FRI0124

PREVENTION OF EXTENSIVE BONE MARROW OEDEMA AND CONSEQUENT RAPID RADIOGRAPHIC PROGRESSION BY SHORT TERM USAGE OF BIOLOGICS IN DRUGS RESISTANT PATIENTS WITH EARLY DESTRUCTIVE RHEUMATOID ARTHRITIS

K. Katayama¹, T. Okubo², T. Sato¹, R. Fukai³, Y. Kon⁴, Y. Makino⁵, S. Kodama⁵, H. Ito⁶, ¹Orthopedic Surgery, ²Radiology, Katayama Orthopedic Rheumatology Clinic; ³Pharmacology, Seien Pharmacy, Asahikawa; ⁴Rheumatology, Sapporo Rheumatology and Immunology Clinic, Sapporo; ⁵Medicine; ⁶Orthopedic Surgery, Asahikawa Medical University, Asahikawa, Japan

Objectives: To investigate possible preventive effect of radiographic joint damage, especially RRP by short term treatment with biologics in non-biological disease-modifying ant-rheumatic drugs(non-bio DMARDs) resistant early RA (Clinical registration number; UMIN-CTR 000013614).

Methods: Fifty early RA patients with extensive BE by hand MRI test despite treatment with non-bio DMARDs were recruited. Among these, 44 patients were diagnosed as RRP. Twenty three patients (male 5, female 18) were treated with combination of non-bio DMARD and biologic DMARDs (Bio group) and 26 patients were treated with enhanced DMARDs therapy using MTX with or without other DMARDs (enhanced DMARDs group). Baseline demographics of both groups were not significantly different (Data not shown). In the Bio group, the following biologics were added: Adalimumab (13 cases), Tocilizumab (3 cases), Abatacept (3 cases), Infliximab (2 cases), Certolizumab (1 case), Golimumab (1 case). In enhanced DMARDs group, mean MTX dose was increased from 7.3 mg/w to 11.3 mg/w or other DMARDs were added. Bone destruction was determined before and 3 or 6 months after treatment by modified total Sharp scoring (mTSS) using by conventional radiography, and expressed as yearly progression of mTSS (Δ mTSS/y). BE score was measured by RAMRIS method using T1 or STIR image of hand MRI (HITACHI, Elis, 0.5T).

Results: Significant reduction in DAS28-ESR values after 3 or 6 months treatment were observed: from 4.2 to 3.3($p=0.0004$) in the enhanced DMARDs group, and 4.37 to 3.0($p<0.0001$) in the Bio groups. Similarly, improvement of BE: 7 out of 26 (26.9%) and 14 out of 23 patients (60.9%), mean Δ mTSS/y: 5.8 and 2.4, incidence of RRP: 9 (34.6%) and 9 (34.6%), and structural remission: 5 (21.7%) and 16 patients (69.6%), in the enhanced DMARDs and the Bio group, respectively. Accordingly, improvement of BE and incidence of structural remission was higher, whereas mean Δ mTSS/y value was significantly lower ($p<0.05$) in the Bio group compared to in the enhanced DMARDs group (table 1, figure 1).

Abstract FRI0124 – Table 1. Comparison between the Enhanced DMARDs group and the Bio group

	Enhanced DMARDs group (n=23)	Bio group (n=26)	P
Δ mTSS/y	5.8	2.4	0.0142*
% RRP	34.6% (9/26)	21.7% (5/23)	n.s
% Structural remission (%)	34.6% (9/26)	69.6% (16/23)	0.0146*
% BE improvement	26.9% (7/26)	60.9% (14/23)	0.0166*

*: significant

Enhanced DMARDs group					Bio group				
BE (0-4)	BE (3-4)	Improve	mTSS/y	Δ mTSS/y	BE (0-4)	BE (3-4)	Improve	mTSS/y	Δ mTSS/y
26	2	0	46	4.8	21	2	0	8	-4.6
27	19	X	14.1	0	28	5	0	30	0
11	4	0	9	0	28	17	X	5.4	0
11	15	X	12	0	23	0	0	6.4	0
33	3	0	11.1	0	29	6	0	8.2	0
29	13	X	48	0	29	0	0	8.4	0
29	1	0	30	0	35	8	0	42	0
15	0	0	12	0	31	9	0	30.8	0
38	38	X	10.7	0	28	8	0	15.1	0
34	24	X	62.4	0.86	16	15	X	21.8	0
38	3	0	15	1.2	27	5	0	31.2	0
19	13	0	96	1.5	26	15	X	20	0
32	18	X	24	1.8	27	7	0	33	0
25	1	0	2	2.7	36	37	X	14.6	0
14	2	0	1.8	2.9	22	6	0	10	0
29	30	X	15.9	3.3	21	3	0	15	0
22	29	X	12	4.4	28	3	0	11.7	1
18	13	X	4.3	6	20	4	0	16.7	2
13	16	X	11	6	18	16	X	12	5.3
29	14	X	5	6.5	26	30	X	32	6
32	32	X	2.8	7.2	24	17	X	8.4	10
36	36	X	24	13	22	34	X	4	12
33	39	X	13	13	42	42	X	37.7	20.6
27	11	X	29.1	25.5					
39	27	X	35	29					
15	26	X	36	33.6					
25.8	16.2		22.5	5.8	26.4	12.6		18.4	2.4

Abstract FRI0124 – Figure 1. Radiographic data

Conclusions: Results of this study indicated that short term (3 or 6 months) treatment with biologics is effective in the reducing BE, and consequently prevent further progression of the disease into RRP status in 80% of early destructive RA despite extensive DMARDs therapy. The effect of withdrawal of biologics in RA improving BE are currently under investigation (figure 1). We consider that a short-term treatment with biologics for early RA patients, who are resistant to

DMARDs and at high risk to transit to RRP, will be an effective and economical treatment strategy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3718

FRI0125

QUANTIFICATION OF TUMOUR NECROSIS FACTOR IN ANKYLOSING SPONDYLITIS PATIENTS DURING ADALIMUMAB TREATMENT

L. Berkhout¹, J. Ruwaard², M.J. l'Ami², G. Wolbink^{1,2}, T. Rispens¹. ¹Department of Immunopathology, Sanquin Research; ²Amsterdam Rheumatology and Immunology Center, Reade, Amsterdam, Netherlands

Background: Tumour necrosis factor- (TNF) inhibitors, including adalimumab, are widely used in the treatment of inflammatory autoimmune diseases. Longitudinal (drug-bound) TNF levels in rheumatoid arthritis (RA) patients increased upon adalimumab treatment, and remained stable over two years follow-up. Low TNF levels at week four were associated with a significantly higher frequency of anti-drug antibodies (ADAs) at subsequent time points, significantly less methotrexate (MTX) use at baseline and a significantly reduced clinical response after 52 weeks (unpublished data).

Objectives: To investigate TNF levels during adalimumab treatment in ankylosing spondylitis (AS) patients and to compare this with TNF levels measured in RA patients.

Methods: Longitudinal TNF levels were quantified in 76 consecutive AS patients during adalimumab treatment, using a competition enzyme-linked immunosorbent assay (ELISA). This ELISA is drug-tolerant, which enables the quantification of TNF in the presence of large amounts of TNF-inhibitor. The relationship between TNF levels, drug levels and ADA detection was evaluated.

Results: At baseline, TNF levels were close to the detection limit, but levels increased during adalimumab treatment (figure 1A; stratified to concomitant MTX use; black lines represent median TNF (IQR)). The increase in TNF was more gradual in patients treated with adalimumab monotherapy, compared to the increase in TNF levels in patients concomitantly treated with MTX (only 9% of the patients). Similar results were found for adalimumab-treated RA patients, stratified to concomitant MTX use (figure 1B; Black lines show median (IQR)). Furthermore, at week four, low TNF levels in AS patients tended to associate with a higher frequency of ADAs after 24 weeks.

Conclusions: This is the first study describing an increase in TNF levels in AS patients during one year of adalimumab treatment. The dynamics in TNF levels is different for patients concomitantly treated with MTX, compared to patients treated with adalimumab monotherapy. Low TNF levels at week four tended to associate with a higher frequency of ADAs, which is potentially associated with the low frequency of MTX use at baseline.