DOI: 10.1136/annrheumdis-2018-eular.6360

SAT0246

AT WHICH POINT AND FOR WHICH REASONS ARE ORAL MTX FORMULATIONS SWITCHED TO INJECTABLE ONES IN RA PATIENTS? COMBINED RESULTS FROM 3 INDEPENDENT OBSERVATIONAL AND CLINICAL TRIALS

R.-M. Flipo^{1,2}, A. Saraux³, C. Hudry^{4,5}, C. Gaujoux-Viala⁶, E. Senbel⁷, S. Tropé⁸, E. Zinovieva^{9,10}, H. Herman-Demars⁹. ¹Rheumatology department, CHRU Roger Salengro, ²University, Lille, ³Rheumatology department, CHU La Cavale Blanche, Brest, ⁴Rheumatology Department, Cochin Hospital, ⁵Institut de Rhumatologie Paris 8, Paris, ⁶Rheumatology department, CHU Carémieu, Nîmes, ⁷Rheumatology office, Marseille, ⁸ANDAR Patients' association, Montpellier, ⁹Medical Department, Nordic Pharma, Paris, France

Background: MTX is considered as a cornerstone in RA treatment since the 1990s and its injectable forms have proven their enhanced clinical and pharmacological efficacy and safety in case of insufficient response or poor tolerance of oral formulations. Few data are available considering the timepoint at which the route of administration is changed in current practice.

Objectives: The objective of this work was to investigate across 3 independent trials if there was a consistency in patterns of MTX oral ->injectable switches in terms of RA characteristics, MTX dosages (before and after the switch) and reasons of passage.

Methods: Three trials were considered for this work: 1/STRATEGIE (observational study designed to investigate the therapeutic strategies used in current practice in RA patients insufficiently responding to initial MTX monotherapy), 2/APRIM (observational study aimed to investigate the treatment adherence of RA patients switching from oral to injectable MTX or between two different MTX prefilled syringes) and 3/SELFi (phase III randomized trial aiming to compare a new MTX autoinjector to the historical MTX prefilled syringe in terms of treatment adherence and functional capacity in RA patients at 6 months). In all three studies we selected baseline data concerning patients switching from oral to injectable MTX at the inclusion visit.

Results:

	STRATEGIE N = 151	APRIM N = 270	SELFi N = 98
RA duration, years (mean±SD) (median (min;max))	4.9±6.1 2.8 (0.0; 29.0)	6.6±8.1 3.0 (0.0; 40.0)	4.5±5.9 2.0 (0.2; 30.5)
MTX treatment duration, years (mean±SD) (median (min;max))	3.6±4.5 1.9 (0.0; 24.3)	3.3±4.2 1.4 (0.0; 23.6)	2.5±2.8 1.4 (0.1; 15.4)
DAS28 (mean±SD)	4.4±0.9	3.9±0.9	3.5±1.2
MTX oral dosage at V0, mg/wk (mean±SD)	15.3±3.7	15.0±4.1	14.8±3.8
MTX injectable dosage at the end of V0, mg/wk (mean±SD)	17.0±4.0	16.3±3.8	17.0±4.0
Distribution MTX dosage unchanged/raised/ reduced	50%/45%/ 5%	62%/34%/ 4%	51%/42%/ 7%

Consistent data were observed across the three considered trials concerning the oral/injectable MTX switch. It occurs after about 3 years of treatment, at a DAS28 of 4 and at an average dose of 15 mg/wk (which is consistent with bioavailability data shown before). In most situations, MTX dosage is unchanged or very slightly raised at the switch timepoint. The main switch reasons were "non-achievement of treatment target" and "RA worsening", the safety reasons were mentioned only in 5% of cases.

Conclusions: Our work showed a consistent pattern across 3 independent trials concerning the oral/injectable MTX switch. It generally occurs at 15 mg/wk, the new injectable dosage being either unchanged or very slightly raised as compared to the last oral one. Surprisingly, the MTX route of administration seems to be modified mostly for efficacy reasons, safety issues being anecdotal.

REFERENCE:

1 Schiff MH, et al. Ann Rheum Dis 2014.

Disclosure of Interest: R.-M. Flipo Consultant for: Nordic Pharma, A. Saraux Consultant for: Nordic Pharma, C. Hudry Consultant for: Nordic Pharma, C. Gaujoux-Viala Consultant for: Nordic Pharma, E. Senbel Consultant for: Nordic

Pharma, S. Tropé Consultant for: Nordic Pharma, E. Zinovieva Employee of: Nordic Pharma, H. Herman-Demars Employee of: Nordic Pharma

DOI: 10.1136/annrheumdis-2018-eular.3709

SAT0247

IMPACT OF GLUCOCORTICOIDS ON EFFICACY AND SAFETY OF TOFACITINIB WITH AND WITHOUT METHOTREXATE AND ADALIMUMAB WITH METHOTREXATE FOR RHEUMATOID ARTHRITIS: RESULTS FROM A PHASE 3B/4 RANDOMISED TRIAL

R. Fleischmann¹, J. Wollenhaupt², S. Cohen¹, J. S. Smolen³, P. Dahl⁴, N. Ilikuni⁵, H. Shi⁶, S. Tatulych⁷, L. Takiya⁸. ¹Metroplex Clinical Research Center and University of Texas Southwestern Medical Center, Dallas, TX, United States, ²Schön-Klinik Hamburg-Eilbek Teaching Hospital of the University of Hamburg, Hamburg, Germany, ³Medical University of Vienna and Heitzing Hospital, Vienna, Austria, ⁴Pfizer Inc, Ballerup, Denmark, ⁵Pfizer Inc, New York, NY, ⁶Pfizer Inc, Collegeville, PA, ⁷Pfizer Inc, Groton, CT, United States

Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Glucocorticoids (GC) are an established therapy in RA that are often used to rapidly reduce pain and inflammation while awaiting the effects of disease-modifying antirheumatic drugs.

Objectives: A post hoc analysis to describe the impact of background GC on the efficacy and safety of tofacitinib with and without methotrexate (MTX) and adalimumab (ADA) with MTX in ORAL Strategy.

Methods: ORAL Strategy (NCT02187055) was a 1-year, double-blind, Phase 3b/4, head-to-head, non-inferiority randomised controlled trial in adult patients (pts) with active RA despite MTX therapy. Pts were randomised 1:1:1 to receive tofacitinib 5 mg twice daily (BID; tofa mono), tofacitinib 5 mg BID + MTX (tofa +MTX) or subcutaneous ADA 40 mg every other week + MTX (ADA+MTX). Pts receiving low-dose GC (≤10 mg/day prednisone or equivalent) before enrolment maintained a stable dose throughout the study period. The following efficacy endpoints were assessed through Month 12 for pts receiving tofa mono, tofa+MTX and ADA+MTX with/without GC: ACR20, ACR50 and ACR70 response rates, proportions of patients achieving low disease activity (LDA; DAS28-4[ESR]≤3.2) and remission (DAS28-4[ESR]≤2.6) and change from baseline (BL) in HAQ-DI (ΔHAQ-DI). Safety endpoints were evaluated throughout the study and included adverse events (AEs), serious AEs (SAEs), discontinuations due to AEs and serious infection events (SIEs).

Results: 1146 patients were randomised and treated; low-dose BL GC were received by 228/384 (59.4%) pts receiving tofa mono (mean [SD] BL GC dose: 7.5 [13.7] mg/day), 215/376 (57.2%) pts receiving tofa+MTX (mean [SD] BL GC dose: 6.5 [2.5] mg/day) and 223/386 (57.8%) pts receiving ADA+MTX (mean [SD] BL GC dose: 6.4 [2.6] mg/day). BL demographics and disease characteristics were generally similar across treatment groups, regardless of BL GC use. Efficacy endpoints (ACR50 response rate, LDA and remission rates, ΔHAQ-DI) were generally similar for each treatment group when stratified by GC use (figure 1, table 1; similar results were seen for ACR20/70 response rates – data not shown). GC use did not appear to be associated with higher rates of AEs, discontinuations due to AEs, SIEs and SAEs; some AE rates were higher with MTX than without MTX (table 2). SIEs in pts using GC included herpes zoster (HZ; tofa mono, n=2) and tuberculous meningitis (tofa+MTX, n=1); in pts not using GC, there was 1 event each of cytomegalovirus chorioretinitis (tofa+MTX), pulmonary TB (tofa+MTX), HZ (ADA +MTX) and varicella (ADA+MTX).

*Interim response (proportion of patients with low disease activity and last observation carried forward for patients with missing data before withdrawal)
ACR50, American College of Rheumatology; ADA, adalimumab 40 mg subcutaneously every two weeks; BID, twice daily; CI, confidence interval; FAS, full analysis set; GC, glucocorticoids; MTX, methotrexate

Figure 1. Proportion of patients achieving ACR50 response according to treatment group and GC use (FAS, with imputation*)