AB0364

EFFICACY OF BARICITINIB (BARI) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) WHOSE RESPONSE WAS INADEQUATE TO TOFACITINIB (TOFA).

T. Yamane¹, A. Hashiramoto². ¹Kakogawa Central City Hospital, Kakogawa, Japan; ²Kobe University Graduate School of Health Sciences, Kobe, Japan

Background: Currently, four types of JAK inhibitors are approved for the treatment of RA in Japan, however, they often show differences in clinical efficacies presumably due to their JAK selectivity.

Objectives: To investigate the efficacy of Bari for patients with Tofa-inadequate response (IR), clinical profiles of seven Tofa IR patients were evaluated.

Methods: We performed a single-center retrospective study on seven Tofa IR patients (female:7) who were switched to Bari. Items evaluated were as follows; patient's baseline characteristics, continuation rate of Bari, swollen joint count, tender joint count, C-reactive protein (CRP), matrix proteinase 3 (MMP3), physician's and patient's visual analog scale (VAS), disease activity assessed by Disease Assessment Score of 28 joints - C-reactive protein (DAS 28-CRP), simplified disease activity index (SDAI) and clinical disease activity index (CDAI) at 2, 4, 8, 12 weeks, and the dosage of prednisone (PSL).

Results: Patient's mean age was 56.4 and mean disease duration was 9.2 years. Tofa had administered for 3.4 months (range 1-10) before switching to Bari. All patients were positive for both anti-citrullinated protein antibodies and rheumatoid factor. The number of prior biologics use was 2.3 (range 1-4). 3 patients had concomitant MTX use (mean dosage 5.3mg/week) and 4 had prednisone (mean dosage 3.3mg/day). Mean swollen joint counts and tender joint counts were 5.0 (range 1-15) and 5.3 (range 1-15), respectively. Physician's and Patient's VAS 0-100 were 71 mm (range 50-90) and 73mm (range 50-80), mean CRP levels were 1.6mg/dl (range 0.01-4.3) and MMP3 levels were 357.3mg/dl (range 27-933). Mean SDAI, CDAI and DAS-28-CRP were 26.3 (range 17-50), 24.7 (range 17-47) and 4.5, respectively. When enrolled, 4 of 7 patients corresponded to moderate disease activity (MDA) and 3 were in high disease activity (HDA) by all composite measures. After switched to Bari, the patient's VAS significantly decreased at week 2 ($P < 0.01$). CDAI, SDAI and DAS28-CRP also showed a significant improvement at week 4, ($P < 0.05$). At week 4, 2 patients discontinued Bari due to the lack of efficacy or acute exacerbation of interstitial pneumonia. Thus, continuation rate of Bari at week 12 was 71.4%. Among 5 patients who continues Bari, all patients achieved low disease activity (LDA) by SDAI and CDAI at week 12. By DAS 28-CRP, 2 patients achieved MDA, 2 achieved LDA and 1 achieved remission (mean 2.6), respectively, at week 12, 3 of 4 patients taking PSL were able to withdraw that before week 12 (Figure).

Conclusion: Result showed the efficacy of Bari for patients with Tofa IR, representing inadequate improvements of patient's VAS with Tofa. The efficacy of Bari can be expected from the early stage and continued up to 12 weeks after switching. This difference in therapeutic effect may be due to each mechanism of action, Bari inhibits JAK1/2, whereas Tofa mainly inhibits JAK1 /3 (1). JAK2 is important for signal by GM-CSF, which has shown potential as an important therapeutic target in RA (2). Inhibition of JAK2 and GM-CSF may be the reason for Bari efficacy in Tofa IR patients.

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AB0365

COMPARISON OF SUSTAINED CLINICAL REMISSION AND/OR LOW DISEASE ACTIVITY RATE BETWEEN RAPIDLY AND GRADUALLY DE-ESCALATION OF BARICITINIB IN RHEUMATOID ARTHRITIS.

M. Yamasaki¹. ¹Shin-Yokohama Arthritis and Rheumatology Clinic, Yokohama, Japan

Background: However baricitinib, an oral selective inhibitor of Janus kinase (JAK) 1 and 2, improved signs and symptoms of rheumatoid arthritis (RA), it is unknown who can taper or stop baricitinib and strategies for de-escalation.

Objectives: We analyze predictors of tapering of withdrawal failure in rheumatoid arthritis (RA) patients treated with baricitinib. This study will assess and compare (1) characteristic of patients who achieve remission (REM) or low disease activity (LDA) as who can taper baricitinib and (2) two de-escalation methods, rapidly and gradually de-escalation in patients who respond first-line therapy.

Methods: Cases were recruited to SHin-yokohama Arthritis REgister (SHARE) between 2015 and 2019 (n=3,674). Patients were diagnosed according to ACR/EULAR 2010 classification criteria, and treated with DMARDs which included baricitinib 2mg/day (n=154). In 154 cases, Clinical Disease Activity Index (CDAI), Health Assessment Questionnaire-Disability Index (HAQ-DI), anti-CCP2 and patients clinical parameters were analyzed. Two de-escalation methods were compared in this study. In rapidly de-escalation methods, baricitinib were stopped in patients with stable REM/LDA over 12 weeks. In gradually de-escalation methods, baricitinib were decreased to 50%, 42%, 28%, 14% in order with stable REM/LDA over 12 weeks.

Results: In 154 (Male 25, Female 129 cases, RA duration 11.4+/-8.0 years) cases, CDAI at baricitinib-start was 20.6+/-12.4 and titer of anti-CCP2 was 242.6+/-516.5 U/ml. 126 cases (81.8%) were more than 2 years of RA duration and 49 cases (31.8%) had persistency of signs and/or symptoms suggestive of inflammatory RA disease activity, despite prior treatment with csDMARDs and at least two biologic DMARDs. 33 cases (21.4%) were biologic DMARDs naive.

(1) "Multivariate logistic regression examined the predictors to detect who can taper baricitinib" However there were no differences in duration of RA, onset age of RA, biologics and/or JAK inhibitors naive, anti-CCP2 titer and CDAI at the start baricitinib, patients who showed decrease of CDAI at 12 weeks were correlated with achievement of remission (REM) or low disease activity (LDA) in patients treated with baricitinib (OR 0.964, 95%CI 0.934-0.996, $p=0.010$). ROC analysis of Δ CDAI at 12 weeks is cut-off value of -6.6 ($p=0.011$).

(2) "Comparison of sustained REM and/or LDA rate between rapidly and gradually de-escalation of baricitinib in rheumatoid arthritis" 11 cases were tapered baricitinib with rapidly de-escalation methods and 60 patients were with gradually de-escalation. Mean times to start taper baricitinib in rapidly and gradually de-escalation group were 4.6+/-1.6 months and 5.9+/-2.2 months respectively. Gradually de-escalation methods showed less relapse rate compared with rapidly de-escalation after tapered baricitinib for 6 months (18.3% vs. 54.5%, $p=0.018$). There were no differences in clinical features such as anti-CCP2, CDAI and administration period of baricitinib between non-relapse and relapse patients in gradually escalation methods.

Conclusion: A combination of Δ CDAI at 12 weeks and tapering baricitinib using gradually de-escalation methods may help to predict successful baricitinib deduction in RA patients with sustained clinical REM and/or LDA.

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16. SLE, Sjögren's and APS - treatment

AB0366

DIFFUSE ALVEOLAR HEMORRHAGE IN LUPUS NEPHRITIS PATIENTS: MULTICENTER RETROSPECTIVE STUDY

S. Abdulaziz¹, H. Halabi², S. Bahlal³, S. Attar³, M. Dessougi⁴, A. Alhouiri⁵, A. Taruti⁶, H. Alrayes⁷, A. H. A. Albeity⁸. ¹King Fahd Hospital, Jeddah, Saudi Arabia; ²King Faisal Specialist Hospital, Jeddah, Saudi Arabia; ³King Abdulaziz University, Jeddah, Saudi Arabia; ⁴Armed Forces Hospital, Riyadh, Saudi Arabia; ⁵Qatif Central Hospital, Dammam, Saudi Arabia; ⁶Qatif Central Hospital, Jeddah, Saudi Arabia; ⁷King Sultan Military Hospital, Riyadh, Saudi Arabia; ⁸King Faisal Specialist Hospital, Jeddah, Saudi Arabia

Background: Diffuse alveolar hemorrhage (DAH) is a rare and potentially lethal complication of systemic lupus erythematosus (SLE) with a high mortality rate. It occurs more frequently in patients with lupus nephritis (LN).

Objectives: The aim of our study is to explore the characteristics of patients that develop DAH with lupus nephritis, risk factors that predispose DAH, treatment response and outcomes.

Methods: Multicenter retrospective cohort study was undertaken including 6 centers in Saudi Arabia from 2002 to 2018. Systemic lupus erythematosus patients meeting the SLICC criteria with lupus nephritis (biopsy proven or proteinuria or renal impairment due to lupus) presenting with diffuse alveolar hemorrhage (fulfilling a predefined criteria) were included in the study. An identical number of control group with lupus nephritis was also studied. Data was obtained from medical records by using a data sheet: demographics including age, gender, diagnosis, date of diagnosis of lupus, date of presentation of alveolar hemorrhage, clinical presentation, detection of alveolar hemorrhage proved by radiology, lavage or biopsy and laboratory parameters: including level of hemoglobin before and during DAH, sign of activity, treatment and outcome of DAH. Identification of risk factors predisposing to DAH in lupus nephritis patients was analyzed.

Results: We identified 23 cases of DAH with lupus nephritis, all fulfilling the criteria. Mean age at presentation of DAH was 31.09 ± 12.6 years ranging from 14-57 years, of which 87 % were females. 13 patients 56.5% had Class 4 LN and 21.7% had Class 4 and 5 LN on renal pathology. DAH occurred at a mean of 6.5 years ± 3.8 in 13/23 patients with LN. Shortness of breath 95%, new chest x ray finding 95.7% and mean drop of haemoglobin of $2.72 \text{ gm/dl} \pm 0.97$ were more frequent at presentation of DAH with LN patients. High SLE disease activity - SELENA SLEDAI 2K was 38.56 ± 19.3 was present at the onset of DAH. All were treated with methylprednisone, 15/23 (65.2%) underwent mechanical ventilation and plasmapheresis was done in 21/23 patients (91.3%). Cyclophosphamide was given in 14/21 patients (60.9%), Intravenous immunoglobulins were given in 14/23 patients (65.2%) and dialysis was done in 12/23 patients (52.2%). Mortality occurred 8 patients 34.8 %. In comparison with the LN group, a mean haemoglobin of 7.56 ± 1.3 , CNS involvement, vasculitis and fever >38° were of statistically significance P value: <0.001, 0.02, 0.03 and 0.03 respectively.

Conclusion: In this multicenter cohort series with DAH in LN patients CNS involvement, vasculitis and fever >38° were associated in the occurrence of DAH. Mortality was low in our cohort in comparison to previous series which may be explained by early diagnosis and use of aggressive management. Well designed prospective studies are required to identify high risk patients for preventing this serious complication.

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AB0367

USING UNSUPERVISED CLUSTERING ANALYSIS OF REAL LIFE DATA FROM AN ONLINE COMMUNITY TO IDENTIFY LUPUS PATIENTS' PROFILES REGARDS TO THEIR TREATMENT PREFERENCES

D. Testa¹, V. Morisseau¹, L. Radoszycki¹, L. Anfray¹, L. Chiche². ¹Carenity, Paris, France; ²European Hospital Marseille, Service de Médecine Interne, Marseille, France

Background: Lupus is a prototype of a chronic complex autoimmune disease. Non-adherence rate to treatment is surprisingly high and impairs its management. Adherence to drug treatment is a complicated and multifactorial phenomenon, including characteristics of treatment.

Objectives: This study used unsupervised clustering analysis to identify profiles among lupus patients with regards to their treatment preferences (apart from efficiency).

Methods: An online survey among adult lupus patients from Carenity was conducted between August 2018 and April 2019. Multiple Correspondence Analysis (MCA) of a French lupus patient dataset was used with 3 unsupervised clustering methods (hierarchical, kmeans and partitioning around medoids).

Results: The 268 participating lupus patients were mostly female (96%), with a mean age of 44.3 years, and 83% fulfilled the ACR SLE diagnostic criteria. Overall, the preferred galenic form was oral (62%), and the most important characteristic was fewer side effects (32%).

A MCA was performed using 8 profile variables and the best unsupervised clustering method for this dataset (hierarchical clustering) identified 3 clusters (Table 1). Cluster 1, main one (59%), comprised patients with few comorbidities, less capacity to identify coming flares, and that wanted mostly (84%) oral treatments with limited side effects, most of them (83%) already on oral treatments. Cluster 2, the smallest one (13%), comprised younger patients, having already participated in clinical trials, favoring implants and the compatibility of treatments with pregnancy. Cluster 3 comprised patients (28%) that had longer lupus duration but less controlled disease with more comorbidities. A third had injectable treatments, wanting mainly implants and injections and with the main goal of reducing corticosteroids. The robustness of these results was confirmed by external validation and sensitivity analyses.

Table 1. Description of the three clusters

	Overall n=268	Cluster 1 n=158	Cluster 2 n=36	Cluster 3 n=74	p-value
Most represented age group (%)	41-50 (32%)	41-50 (41%)	31-40 (42%)	51-60 (39%)	< 0.001
Comorbidities 0 / ≥ 4	20% / 37%	30% / 4%	14% / 8%	3% / 36%	< 0.001
Ability to identify coming flare	82%	73%	97%	93%	< 0.001
Current lupus control (no or poor)	26%	20%	25%	38%	< 0.05
Current galenic (inj. / oral)	12% / 76%	2% / 83%	8% / 78%	35% / 61%	< 0.001
Trial participation	7%	0%	50%	1%	< 0.001
Ideal galenic oral	62%	84%	50%	20%	< 0.001
implant	19%	9%	33%	32%	
home / auto-inj.	14% / 9%	6% / 2%	11% / 11%	32% / 22%	
hospital inj.	6%	1%	5%	15%	
Top ranked drug characteristics ^{\$}	Side effects (32%)	Side effects (41%)	Pregnancy (55%)	Cortisone sparing (24%)	< 0.001

^{\$}among the 10 following items: less side effects, compatibility with pregnancy, better long term tolerance, less costly for collectivity, more convenient place for administration, easier administration, less medical follow-up needed, less risk of infection, cortisone sparing effect, shorter time of administration. P-values obtained after χ^2 tests. Inj.: injection.

Conclusion: Most lupus patients preferred a drug galenic favoring the conservation of their autonomy. The identified clusters could help physicians to tailor their therapeutic proposition taking into account patients' preferences and to maximize therapeutic adherence. Our study also highlights the potential of using unsupervised machine learning techniques in combination with direct-access patient community data to provide new a priori knowledge in the field of rare and complex chronic diseases.

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AB0368

TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH BELIMUMAB – PROSPECTIVE OBSERVATION OVER 2 YEARS

S. Dimitrov¹, S. Hristova², S. Bogdanova-Petrova², T. Shivacheva². ¹University Hospital St Marina, Rheumatology, Varna, Bulgaria; ²University Hospital St Marina, Varna, Bulgaria

Background: Systemic lupus erythematosus (SLE) is autoimmune connective tissue disorder of unclear etiology. It is characterized by autoantibody production and a variety of clinical manifestations. The introduction of biological treatment over the past few years provided an opportunity for a disease control.

Objectives: The aim was to assess the effectiveness and safety profile of Belimumab in the treatment programs of SLE patients during a 2 year period.

Methods: We initiated a prospective observational study of SLE patients in the Rheumatology Department in University Hospital St Marina – Bulgaria. The study comprises data from 26 patients at baseline before Belimumab treatment initiation and data after 6, 12, 18 and 24 months of treatment. All patients were with moderate disease activity according to SELENA – SLEDAI index and were on treatment with immunosuppressive drug (azathioprine) and glucocorticoids (GCs). We observed the change in the dosage of glucocorticoids over the observed period, the number of flares of SLE, as well the SELENA – SLEDAI index change. Safety profile of Belimumab was also registered.

Results: We included 26 patients with SLE over a period of 4 years – between 2015 and 2019. The mean age was 45.8 ± 11.4 years and 94% were Caucasian females. All patients were on a stable dosage of GCs at least 3 months before the first infusion of Belimumab and azathioprine 100 mg daily. Ninety percent of patients were diagnosed with SLE for more than 6 years according to ACR – SLE criteria. All of SLE patients were with moderate disease activity. Main reasons for biological treatment decision were persistent mucocutaneous manifestations