Background: The incidence and factors related to an inadequate response to denosumab (Dmab) treatment remain unclear.

Objectives: To describe clinical, analytical and densitometric characteristics of patients with inadequate response (IR) to Dmab in clinical practice. IR was defined as the presence of a new fracture [fxs-IR] or a significant decrease in BMD ($\geq 5\%$ lumbar or $\geq 4\%$ femoral) [BMD-IR].

Methods: retrospective study of patients with IR to Dmab treatment. Data of demographic variables, risk factors for osteoporosis, history of fractures, previous anti-osteoporotic treatment, densitometric and analytical parameters were collected before and after IR.

Results: 22 patients were included (19W:3M) with mean age of 75 ± 10 years. The causes of osteoporosis were: postmenopausal (50%), induced by glucocorticoids (22.7%), alcoholic (9.09%) and multifactorial (18.8%). Most patients were previously treated with bisphosphonates (59.09%, duration 5.2 ± 2.6 y) and had previous vertebral fractures (54.54%, median 3).

During Dmab treatment, 10 patients presented a BMD-IR (with a mean bone loss up to -3.5% at femur and -5.8% at lumbar spine) and 12 had fxs-IR (vertebral [n=8], humerus [n=1], pelvis [n=1], tibia [n=1]). No significant differences were observed in duration of Dmab between both IR groups (Fxs-IR: 3.2 ± 1.9 vs BMD-IR: 2.4 ± 1.2 y). In the BMD-IR, the BMD loss was higher at lumbar spine than at total hip ($-6.6\% \pm 3.7$ vs $-1.9\% \pm 4.8$). Only 1 patient of the fxs-IR had a secondary cause of IR (myeloma multiple).

In the fxs-IR group, most patients started combined treatment with teriparatide (n=4), 1 changed to teriparatide and 7 remained with Dmab. In the BMD-IR group, most maintained Dmab treatment (n=8) and 2 switched to zoledronate.

Conclusion: Most patients who developed IR to Dmab had been previously treated with bisphosphonates and had previous fragility fractures and appears within the first 3 years of treatment. BMD loss seems to be more marked at spine than total hip. Only one patient had a secondary cause of IR.

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AB0915

BONE MINERAL DENSITY AND FRACTURE FREQUENCY IN PREMENOPAUSAL WOMEN WITH RHEUMATIC DISEASES

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Background: The onset of the disease in young and middle age is typical for rheumatic diseases (RDS), but most studies on osteoporosis were conducted in patients (pts) older than 50 years, which included postmenopausal women.

Objectives: To assess bone mineral density (BMD), fracture frequency and the factors associated with low BMD in premenopausal women with RDs.

Methods: 160 women (median age, 36 [29; 43] years): 120 pts with RDs (43 rheumatoid arthritis (RA), 53 systemic sclerosis (SSc) and 24 psoriatic arthritis (PsA)) and 40 age-matched healthy controls were enrolled in the study. We performed a dual-energy X-ray absorptiometry (DXA, Hologic Discovery A, USA) to measure BMD in lumbar spine, femoral neck and total hip. BMD decreasing grade was evaluated by the Z-score $< -2SD$. All pts were interviewed using a unified questionnaire including assessment of daily dietary calcium intake. Serum vitamin D, C-reactive protein and erythrocyte sedimentation rate (ESR) measurements were done.

Results: 25% pts with RDs and only 8% healthy controls have low BMD ($p=0.02$). RA, SSc and PsA pts had low BMD in 37%, 21% and 13%, respectively, that was more often than in healthy women ($p=0.004$, $p=0.046$ and $p=0.081$, respectively). 9.3% RA pts and 7.5% SSc pts had low energy fractures. BMD of RDs pts in all areas of measurement demonstrated a direct correlation with height, weight, body mass index, and serum vitamin D concentration and an inverse correlation with the cumulative dose of glucocorticoids. Also, proximal femur BMD inversely correlated with RDs duration. BMD of femoral neck and total hip inversely correlated with C-reactive protein level in SSc pts. In RA women we found a direct correlation between lumbar spine and femur neck BMD and ESR.

Conclusion: 25% of premenopausal women with RDs had reduced BMD and needed monitoring and osteoporosis prevention, while 9.3% pts with RA and 7.5% women with SSc needed anti-osteoporotic treatment.

Disclosure of Interests: None declared

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AB0916

FACTORS THAT DEMONSTRATED SIGNIFICANT CORRELATION WITH BONE MINERAL DENSITY GAIN WITH DENOSUMAB ADMINISTRATION FOR PATIENT WITH RHEUMATOID ARTHRITIS

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Background: Denosumab, a monoclonal antibody of receptor activator of NF- κ B ligand promotes a strong action for bone mineral density (BMD) gain. This agent is often used for patient with rheumatoid arthritis (RA) because of its strong anti-osteoclastogenesis action, with that joint structural damage is induced. However, factors what affects BMD gain for patient with RA is still unclear.

Objectives: Factors that may affect BMD gain for patient with RA is evaluated statistically.

Methods: Patients with RA to whom denosumab is administrated consecutively three shots or more were picked up. BMD in lumbar spine (LS) and femoral neck (FN) measured with dual-energy X-ray absorptiometry was routinely measured at the initial administration (BL). BMDs were measured every six months when another denosumab is administrated. Change of BMD for each bone was calculated. Patient's age at BL, at onset of RA, disease duration, sex, anti-cyclic citrullinated polypeptide antibodies (ACPA), whether denosumab is naïve, body mass index (BMI) at BL were harvested. BMD in each bone, serum tartrate resistant acid phosphatase 5b (TRACP5b), total type one procollagen-N-peptide (P1NP), calcium (Ca), creatinine (Cr), cystatin C (CysC), estimated glomerular filtration ratio based on CysC (eGFR), serum Cr-to-CysC ratio (Cr/CysC), and Barthel Index, were measured at BL and every six months thereafter. Relationship between BMD gain from BL to second administration and such like factors at BL were evaluated with linear regression analysis at first with univariate model and then multivariate model with factors that demonstrated statistical significance within 5%. Binary logistic regression analysis for these factors was also performed according to BMD gain. These procedures were performed as a same manner regarding with BMD gain from BL to third administration.

Results: A total of 397 patients with 43 males (10.4%) and 354 females (89.6%) were recruited. Average age was 81.3 and average disease duration of RA was 6.9 years. 227 patients (57.4%) was denosumab naïve, and prior to BL, 170 patients were already administered with alendronate in 26, risedronate in 26, minodronate in 23, ibandronate in 12, raloxifene in 39, bazedoxifene in 7, teriparatide in 36.

BMD gain in LS from BL to the second administration demonstrated significant correlation with age and TRACP5b at BL with univariate model, and only aging correlated significant negative correlation with BMD gain with multivariate model. In binary logistic regression analysis, aging demonstrated no significant regression with BMD gain. From BL to third administration, BMD gain also demonstrated significant correlation with aging, but no correlation with TRACP5b, but Cr/CysC at BL. These two factors also demonstrated significant correlation with BMD gain in LS, in these aging demonstrated negative and Cr/CysC demonstrated positive correlation. Cr/CysC demonstrated significant regression with BMD gain in LS from BL to the third with binary logistic regression analysis.

BMD gain in FN from BL to the second administration demonstrated significant correlation with age, BMD in FN at BL, and ACPA with univariate model, and all of the three demonstrated significant correlation with BMD gain with multivariate model. However, no factors demonstrated significant regression with BMD gain with binary logistic regression analysis. From BL to third administration, BMD gain in FN demonstrated significant correlation with aging and BMD in FN at BL. However, BMD in FN at BL demonstrated the only factor to correlate with BMD gain in FN. BMD in FN at BL demonstrated significant regression with BMD gain in FN from BL to the third with binary logistic regression analysis.

Conclusion: These results suggested that BMD gain in LS and FN was affected by different factors. These results may be helpful reference in choosing denosumab against osteoporosis in RA patient.

Disclosure of Interests: None declared

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Crystal diseases, metabolic bone diseases other than osteoporosis

AB0917

AGE PLAYS A CRUCIAL ROLE IN CRYSTAL ARTHRITIS SEVERITY – A SYNIOVAL FLUID STUDY

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Background: Incidence and severity of gout and calcium pyrophosphate deposition disease (CPPD) increase with age (1). Aging is associated with immune senescence, leading to a deregulation of the innate immune system and hence inflammation (2). MRI studies hinted on a significantly higher synovial inflammation in older compared to younger arthritis patients (3). Whether inflammatory

responses to synovial crystals are more pronounced in elderly patients or not is unknown.

Objectives: To test the hypothesis whether aging associates with a more pronounced synovial inflammation in response to urate and CPP crystals.

Methods: Gout or CPPD patients with a synovial fluid (SF) aspiration were included. Clinical, blood and synovial parameters were recorded. In the Cytokine study, SF was analyzed for interleukin (IL)-1-beta, IL-6, IL-8, IL-10, IL-12p70, interferon-gamma (IFN-gamma), tumor necrosis factor-alpha (TNF-alpha), IL-17, and transforming growth factor-beta (TGF-beta) by multiplexed cytokine analysis.

In the Cell study, SF samples were immunophenotyped by flow cytometry, including surface markers CD4+ (CD3+), CD8+ (CD3+), and following stimulation for intracellular IFN-gamma and IL-17. The patients were divided into two groups by age median-split.

Statistical analysis

Categorical variables were reported as frequencies. Continuous variables were compared using Student's t-test or in case of non-normal distribution Mann-Whitney U test.

Table 1. Patients Characteristics

Medians, (IQR), Frequencies in %	Cytokine study (n=15)	Cell study (n=19)
Age [years]	76.6 (69.5; 83.0)	59.0 (54.5; 76.0)
Age Median Split	75	65
Male	80.0%	68%
Gout; CPPD patients [n pat]	10; 5	10; 9
crystals*		
Oligo-/Polyarticular [n pat]	7	8

IQR=Interquartile ranges, CPPD=Calcium pyrophosphate deposition disease, n pat=number of patients

Cytokine study

Median C-reactive (CRP), SUA levels and synovial cell counts were higher in the older patient group. Serum creatinine levels were similar between the two groups. Synovial IL-1-beta, IL-8, and IL-17 levels were significantly higher in the older subjects. Age was correlated with SF IL-1-beta ($r=0.62$, $p=0.02$), IL-17 ($r=0.63$, $p=0.04$) and IL-8 ($r=0.54$, $p=0.04$) levels.

Cell study:

Median CRP was higher in older patients: 87 mg/l (IQR 65; 115) vs. 20 mg/l (IQR 7; 65, $p=0.0129$). Although not significant, a higher frequency of total Th17 (both CD4+IL17+ and CD8+IL17+) T-cells were seen in the SF of the older patient group. The remaining T-cell subsets were comparable between the two groups.

Conclusion: Gout and CPPD are paradigms for auto-inflammatory diseases. We here show an important autoinflammation enhancing cofactor: age. Inflammation measured as serum CRP, SF-IL-8, SF-IL-1-beta, and SF-IL-17 was pronounced in the older patients. Moreover, the adaptive immune system with a predominant Th-17 immune response was more prominent in the older patient group. High IL-17 concentrations may promote differentiation of T-cells in Th-17 cells and thus perpetuate inflammation in older patients with crystal arthritis (4).

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AB0918

FACTORS ASSOCIATED WITH ACHIEVEMENT OF TARGET SERUM URIC ACID IN PATIENTS WITH NON-TOPHACEOUS GOUT ATTENDING PRIMARY CARE CLINICS.

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Background: Gout is characterised by deposition of monosodium urate crystal in the synovial fluid of joint and other tissues, in the presence of elevated serum uric acid (SUA). Dose-escalation strategy with allopurinol as first-line urate lowering

therapy (ULT) was shown to be cost effective and a target SUA of less than 360µmol/L was recommended in non-tophaceous gout.¹ Some of the barriers to treatment effectiveness were related to physician and patient-related factors.^{2,3}

Objectives: To investigate the factors associated with achievement of target SUA in patients with non-tophaceous gout attending primary care clinics.

Methods: A cross-sectional study was conducted over four months on patients with gout attending 21 primary care clinics in Selangor, an urbanised state in Malaysia. The demographic and clinical data, including the most recent SUA within six months of study participation, were obtained from patients' interview and medical records. Obesity was defined as body mass index (BMI) of >27.5kg/m². Data was analysed for patients with non-tophaceous gout. Comparison between patients who achieved and did not achieve target SUA, defined as <360µmol/L, was performed using chi-square and student t-test for categorical and continuous data, respectively.

Results: Four hundred and twenty-six patients with gout participated in this study and 343 (80.5%) patients had non-tophaceous gout. Their mean age was 57.7 (±12.9) years. Majority were men (280 patients), Malay (260 patients) and had at least a secondary education (223 patients). There were high prevalence of cardiovascular co-morbidities; hypertension in 279 (81.3%), dyslipidaemia in 235 (68.5%), diabetes mellitus in 154 (44.9%) and obesity in 167 of 265 (63%). There were 280 patients diagnosed with gout for more than six months and 201 (71.8%) had recent SUA; 44 (21.9%) achieved target SUA and 157 (78.1%) did not achieve target SUA. The factors found to be significantly different between the two groups were age, ethnicity, education level, BMI and SUA level before ULT initiation. (Table 1) The mean allopurinol dose were similar between patients who achieved and did not achieve target SUA (191.3±80.8mg vs 197.1±72.5mg, $p=0.56$) despite significant difference in the mean SUA (301.5±70.3µmol/L vs 488.3±93.1µmol/L, $p<0.01$).

Table 1. Comparison between patients who achieved and did not achieve target SUA level.

Factors	Target SUA achieved, mean (±SD)	Target SUA not achieved, mean (±SD)	p-value
Age, years	63.9 (8.9)	58.1 (12.5)	<0.01
Gender*			0.92
• Male	35 (21.7)	126 (78.3)	
• Female	9 (22.5)	31 (77.5)	
Ethnic*			0.03
• Malay	30 (19.1)	127 (80.9)	
• Others	14 (35)	26 (65)	
Education*, n=181			0.14
• Primary	17 (35.4)	31 (64.6)	
• Secondary and beyond	24 (18.0)	109 (82.0)	
Disease duration, years	94.5 (99.9)	96.39 (94.8)	0.91
BMI, kg/m ²	28.3 (4.3)	31.1 (7.8)	<0.01
SUA before ULT, µmol/L	553.2 (109.2)	603.2 (98.5)	0.03
Recent SUA, µmol/L	301.5 (70.3)	488.3 (93.1)	<0.01
Allopurinol dose, mg	191.3 (80.8)	197.1 (72.5)	0.67

*no of patients

Conclusion: There was a low percentage of patients who achieved target SUA in primary care clinics. Older age, ethnicity other than Malay, lower BMI and lower SUA level before ULT initiation were significantly associated with achievement of target SUA. Higher education was significantly associated with failure to achieve target SUA and in these patients, allopurinol was not titrated according to SUA level.

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AB0919

WHAT IS LOWER EXTREMITY ENTHESEAL INVOLVEMENT IN ACUTE GOUT ATTACK? AN ULTRASOUND-STUDY

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