi², E. Y. Lee³. ¹Division of Rheumatology, Department of Internal Medicine, Jeju National University School of Medicine, Jeju National University Hospital, Rheumatology, Seoul, Korea, Rep. of (South Korea); ²Seoul National University Graduate School, Biomedical Science, Seoul, Korea, Rep. of (South Korea); ³Seoul National University College of Medicine, Rheumatology, Seoul, Korea, Rep. of (South Korea)

Background: Since tofacitinib is a tsDMARD with a different mechanism of action compared to bDMARDs, along with the fact that recent releases of bDMARDs or tsDMARDs have led to numerous possible switching patterns, there is a need for comparative studies of bDMARDs and tofacitinib with subsequent drug survival among RA patients.

Objectives: To determine the association of first, second, and third-line biologic disease-modifying antirheumatic drugs (bDMARDs) and tofacitinib with drug survival among rheumatoid arthritis (RA) patients.

Methods: The study population was composed of 8,018 seropositive RA patients who were prescribed bDMARDs or tofacitinib between January 2014 and January 2019 from the Korean Health Insurance Review and Assessment Service database. First, second, and third-line choice of tumor necrosis factor inhibitors (TNFi) including etanercept, infliximab, adalimumab, and golimumab, as well as non-TNFi including tocilizumab, rituximab, tofacitinib, and abatacept were assessed. Multivariate Cox proportional hazards regression was used to determine the adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for drug failure according to bDMARD or tofacitinib choice starting from the initial prescription date.

Results: Compared to first etanercept users, patients with first tocilizumab (aHR 0.56, 95% CI 0.46-0.68), tofacitinib (aHR 0.27, 95% CI 0.18-0.42), or abatacept (aHR 0.83, 95% CI 0.69-0.99) had lower risk of drug failure. Second choice of tocilizumab (aHR 0.38, 95% CI 0.25-0.55), tofacitinib (aHR 0.23, 95% CI 0.15-0.37), or abatacept (aHR 0.54, 95% CI 0.35-0.84) was associated with lower drug failure risk compared to second etanercept users. Finally, third choice of tocilizumab (aHR 0.32, 95% CI 0.16-0.62) or tofacitinib (aHR 0.35, 95% CI 0.19-0.63) was associated with lower drug failure risk compared to third TNFi users.

Conclusion: First and second-line tocilizumab, tofacitinib, or abatacept may lead to improved drug survival. Third choices of tocilizumab or tofacitinib may be beneficiary in reducing drug failure risk among RA patients.

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