Results: In all machine learning methods, the accuracy and the area under the receiver operating characteristic (AUROC) were 57.2%~74.5%, 0.547~0.747, respectively (Table 1). The accuracy and AUROC of each biologics were similar between machine learning methods. Figure 2 showed interpretation of feature importance with the Shapley plot for remission. The most important feature was age in adalimumab (younger were closer to remission), daily corticosteroid dose in etanercept, golimumab, and all TNF inhibitors (using fewer doses daily were closer to remission), baseline erythrocyte sedimentation rate in infliximab (lower ESR were closer to remission), disease duration in abatacept (longer disease durations showed difficulty determining remission), baseline c-reactive protein in tocilizumab (higher CRP were closer to remission).

Table 1. Predicting remission for all biologics in various machine learning method.

	Measure	Lasso	Ridge	SVM	Random Forest	XGBoost	No info rate	Sample
Abatacept	Accuracy	74.1%	74.1%	70.6%	71.8%	68.8%	70.6%	216
	AUROC	0.725	0.742	0.707	0.677	0.647	0.500	
Adalimumab	Accuracy	73.6%	72.0%	70.4%	72.0%	70.4%	68.8%	315
	AUROC	0.710	0.729	0.700	0.675	0.663	0.500	
Etanercept	Accuracy	72.0%	72.0%	70.0%	71.5%	70.0%	68.0%	250
	AUROC	0.741	0.747	0.726	0.719	0.704	0.500	
Golimumab	Accuracy	71.3%	68.5%	66.7%	68.5%	68.5%	68.5%	138
	AUROC	0.746	0.727	0.701	0.690	0.655	0.500	
Infliximab	Accuracy	72.8%	73.5%	67.6%	73.5%	69.1%	72.5%	172
	AUROC	0.663	0.683	0.616	0.597	0.527	0.500	
TNF inhibitors	Accuracy	73.9%	74.5%	73.9%	74.2%	73.6%	70.3%	875
	AUROC	0.739	0.741	0.726	0.747	0.724	0.500	
Tocilizumab	Accuracy	62.4%	63.6%	62.4%	59.5%	57.2%	59.5%	436
	AUROC	0.633	0.640	0.633	0.615	0.547	0.500	

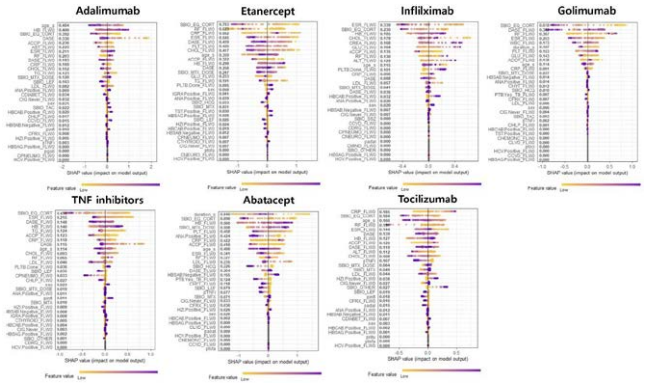

Figure 2. Shapley plots and SHAP values for the feature importance from clinical information in patients with RA.

Conclusion: We developed machine learning models for predicting remission as a response to each biologics in active RA patients based on their clinical profiles, and found important clinical features using explainable AI. This approach may support clinical decisions to improve treatment outcomes in patients with RA.
Disclosure of Interests: None declared
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OP0024 USE OF HYDROXYCHLOROQUINE AND RISK OF HEART FAILURE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Hydroxychloroquine (HCQ) is a disease-modifying anti-rheumatic drug (DMARD) used as a long-term treatment for rheumatoid arthritis (RA) patients. Cardiotoxicity is a rare but potentially life-threatening side effect of HCQ and may present as conduction disorders, cardiomyopathy, and resulting heart failure (HF). The evidence of cardiotoxicity associated with the use of HCQ largely relies on case reports and case series while large cohort studies on the subject are lacking.
Objectives: To examine the relationship between the use of HCQ and risk of developing HF in RA.
Methods: In this nested case-control study, cases were Olmsted county, Minnesota residents with incident RA (based on 1987 ACR criteria) in 1980-2013 who developed HF after RA incidence. Each case was matched on year of birth, sex and year of RA incidence with an RA control who did not develop HF. Each non-HF control was assigned an index date corresponding to the HF diagnosis date of the case. Controls were allowed to later become cases to avoid bias. HF was defined using the Framingham criteria. Data on HCQ use including start and stop dates and dose changes was manually abstracted via medical record review, and used to calculate HCQ duration and cumulative dose. Age-adjusted logistic regression models were used to examine the association between HCQ and HF.
Results: From a cohort of 1078 subjects, the study identified 143 RA cases diagnosed with HF (mean age 65.8, 62% females) and 143 non-HF RA controls (mean age 64.5, 62% female). Cases and controls had similar RA duration, proportion of patients positive for rheumatoid factor (RF) and/ or cyclic citrullinated antibody (CCP), body mass index, and smoking status (Table). The duration of HCQ use prior to the diagnosis of HF was 2.8 years in cases and 2.6 years in controls. A total of 71 cases and 69 controls used HCQ at some time before index date. Among these, the median (interquartile range) duration of HCQ use was 2.8 (0.6, 10.0) years for cases and 2.5 (0.7, 8.2) for controls. The median cumulative dose of HCQ was 371 g and 302 g in cases and controls, respectively, with 55% of cases receiving a cumulative dose of ≥ 300 g compared to 54% in controls. HCQ cumulative dose was not associated with HF (Odds Ratio [OR]: 0.96 per 100g increase in cumulative dose, 95% confidence interval [95% CI]: 0.90-1.03). Likewise, no association was found for patients with a cumulative dose ≥300g (OR 0.92, 95% CI 0.41-2.08). The duration of use of HCQ prior to index was not associated with HF (OR 0.98, 95% CI 0.91-1.05). Retinal toxicity rates were similar in cases and controls.

Table. Characteristics of patients with rheumatoid arthritis with and without heart failure.

Variable	HF	non-HF
Age at RA diagnosis (years)	65.8 ± 12.3	64.5 ± 12.5
Female	62%	62%
RA duration at baseline (years)	11.3 ± 8.5	10.3 ± 8.2
RF positive	66%	65%
CCP positive	46%	53%
RF/ CCP positive	68%	66%
BMI (at RA diagnosis)	28.6 ± 6.5	27.7 ± 5.4
Smoking status at RA incidence		
Former	45%	41%
Current	22%	22%

Conclusion: Use of HCQ was not associated with development of HF in patients with RA in this study. While there was no statistically significant association between the cumulative dose of HCQ and HF, the confidence interval for HCQ dose ≥300 g was wide suggesting that more studies are needed to understand the impact of higher doses of HCQ on development of HF in RA.
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OP0025 DRUG RETENTION OF 7 BIOLOGICS AND TOFACITINIB IN BIOLOGICS-NAÏVE AND BIOLOGICS-SWITCHED PATIENTS WITH RHEUMATOID ARTHRITIS -THE ANSWER COHORT STUDY

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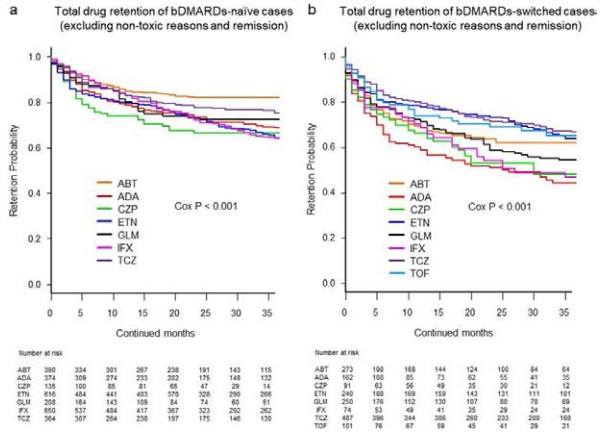
Background: EULAR recommendation announced that biological disease-modifying antirheumatic drugs (bDMARDs) and janus kinase inhibitors (JAKi) are considered as equivalent in the treatment of rheumatoid arthritis (RA). However, we still lack reliable evidence of direct comparison between these agents' retention, which may reflect both effectiveness and safety.

Objectives: The aim of this multi-center (7 university-related hospitals), retrospective study is to clarify retention rates and reasons for discontinuation of 7 bDMARDs and tofacitinib (TOF), one of the JAKi, in both bDMARDs-naïve and bDMARDs-switched cases.
Methods: This study assessed 3,897 patients and 4,415 treatment courses of with bDMARDs and TOF from 2001 to 2019 (2,737 bDMARDs-naïve patients and 1,678 bDMARDs-switched patients [59.5% switched to their second agent], female 82.3%, baseline age 57.4 years, disease duration 8.5 years; rheumatoid factor positivity 78.4%; DAS28-ESR 4.3; concomitant prednisolone [PSL] 6.1 mg/day [42.4%] and methotrexate [MTX] 8.5 mg/week [60.9%]). Treatment courses included abatacept (ABT; n=663), adalimumab (ADA; n=536), certolizumab pegol (CZP; n=226), etanercept (ETN; n=856), golimumab (GLM; n=458), infliximab (IFX; n=724), tocilizumab (TCZ; n=851), and TOF (n=101/only bDMARDs-switched cases). Reasons for discontinuation were classified into four categories by each attending physician: 1) lack of effectiveness, 2) toxic adverse events, 3) non-toxic reasons, and 4) remission. Retention rates of each discontinuation reason were estimated at 36 months using the Kaplan-Meier method and adjusted for potential clinical confounders (age, sex, disease duration, concomitant PSL and MTX, starting date and number of switched bDMARDs) using Cox proportional hazards modeling.
Results: Adjusted drug retention rates for each discontinuation reason were as follows: lack of effectiveness in the bDMARDs-naïve group (from 70.8% [CZP] to 85.1% [ABT]; P=0.001 between agents) and the bDMARDs-switched group (from 52.8% [CZP] to 78.7% [TCZ]; P<0.001 between agents). Toxic adverse events in the bDMARDs-naïve group (from 86.9% [IFX] to 96.3% [ABT]; P<0.001 between agents) and the bDMARDs-switched group (from 81.1% [ADA] to 95.4% [ETN]; P=0.01 between agents). Finally, overall retention rates excluding discontinuation for non-toxic reasons or remission ranged from 64.2% (IFX) to 82.0% (ABT) (P<0.001 between agents) in the bDMARDs-naïve group (figure a) and from 44.2% (ADA) to 66.8% (TCZ) (P<0.001 between agents) in the bDMARDs-switched group (figure b).
Conclusion: Remarkable differences were observed in drug retention of 7 bDMARDs and TOF between bDMARDs-naïve and bDMARDs-switched cases.



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Vasculitis

OP0026

A RANDOMIZED, CONTROLLED TRIAL OF RITUXIMAB VERSUS AZATHIOPRINE AFTER INDUCTION OF REMISSION WITH RITUXIMAB FOR PATIENTS WITH ANCA-ASSOCIATED VASCULITIS AND RELAPSING DISEASE

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Background: Rituximab (RTX) is an effective therapy for induction of remission in ANCA-associated vasculitis (AAV). However, the effect of RTX is not sustained, and subsequent relapse rates are high, especially in patients with a history of relapse.
Objectives: The RITAZAREM trial is an international, multi-center, open-labelled, randomized, controlled trial of patients with AAV with relapsing disease comparing the efficacy, after induction of remission with RTX, of two relapse-prevention strategies: repeat dosing of RTX or daily oral azathioprine (AZA).
Methods: Patients with AAV were recruited at the time of relapse and received induction therapy with RTX and glucocorticoids. If remission was achieved by month 4, patients were randomized in a 1:1 ratio to receive either RTX (1000 mg every 4 months for 5 doses) or AZA (2 mg/kg/day) as maintenance therapy. Patients were followed for a minimum of 36 months, with the primary outcome being time to disease relapse.
Results: 190 patients were enrolled and 170 randomized at 4 months (85 to RTX; 85 to AZA). The data are complete on all patients up to at least month 24. Median age was 59 years (range 19-89), with a prior disease duration of 5.3 years (0.4-38.5). 123/170 (72%) patients had a history of testing positive for anti-proteinase 3 ANCA; 47/170 (28%) for myeloperoxidase ANCA; 104/170 (61%) were enrolled having suffered a major relapse, and 48/170 (28%) received a pre-specified higher dose glucocorticoid induction regimen (Table 1).

Table 1. Baseline characteristics of patients enrolled in RITAZAREM trial

	Rituximab (N=85)	Azathioprine (N=85)	Total (N=170)
Age, years: median (range)	57 (18-89)	61 (27-83)	59 (18-89)
Female, number (%)	42 (49.4%)	44 (51.8%)	86 (50.6%)
Disease duration, years: median (range)	5.8 (0.4-38.5)	4.9 (0.4-25.8)	5.3 (0.4-38.5)
Prior cyclophosphamide therapy			
Number of patients (%)	67/85 (78.8%)	66/85 (77.6%)	133/170 (78.2%)
Cumulative dose, grams (g): median (range)	7.1 g (0.2-301)	12 g (1.0-146)	10 g (0.2-301)
Prior rituximab therapy			
Number (%) patient	33/85 (38.8%)	27/85 (31.8%)	60/170 (35.3%)
Cumulative dose, grams (g): median (range)	3.2 g (2.0-16.0)	5.4 g (1.5-14.0)	3.9 g (1.5-16.0)
Glucocorticoid induction regimen			
1mg/kg/day starting dose	24/85 (28.2%)	24/85 (28.2%)	48/170 (28.2%)
0.5mg/kg/day starting dose	61/85 (71.8%)	61/85 (71.8%)	122/170 (71.8%)
ANCA type			
Anti-proteinase 3	61/85 (71.8%)	62/85 (72.9%)	123/170 (72.4%)
Anti-myeloperoxidase	24/85 (28.2%)	23/85 (27.1%)	47/170 (27.6%)
Relapse type upon entry into trial			
Severe	52/85 (61.2%)	52/85 (61.2%)	104/170 (61.2%)
Non-severe	33/85 (38.8%)	33/85 (38.8%)	66/170 (38.8%)

RTX was superior to AZA in preventing disease relapse with a preliminary overall hazard ratio (HR) estimate of 0.36 (95% CI 0.23-0.57, p <0.001) and a during-treatment HR estimate of 0.30 (95% CI 0.15-0.60, p<0.001) (Figure 1). After adjustment, none of the randomization stratification covariates (ANCA type,