At least one TESAE (subcutaneous abscess, pulmonary tuberculosis, staphylococcal sepsis, toxic shock syndrome, cervix carcinoma, obstructive pancreatitis, diabetic vascular disorder) was reported in 8 (5.6%) of OKZ groups, numerically higher than 4(2.8%) in PBO. There was one death due to septic shock in the OKZ q2w arm. **Conclusion:** Treatment with OKZ over a 24-week period was associated with significant improvements in the signs, symptoms and physical function of RA, with a safety profile consistent with Phase II data for OKZ and with the data for the agents with similar mechanism of action.

There were no discernible differences between the two regimens of OKZ in efficacy or safety outcomes.

References:

- [1] Genovese MC et al. *Ann Rheum Dis.* 2014 Sep; 73:1607; 2. Takeuchi T, et al. *Mod Rheumatol.* 2016; 26:1

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OP0022

RISK OF DIVERTICULITIS AND GASTRO-INTESTINAL PERFORATION IN RHEUMATOID ARTHRITIS TREATED WITH TOCILIZUMAB COMPARED TO RITUXIMAB AND ABATACEPT: A PROSPECTIVE PROPENSITY-MATCHED COHORT STUDY

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Background: There are discordant results regarding a potential increased risk of gastro-intestinal perforation (GIP) in rheumatoid arthritis (RA) patients treated with tocilizumab (TCZ) compared to conventional synthetic disease modifying anti rheumatic drugs (csDMARDs) or TNF inhibitors (TNFi) (1–3).

Objectives: The aim of our study was to compare the risk of diverticulitis and GIP in RA patients treated with TCZ compared to rituximab (RTX) and abatacept (ABA).

Methods: We conducted a multicentric study of patients with RA, prospectively followed in 3 observational French registries evaluating the effectiveness and safety of RTX (Autoimmunity and Rituximab (AIR)), ABA (Orencia and Rheumatoid Arthritis (ORA)), and TCZ (REGistry–RoAcTEmma (REGATE)). Using a propensity score approach, we compared the risk of diverticulitis or GIP during treatment with TCZ vs RTX and ABA. The following covariates were included in the propensity score: age, sex, history of diabetes and neoplasia, Charlson Comorbidity Index, number of previous csDMARDs and TNFi, history of TNFi, daily dose of glucocorticoids (GCs) at baseline, co-treatment with a csDMARDs, average DAS28 during follow-up, duration of RA, and exposure time to the considered bDMARDs.

Results: 4501 patients (1496 treated by TCZ, 1986 by RTX and 1019 by ABA) were included. 21 and 9 GIP occurred in the TCZ treated patients, compared to 10 and 8 in the RTX treated patients and 10 and 2 in the ABA treated patients (corresponding incidence rate (IR) are shown in table 1). Two deaths occurred in patients experiencing GIP: 1 (12.5%) due to undetermined rectal perforation among a RTX treated patient, and 1 (11.1%) due to a perforated ulcer among a TCZ treated patient. Based on inverse probability weighting (IPW), there was an increased risk of diverticulitis and GIP in the TCZ treated patients compared with RTX or ABA (table 1). In a subgroup analysis, we confirmed an increased risk of GIP due to diverticulitis but

not to any other etiology. Older age ($p=0.05$), GCs at baseline ($p=0.10$) and average daily dose of GCs during follow-up ($p=0.08$) seemed associated with GIP only in univariate analysis. Compared to RTX and ABA, diverticulitis and GIP among TCZ patients occurred earlier after the last perfusion ($p=0.01$), with atypical clinical presentation (slow transit in 30%, $p=0.04$) and lower acute phase reactants when the event occurred (C-reactive protein: 31.2 ± 58.4 vs 88.2 ± 89.6 mg/L, $p=0.005$). Perforated diverticulitis seemed to have higher dose of GCs at the time of the event compared to diverticulitis without perforation in univariate analysis ($p=0.06$).

Conclusion: TCZ was associated with an increased risk of diverticulitis, and GIP due to diverticulitis, compared to RTX and ABA. Our study confirms an increased risk of GIP in RA patients treated with TCZ, which might be explained by an increased risk of diverticulitis with misleading clinical presentation.

References:

- [1] Strangfeld A et al. *Ann Rheum Dis.* 2016 Jul 12
[2] Xie F, Yun H et al. *Arthritis Rheumatol.* 2016 May 1
[3] Barbulescu A et al. OP0231, *Ann Rheum Dis.* 2018 Jun 1; 77(Suppl 2):164–5.

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OP0023

PREDICTION OF REMISSION FOR EACH BIOLOGICS BASED ON PATIENT'S CLINICAL INFORMATION BEFORE STARTING BIOLOGICS USING EXPLAINABLE ARTIFICIAL INTELLIGENCE: DATA FROM THE KOREAN COLLEGE OF RHEUMATOLOGY BIOLOGICS REGISTRY

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Background: Many studies have identified predictive factors of response to biologics in patients with rheumatoid arthritis (RA). However, there is still a lack in using them in daily clinical practice. Therefore, it is necessary to develop a method that can assist the physician in selecting effective biologics.

Objectives: The purpose of this study is to establish machine learning model that predicts remission in patients treated with biologics using data of RA patients from the Korean College of Rheumatology Biologics (KOBIO) registry, and to identify the important features that have the most influence on the response to biologics using explainable artificial intelligence (AI).

Methods: A total of 1,527 patients who started with biologics such as etanercept, adalimumab, golimumab, infliximab, abatacept, and tocilizumab from December 2012 to June 2019 were enrolled. Remission was predicted using 46 variables corresponding to baseline profiles at the starting of each biologics. We used five machine learning methods such as lasso, ridge, SVM, random forest, and XGBoost. For explainability of those models, we used Shapley plot to interpret the feature importance for each biologics.

Table 1. Incidence (/1000 PY) and risk of diverticulitis or GIP

Exposition (PY)	AE (n)		IR		AE (n)		IR		AE (n)		IR	IPW analysis			
	TCZ (ref)		RTX		ABA		TCZ vs RTX		TCZ vs ABA		OR [95 CI]		p		
	3 990		6 322		2 389										
Diverticulitis	21	5.3	10	1.6	10	4.2	4.5 [2.6-7.6]	<0.0001	3.4 [1.7-6.5]	<0.0001					
GIP	9	2.3	8	1.3	2	0.8	2.8 [1.5-5.1]	0.001	5.4 [1.4-19.9]	0.01					
* Diverticular GIP	6	1.5	3	0.5	2	0.8	3.8 [1.7-8.5]	0.001	6.9 [1.9-25.4]	0.004					
* Due to another etiology	3	0.7	5	0.8	0	0	1.4 [0.5-3.9]	0.5	-	-					

AE=adverse events; PY=person-years

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 ≥ 300 g (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 $\pm$ 12.3	64.5 $\pm$ 12.5
Female	62%	62%
RA duration at baseline (years)	11.3 $\pm$ 8.5	10.3 $\pm$ 8.2
RF positive	66%	65%
CCP positive	46%	53%
RF/CCP positive	68%	66%
BMI (at RA diagnosis)	28.6 $\pm$ 6.5	27.7 $\pm$ 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.