FRI0070

COST-EFFECTIVENESS OF BIOLOGIC AGENTS FOR RHEUMATOID ARTHRITIS WAS SUPERIOR TO TRADITIONAL/CONVENTIONAL DMARDS WHEN ANALYSED WITH NUMBER NEEDED TO TREAT(NNT) METHOD

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Background: Recently biologic agents are widely used for patients with rheumatoid arthritis (RA). Biologic agents are reported to have higher effectiveness than other disease-modifying anti-rheumatic drugs (DMARDs) including methotrexate (MTX), however, those new agents are more expensive.

Objectives: This study evaluated the cost-effectiveness of biologic agents for RA using number needed to treat (NNT) method. NNT is an index for determining the number of patients who need to be treated in order to reach a patient toward to clinical goal when a new treatment is introduced.

Methods: Fifty-three patients with RA was included in this study. These patients were introduced biologic agents between September 2012 to ^{March 2017} and continued same agent up to 24 weeks. NNT was calculated based on disease activity score (DAS28-ESR) and clinical disease activity index (CDAI) at 24 weeks. Ninety-four patients were investigated as a control group who treated with DMARDs. In addition, actual healthcare cost including doctor's fee, laboratory examination, prescription fee, and cost of biologic agents in each patient were calculated based on hospital's medical receipt, then averaged and compared between two groups.

Results: In biologic group, tocilizumab (TCZ) were used for 20 patients, golimumab (GLM) for 14 patients, etanercept (ETN) for 13 patients, and other biologics for six patients. In control group, 66 patients administered MTX and/or conventional DMARDs (csDMARDs), and 28 patients administered only csDMARDs. In biologic group, 53 patients (79.2%) achieved remission in DAS28-ESR, and 24 patients (45.2%) achieved remission in CDAI. On the other hand, the rate of remission was 61.7% and 23.4% respectively in control group. NNT was 1.26 (DAS28) and 2.21 (CDAI) in biologic group, and 1.62 and 4.27 respectively in control group. In biologic group, NNT based on DAS28-ESR of each agent was 1.11 of TCZ, 1.30 of ETN, 1.40 of GLM, and 1.50 of others (table 1). The total actual healthcare cost in the study period was 7,812.5 Euro (1044066 JPY; 1 Euro=133.6 JPY, in December 2017) in biologic group and 583.8 Euro (78020 JPY) in control group.

	Number	Ave. DAS28-ESR	Remission	ARR	NNT
Biologic group	53	1.92	42	0.79	1.26
TCZ	20	1.58	18	0.90	1.11
GLM	14	2.10	10	0.71	1.40
ETN	13	2.05	10	0.77	1.30
others	6	2.56	4	0.67	1.50
Control group	97	2.39	58	0.62	1.62
MTX	66	2.30	41	0.61	1.61
csDMARDs	28	2.63	17	0.61	1.65

	Number	Ave. CDAI	Remission	ARR	NNT
Biologic group	53	4.31	24	0.45	2.21
TCZ	20	2.94	11	0.55	1.82
GLM	14	5.10	5	0.36	2.80
ETN	13	4.52	7	0.54	1.86
others	6	6.58	1	0.17	6.00
Control group	94	5.43	22	0.23	4.27
MTX	66	5.19	16	0.24	4.13
csDMARDs	28	6.00	6	0.21	4.67

Conclusions: The total actual health care cost of biologic group was much higher than DMARDs group, however, the cost-effectiveness of biologics was superior to DMARDs from the stand point of NNT.

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FRI0071

OUTCOMES FROM RHEUMATOLOGY AND REPRODUCTIVE HEALTH CLINIC 2013–2016

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Background: A multidisciplinary approach to pregnancy in women with rheumatic diseases will ensure best outcomes for mother and baby.¹

Objectives: In 2013, we developed a dedicated nurse-led multidisciplinary Rheumatology Reproductive Health Clinic (RRHC) in order to provide a multidisciplinary service.

Methods: 98 women attended the RRHC from January 2013–16. They were prospectively assessed for age, diagnosis, medications, use of assisted reproductive technology (ART) and pregnancy outcomes.

Results: The mean (range) age was 35 years.^{19–48} The majority of patients had rheumatoid or psoriatic arthritis. The characteristics of the patients is summarised in table 1 and their outcomes in table 2. 24 women were on a biologic DMARD therapy at the time of conception. 10 discontinued in the first semester and 5 in the second trimester. 9 continued throughout their pregnancies. 90% of women surveyed were "very satisfied" with the physical and emotional support received in the clinic.

Abstract FRI0071 – Table 1. Patient Characteristics

Diagnosis	Number of Patients
Rheumatoid Arthritis	41
Psoriatic Arthritis	16
Ankylosing Spondylitis	8
Systemic Lupus erythematosus	7
Juvenile Idiopathic Arthritis	3
Chronic Regional Pain Syndrome	3
Granulomatosis with Polyangiitis	3
Reactive Arthritis	2
Behçet's Disease	2
Sicca Syndrome	2
Takayasu's Arteritis	2
Raynaud's Syndrome	2
Fibromyalgia Syndrome	2
Sarcoidosis	1
Mixed Connective Tissue Disease	1
Systemic Sclerosis	1
Total	98

Abstract FRI0071 – Table 2. Outcomes

Outcome	Number of Patients
Information gathering only	10
Pregnancy achieved	62
Using Assisted Reproductive Technology	3
Actively trying to achieve	26
Total number of pregnancies	88
Births	76
Mothers who had one birth only	49
Mothers who had two births (including one set of twins)	27
1st trimester pregnancy loss	11
2nd trimester pregnancy loss	1
Neonatal death (renal aplasia diagnosed in utero)	1
Breastfeeding continued to 6 week postpartum review	21
Total number of women	98

Conclusions: This is the first report of results from a multidisciplinary RRHC. These data show high levels of successful pregnancy outcomes and patient satisfaction.

The majority of patients had an inflammatory arthritis. Successful pregnancy outcomes were achieved in 70% of women actively trying to conceive. 38% of

patients on biologic DMARDs continued these throughout pregnancy. There were comparable miscarriage rates observed when compared with the general population (14% versus 20%).² Breastfeeding rates were low at 28% compared to the figure of 55% for the general population in Ireland.³ Most patients were "very satisfied" with the service.

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FRI0072

THE IMPACT OF ANTI-TNF-THERAPY ON ENDOTHELIAL FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS OR ANKYLOSING SPONDYLITIS

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Background: Increased mortality in chronic rheumatic diseases is mostly attributed to cardiovascular events (CVE). Assessment of endothelial dysfunction can help to identify patients at risk for major CVE. Studies have shown that the underlying endothelial dysfunction in rheumatoid arthritis is closely associated with inflammation. Only limited information is available whether the blockade of TNF α can restore endothelial function.

Objectives: To investigate parameters of endothelial function before and after initiation of immunosuppressive therapy (anti-TNF-therapy or methotrexate) in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or ankylosing spondylitis in an open-label, prospective study.

Methods: Patients with active RA, PsA or SpA were eligible for inclusion with active disease and when new treatment with sDMARD (methotrexate) or bDMARD (anti-TNF-therapy) was started. Study visits were performed at baseline, at 3 and at 12 months. Clinical disease activity and inflammation marker were obtained. Systemic Coronary Risk Evaluation (SCORE) and measurement of intima media thickness (IMT) were performed to assess baseline cardiovascular (CV) risk. Endothelial function was measured as arterial dilatation (artFID), arterial constriction (artFIC) and venous dilatation (venFID) in response to flicker light by dynamic vessel analysis (DVA; IMEDOS) and by peripheral arterial tonometry (EndoPAT) as reactive hyperemia index (RHI). For the primary endpoint, we analysed the endothelial function before and during treatment (month 12). Secondary endpoints were ACR20/50 response for RA and PsA and ASAS20 response for SpA. A comparison was made for changes in endothelial function in responder and non-responder to immunosuppressive treatment.

Results: 62 patients (37 RA, 13 PsA, 14 SpA) were included (mean age 51.3 $\pm$ 14.9 years, 46.8% females). The mean ten-year risk of fatal cardiovascular disease (SCORE) was estimated with 2.2% (95%CI: 1.5–3.0). Mean IMT was 0.59 $\pm$ 0.13 mm. Treatment was initiated with etanercept (n=21), certolizumab (n=10), infliximab (n=2), adalimumab (n=13), golimumab (n=4) or methotrexate (n=12). Response to treatment after 3 (n=57) and 12 months (n=32) measured by ACR20/50 (RA and PsA) and ASAS20 (SpA) was found in 33.3/16.7% and 57.2% (month 3) and 29.2/20.8% and 50.0% (month 12). artFID increased (3.1% $\pm$ 2.8% to 4.0 $\pm$ 3.2%; p<0.05), while artFIC and venFID remained unchanged (–0.3 $\pm$ 1.6% to –0.2 $\pm$ 2.1%; p=0.613, 3.7 $\pm$ 3.0% to 3.9% $\pm$ 2.2%; p=0.383). RHI did not change (1.9% $\pm$ 0.5% to 1.8 $\pm$ 0.5%; p=0.166). There were no differences in changes of endothelial function between responder and non-responder to immunosuppressive therapy or between anti-TNF-therapy and methotrexate.

Conclusions: Our data indicate, that patients with active RA, PsA or SpA are at risk for cardiovascular events. Immunosuppressive treatment can improve endothelial function at retinal arteries but has no effect on reactive hyperemia index at peripheral arteries. The effect of immunosuppressive treatment on parameters of endothelial function was not different in responders or non-responders and did not depend on whether the patients were treated with anti-TNF-therapy or methotrexate.

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FRI0073

CHANGES OF BONE MINERAL DENSITY OVER 10 YEARS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Patients with Rheumatoid Arthritis (RA) have been shown to have an increased risk of osteoporosis and fractures. Most studies on RA and osteoporosis are cross-sectional. There are very few studies on changes in bone mineral density (BMD) over time.

Objectives: To study changes in BMD in men and women with early RA over a period of ten years.

Methods: An inception cohort of consecutive patients with early RA (n=233, symptom duration <12 months), recruited 1995–2005, was investigated. Patients were followed according to a structured program, including dual-energy X-ray absorptiometry (DXA) of the left femoral neck and the lumbar spine (L2–L4) at inclusion and after 2, 5 and 10 years. Z-scores (standard deviations above or below the mean BMD for the given age and sex) were calculated using a cohort of healthy individuals from the same area as a reference population. The mean Z-score over the study period was estimated using mixed linear effect models. Changes in Z-scores between follow-up visits were analysed using the paired T-test. Data are presented as mean (95% confidence interval (CI)).

Results: At inclusion, 219 patients were examined with DXA. The corresponding numbers at 2, 5 and 10 years were 196, 172 and 121. Among those with baseline DXA data, mean age was 60 years, mean symptom duration 7.4 months and 70% were women. Men were older (mean age 63 vs 59 years) and more often treated with corticosteroids (49% vs 35%) than women at inclusion. The majority of men and women were on disease modifying anti-rheumatic drugs (86% vs 81%). More women were treated for osteoporosis (bisphosphonates and/or calcium and vitamin D) and of the women, 16% were on oestrogen at inclusion.

At the femoral neck, the mean Z-score over 10 years of time was –0.07 (–0.22; 0.08) in women and –0.33 (–0.57; –0.08) in men. Men had significantly lower BMD at the femoral neck than expected by age at inclusion (estimated by the intercept Z-score value –0.35; 95% CI –0.61; –0.09), whereas there was no significant overall change in Z-score over time in men or women. At the lumbar spine, the mean Z-score for women was 0.06 (–0.10; 0.21) and for men –0.05 (–0.29; 0.19). There was a significant increase in Z-scores at the lumbar spine over time in both groups (change/year 0.04 (0.03; 0.05) in women and 0.02 (0.00; 0.05) in men).

The paired comparisons of BMD at different follow-up visits are shown in table 1. In the femoral neck, Z-scores for men decreased significantly from inclusion to the 5 year follow-up visit. After 5 years, no further reduction was seen. Lumbar spine BMD Z-scores increased in both men and women over the study period.

Abstract FRI0073 – Table 1. Bone mineral density (femoral neck and lumbar spine – L2–L4) in the early RA cohort, by sex. Pairwise comparisons of different follow-up visits.

Follow-up (years)	Patients with data at inclusion and 2 years		Patients with data at 2 years and 5 years		Patients with data at 5 years and 10 years		Patients with data at inclusion and 5 years		Patients with data at inclusion and 10 years	
	0	2	2	5	5	10	0	5	0	10
L2-L4	135		119		97		117		87	
Women	Z-score mean		0.04		0.09		0.12		0.08	
	95% CI		–0.13; 0.21		–0.07; 0.25		–0.06; 0.30		0.07; 0.45	
	Mean change (95% CI)		0.05 (–0.01; 0.11)		0.14 (0.05; 0.23)		0.21 (0.02; 0.39)		0.18 (0.07; 0.29)	
Men	Z-score mean		–0.12		–0.08		–0.19		–0.10	
	95% CI		–0.39; 0.15		–0.37; 0.21		–0.47; 0.09		–0.45; 0.14	
	Mean change (95% CI)		0.04 (–0.04; 0.12)		0.08 (–0.01; 0.15)		0.29 (0.12; 0.45)		0.23 (0.08; 0.39)	
NECK	135		119		97		117		87	
Women	Z-score mean		–0.02		–0.08		–0.14		–0.08	
	95% CI		–0.19; 0.15		–0.24; 0.08		–0.32; 0.05		–0.15; 0.36	
	Mean change (95% CI)		–0.06 (–0.13; 0.04)		–0.08 (–0.04; 0.19)		–0.05 (–0.19; 0.09)		0.01 (–0.09; 0.12)	
Men	Z-score mean		–0.23		–0.32		–0.42		–0.41	
	95% CI		–0.51; 0.05		–0.59; –0.05		–0.61; –0.04		–0.70; –0.11	
	Mean change (95% CI)		–0.09 (–0.26; 0.02)		–0.10 (–0.22; 0.03)		0.11 (–0.07; 0.30)		0.46 (0.20; 0.70)	

Conclusions: In this study of patients with early RA, men had low femoral neck BMD at study start and kept losing bone mass during the first 5 years of follow up. Lumbar spine BMD Z-scores in both women and men increased significantly over the study period. Potential explanations for the low femoral neck BMD in men include exposures that may predispose to both RA and low BMD, such as smoking and low androgen levels. The increasing lumbar spine BMD could be due to more extensive anti-osteoporotic treatment compared to the reference population, and possibly more artefacts, such as extensive aortic calcification or degenerative spinal changes, in patients with RA.

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