SAT0185 **BIO-HOLIDAY THERAPY WITH A TIGHT CONTROL STRATEGY IN RHEUMATOID ARTHRITIS PATIENTS WITH CLINICAL DISEASE ACTIVITY INDEX REMISSION ENABLES MAINTENANCE OF BONE METABOLISM STATUS**

E. Torikai, M. Suzuki, Y. Matsuyama. *Orthopaedic Surgery, Hamamatsu University School of Medicine, Hamamatsu, Japan*

Background: The cost of Bio therapy has become a major problem in health economics and is unaffordable for some patients. Thus, it is important to consider whether we should discontinue or extend the interval of Bio. At EULAR 2016, we reported that maintaining disease activity, radiographic progression, and physical function via Bio-holiday therapy in rheumatoid arthritis (RA) patients with clinical disease activity index (CDAI) remission under a tight control strategy is possible. Osteoporosis is another issue for RA patients. RA patients generally develop osteoporosis more frequently than healthy individuals because of increased bone resorption and inhibited bone formation.
Objectives: To investigate bone metabolism markers and bone mass index of RA patients with CDAI remission who underwent Bio-holiday therapy.
Methods: Sixty-four RA patients with CDAI remission were included and were classified into two groups. Bio-holiday group (group H) comprised 34 patients [golimumab (GLM) and tocilizumab (TCZ), 18 and 16 patients, respectively] and in which patients were taken off Bio if they achieved CDAI remission. Patients visited our clinic at least once every 2 months and were treated with Bio within 3 months after falling out of CDAI remission. They could be taken off Bio again when they reached CDAI remission. The Bio group (group C) comprised 30 patients (GLM and TCZ, 16 and 14 patients, respectively). The mean ages of groups H and C were 52.9 and 55.6 years, respectively, and the mean disease durations were 3.98 and 4.13 years, respectively. There were no statistical differences between the backgrounds of the two groups. We compared the change in bone metabolism makers [urine type I collagen cross-linked N-telopeptide (NTX), serum tartrate-resistant acid phosphatase 5b (TRACP5b), serum bone-specific alkaline phosphatase (BAP), and serum osteocalcin (OC)] and bone mineral density (BMD) of lumber spine (L-spine) and femoral neck (FN) between both groups for 2 years.
Results: The mean withdrawal periods were 12.1 and 8.8 months with GLM and TCZ, respectively. Three and four patients dropped out because of financial constraints in the in the groups H and C, respectively. One patient in each group dropped out because of RA flare-up. No patients in either group discontinued their therapy because of adverse events. Besides one patient who dropped out because of RA flare-up, all remaining patients in the group H were able to achieve CDAI remission without delay. There were no statistical differences in CDAI throughout the study period (Fig.1). There were no statistical differences in any of the bone metabolism makers throughout the study period (Table.1) and BMD of L-spine (Fig. 2(a)) and FN (Fig. 2(b)) at baseline and last evaluation.

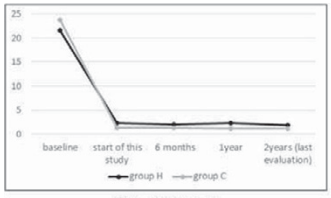

Fig.1 CDAI score

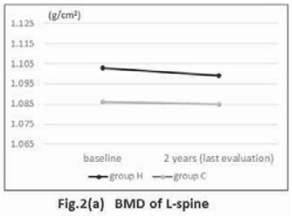

Fig.2(a) BMD of L-spine

[group H]	Start of this study	1 year	2 years
NTX(nmolBCE/mmolCr)	42.6± 24.7	44.3± 27.3	42.1± 26.6
TRCP5b (mU/dL)	355± 170	347± 156	364± 183
BAP (μg/L)	15.5± 6.1	16.5± 6.3	15.9± 6.0
OC (ng/mL)	11.9± 6.5	10.8± 6.2	11.3± 6.6
[group C]	Start of this study	1 year	2 years
NTX (nmolBCE/mmolCr)	40.3± 25.1	44.1± 28.4	43.5± 28.0
TRCP5b (mU/dL)	349± 169	352± 176	358± 165
BAP (μg/L)	15.9± 5.9	16.2± 6.1	16.4± 6.3
OC (ng/mL)	10.6± 5.9	10.9± 5.8	10.8± 6.2

Table.1 bone metabolism makers

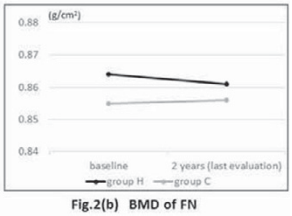

Fig.2(b) BMD of FN

Conclusions: We conclude that maintaining disease activity bone metabolism status via Bio-holiday therapy for RA patients with CDAI remission under a tight control strategy is possible. Given that the flare-up rate in RA patients with deep remission is not high, it is not difficult to resume Bio therapy and gain CDAI remission. Furthermore, this treatment is financially durable. Therefore, we recommend Bio-holiday therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2088

SAT0186 **EFFECTS OF DENOSUMAB, A SUBCUTANEOUS RANKL INHIBITOR, ON THE PROGRESSION OF STRUCTURAL DAMAGE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH CSDMARDS: RESULTS FROM THE 12-MONTH DOUBLE BLIND PHASE 3, DESIRABLE STUDY**

T. Takeuchi[1], Y. Tanaka[2], S. Soen[3], H. Yamanaka[4], T. Yoneda[5], S. Tanaka[6], T. Nitta[7], N. Okubo[7], H.K. Genant[8], D. van der Heijde[9]. *[1]Keio University School of Medicine, Tokyo; [2]University of Occupational and Environmental Health, Kitakyushu; [3]Kindai University Nara Hospital, Ikoma; [4]Institute of Rheumatology Tokyo Women's Medical University, Tokyo, Japan; [5]Indiana University School of Medicine, Indianapolis, United States; [6]The University of Tokyo; [7]Daiichi Sankyo Co. Ltd, Tokyo, Japan; [8]University of California, San Francisco, United States; [9]Leiden University Medical Center, Leiden, Netherlands*

Background: Denosumab is a fully human monoclonal antibody (IgG_2 subclass) that inhibits bone resorption by inhibiting RANKL, a key mediator of osteoclast formation, function, and survival.
Objectives: To evaluate the effect of denosumab 60 mg every 6 months (Q6M) or every 3 months (Q3M) on the progression of joint damage in Japanese patients with RA on csDMARD background treatment.
Methods: DESIRABLE is a 12-month randomized, double-blind, placebo-controlled, parallel-group study in patients with RA receiving csDMARD treatment. Subjects fulfilling the 1987 ACR criteria or 2010 ACR-EULAR criteria were randomized (1:1:1) to denosumab 60 mg Q6M, denosumab 60 mg Q3M, or placebo. The primary endpoint is the change from baseline to 12 months in the van der Heijde modified total Sharp score (mTSS). Radiographs of hands and feet at baseline, 6 months and 12 months were scored with blinded time order by 2 readers independently. Average score of the 2 readers is used for the analysis. Comparisons of each denosumab group with placebo for the change from baseline were performed using van Elteren stratified rank test adjusting for baseline glucocorticoid use. Missing scores were imputed using linear extrapolation/interpolation.
Results: Among 679 patients randomized, 667 (placebo, n=223; Q6M, n=222; Q3M, n=222) received at least one dose of study drug, and 60 (placebo n=15; Q6M, n=23; Q3M, n=22) were discontinued during the study. Demographic and baseline characteristics were similar across the groups (Table 1). Mean change from baseline in mTSS and erosion score (ES) at 12 months was significantly lower with both denosumab 60 mg Q6M and Q3M compared with placebo, with no obvious evidence of an effect on joint space narrowing (JSN) score for denosumab. (Table 2).
Consistently, the percent of nonprogressors (ie, mTSS change $\leq$0.5) at 12 months was significantly greater with denosumab 60 mg Q6M (75.6%, p=0.010) and Q3M (78.1%, p=0.001) compared with placebo (64.2%).
Incidence of adverse events (AEs), serious AEs, and AEs leading to discontinuation of study drug were similar across treatment groups. No events of osteonecrosis of the jaw or atypical femoral fracture were observed.

Table 1. Baseline demographics and characteristics

Characteristic	Placebo N = 218	Denosumab 60 mg Q6M N = 217	Denosumab 60 mg Q3M N = 219
Female	167 (76.6)	168 (77.4)	154 (70.3)
Age (years)	55.8 ± 11.7	58.1 ± 12.3	58.2 ± 12.0
Disease duration (years)	2.1 ± 1.3	2.2 ± 1.3	2.2 ± 1.3
Rheumatoid factor positive	137 (62.8)	140 (64.5)	128 (58.4)
MTX use	190 (87.2)	176 (81.1)	189 (86.3)
Glucocorticoid use	69 (31.7)	73 (33.6)	68 (31.1)
DAS28-CRP	3.4 ± 1.0	3.6 ± 1.1	3.5 ± 1.0
mTSS	13.1 ± 21.4	15.9 ± 22.2	15.2 ± 19.0

Data presented are Mean ± SD or n (%).

Table 2. Change from baseline in mTSS, ES and JSN at 12 months

Characteristic	Placebo N = 218	Denosumab 60 mg Q6M N = 217	Denosumab 60 mg Q3M N = 219
mTSS	1.49 ± 3.76	0.99 ± 3.77 (p = 0.024)	0.72 ± 2.32 (p = 0.006)
Erosion score	0.98 ± 2.48	0.51 ± 2.15 (p = 0.010)	0.22 ± 0.95 (p < 0.001)
JSN score	0.51 ± 1.72	0.48 ± 2.08 (p = 0.257)	0.50 ± 1.76 (p = 0.533)

Data presented are Mean ± SD

Conclusions: Denosumab inhibited the progression of joint destruction significantly more than placebo and was generally well tolerated in Japanese patients with RA on csDMARDs. Denosumab has potential to be a new therapeutic option to inhibit structural progression for patients with RA.
Disclosure of Interest: T. Takeuchi Grant/research support from: Astellas, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, AYUMI Pharmaceutical, Takeda, Teijin Pharma, AbbVie, Asahi Kasei Pharma, and Taisho Toyama, Consultant for: AstraZeneca, Eli Lilly, Novartis, Mitsubishi Tanabe, Asahi Kasei Pharma, AbbVie, Daiichi Sankyo, Bristol-Myers Squibb, Nipponkayaku, Janssen, Merck Serono, Takeda, Astellas, and Pfizer, Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Eisai, Janssen, Mitsubishi Tanabe, Pfizer, Takeda, Astellas, Daiichi Sankyo, Celtrion, and Nipponkayaku, Y. Tanaka Grant/research support from: BMS, MSD, Chugai, Mitsubishi Tanabe, Astellas, AbbVie, and Daiichi Sankyo, Speakers bureau: UCB Pharma, Mitsubishi Tanabe, Abbott, AbbVie, Eisai, Chugai, Janssen, Pfizer, Takeda, Astellas, Daiichi Sankyo, GSK, AstraZeneca, Eli Lilly, Quintiles, MSD, and Asahi Kasei Pharma, S. Soen Grant/research support from: Eisai, Daiichi Sankyo, and Takeda, Speakers bureau: Asahi Kasei Pharma, Astellas, Eisai, MSD, Ono Pharmaceutical, Daiichi Sankyo, Takeda, Chugai, Teijin