THU0646 INTERCHANGEABILITY FROM INFLIXIMAB ORIGINATOR TO INFLIXIMAB BIOSIMILAR: EFFICACY AND SAFETY IN A PROSPECTIVE OBSERVATIONAL STUDY ON 89 PATIENTS

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Background: Biosimilar biologic disease modifying anti-rheumatic drug (bsDMARD) are supposed to offer a real economic advantage for these diseases for the same health benefit. While the administration of a biosimilar to a new patient is widely accepted, the switch from a biologic originator DMARD (boDMARD) to its biosimilar remains questioned.

Objectives: This study aimed to assess the safety and efficacy of switching from an IV anti-TNF boDMARD to its bsDMARD in patients with rheumatic arthritis, spondyloarthritis, psoriatic arthritis, juvenile arthritis and uveitis.

Methods: Prospective real-life study in the rheumatology unit of La Pitié-Salpêtrière Hospital, from February 2016 to December 2016. Patients initially treated with the boDMARD infliximab (Remicade®), all switched to infliximab bsDMARD (Inflectra®) after patient's information by a rheumatology nurse. The dose and administration schedule remained unchanged at the switch. Our primary endpoint was infliximab maintenance rate. Secondary endpoints were evolution of disease activity, as well as evolution of both infliximab trough levels and anti-drug antibody (ADA) serum levels before and after the switch. In addition, safety events were also monitored.

Results: We identified 89 patients – spondyloarthritis (61%), rheumatic arthritis (27%), psoriatic arthritis (11%), juvenile arthritis and uveitis (1%) – in rheumatology who have been switched to boDMARD infliximab to its bsDMARD. Clinical assessment was based on DAS28 (peripheral joint involvement) or BASDAI (axial involvement) scores. 93% of patients remained treated with infliximab: 6 patients (7%) stopped the treatment due to a loss of efficacy. As shown in Figure 1, there is no significant change in disease activity before and after having switched patients to infliximab biosimilar. The ADA dose were detected in 10 patients, 7 with high titer (>200ng/mL) and 3 with moderate titer (between 50 and 200 ng/mL). It was significantly correlated with low trough levels of IFX (<0.3µg/mL). Among them, 6 (4 with high titer; 2 with moderate titer) also had a poor clinical response before switch (refractory patients). 4 ADA-positive patients (3 with high titer; 1 with moderate titer) were still good clinical responders.

Conclusions: The interchangeability of infliximab boDMARD to its bsDMARD does not rise any efficacy and safety concern in our experience. The role of drug and ADA monitoring during the switch remains to be further explored.

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THU0647 INTERACTIONS BETWEEN STEPS PER DAY AND RISK FACTORS FOR OSTEOARTHRITIS ON MRI-DETECTED OSTEOPHYTES IN A POPULATION BASED COHORT STUDY

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Background: It is clear that exercise helps the symptoms of osteoarthritis. However, the relationship between physical activity (PA) and progression of knee osteoarthritis (OA) remains controversial. Moreover, no guideline on the amount of PA to prevent OA progression in general older population has been recommended, and it is still uncertain whether PA should be promoted among subgroups with knee OA such as female gender, obesity, radiographic osteoarthritis (ROA) and knee injury history. Osteophyte (OP) has long been viewed as a defining structural feature of knee OA. Recently, MRI-detected OPs have been shown to be more sensitive to change than radiographs.

Objectives: The aims of this study were to describe the longitudinal association between objectively-measured PA and knee MRI-detected (OPs), and to test the interactions between PA and gender, obesity, ROA or knee injury history on the increases in MRI-detected OPs.

Methods: 408 community-dwelling adults aged 51–81 were randomly selected from local community and measured at baseline and 2.6 years later. T1-weighted fat suppressed MRI was used to evaluate knee OPs at baseline and after 2.6 years. PA was assessed at baseline by pedometers (steps per day) and categorized as 3 groups: low PA (≤7499 steps per day), moderate PA (7500 to 9999 steps per day) and high PA (≥10000 steps per day). Radiographs were obtained and scored for individual features of radiographic osteoarthritis (ROA). Knee injury history was recorded by questionnaire and body mass index (BMI) was calculated. Logistic regression and log binomial regression were used in longitudinal analyses.

Results: In total study sample, doing moderate PA was associated with reduced risk of an increase in MRI-detected OPs, comparing to low PA (RR=0.73, p=0.03).

There were significant interactions between PA and gender, obesity, ROA or knee injury history (all p<0.05) for an increase in MRI-detected OPs. In stratified analyses, moderate PA was protective against an increase in MRI-detected OPs in females (OR=0.23, p<0.01), obese participants (OR=0.23, p<0.01), participants with ROA (OR=0.45, p=0.02) and participants with knee injury history (OR=0.05, p=0.02). These significant associations still existed after further adjustments for age, sex, BMI, ROA and/or knee injury history (where appropriate). High PA was not associated with an increase in MRI-detected OPs in total sample or the stratified analyses but there were relatively few in this category.

Conclusions: Moderate PA is protective for change in MRI-detected OPs in older adults, especially in those with female gender, ROA, obesity and knee injury history. This implies older people with above risks of knee OA may need to aim for a range from 7500 to 9999 steps per day.

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THU0648 USE OF OUTPATIENT RHEUMATOLOGIC HEALTH CARE SERVICES BEFORE AND AFTER SWITCH FROM ORIGINATOR TO BIOSIMILAR INFLIXIMAB

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Background: According to Danish national guidelines issued in 2015, pts (pts) with inflammatory rheumatic diseases in routine care treatment with originator infliximab (INX) must switch to the cheaper biosimilar infliximab (CT-P13). This switch was done for economic reasons (CT-P13 64% cheaper than INX). Since any treatment change potentially induces additional guidance of pts and use of hospital services, it is relevant to investigate whether the switch affected use of hospital resources.

Objectives: To study difference in rates of outpatient activities and services provided 6 months before vs after the switch to CT-P13 for pts treated at rheumatologic departments which provide infliximab treatment.

Methods: The switch population and switch dates were identified in the Danish quality registry, DANBIO (1). Vital status was validated in the Central Person Registry. The Danish National Patient Registry (NPR) provided information regarding outpatient contacts and services. The use of 16 types of services relevant to the rheumatologic specialty was identified and included outpatient visits, infliximab infusion, nurse counselling, phone consultation, and rheumatologic ultrasound. Number of days with these services was counted. Services performed on the switch date were analyzed separately. Thus, for each patient the following rates were calculated 6 months before and after the switch: 1) days with at least one outpatient service provided, and 2) number of services provided. In addition, the weekly rate of days with services was calculated.

Only pts who were alive and could be followed in the NPR for 6 full months after the switch were included.

Paired t-tests were used to compare rates before and after switch. A graphical interrupted time series analysis was conducted for weekly number of services provided.

Results: Among 802 pts identified, 769 had available NPR outpatient data from hospital departments of rheumatology. The 769 pts had 1484 outpatient treatment contacts at the included rheumatology departments with a total of 9243 days with services provided (including 693 on the switch date). The mean rate of days with services provided was 5.4 before the switch and 5.7 after switch (p=0.0003). The

Figure Weekly rate of days with services per patient according to switch date

weekly rate of days with services showed no obvious differences before and after the switch but had a clear 8-week pattern (corresponding to the average infusion interval) (Figure).

The total number of services provided was 19,752 (2,019 of these on the switch date). There were significant increases in the rates before vs after switch for 6 of the 16 service categories, although the mean rates were small: telephone consultations (mean rate 1.0 before vs. 1.2 after), patient guidance (0.5 vs. 0.4), intravenous medication (0.0 vs. 0.1), clinical controls (2.1 vs. 2.3) and clinical investigations (0.3 vs. 0.5), whereas the rate of infliximab treatment decreased (3.1 vs 3.0) (all $p < 0.05$, insignificant results not shown).

Conclusions: This analysis showed that there were only small differences in the rates of days with outpatient services and rates of services 6 months before and after the switch from original to biosimilar infliximab. Thus, it is unlikely that the switch is associated with substantially higher cost of health care resources.

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THU0649 MANDATORY CHOICE OF FIRST bDMARD IN DENMARK – AN OPPORTUNITY TO STUDY REAL-LIFE EFFECTIVENESS? RESULTS FROM THE DANBIO REGISTRY

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Background: In Denmark, biological treatments (bDMARDs) are tax paid. Since year 2013, The Danish Council for the Use of Expensive Hospital Medicines (RADS) has issued recommendations with annual updates regarding RA patients (pts) initiating biological treatment, dictating a mandatory choice of the cheapest bDMARD (1). Furthermore, the percentage of pts expected to be treated according to the RADS recommendation per year is stated. For pts treated with concomitant methotrexate (MTX) recommendations on first line, first choice bDMARD were: Jan 1st 2013-June 30th 2014: certolizumab pegol (in 80% of pts); July 1st 2014 - June 30th 2015: abatacept (80%); July 1st 2015-June 30th 2016: biosimilar infliximab (CT-P13) (50%). The nationwide Danish DANBIO registry collect data prospectively and covers >90% of adults with rheumatological diseases treated with bDMARDs in routine care (2).

Objectives: To characterize Danish RA pts initiating first line, first choice treatment with a bDMARD in combination with MTX in the three RADS periods and to explore the degree of compliance to RADS recommendations. Furthermore, to investigate differences in baseline characteristics between those pts who were compliant to RADS guidelines and those who were not.

Methods: For each of the three RADS' periods bio-naïve pts with RA were identified in DANBIO and compliance to RADS recommendations was assessed. Baseline characteristics of those who started first choice bDMARD treatment according to RADS were compared with those who started another biologic instead. Comorbidities and previous hospitalized infections were identified in the Danish National Patient Registry. Comorbidities from Charlson Comorbidity Index were summarized except category number 7, connective tissue disease.

Results: For all three RADS periods, age, gender, functional status and disease activity were typical for pts with RA. Age was median: 57 years, range 18–88 years and disease duration: 3 years, range 0–54 years. 16–22% of pts had ≥ 1 comorbidity and 7–9% had ≥ 1 hospitalized infection the previous year. In each of the three RADS periods, 71%, 66% and 60% of pts followed the RADS recommendations, respectively (Table). The table shows differences between those who started first choice bDMARD treatment according to RADS, and those who did not. Overall, pts who complied to RADS had higher DAS28 and patient VAS global. Characteristics of pts who followed RADS recommendations in the three periods appeared similar.

Conclusions: In this nationwide study of >600 RA pts, pts' clinical characteristics

Table 1: Characteristics of RA pts initiating treatment with first bDMARD in combination with MTX stratified by compliance to the recommendations of RADS or not in the three time periods.

	Certolizumab pegol		Abatacept		CT-P13	
Time periods, MM.YY	01.13-06.14		07.14-06.15		07.15-06.16	
Recommended compliance (%)	80		80		50	
Actual compliance to RADS (%)	71		66		60	
Baseline characteristics	RADS	Not RADS	RADS	Not RADS	RADS	Not RADS
Number of pts	328	135	210	109	200	131
Age (years)	57	58	57	59	59	56
Female (%)	71	80	73	71	69	71
IgM-RF positive (%)	61	61	67	69	64	70
Anti-CCP positive (%)	74	73	77	83	70	71
Disease duration (years)	3	5	3	4	4	2
DAS28	4.6	4.3	4.5	4.3	4.6	4.5
HAQ	1.1	1.1	1.1	0.9	1.0	1.0
Patient global VAS (mm)	70	57	73	53	69	67
Comorbidities ≥ 1 (%)*	22	33	16	28	24	20
No. of comorbidities (mean)**	1.3	1.5	1.2	1.6	1.3	1.4
Hosp. infections ≥ 1 (%)***	8	10	7	9	9	9

Variables are medians unless otherwise mentioned. **Numbers in bold:** $p < 0.05$ for comparison between RADS/not RADS, (Mann Whitney and Chi-square test) * From baseline and 10 years back;

In pts with ≥ 1 comorbidity; * From baseline and 1 year back;

Abbreviations: DAS28 Disease activity score in 28 joints; HAQ health assessment questionnaire;

VAS: visual analogue scale

were more heterogeneous than in clinical trials, reflecting routine care. Overall, compliance to recommendations was good. Thus, the national guidelines in Denmark with mandatory choice of the first biological drug may provide an interesting opportunity to study effectiveness of bDMARDs in routine care. This highlights observational studies as a valuable supplement to RCTs.

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THU0650 THE EFFECT OF ANTI-TNF THERAPY ON WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS OVER ONE YEAR – REAL LIFE DATA FROM THE CZECH BIOLOGICS REGISTRY ATTRA

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Objectives: To assess the effect of anti-TNF therapy on work productivity using the Work Productivity and Activity Impairment-Specific Health Problem (WPAI-SHP) questionnaire in patients with RA, PSA and AS in the real life setting. In the Czech Republic, anti-TNF therapy is reimbursed for RA if DAS28 > 5.1 despite therapy with csDMARDs, for PSA if disease is not "adequately controlled" with csDMARDs, and for AS if BASDAI > 4 and CRP/ESR elevated above normal.

Methods: WPAI-SHP scores were collected for all patients enrolled in ATTRA since 2012 at baseline and after 12 months of anti-TNF exposure. Bio-naïve patients with RA (n=352), AS (n=442) and PSA (n=133) starting anti-TNF therapy with available baseline data on demography, disease duration and physical function, and WPAI-SHP at baseline and at 12 months were included in this analysis. Patients older than 60 years, on maternity leave or students were excluded. Only patients working for pay at baseline were assessed for WPAI-SHP summary scores: absenteeism (mean % work time missed), presenteeism (mean % productivity loss at work), overall work impairment (mean % overall work productivity loss), and activity impairment (mean % productivity loss in regular activities).

Results: Baseline characteristic were significantly different between diagnoses (Table 1). Working status changed significantly only in patients with RA (employed