Table 1. Efficacy endpoints at Week 12

Endpoint ^a	UPA 15mg QD (n=169)	PBO (n=169)
Primary endpoint		
ACR20, %	71.6***	31.4
Secondary endpoints		
Δ DAS28(CRP)	-2.56***	-0.95
Δ HAQ-DI	-0.62***	-0.18
Δ SF-36 PCS	8.93***	3.36 ^d
DAS28(CRP) ≤3.2, %	46.2***	13.6
DAS28(CRP) <2.6, %	29.6***	5.3
CDAI ≤10, %	35.5***	11.2
ACR50, % ^b	40.8***	8.3
ACR70, % ^b	21.3***	3.6
ACR20 at Week 1, % ^b	25.4***	5.9

***p<0.001 vs PBO

^aNRI for binary endpoints; ANCOVA with multiple imputation for DAS28(CRP) and HAQ-DI; mixed model repeated measures for other continuous endpoints

^bUnranked secondary endpoint. ^cn=143. ^dn=149

the primary endpoint of ACR20 (71.6% vs 31.4%, p<0.001). UPA also demonstrated statistically significant improvements in all ranked secondary endpoints vs PBO at Week 12 (Table 1), including mean change in DAS28(CRP), HAQ-DI, and SF-36 PCS, and patients achieving DAS28(CRP) ≤3.2, DAS28(CRP) <2.6, and CDAI ≤10. Greater responses were also seen with UPA vs PBO for other key secondary endpoints including ACR50 and ACR70. Onset of UPA action was rapid with more patients on UPA achieving ACR20 by Week 1 (25.4% vs 5.9%, p<0.001). The frequency of AEs (61.5% vs 49.1%) and serious AEs (7.1% vs 3.0%) was higher with UPA vs PBO. The frequency of AEs of special interest was generally similar between UPA and PBO, with the exception of herpes zoster (1.8% vs 0.6%), hepatic disorders (9.5% vs 7.1%), neutropenia (3.0% vs 0%), and elevated creatine phosphokinase (1.8% vs 0.6%), which were higher with UPA. One case of breast cancer (on Day 1 of study) and one VTE (pulmonary embolism and deep vein thrombosis in a patient with history of deep vein thrombosis) were reported with UPA treatment.

Conclusion: Efficacy of UPA was demonstrated in this csDMARD-IR population from China, Brazil, and South Korea. The safety of UPA was comparable with the global Phase 3 program.

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SAT0161

THE ANALGESIC EFFECT OF TOFACITINIB MAY HAVE CLINICAL SIGNIFICANCE IN PATIENTS WITH RHEUMATOID ARTHRITIS. DATA FROM THE MOSCOW UNIFIED REGISTER OF ARTHRITIS (MUAR)

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Background: Some theoretical data suggest that the JAK-kinase blocker tofacitinib (TOFA) may have a direct analgesic effect.

Objectives: to evaluate the clinical significance of the analgesic effect in patients with rheumatoid arthritis (RA) in real clinical practice.

Methods: Hypothesis being tested: the analgesic effect of TOFA may be manifested by a decrease in the ratio of subjective to objective indicators of arthritis activity.

Data from RA patients receiving biologics (bDMARD) and/or TOFA and included in the MUAR register were analyzed. The tender joints count (TJC),

Table. Ratios of objective and subjective indicators during the treatment with tofacitinib and with tDMARDs therapy in general

Index	Unadjusted values		Identified confounders	Adjusted values (TOFA)	Significance of difference TOFA from average values
	TOFA	Average			
TJC / (SJC +1)	1,93 ± 2,40	2,40 ± 2,78	Age, year of inclusion in registry	1,95 ± 0,45	0,014
HAQ/ (SJC +1)	0,78 ± 0,60	0,89 ± 0,64	Age, year of inclusion in registry, duration of RA, duration of treatment	0,583 ± 0,114	0,039
RAPID3 / (SJC +1)	6,69 ± 4,96	8,13 ± 5,36	Age, year of inclusion in registry, duration of treatment	6,75 ± 0,80	0,001
TJC / (CRP +1)*	1,15 ± 1,83	1,17 ± 1,73	Morning stiffness duration at the RA onset	1,15 ± 0,18	0,263
HAQ/ (CRP +1)*	0,38 ± 0,36	0,40 ± 0,41	Gender, RA duration	0,342 ± 0,04	0,123
RAPID3/(CRP +1)*	3,26 ± 2,74	3,78 ± 3,71	BMI, duration of treatment	3,47 ± 0,43	0,527

* - when calculating the indices, episodes of treatment with tocilizumab (n = 113) were excluded, CRP - level of C-reactive protein, mg/l; TJC - tender joints count, SJC - swollen joints count, TOFA - tofacitinib, RA - rheumatoid arthritis, BMI - body mass index.

the HAQ-DI functional ability index, and the RAPID3 disease activity index were considered as subjective estimates. The swollen joints count (SJC) and the level of CRP were treated as objective indicators. The estimation of quotients from the division of subjective indicators into objective ones in all combinations is made.

Taking into account the observational nature of the study, we searched for confounders for each of these ratios. Comparison of the calculated indices during the treatment with various targeted DMARDs (tDMARDs) was made with an adjustment for the detected confounders.

Results: the analysis included 944 treatment episodes in 832 patients, including 93 episodes of TOFA treatment. The average age was 55.3 ± 12.4 years, women - 698 (83.9%), seropositive for RF -672 (80.8%). The analysis of the adjusted values showed that the ratios of the TJC, HAQ-DI and RAPID3 to the SJC during the treatment with TOFA was significantly lower than with tDMARDs on average. There were no significant differences in the ratios of objective indicators to the CRP level (Table).

Conclusion: the severity of subjective feelings and functional disorders in RA patients receiving TOFA may be less with the same level of objective signs of arthritis compared with bDMARDs.

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SLE, Sjögren's and APS - treatment

SAT0162

WITHDRAWAL OF LOW-DOSE STEROIDS IN SYSTEMIC LUPUS ERYTHEMATOSUS IN REMISSION: PREDICTORS OF FLARES AND DIFFERENCE IN OUTCOMES IN SEROLOGICALLY ACTIVE CLINICALLY QUIESCENT PATIENTS

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Background: According to the recent recommendations for Systemic Lupus Erythematosus (SLE), a progressive tapering until withdrawal of glucocorticoids (GC) is considered one of the main goals of SLE management (1). However, which patient may be a candidate for safe GC withdrawal has not been determined yet and a proportion of patients are kept on long-term low-dose prednisone despite clinical remission.

Objectives: to evaluate the rate of low-dose GC withdrawal in SLE patients in remission and to identify predictors of flares.

Methods: Eligible patients were SLE patients according to the ACR criteria (2) who were in prolonged clinical remission defined by a cSLEDAI=0 for at least 2 years and on a stable SLE treatment (immunosuppressive drugs and/

or hydroxychloroquine (HCQ) and daily 5 mg prednisone). A SACQ period was defined as at least 1-year period with persistent serologic activity without clinical manifestations. Flares were defined by SLEDAI-2K Flare Index (3). Damage was assessed by SLICC damage index (SDI). Data were compared by the unpaired student's t test or chi-squared test as appropriate. Predictors of flares after GC withdrawal were analyzed by Cox regression.

Results: Out of 246 SLE patients registered in the Naples Lupus Clinic database, 132 eligible patients were identified. Among them, we selected 57 (43%) patients in whom a GC withdrawal was attempted. 75 (57%) patients were in the prednisone maintenance group.

There were no significant differences between the two treatment groups (table 1). The proportion of patients experiencing a flare was not significantly lower in the maintenance group than in the withdrawal group (15/75 vs 16/57; $p=0.28$). Moreover, the proportion of patients who had an increase in the SDI at the end of follow up was similar between the two groups (14/75 vs 8/57; $p=0.48$). However, among the withdrawal group, the rate of flares was significantly higher in SACQ patients (10/22 vs 6/35; $p=0.02$), while the majority of serologically inactive patients (82%) successfully stopped GCs without subsequent flares. At Cox regression analysis (Table 2), duration of HCQ therapy and >4 year remission at withdrawal were protective factors, while a SACQ disease and history of lupus nephritis (LN) increased the risk of disease flare.

Table 1. Baseline characteristics of 132 patients at study entry

Characteristics	Withdrawal group (n=57)	Maintenance group (n=75)	p-value
Female, no. (%)	54 (94)	70 (93)	0.73
Age, years	26.7±10.1	28.5±11.7	0.37
Disease duration, years	8.5±2.9	9.1±12.9	0.73
History of lupus nephritis, no. (%)	13(22)	22(29)	
SDI score	0.40±0.7	0.57±0.8	0.26
Immunosuppressive drugs, no. (%)	31 (54)	33(44)	0.16
HCQ, no. (%)	52 (91)	66 (88)	0.06
Low C3, no. (%)	28 (49)	41(54)	0.52
Increased dsDNA Ab, no. (%)	11 (19)	19 (25)	0.41

Table 2. Factors predicting lupus flares during follow-up at Cox regression analysis

Variables	HR	95% CI	p value
SACQ	2.99	1.08 – 8.25	0.03
Age	0.97	0.93 – 1.02	0.29
Disease duration	0.99	0.94 – 1.04	0.84
History of LN	3.38	1.22–9.33	0.01
SDI score	1.13	0.63 – 2.01	0.66
Immunosuppressive drugs	2.39	0.86 – 6.62	0.09
HCQ, ever	2.92	0.43 – 35.2	0.95
Duration of HCQ	0.84	0.72 – 0.98	0.03
5years remission	0.12	0.04 – 0.39	0.0003

Conclusion: GC withdrawal is an achievable target in SLE and may be attempted in patients in complete remission. In SACQ patients, maintenance of 5mg prednisone is superior to its withdrawal in order to prevent flares. Long-term HCQ therapy and prolonged remission can significantly reduce the risk of disease relapse after GC withdrawal.

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SAT0163

IMMUNOSUPPRESSANT WITHDRAWAL AFTER REMISSION ACHIEVEMENT IN LUPUS NEPHRITIS: EFFECT ON FLARE OCCURRENCE

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Background: Whether and when immunosuppressive therapy may be safely withdrawn in patients with lupus nephritis (LN) is still poorly defined. Indeed, there is no clear agreement about the optimal duration of maintenance treatment.

Objectives: We aimed at assessing the rate and predictors of flare after IS withdrawal in patients with LN in remission.

Methods: Patients with systemic lupus erythematosus (SLE) (ACR criteria) and biopsy-proven LN diagnosed between 1990 and 2019, ever treated with IS and currently in follow-up were considered. IS discontinuation was defined as the complete withdrawal of any immunosuppressive drug in patients in remission. Remission was defined as normal serum creatinine, proteinuria <0.5g/24h, inactive urine sediment, and no extra-renal SLE activity (clinical SLE Disease Activity Index [c-SLEDAI]-2K=0) on a stable immunosuppressive and/or antimalarial therapy and/or on prednisone ≤5mg/day. Flares were defined according to SLEDAI Flare Index; renal flare was defined as an increase of proteinuria >0.5g/24h requiring an increase in corticosteroid therapy or the reintroduction of IS. Predictors of a subsequent flare were analyzed by multivariate logistic regression analysis.

Results: Out of 456 SLE patients regularly followed-up, 206 (45.1%) had LN and were considered in our study. Eighty-three patients (40.3%) discontinued IS after remission achievement (Table 1). After stopping therapy, patients were followed for a mean±SD of 99±77 months (range 12-378). Nineteen patients (22.8%) developed a flare after IS discontinuation, after a mean±SD follow-up of 78±68 months (range 7-312), and were re-treated; among them, 6 patients (7.2%) experienced a renal and 13 (15.6%) an extra-renal flare. Compared to patients who flared, patients in persistent IS-free remission had longer remission before IS withdrawal (51.2±31.5 vs. 29.3±16.5 months, $p<0.001$), and continued antimalarials after IS discontinuation ($p=0.005$). No differences in flare occurrence according to the type of IS discontinued were found. At multivariate analysis, therapy with antimalarials was the strongest protective factor against disease flare (OR 0.06, 95% CI 0.11-0.41, $p=0.004$) (Table 2). At last follow-up, mean±SD SLEDAI-2K was 3.1±2.8 and 1.5±1.6 in patients who experienced or not a flare after IS discontinuation, respectively ($p=0.058$). Indeed, 10/19 patients (52.5%) who developed a flare re-achieved remission.

Table 1. Characteristics of 83 patients with LN in remission who discontinued immunosuppressive therapy, overall and according to flare occurrence

	Total patients (83)	Patients with flare (19)	Patients with- out flare (64)	P value
Female, N(%)	72 (88.7)	16 (84.2)	56 (87.5)	ns
Age at 2019, years	43±11	39±11.5	45±10.4	0.049
SLE duration at 2019, years	18±9	16.7±9.0	18.6±8.6	ns
SLE duration at IS discontinuation, years	9.7±7.6	7.1±6.1	10.5±7.8	ns
Time to achieve remission, months	27±37	22.1±35.6	28.5±37.6	ns
Remission duration at IS discontinuation, months	46±30	29 ±16.5	51±31.5	<0.001
IS therapy duration, years	6.7±4.3	5.2±3.8	7.1±4.2	0.061
Anti dsDNA, N(%)	65 (78.3)	18 (95)	47 (73)	0.059
HCQ after IS discontinuation, N(%)	67 (80.7)	12 (63.1)	55 (85.9)	0.005

IS, immunosuppressant; HCQ, hydroxychloroquine

Table 2. Multivariate logistic regression: predictors of flare occurrence

Dependent variable: flare occurrence	OR	95% CI	p value
Number of ISs, ever	3.264	1.030-10.342	0.044
HCQ therapy after IS discontinuation	0.096	0.014-0.652	0.017
Remission duration at IS discontinuation	0.954	0.912-0.997	0.037
Cyclophosphamide, ever	0.065	0.008-0.548	0.012

IS, immunosuppressant; HCQ, hydroxychloroquine

Conclusion: Based on our experience, withdrawal of IS is feasible in selected patients with LN, i.e. patients who achieved stable remission and received maintenance therapy with antimalarials. Patients who experience new flares can re-achieve remission with an appropriate treatment.

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