important to exert certain efficacy of MTX. We previously reported in retrospective study that MTX-PG concentration in RA patients keeping remission for long time was associated with several SNPs²), and some of the results were confirmed in this prospective study.

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SAT0239

RAPID RESPONSE WITH UPADACITINIB TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO CSDMARDS OR bDMARDS

O. FitzGerald¹, A. Rubbert-Roth², K. Chen³, S. Meerwein⁴, J. Enejosa³, T. Shaw³, A. F. Wells⁵. ¹St. Vincent's Univ Hospital and Conway Inst Univ College Dublin, Dublin, Ireland, ²Kantonsspital St. Gallen, St Gallen, Switzerland, ³AbbVie, N Chicago, United States, ⁴AbbVie Deutschland, Ludwigshafen, Germany, ⁵Rheum and Immunotherapy Ctr, Franklin, United States

Background: Upadacitinib (UPA), an oral JAK inhibitor selective for JAK1, demonstrated efficacy in patients (pts) with moderate to severe rheumatoid arthritis (RA) with an inadequate response (IR) to csDMARDs or bDMARDs in the SELECT-NEXT¹ and SELECT-BEYOND² trials, respectively.

Objectives: To investigate the speed of response to UPA across disease measures in csDMARD- and bDMARD-IR pts.

Methods: 661 pts in NEXT and 498 in BEYOND received UPA 15 mg or UPA 30 mg once daily (QD) or placebo (PBO) for 12 weeks (wks)^{1,2}. Time to first achievement of clinically meaningful outcomes, including ACR20/50, DAS28-CRP≤3.2 and Low Disease Activity (LDA) measures of CDAI (≤10) and SDAI (≤11) was evaluated. The cumulative incidences of ACR20/50, DAS28-CRP≤3.2 and LDA by CDAI and SDAI over 12 wks were estimated. Hazard ratios between UPA and PBO were obtained using Cox proportional hazards model with treatment group, corresponding baseline values and main stratification factors, without control for multiple comparisons. All analyses were based on observed data without imputation.

Table 1. Summary of Median Time (in Weeks) to Achieve First Response Over 12 Weeks

		csDMARD-IR			bDMARD-IR		
		N	Median (Q1, Q3)	HR	N	Median (Q1, Q3)	HR
ACR20	PBO	221	12.1 (2.9, NE)		169	11.9 (2.3, NE)	
	UPA 15	219	4.1 (2, 12.1)	2.1***	164	4.1 (1.3, 12.1)	2.0***
	UPA 30	216	2.4 (1.3, 8.1)	2.5***	164	2.7 (1.6, 12.1)	2.0***
ACR50	PBO	221	12.9 (4.2, NE)		169	NE (NE, NE)	
	UPA 15	219	12.3 (4.3, NE)	2.4***	164	12.7 (8, NE)	2.8***
	UPA 30	216	8.6 (4.1, 13.4)	3.4***	165	12.1 (4.1, NE)	3.6***
DAS28-CRP ≤3.2	PBO	221	NE (12.1, NE)		166	NE (12.2, NE)	
	UPA 15	214	12.1 (4.1, 13)	2.9***	163	12.2 (4.1, NE)	2.8***
	UPA 30	215	8.1 (2.6, 12.7)	3.9***	163	8.7 (4.1, 13)	3.2***
CDAI LDA	PBO	210	NE (12.1, NE)		159	NE (NE, NE)	
	UPA 15	206	12.3 (8, 13)	2.2***	156	13.1 (8.1, NE)	2.1***
	UPA 30	209	12.1 (4.1, 13.3)	2.6***	156	12.3 (4.3, NE)	2.5***
SDAI LDA	PBO	210	NE (12.1, NE)		160	NE (12.3, NE)	
	UPA 15	206	12.3 (4.1, 13)	2.6***	156	12.4 (7.7, NE)	2.2***
	UPA 30	209	12 (4.1, 13.4)	3.2***	156	12.1 (4.1, NE)	2.7***
TK68 50% Improvement	PBO	221	8.1 (2.3, NE)		169	8.1 (2.1, 12.4)	
	UPA 15	220	4.1 (2, 12.1)	1.6***	164	4.1 (1.3, 12.1)	1.5**
	UPA 30	216	4.1 (2.1, 8.6)	1.7***	165	4.1 (2, 8.4)	1.5**
SK66 50% Improvement	PBO	221	4.4 (2.1, 12.9)		169	4.1 (2.1, 12.3)	
	UPA 15	220	4.0 (1.4, 8.1)	1.5***	164	2.3 (1.3, 8.4)	1.4**
	UPA 30	216	2.2 (1.3, 8.1)	1.6***	165	3.9 (1.4, 8.1)	1.4**

HR, hazard ratio; NE (not estimable) indicates that the response was not reached within the 12-week period. ***p<0.001

HR, hazard ratio; NE (not estimable) indicates that the response was not reached within the 12-week period. ***p<0.001

Results: Pts had a disease duration of 7 and 13 years in NEXT and BEYOND respectively.^{1,2} In BEYOND, pts were treatment-refractory as evidenced by 53% having received ≥2 prior bDMARDs². Median times to achieve ACR20 were similar, irrespective of pt population, being 4 wks for UPA 15 mg QD and 2–3 wks for

UPA 30 mg QD vs 12 wks on PBO (p<0.001). In general, the median times to achieve ACR50 and DAS28-CRP≤3.2 for UPA 15 mg and 30 mg QD were ~12 wks and ~8 wks for both csDMARD-IR and bDMARD-IR pts, whereas the median was not reached for pts on PBO during the first 12 wks (p<0.001, table 1). The median time to LDA by CDAI and SDAI was ~12 wks across UPA doses and populations, but was not reached for pts receiving PBO within that time. Pts receiving UPA were 2–4 times more likely to achieve clinical responses vs pts receiving PBO. In general, both UPA doses performed similarly across pt populations, with numerically quicker responses observed in pts receiving UPA 30 mg vs UPA 15 mg QD. Median times to achieve 20% and 50% improvements in tender and swollen joint counts were 1–2 wks and 2–4 wks respectively, for both UPA doses, irrespective of pt population. Median times to achieve 20% improvements in morning stiffness duration and severity were approximately 2 wks in each of the UPA arms vs 4 wks on PBO (p<0.001).

Conclusions: Pts receiving UPA at either 15 mg or 30 mg QD were more likely to achieve clinical responses at significantly earlier time points when compared with pts receiving PBO. Irrespective of being csDMARD-IR or bDMARD-IR, times to achieve various clinical responses were consistent between pt populations.

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SAT0240

VAGUS NERVE STIMULATION IN PATIENTS WITH RHEUMATOID ARTHRITIS: TWO-YEAR SAFETY AND EFFICACY

F. A. Koopman¹, A. Musters¹, M. J. Backer¹, D. Gerlag¹, S. Miljko², S. Grazio³, S. Sokolovic⁴, Y. A. Levine⁵, N. de Vries¹, P.-P. Tak¹. ¹Academic Medical Center/University of Amsterdam, Amsterdam, Netherlands, ²University Clinical Hospital, Mostar, Bosnia and Herzegovina, ³Clinical Hospital Center Sestre Milosrdnice, Zagreb, Croatia, ⁴Sarajevo University Clinical Center, Sarajevo, Bosnia and Herzegovina, ⁵SetPoint Medical, Inc, Valencia, United States

Background: Rheumatoid arthritis (RA) is a debilitating chronic disease with an unmet need for additional therapeutic approaches. Activating neuro-immune reflex pathways by stimulation of the vagus nerve (VNS) could represent a novel means of treating RA [1] and other immune-mediated inflammatory diseases. Last year we reported a 12-week proof-of-concept study using a VNS device, approved for drug-resistant epilepsy, showing reduction in the DAS28-CRP clinical disease activity score, with concomitant reductions in TNF and IL-6 levels [2].

Objectives: To understand the long term safety and efficacy of this novel treatment approach, we followed the patients in a 24 months long-term extension study and report on the safety and clinical efficacy data.

Methods: VNS devices were implanted into 17 RA patients, mostly with insufficient response to multiple conventional and biologic disease-modifying antirheumatic drugs (DMARDs), on stable background of methotrexate (≤25 mg weekly) therapy. The devices electrically stimulated the vagus nerve, 1–4 min/day, over a 12 week open label period. On completion, subjects were offered to enroll into a follow-up study, where the study physicians were given flexibility to alter VNS dosing parameters and/or to add a biologic DMARD to the treatment regimen. DAS28-CRP and Health Assessment Questionnaire-Disability Index (HAQ-DI) were collected over 2 years.

Results: All subjects electively continued on VNS treatment through 24 months of the long term follow-up study. Biologic DMARDs were started in 1 and restarted in 8 of 17 subjects; of these, 4 were non-responders to VNS, and 5 had stable improvement but had not yet achieved disease remission on VNS alone (table 1). At the start of the follow-up study, the mean DAS28–28 and HAQ-DI were significantly reduced compared to the pre-implant baseline (mean difference±SE in DAS28-CRP = -1.60±0.37, p<0.0001; mean difference±SE in HAQ-DI = -0.44±0.21, p<0.037), and the depth of effect was retained through 24 months. At 24 months, there was no significant difference in DAS28-CRP between the subjects using VNS monotherapy or those using a combination of VNS and biologic

DMARDs (VNS monotherapy= 3.76±1.77 vs. VNS and biologic DMARD= 3.21±1.44, $p<0.54$). No difference in the adverse events profile between the two groups was seen.

Table 1 Two Year Efficacy of VNS Treatment. Mean DAS28-CRP at primary study baseline (month -3-5) and at visits over 2 years of long term follow up (months 0-24). **Conclusions:** The data presented here demonstrate that VNS in subjects with RA is associated with a substantial reduction in disease activity that is sustained for 24 months without untoward safety signals. In addition, the data suggest that biological DMARDs can be initiated safely in combination with VNS treatment, though this requires further study in larger cohorts. These results support further development of VNS devices as an alternative therapeutic approach for RA treatment, which potentially can safely be combined with biologic DMARDs.

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SAT0241

PATIENTS' PERSPECTIVE ON THE EFFICACY AND RISKS OF GLUCOCORTICOIDS IN RA – AN INITIATIVE UNDER THE GLORIA PROJECT

P.D. Carvalho¹, N. Goel², M. Voshara³, M. Boers^{4,5}, J.A.P. D. Silva⁶. ¹*Serviço de Reumatologia, Centro Hospitalar e Universitário do Algarve, Faro, Portugal*, ²*QVIA, Duke University School of Medicine, Durham, NC, United States*, ³*Department Psychology, Health and Technology, University of Twente, Twente*, ⁴*Department of Epidemiology and Biostatistics, ⁵Amsterdam Rheumatology and Immunology Center, VU University Medical Center, Amsterdam, Netherlands*, ⁶*Faculty of Medicine and University Hospital, Coimbra, Portugal*

Background: The Glucocorticoid Low-dose Outcome in Rheumatoid Arthritis Study (GLORIA) is an international investigator-initiated pragmatic randomised trial designed to study the effects of low dose glucocorticoids (GC) in elderly patients with Rheumatoid Arthritis (RA). The research team is also committed to promote a better understanding of the risks and benefits of these drugs among health professionals and patients. In order to achieve these goals, it is important to assess the current concepts and concerns of patients regarding GC.

Objectives: In this study, we evaluated the beliefs about GC in RA patients who are, or have been treated with GC.

Methods: Patients with RA from three different countries (United States (US), Portugal, and the Netherlands) completed an online survey which was presented in their native language.

Members of People with Arthritis and Rheumatism, and national associations were involved in the development of the questionnaire. In Europe, patients were invited to participate through national patients' organizations, and SurveyMonkey[®] was used to disseminate the online surveys. In the US, patients were invited to participate and surveyed through MediGuard.org.

Patients with RA from three different countries (United States (US), Portugal, and the Netherlands) completed an online survey which was presented in their native language.

Members of People with Arthritis and Rheumatism, and national associations were involved in the development of the questionnaire. Participants were asked to agree or disagree with statements on a 5-point scale. In Europe, patients were invited to participate through national patients' organizations, and SurveyMonkey[®] was used to disseminate the online surveys. In the US, patients were invited to participate and surveyed through MediGuard.org.

Results: Data was collected from 314 RA patients with exposure to GCs (table 1). Mean education level was around 15 years and duration of GC exposure was

skewed (median 48 months [inner quartiles 8, 120]). The majority of US patients had received prednisone and in Europe, prednisolone. The majority of participants in all three regions had already read articles or pamphlets on the benefits or harms related to GC therapy.

Regarding GC risk, about half of the European patients stated that they had already suffered a serious adverse event (SAE) due to GC. US patients were not asked if they suffered GC-related SAE due to regulatory reporting rules, but 82% showed concern about experiencing an SAE from GC use.

Regarding GC efficacy, high levels of endorsement were found for the three questions asked: more than 78% of patients considered that GC were very useful in their case, more than 61% considered that GC were effective even in low doses, and more than 60% agreed that GC improved RA symptoms within days.

Table 1 Patient beliefs about GC from surveys in USA, Portugal and The Netherlands.

	USA	Portugal	Netherlands
Number of patients	139	131	44
Education, mean ± SD (years)	14 ± 3	15 ± 5	16 ± 4
GC prescribed (%)			
Prednisone	78	18	33
Prednisolone	11	73	62
Methylprednisolone	9	10	5
Other	1	0	0
Treatment duration, median (inner quartiles, months)	24 (5-84)	120 (36-180)	36 (4-108)
Have you read any articles or pamphlets on the benefit or harm of GC therapy? (%)	72	64	75
Level of agreement for statements (%)*			
If I take GC, I am concerned that I may suffer a serious adverse event	82 (55)	NA	NA
I have suffered serious adverse events due to GC	NA	48 (18)	51 (23)
GC are or have been very useful to me	79 (56)	86 (55)	85 (69)
At a dose of less than or equal to 7.5 mg of prednisolone/day, GC:			
- are very effective in the control of signs and symptoms of RA	61 (38)	78 (41)	69 (44)
- improve RA symptoms within days	60 (41)	74 (45)	69 (49)

* Total of 'slightly agree' and 'agree' in parentheses the percentage of 'agree';

SD: Standard Deviation; GC: Glucocorticoid; RA: Rheumatoid Arthritis; NA: Not Asked.

Conclusions: Patients with RA exposed to long-term GC report a high prevalence of SAE or fear thereof. This is accompanied by a strong conviction that GC are very useful and effective for the treatment of their RA, even at low dosages.

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SAT0242

EFFECTIVENESS OF CONVENTIONAL DMARD THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED UNDER A TREAT TO TARGET MODEL – LESSONS FROM A REAL-LIFE COHORT

P. Santos-Moreno¹, D. Buitrago-Garcia², L. Villarreal³, M. Cabrera³, E. Castillo¹, E. Cardozo¹, S. Farietta¹, R. Giraldo¹, D. Gomez¹. ¹*Rheumatology, Biomab, Center For Rheumatoid Arthritis, Bogota*, ²*Epidemiology, SIIES*, ³*Health services, Biomab, Center For Rheumatoid Arthritis, Bogota, Bogota, Colombia*

Background: Rheumatoid arthritis (RA) is a common chronic inflammatory disease. It is characterized by progressive, joint damage, impaired joint function and pain, the disease causes disability and reduces quality of life. Treat-to-target (T2T) is an acknowledged management strategy for RA; it proposes that the therapeutic target in RA should be a state of remission or low disease activity. There are two types of pharmacological therapy available: biological DMARDs that are considered highly expensive for our countries and conventional DMARDs which have demonstrated effectiveness and is a low-cost treatment (1,2).

Objectives: The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) using a T2T strategy during three years in a cohort of patients receiving conventional DMARDs.

Methods: A descriptive cohort study was conducted. Medical records of patients from specialized in RA center were reviewed during 2015–2017; those patients were followed-up under T2T standards and a multidisciplinary approach. Clinical follow-up was according to DAS28: every 3–5 weeks (DAS28 >5.1), every 7–9 weeks (DAS28 ≥3.1 and ≤5.1), and every 11–13 weeks (DAS28 <3.1). Therapy had to be adjusted with DAS28 >3.2 unless patient's conditions don't permit it; We divided patients in four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and severe disease activity (SDA) patients and the aim of the study was to look at what percentage of patients reached LDA or REM. Descriptive epidemiology was done, we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates.