FRI0279

USE OF TNF-INHIBITORS BEFORE, DURING AND THE FIRST YEAR AFTER PREGNANCY IN WOMEN WITH SPONDYLOARTHRITIS

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Background: Treat to target is a goal in pregnant women with spondyloarthritis. There is increasing evidence on safe use with TNF inhibitors during pregnancy (1). Adjusted use of TNF inhibitors preconception and throughout pregnancy may stabilize disease activity and prevent flares (2). Low disease activity is also beneficial for the fetus.

Objectives: To study the use of TNF-inhibitors among women with spondyloarthritis in Norway before, during and after pregnancy.

Methods: RevNatus is a Norwegian, nationwide quality register that monitors treatment of inflammatory rheumatic diseases before, during and after pregnancy. Data from RevNatus in the period October 2017 to October 2019 were used to map the use of all types of TNF inhibitors among 208 women with spondyloarthritis, fulfilling the ASAS criteria.

The use of medication was reported at the time of visit in outpatient clinic. The frequency of use of TNF inhibitors is registered at seven timepoints from pre-pregnancy to twelve months after delivery.

Results: The use of TNF-inhibitors was reported at each visit for all the women with spondyloarthritis. Most women are not using TNF inhibitors before and beyond conception. Most of the women continuing TNF inhibitors beyond conception, used certolizumab, etanercept, or adalimumab. Infliximab or golimumab were not used in pregnancy (tabell 2).

Table 2:

SPA	Certolizumab	Etanercept	Adalimumab	Golimumab	Infliximab	No TNF-inhibitor
Before Pregnancy n=139	10% (14)	8% (11)	6% (9)		6% (9)	69% (96)
1.trimester n=102	7% (7)	7% (7)	2% (2)			84% (86)
2.trimester n=104	7% (7)	6% (6)	1% (1)			87% (90)
3. trimester n=95	3% (3)	2% (2)	1% (1)			94% (89)
6 weeks post partum n=100	15% (15)	10% (10)	8% (8)	3% (3)		64% (64)
6 months post partum n=82	19% (16)	12% (10)	7% (6)	2% (2)	2% (2)	55% (46)
12 months post partum n=74	22% (16)	15% (11)	7% (5)	4% (3)	5% (4)	47% (35)

Conclusion: A majority of the women with spondyloarthritis were not treated with TNF inhibitors before or during pregnancy. Only a few of the women with spondyloarthritis continued treatment with TNF inhibitors during pregnancy.

References:

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FRI0280

COMPARATIVE DRUG SURVIVAL OF TNF INHIBITORS AND SECUKINUMAB IN BIOLOGIC NAÏVE PATIENTS WITH ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS

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Background: Secukinumab (SEC) was approved for treating ankylosing spondylitis (AS) and psoriatic arthritis (PsA) in the UK in 2016/17 respectively, providing an alternative mechanism of action to TNF inhibitors (TNFi), which were, until that time, the most frequently prescribed biologic therapies for these rheumatic

conditions. SEC's efficacy and safety has been shown in clinical trials^{1,2}, but real world data on its survival remains scarce.

Objectives: This study aimed to compare SEC and TNFi drug survival in AS and PsA biologic naïve patients.

Methods: Observational retrospective study of consecutive biologic naïve patients attending the Dudley Group NHS Foundation Trust (DGFT) with a clinical diagnosis of AS (fulfilling ASAS criteria) or PsA (fulfilling CASPAR criteria) who received at least one dose of biologic therapy between 01/07/2017 and 30/09/2019, with a follow-up period until December 31st, 2019. The biologics database, patient medical records and investigations were reviewed and data on demographics, disease characteristics, previous cDMARD therapy and reasons for discontinuation of biologic were collected. Analysis was performed using descriptive statistics, Kaplan-Meier plots and Cox regression on SPSS version 23.

Results: We identified 153 AS or PsA patients starting biologic therapy in this time interval. 103 (68.7%) were biologic naïve, commencing either TNFi (38, 36.9%), SEC (63, 61.1%) or Ixekizumab (2, 1.9% -excluded from analysis) for AS (45.5%) and PsA (54.5%). The patients were evenly distributed in terms of sex (female 50.5%), had a mean ($\pm$ SD) age of 45 ($\pm$ 13.8) years and a median (IQR) disease duration of 5 (7.7) years. The median (IQR) follow up time was 13 (13) months.

The overall 1 and 2-year drug survival was 86.8% and 79.3% respectively for TNFi and 81.5% and 77.4% for SEC treated patients. There was no statistically significant difference between the estimated means for drug survival time for the two treatment modalities (TNFi: 24.4 vs SEC:22.9 months, *log rank*:0.991) (Figure 1). The analysis of SEC's drug survival in AS in comparison to PsA did not show statistically significant difference (21.8 vs 22.0 months respectively, *log rank*: 0.419). We observed a trend for worse TNFi survival in AS compared to PsA, but this did not reach statistical significance (18.9 vs 26.1 months respectively, *log rank*: 0.09).

Figure 1. Comparative cumulative drug survival (months) in biologic naïve AS and PsA patients

No significant difference in reasons for discontinuation between treatments was observed. Age, sex, disease duration, previous DMARD use and extra-articular manifestations were variables that were not associated with drug survival on Cox regression analysis.

Conclusion: The estimated 1 year drug survival for TNFi and SEC was 86.8% and 81.5% respectively. Data from our cohort of real-life previously biologic naïve patients with AS and PsA showed no difference in drug survival and reasons for discontinuation between TNFi and SEC. Age, sex, previous DMARD use and extra-articular manifestations were not predictors for drug survival.

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FRI0281

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN PATIENTS WITH STABLE ANKYLOSING SPONDYLITIS RECEIVING TUMOR NECROSIS FACTOR INHIBITOR: CONTINUED VS WITHDRAWN

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Background: A recent recommendation from the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network (ACR/SAA/SPARTAN) suggests withdrawing non-steroidal anti-inflammatory drugs (NSAIDs) in patients with stable ankylosing spondylitis (AS) receiving tumor necrosis factor inhibitor (TNFi) and NSAIDs.¹ However, the level of evidence for this statement is very low with lack of evidence supporting this recommendation. No studies have directly compared stable AS patients receiving TNFi with NSAIDs, and those receiving TNFi without NSAIDs.

Objectives: To compare the disease activity in stable AS patients receiving TNFi, according to the use of NSAIDs.

Methods: In total, 189 patients with stable AS receiving TNFi were included. Patients were classified into NSAID withdrawn group (n=48) and NSAID continued group (n=141), according to the use of NSAIDs. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were measured every 3 months, and Bath ankylosing spondylitis disease activity index (BASDAI) was measured every 6 months as parameters to evaluate disease activity. ESR, CRP, and BASDAI at each time point, and time-averaged values of each parameter during the observation period of one-year were compared between the two groups. Repeated-measure ANOVA was performed to compare changes in disease activity parameters during the observation period between the two groups.

Table. Disease activity measures during observation period

	NSAID withdrawn (N = 48)	NSAID continued (N = 141)	P value
At 3 months			
ESR (mm/hr), median (IQR)	5.0 (2.0–14.0)	7.0 (2.0–15.0)	0.712
CRP (mg/L), median (IQR)	0.5 (0.2–1.5)	0.8 (0.3–1.8)	0.613
At 6 months			
ESR (mm/hr), median (IQR)	5.0 (2.0–15.0)	7.0 (2.0–15.0)	0.278
CRP (mg/L), median (IQR)	0.6 (0.3–1.8)	0.8 (0.3–2.1)	0.335
BASDAI, mean ± SD	2.019 ± 0.569	2.226 ± 1.028	0.187
At 9 months			
ESR (mm/hr), median (IQR)	4.5 (2.0–13.8)	7.0 (2.8–17.0)	0.261
CRP (mg/L), median (IQR)	0.5 (0.3–1.6)	0.8 (0.3–2.2)	0.129
At 12 months			
ESR (mm/hr), median (IQR)	6.0 (2.0–13.0)	9.0 (3.0–19.0)	0.050
CRP (mg/L), median (IQR)	0.6 (0.3–2.1)	1.0 (0.4–3.1)	0.151
BASDAI, mean ± SD	2.168 ± 1.066	2.197 ± 1.002	0.867
Time-averaged values			
ESR (mm/hr), median (IQR)	5.3 (2.6–15.2)	8.4 (3.8–14.7)	0.096
CRP (mg/L), median (IQR)	0.8 (0.4–1.8)	1.1 (0.5–2.9)	0.136
BASDAI, mean ± SD	2.137 ± 0.557	2.227 ± 0.706	0.421

Abbreviations: NSAIDs, non-steroidal anti-inflammatory drugs; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BASDAI, Bath ankylosing spondylitis disease activity index.

Results: The level of ESR, CRP, and BASDAI at baseline and during the observation period did not differ between the two groups. The time-averaged values of ESR (p=0.096), CRP (p=0.136), and BASDAI (p=0.421), and changes of ESR (p=0.101), CRP (p=0.714), and BASDAI (p=0.613) during the observation period were not significantly different between the two groups.

Conclusion: The continued use of NSAIDs in patients with stable AS receiving TNFi had no additional benefit in controlling the disease activity, as compared to patients who withdrew NSAIDs. Considering the risk of toxicity of long-term NSAID use, withdrawal of NSAIDs in stable AS patients receiving TNFi may be preferable.

References:

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FRI0282

CONVENTIONAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS THERAPY HAS NO EFFICACY IN SLOWING SPINAL RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS: RESULTS FROM 18-YEAR LONGITUDINAL DATA

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Background: In the treatment of ankylosing spondylitis (AS), conventional disease-modifying antirheumatic drugs (cDMARDs) are generally recommended only in patients with peripheral arthritis. However in daily clinical practice, sulfasalazine (SSZ) and methotrexate (MTX) have still been considered on the basis of their anti-inflammatory effect when non-steroidal anti-inflammatory drugs (NSAIDs) are not available and when it is difficult to start tumor necrosis factor (TNF) inhibitors. Nonetheless there is few data about the impact of the cDMARDs on the prognosis of spinal progression.

Objectives: The aim of this study was to investigate the effectiveness of SSZ and MTX on the spinal radiographic progression in patients with AS.

Table 1. Association of clinical covariates and DMARD intervals with the rate of mSASSS change

Variable	Multivariate analysis			
	Model 1		Model 2	
	β (95% CI)	p	β (95% CI)	p
On-DMARD intervals	-0.081 (-0.276 to 0.115)	0.418		
On-SSZ intervals			-0.001 (-0.211 to 0.189)	0.913
On-MTX intervals			-0.180 (-0.439 to 0.078)	0.172
Sex (female)	-0.449 (-0.782 to -0.117)	0.008	-0.440 (-0.775 to -0.105)	0.010
Age	0.012 (-0.001 to 0.026)	0.061	0.012 (-0.001 to 0.025)	0.076
Eye involvement	0.572 (0.264 to 0.880)	< 0.001	0.577 (0.268 to 0.886)	< 0.001
Peripheral joint involvement	-0.508 (-0.810 to -0.206)	0.001	-0.513 (-0.817 to -0.210)	0.001
HLA-B27 positivity	†		†	
NSAIDs	†		†	
Glucocorticoids	†		†	
ESR (log)	0.176 (0.087 to 0.265)	< 0.001	0.178 (0.088 to 0.268)	< 0.001
BASDAI (square root)	†		†	

†Not included in the model because the value did not show potentially significant association in univariate analysis (p > 0.1).

Methods: A total of 301 patients who have been treated with cDMARDs were enrolled from 1,280 patients in a single center cohort during 18 years of follow up. For each patient, time intervals of periods were created according to the prescription records. 'On-DMARD' intervals were time intervals of periods with SSZ or MTX treatment and 'off-DMARD' intervals were time intervals of periods without both SSZ and MTX treatment. The intervals were the periods excluding the treatment periods of TNF inhibitors. Radiographic progression was evaluated by the rate of Modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) change, an increase or decrease of mSASSS change per year. A generalized estimating equation models with adjustment for confounding covariates were used to evaluate the efficacy of cDMARDs on the radiographic progression.

Results: The number of 732 on-DMARD intervals and 1,027 off-DMARD intervals were obtained. Among the on-DMARD intervals, the proportion of intervals treated with SSZ (on-SSZ intervals), MTX (on-MTX intervals) and both of them (on-SSZ/MTX intervals) were 96.2%, 19.9% and 16.1%, respectively. In the multivariable regression analysis, there was no significant decrease in the rate of mSASSS change during cDMARDs therapy (β = -0.081, p = 0.418) (Table 1). And the mean rate of mSASSS change were 0.61 during on-DMARD intervals and 0.69 during off-DMARD intervals after adjustment of other covariates.

Conclusion: Treatment with cDMARDs in AS did not show significant impact in retarding spinal progression. In patients with AS, treatment with biologics rather than cDMARDs may be more effective in slowing radiographic progression.