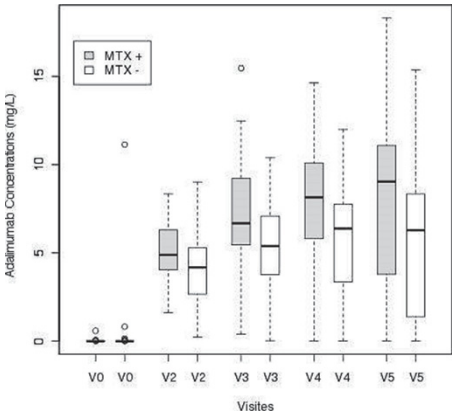
However, anti-drug antibodies (ADA) may be responsible for decreased efficacy. Methotrexate reduces adalimumab immunogenicity in rheumatoid arthritis (1).
Objectives: The aim of the study was to evaluate the effect of methotrexate on ADA detection in SpA patients receiving adalimumab.
Methods: One hundred and ten SpA patients eligible for adalimumab 40 mg S/C eow were randomized on a 1:1 ratio to receive MTX 10 mg s/c every week, 2 weeks prior (V0) adalimumab (MTX+), or adalimumab alone (MTX-). ADA detection and adalimumab concentration were assessed 4 weeks (V2), 8 weeks (V3), 12 weeks (V4) and 26 weeks (V5) after starting adalimumab (V1). The main outcome was the percentage of positive patients for ADA detection at V5 or last available visit.
Results: Patients' characteristics (sex, previous TNF inhibitors, disease duration, HLA B27 +/-, BMI) were comparable between the two groups. One hundred and seven patients were analyzed, 55 in the MTX+ group versus 52 in the MTX- group. ADA were detected at V5, in 39/107 (36.4%) patients; 13/52 (25%) in the MTX+ group versus 26/55 (47.3%) in the MTX- group (p=0.03). Adalimumab concentrations were statistically higher in the MTX+ group as compared with the MTX- group at V2, V3, V4 and V5 (Figure 1). There was no difference in terms of adverse events and efficacy between the two groups.



Conclusions: MTX reduces immunogenicity and ameliorates pharmacokinetics of adalimumab in SpA patients. The clinical impact of this combination requires longer period studies.
References:
[1] Krieckaert CL, Nurmohamed MT, Wolbink GJ. Ann Rheum Dis 2012.
Acknowledgements: The authors thank Bruno Giraudeau for his methodological advice in the study design; Yoann Desvignes for technical support with the study protocol; Elody Marnat for data management; Coraline Gadras and Céline Vignault for blood sample management; Anne-Claire Duveau for technical assistance. This work was promoted by the Regional University Hospital Center of Tours and supported by grants from the French Ministry for Health and Sport within the framework of the "Programme Hospitalier de Recherche Clinique 2011" and received fundings from the "Lions Club, Tours Val de France" and from Nordic Pharma who provided subcutaneous methotrexate. This work was a collaborative venture by HUGO (Hôpitaux Universitaires du Grand Ouest – Western France University Hospitals Network).
Disclosure of Interest: E. Ducourau: None declared, T. Rispens: None declared, E. Dernis: None declared, F. Le Guilchard: None declared, L. Andras: None declared, A. Perdriger: None declared, E. Lespessailles Grant/research support from: MSD, Novartis, UCB, Pfizer, Consultant for: MSD, Novartis, UCB, Pfizer, A. Martin: None declared, G. Cormier: None declared, T. Armingeat: None declared, V. Devauchelle-Pensec: None declared, E. Solau-Gervais: None declared, B. Le Goff: None declared, A. de Vries: None declared, E. Piver: None declared, D. Ternant Consultant for: Sanofi, Amgen, P. Goupille Consultant for: Abbvie, Biogaran, BMS, Hospira, Janssen, MSD, Pfizer, Sanofi-Genzyme, UCB, D. Mulleman Grant/research support from: Nordic Pharma, Abbvie, Consultant for: MSD, Novartis, UCB, Pfizer
DOI: 10.1136/annrheumdis-2017-eular.1527

THU0350 EFFECT OF NSAID CONSUMPTION ON CARDIOVASCULAR EVENTS IN SPONDYLOARTHRITIS

E. Rivière[1,2], A. Etcheto[3], F. Van den Bosch[4], D. Van der Heijde[5], R. Landewé[6], M. Dougados[3], A. Molto[3] on behalf of ASAS-COMOSPA taskforce.
[1]Rheumatology, Bicêtre Hospital, INSERM U1184, le Kremlin Bicêtre; [2]Rheumatology B, Cochin Hospital; [3]Rheumatology B, Cochin Hospital, INSERM U1153, Paris, France; [4]Rheumatology, Ghent Universituy Hospital, Ghent, Belgium; [5]Rheumatology, Leiden University Medical Center, Leiden; [6]Rheumatology and Immunology Center, ARC, Amsterdam and Zuyderland Hospital Heerlen, Amsterdam, Netherlands

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) have been reported to increase cardiovascular (CV) risk. Studies on NSAIDs safety in patients with spondyloarthritis (SpA) are rare and contradictory. However, this question is highly relevant for these patients with chronic NSAIDs use and increased CV risk (1).
Objectives: The objective of this study was to determine the relationship between NSAIDs use and the occurrence of CV events, including myocardial infarction (MI) and stroke, in patients with SpA.
Methods: This is an ancillary study of the observational, cross-sectional, multicenter, international ASAS-COMOSPA study. The inclusion criteria were: age >18 years and SpA diagnosis. In order to overcome prescription bias when comparing patients who ever received/did not receive NSAIDs, a propensity score (PS) to predict NSAIDs intake was calculated. Patients who had never received NSAIDs were matched to patients who ever received an NSAID according to the PS. In this matched population, the probability for a patient to present a CV event was estimated by logistic regression. Furthermore, in the global population of the study, factors associated with the occurrence of CV event were explored by logistic multivariate analysis, here including the NSAIDs score (2) of the last three months, age and gender, and using the PS as an adjustment variable.
Results: Of the 3984 patients enrolled in the study, data on CV event occurrence were available for 3961 patients. Among them, 3548 patients received NSAIDs (89.6%) and 378 had never received NSAIDs (10.4%). Patients who had never received NSAIDs had more often inflammatory bowel disease (9.9% vs 5.3%), and a less severe disease (% of bamboo patients: 2.0% vs 7.6%). Among the 756 matched patients, 29 (3.8%) patients reported a CV event (21 MI, 13 strokes and 5 MI + stroke). The number of patients with CV event was not significantly different between the two groups, ever and never NSAIDs exposure respectively (16 (2,1%) vs 13 (1,7%), OR =1.86 [0.496–6.989]). No difference was observed between the two groups for MI and stroke compared separately (12 (1,6%) vs 9 (1,2%), OR =2.96 [0.417–21.013] and 8 (1,1%) vs 5 (0,7%), OR =0.926 [0.288–22.108] respectively). In the second model, where PS was used as a covariate, the occurrence of overall CV event was independently associated with age (OR =2.7 [2.3–3.2]) and male sex (OR =1.9 [1.2–3.0]), but not with the NSAIDs score (OR =1.0 [0.9–1.1]).
Conclusions: The use of NSAIDs does not seem to be associated with the occurence of CV event in patients with SpA, however it cannot be excluded that the study is underpowered. Further prospective studies are needed to confirm these results.
References:
[1] Haroon NN, et al. Ann Intern Med. 2015;163(6):409–16.
[2] Dougados M, et al. Ann Rheum Dis. 2011;70(2):249–51.
[3] Moltó A, et al. Ann Rheum Dis. 2016;75(6):1016–23.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2665

THU0351 ADALIMUMAB TAPERING WITH COMBINED METHOTREXATE CAN BE EFFECTIVE AS MAINTENANCE THERAPY IN SPA-RELATED UVEITIS

F. Lian, J. Zhou, Y. Wang, H. Xu, L. Liang, X. Yang. *Dept. of Rheumatology, 1St Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China*

Background: Anti-TNF agents have deeply improved the therapeutic efficacy of spondyloarthritis (SpA)-related uveitis [1]. Despite the benefits of anti-TNF drugs, patients need to stay on this treatment for a long time. There has been a clear medical need to consider the long-term safety and increased drug costs. Unanswered question for physicians is whether TNF blockers can be reduced or even stopped in SpA-related uveitis, or how can it be reduced in patients have achieved remission or LDA. The current study aimed to investigate the effectiveness and safety of adalimumab tapering strategy in SpA-related uveitis. We tried to find a way in balancing the quality of the patients' lives, the side effects and the cost-effectiveness.
Objectives: The aim of this study was to evaluate the effectiveness of tapering of adalimumab combined with MTX in patients with spondyloarthritis (SpA)-related uveitis.
Methods: We performed a retrospective analysis. SpA patients with uveitis admitted to a south China hospital were enrolled. Demographic information, clinical characteristics, laboratory findings, intraocular inflammation, visual acuity, and macular thickness were documented every 3 to 6 months.
Results: In 32 cases of SpA-related uveitis who achieved clinical remission for at least 6 months after receiving a standard dose of adalimumab in combination of MTX, adalimumab was tapered and MTX was continued. Dosing interval of adalimumab were spaced by 30% every 3 months up to complete stop. Twenty-six cases without MTX were analyzed for comparison. No significant difference of demographic characteristics and BASDAI, CRP, ESR was found between the two groups at the baseline. During the first 12 months of adalimumab tapering, the mean BASDAI remained stable in both groups. No recurrent uveitis was found in the group with combined MTX. In the group without combined MTX, 2 patients (2/26, 7.7%) presented increased anterior chamber inflammation and visual acuity. At the end of 24 months, mean BASDAI, CRP and ESR remained low in both groups. Two cases (2/32, 6.3%) in the group of combined MTX were documented increased BASDAI higher than 4, but no recurrent uveitis was observed. Altogether 5 cases (5/32, 15.6%) in the group of combined MTX had recurrent uveitis, in which 4 cases (4/5, 80%) initiated adalimumab tapering at 6 months' remission. In comparison, 8 cases (8/26, 30.8%, $p<0.001$) in the group without combined MTX had recurrent uveitis, in which 6 cases initiated

adalimumab tapering at 6 months' remission and 2 cases initiated adalimumab tapering at 9–12 months' remission. No patients had recurrent uveitis at 12 months' remission or longer in both groups. Adalimumab plus MTX were well tolerated in all patients.

Conclusions: For maintaining remission of SpA-related uveitis, adalimumab tapering can be effective when combined with MTX. Initiation of the tapering after 12 months' remission largely lower the rate of recurrence.

References:

[1] Jaffe GJ, Dick AD, Brézin AP, et al. Adalimumab in Patients with Active Noninfectious Uveitis. N Engl J Med. 2016 Sep 8; 375(10):932–43.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2507

THU0352 TOFACITINIB TREATMENT IS ASSOCIATED WITH ATTAINMENT OF THE MINIMALLY IMPORTANT REDUCTION IN AXIAL MRI INFLAMMATION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

W.P. Maksymowych[1], D. van der Heijde[2], X. Baraliakos[3], A. Deodhar[4], M. Brown[5], S.P. Sherlock[6], D. Li[7], D. Fleishaker[8], T. Hendrikx[7], K.S. Kanik[8].
[1]University of Alberta, Edmonton, AB, Canada; [2]Leiden University Medical Center, Leiden, Netherlands; [3]Rheumazentrum Ruhrgebiet, Herne, Germany; [4]Oregon Health & Science University, Portland, OR, United States; [5]Queensland University of Technology, Brisbane, Australia; [6]Pfizer Inc, Cambridge, MA; [7]Pfizer Inc, Collegeville, PA; [8]Pfizer Inc, Groton, CT, United States

Background: Tofacitinib is an oral Janus kinase inhibitor. The minimally important changes (MICs) for the SPondyloArthritis Research Consortium of Canada (SPARCC) MRI sacroiliac joint (SIJ) and spine scores based on agreement with global change scores by readers are ≥2.5 and ≥5, respectively.[1]

Objectives: To assess whether MIC in SIJ and spine can discriminate between tofacitinib and placebo (PBO) in patients (pts) with ankylosing spondylitis (AS) and if this is concordant with clinical responses.

Methods: In this 16-week (wk), Phase 2, double-blind, dose-ranging study (NCT01786668),[2] 207 adult pts meeting modified New York AS criteria were randomised 1:1:1:1 to PBO or tofacitinib 2, 5 or 10 mg twice daily (BID) for 12 wks. Clinical endpoints included in this post-hoc analysis were: Assessment of SpondyloArthritis International Society 20% improvement (ASAS20) and ASAS 40% improvement (ASAS40) response rates, AS disease activity score major improvement (ASDAS MI; change ≥2.0 from baseline), ASDAS inactive disease (ASDAS ID; <1.3), Bath AS disease activity index (BASDAI), Bath AS functional index (BASFI) and back pain. Pts (%) achieving MIC in SIJ, spine and both SIJ and spine, in tofacitinib and PBO groups, were summarised based on observed data, and pooled tofacitinib (5 and 10 mg BID) vs PBO data were compared using Fisher's exact test. Concordance between achieving MIC and Wk 12 clinical responses was assessed. Wk 12 clinical responses were compared between pts achieving/not achieving MIC.

Results: MRI data for 164 pts were evaluated. Baseline demographics were generally balanced between treatment groups and typical of AS populations.[2] Tofacitinib 2, 5 and 10 mg BID improved mean (range) SPARCC scores vs PBO (SIJ: -2.2 [-22.0, 10.5], -3.5 [-34.5, 11.0], -3.6 [-29.0, 0.5] vs -0.7 [-9.5, 6.5]; spine: -3.2 [-34.5, 20.5], -5.5 [-36.5, 8.0], -6.7 [-32.5, 7.5] vs -0.8 [-8.0, 14.0]). Approximately 3 times more pts achieved MIC in SIJ or spine in the pooled tofacitinib group vs PBO (SIJ: 34.1% vs 11.8%, $p<0.05$; spine: 38.6% vs 11.8%, $p<0.01$). Achieving MIC in SIJ and spine correlated with clinical response. In pts on tofacitinib, ASAS20, ASAS40 and ASDAS MI responses were more likely in pts achieving MIC in SIJ or spine (Table) vs not achieving MIC. Compared with not achieving MIC, pts on tofacitinib achieving MIC in SIJ had larger improvements in BASDAI, BASFI and back pain.

Conclusions: Pts who received tofacitinib who had AS experienced clinically meaningful reductions in axial MRI inflammation. Pts achieving MIC for MRI inflammation had increased clinical response rates.

References:

[1] Maksymowych WP et al. J Rheumatol 2012; 39: 1666–1674.
[2] van der Heijde D et al. Ann Rheum Dis 2016; In press.

Acknowledgements: Previously presented at ACR 2016 and reproduced with permission. This study was sponsored by Pfizer Inc. Editorial support was provided by A Pedder of CMC and funded by Pfizer Inc.

Disclosure of Interest: W. Maksymowych Grant/research support from: AbbVie, Pfizer Inc, Sanofi, UCB, Consultant for: AbbVie, Amgen, Eli Lilly, Janssen, Merck, Novartis, Pfizer Inc, Sanofi, UCB, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Meyers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli Lilly, Galapagos, Janssen, Merck, Novartis, Pfizer Inc, Roche, Sanofi-Aventis, UCB, Employee of: Imaging Rheumatology BV, X. Baraliakos Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Novartis, Pfizer Inc, Roche, MSD, UCB, A. Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer Inc, UCB, M. Brown Grant/research support from: AbbVie, Janssen, Leo Pharma, UCB, Consultant for: AbbVie, Janssen, Novartis, Pfizer Inc, UCB, Speakers bureau: AbbVie, Janssen, Novartis, Pfizer Inc, UCB, S. Sherlock Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, D. Li Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, D. Fleishaker Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, T. Hendrikx Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Kanik Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

Table. Relationship between Wk 12 clinical response rates and achievement of MIC

	ASAS20 n/N (%)	ASAS40 n/N (%)	ASDAS MI n/N (%)	ASDAS ID n/N (%)
Placebo				
SIJ ≥MIC (2.5)	3/4 (75.0)	1/4 (25.0)	0/4	0/4
SIJ <MIC (2.5)	14/29 (48.3)	6/29 (20.7)	3/28 (10.7)	3/28 (10.7)
Spine ≥MIC (5)	3/4 (75.0)	2/4 (50.0)	2/4 (50.0)	1/4 (25.0)
Spine <MIC (5)	14/29 (48.3)	5/29 (17.2)	1/28 (3.6)	2/28 (7.1)
Tofacitinib 2 mg BID				
SIJ ≥MIC (2.5)	9/12 (75.0)	7/12 (58.3)	5/12 (41.7)	2/12 (16.7)
SIJ <MIC (2.5)	15/29 (51.7)	12/29 (41.4)	3/30 (10.0)	4/30 (13.3)
Spine ≥MIC (5)	11/12 (91.7)	8/12 (66.7)	4/12 (33.3)	3/12 (25.0)
Spine <MIC (5)	13/28 (46.4)	11/28 (39.3)	4/29 (13.8)	3/29 (10.3)
Tofacitinib 5 mg BID				
SIJ ≥MIC (2.5)	15/17 (88.2)	10/17 (58.8)	6/17 (35.3)	2/17 (11.8)
SIJ <MIC (2.5)	21/25 (84.0)	12/25 (48.0)	5/26 (19.2)	5/26 (19.2)
Spine ≥MIC (5)	12/14 (85.7)	8/14 (57.1)	5/15 (33.3)	3/15 (20.0)
Spine <MIC (5)	24/28 (85.7)	14/28 (50.0)	6/28 (21.4)	4/28 (14.3)
Tofacitinib 10 mg BID				
SIJ ≥MIC (2.5)	9/13 (69.2)	8/13 (61.5)	4/13 (30.8)	4/13 (30.8)
SIJ <MIC (2.5)	18/31 (58.1)	12/31 (38.7)	9/31 (29.0)	4/31 (12.9)
Spine ≥MIC (5)	13/18 (72.2)	10/18 (55.6)	7/18 (38.9)	2/18 (11.1)
Spine <MIC (5)	14/26 (53.9)	10/26 (38.5)	6/26 (23.1)	6/26 (23.1)
Pooled tofacitinib 5 and 10 mg BID				
SIJ ≥MIC (2.5)	24/30 (80.0)	18/30 (60.0)	10/30 (33.3)	6/30 (20.0)
SIJ <MIC (2.5)	39/56 (69.6)	24/56 (42.9)	14/57 (24.6)	9/57 (15.8)
Spine ≥MIC (5)	25/32 (78.1)	18/32 (56.3)	12/33 (36.4)	5/33 (15.2)
Spine <MIC (5)	38/54 (70.4)	24/54 (44.4)	12/54 (22.2)	10/54 (18.5)

ASAS, Assessment of SpondyloArthritis International Society; ASDAS, ankylosing spondylitis disease activity score; BID, twice daily; ID, inactive disease; MI, major improvement; MIC, minimally important change; SIJ, sacroiliac joints; Wk, week

DOI: 10.1136/annrheumdis-2017-eular.2447

THU0353 CHANGE IN MRI STRUCTURAL LESIONS IN THE SACROILIAC JOINT AFTER TWO YEARS OF ETANERCEPT THERAPY IN COMPARISON TO A CONTEMPORARY CONTROL COHORT IN NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

W.P. Maksymowych[1], M. Dougados[2], R.G. Lambert[1], R. Landewe[3], A. Molto[2], P. Claudepierre[4], M. de Hooge[5], R. Bonin[6], J.F. Bukowski[6], H. Jones[6], I. Logeart[7], R. Pedersen[6], A. Szumski[8], B. Vlahos[6], D. van der Heijde[5].
[1]University of Alberta, Edmonton, Canada; [2]Paris Descartes University, Hôpital Cochin, Paris, France; [3]Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands; [4]Universite Paris Est Creteil, Creteil, France; [5]Leiden University Medical Center, Leiden, Netherlands; [6]Pfizer, Collegeville, United States; [7]Pfizer, Paris, France; [8]InVentiv Health, Princeton, United States

Background: Demonstrating a structural effect of TNF inhibitors in axial SpA (axSpA) is challenging.

Objectives: To compare 2 yrs of structural lesion changes on T1W MRI in the sacroiliac joints (SIJ) of pts receiving etanercept (ETN) in a clinical trial to similar pts not receiving biologics in a cohort study.

Methods: Pts had recent onset non-radiographic (nr)-axSpA fulfilling ASAS criteria. Study group: pts receiving ETN 50 mg once weekly for 2 yrs in EMBARK (NCT01258738). Control group: pts in a longitudinal cohort study not receiving biologics for 2 yrs (DESIR, NCT01648907). Outcome measure: change in structural lesions of erosion, backfill, fat metaplasia, and ankylosis. MRI images were read by 3 experienced readers unaware of image chronology and pt group, using the SpondyloArthritis Research Consortium of Canada SIJ Structural Score (SSS).[1] For each group, differences were calculated between percentages of patients experiencing increases and decreases in structural lesion scores over 2

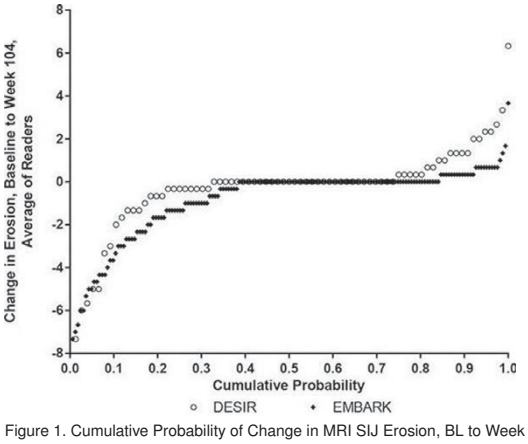


Figure 1. Cumulative Probability of Change in MRI SIJ Erosion, BL to Week 104.