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## AB0440 IMPACT OF VITAMIN D DEFICIENCY UPON DISEASE ACTIVITY AND IMMUNE DISORDER IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** Emerging evidence suggests that vitamin D plays an important role in immune regulation.
**Objectives:** The objective of this work was to determine if patients with rheumatoid arthritis (RA) are at risk for vitamin D deficiency and whether vitamin D levels correlate with disease activity or immune disorders.
**Methods:** This study was a retrospective research. RA patients who had vitamin D levels and immune function indexes of each other were included. Patients receiving or have received vitamin D, corticosteroids, disease-modifying anti-rheumatic drugs or a tumor necrosis factor antagonist and those who had hepatic or renal insufficiency were excluded. Multivariate analysis was performed to examine correlations and control for confounding factors.
**Results:** As suggested threshold (≤25 ng/ml), the overall prevalence of vitamin D insufficiency was 265 of 280 (94.8%). Mean serum vitamin D insufficiency levels of 11.15±4.74 ng/ml for RA patients were significantly lower compared to controls (31.62±6.46) (p=0.001). Among all the subjects, 208 (72.7%) were females. Vitamin D levels in high disease activity group were lower compared to vitamin D level in patients with low and moderate disease activity (DAS-28 score >5.1, 3.2–5.1, <3.2, respectively, p<0.001) and vitamin D levels had an inverse correlation with DAS28 score (β-coefficient-0.164, p=0.018, per 1 ng/ml). In patients with RA, the levels of vitamin D were moderately and inversely associated with Th 17 (β-coefficient-0.158, p=0.019, per 1 ng/ml). However, no significant relationship was found between vitamin D and these variables (T cell, B cell, NK cell, Treg, Th1, Th2, Th17/Treg) in patients.
**Conclusions:** Lower levels of vitamin D are associated with worse DAS28 and higher levels of Th17 with RA, especially in female patients. The levels of 1,25-dihydroxycholecalciferol (1,25$(OH)_2D_3$) could be a marker to monitor the disease activity in RA patients and vitamin D may be an alternative supplementary treatment for RA.
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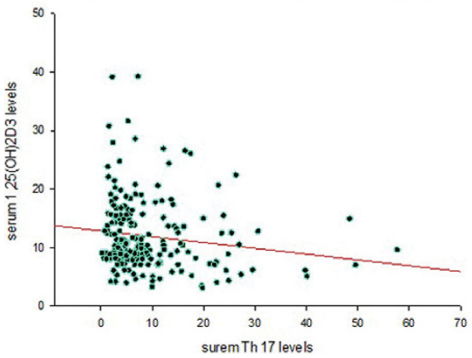
Table 1. Disease activity, immune function indexes with RA as mean ± standard deviation or number (%) for total group and based on vitamin D status

| Variables | All patients N=280 | Patients with Vitamin D insufficiency N=265 | Patients without Vitamin D insufficiency N=15 | P (Insufficiency vs no insufficiency) |
|---|---|---|---|---|
| Women | 208 (72.7) | 201 (74.2) | 7 (33.3) | 0.012 |
| Age (yr) | 56.421±12.325 | 56.109±12.225 | 61.933±13.215 | 0.075 |
| Disease duration (yr) | 9.004±9.336 | 9.017±9.374 | 8.782±8.938 | 0.925 |
| ESR | 59.064±36.483 | 59.325±36.731 | 54.467±32.544 | 0.617 |
| DAS 28 | 4.754±1.429 | 4.768±1.426 | 4.508±1.526 | 0.494 |
| T cell | 1242.473±585.533 | 1249.317±586.751 | 1122.933±569.670 | 0.417 |
| B cell | 204.397±182.279 | 208.206±185.967 | 137.867±72.572 | 0.146 |
| NK cell | 237.419±187.449 | 233.782±188.784 | 300.933±153.989 | 0.178 |
| Th1 | 88.290±116.113 | 87.583±116.660 | 103.377±108.907 | 0.691 |
| Th2 | 12.729±10.819 | 12.852±10.992 | 10.121±5.788 | 0.461 |
| Th17 | 9.271±9.023 | 9.330±9.145 | 8.010±6.059 | 0.669 |
| Treg | 33.710±28.519 | 34.060±29.025 | 26.257±12.426 | 0.424 |
| Th17/Treg | 0.421±0.639 | 0.421±0.647 | 0.411±0.445 | 0.964 |

Table 2. Multivariate associations of serum 1,25$(OH)_2$ $D_3$ concentrations with RA (n=280)

| Variables | β-coefficient | 95% CI | p |
|---|---|---|---|
| Gender | -0.241 | -5.337 to -1.562 | 0.001 |
| Age | 0.182 | 0.024 to 0.168 | 0.009 |
| DAS 28 | -0.164 | -1.243 to -1.116 | 0.018 |
| Th 17 | -0.158 | -0.199 to -0.018 | 0.019 |

Figure 3: The correlations between of serum 1,25$(OH)_2D_3$ levels and Th 17 levels.




## AB0441 USING OF SUBCUTANEOUS METHOTREXATE IN AGED PATIENTS WITH SEROPOSITIVE RA

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**Background:** Increasing life expectancy is a global process involving multiple nations, thus deeper insights into methotrexate (MTX) therapeutic potential in aged people is of paramount importance, as MTX still remains an anchor DMARD in RA management.
**Objectives:** To assess the results of 12-months therapy with subcutaneous MTX (SC MTX) injections in RA patients aged more than 60 years.
**Methods:** The 12 months open study included pts with active RA (DAS28 >3,2), meeting ACR/EULAR (or ACR 1987) criteria, with RA lasting up to 3 years, and naïve to SC MTX. All pts were RF and/or ACPA-positive, 68% had increased BMI, 31% - obesity, 8% were smokers, 25% were taking oral GCS (≤10 mg/day equivalent to *prednisolone*).All pts were administered SC MTX monotherapy once a week as a DMARD, starting at 10–15 mg/week, with subsequent 5 mg up-titration each 1–2 weeks (to max 30 mg/week) up to achieving the target (remission or minimum disease activity) or up to emergence of an adverse drug reaction (ADR). Folic acid (min 5 mg/week) was administered at any day(s) except for the day of SC MTX injection for ADR prophylaxis. Disease activity was scored using DAS28. GEBA were administered in pts with insufficient SC MTX clinical effect. Pts were monitored within universal institutional REMARKA program, envisaging physical examination, blood analysis and biochemistry panel (including liver enzymes and creatinine). STATISTICA 10 software was used for data processing.
**Results:** 32 RA pts (28 females, 4 males) were included (mean disease duration 12±10 months, mean age - 65,7±4,7 years, mean DAS28 score -5,6±0,9. Cumulative SCMT dose by the end of the study reached 264±180 mg). The therapeutic target (remission or minimum disease activity based on DAS28 score) was achieved in 20 pts receiving SCMT monotherpay, 12 pts required administration of GEBAs. Adverse drug reactions (ADRs) were documented in 10 pts, including cases of more than one ADR at a time: breast abscess (1), alopecia (2), diarrhea (2), skin rash (1), a metallic aftertaste (1), local post-injection reactions (1), nausea (2), elevation of liver enzymes (3), leucopenia (1), pneumonia (1). There were 5 cases of SC MTX monotherpay discontinuation (2 - temporary, and 3 - permanent). The majority of pts (88%) could manage self-injection without additional training or assistance from medical staff.
**Conclusions:** 62,5% of aged RA pts participating in the study managed to achieve the therapeutic target after 12 months of SC MT monotherapy, although 31% ADRs rate required temporary (2)/permanent (3) SCMT discontinuation.
**Disclosure of Interest:** None declared
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# SLE, Sjögren's and APS - treatment

## AB0442 REAL-LIFE EXPERIENCE WITH BELIMUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): CONTROL OF DISEASE ACTIVITY AND FLARES IN A MULTICENTER COHORT

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**Background:** Data on the efficacy of belimumab in SLE mainly originate from large randomized clinical trials, whereas reports from real-life clinical practice are lacking.
**Objectives:** To describe the clinical experience from the use of belimumab in Greece since the approval of the drug.
**Methods:** Multicentre observational study of patients receiving belimumab, with documentation of disease activity (SLEDAI-2K index), achievement of low disease

activity states [remission (SLEDAI-2K=0) and lupus low disease activity state (LLDAS)], accrual of irreversible damage (SLICC damage index, SDI), number and severity of flares, and side-effects. Analyses were performed at quarterly intervals and only patients with at least 3 months of follow-up were included in the study.

**Results:** A total of 56 patients were included [53 women (94.6%), mean (SD) age 46.3 (12.7) years]. Evidence of serologic activity (low C3/C4 and/or high anti-ds DNA) was evident in 30 patients (53.5%). Most frequent manifestations were arthritis (82.1%), inflammatory rash (73.2%), active hair loss (57.1%), mucosal ulcers (26.8%) and leukopenia (10.7%).

Median (range) duration of follow-up was 9.1 (2.9 - 34.6) months. We observed a significant decrease in the SLEDAI-2K, physician global assessment (PGA) and daily prednisone dose over time, starting as early as 3 months after belimumab initiation (Table 1). This effect was significantly more pronounced in patients who were serologically active (SA) at baseline, even after exclusion of the serologic component of the SLEDAI [median (range) *clinical* SLEDAI-2K for SA patients: 7 (1–24) at baseline vs. 2 (0–16) at 6 months and 2 (0–16) at 12 months, $p<0.0001$ and p=0.013, respectively; for serologically inactive patients: 6 (2–23) at baseline vs. 6 (0–14) at 6 months and 5 (0–18) at 12 months, p=0.017 and p=0.024, respectively]. For patients with $\geq$12 months of follow-up (n=20), belimumab treatment resulted in a significant decrease in flare rate [median (range) total number of flares for the 12 months before and after belimumab treatment, 3 (0–7) and 0 (0–2), respectively, $p<0.0001$). 10 patients (17.8%) discontinued belimumab due to inefficacy after a median (range) 7.1 (5.5 - 20.4) months of therapy and 5 patients discontinued due to planned pregnancy. There were no drug discontinuations due to side-effects.

**Table 1.** Changes in disease activity and daily prednisone dose during treatment with belimumab

| | Baseline (reference) n=56 | 3 months n=56 | 6 months n=47 | 9 months n=26 | 12 months n=22 | 18 months n=10 | p value |
|---|---|---|---|---|---|---|---|
| SLEDAI, median (range) | 8 (2-28) | 6 (0-24)* | 4 (0-20)* | 4 (0-18)* | 4 (0-18)* | 3 (0-14)** | *p<0.001 **p=0.01 |
| | Baseline (reference) | 3 months | 6 months | 9 months | 12 months | 18 months | p value |
| PGA, median (range) | 1.9 (1-3) | 1.5 (0.3-3)* | 1.5 (0.5-3)* | 1.5 (0-2.2)* | 1.15 (0-3)* | 1 (0-2)*** | *p<0.001 **p=0.18 ***p=0.01 |
| | Baseline (reference) | 3 months | 6 months | 9 months | 12 months | 18 months | p value |
| Pr dose, median (range) | 7.5 (0-40) | 7.5 (0-30)* | 5 (0-25)* | 5 (0-10)* | 5 (0-30)** | 4.3 (0-7.5)*** | *p<0.001 **p=0.001 ***p=0.021 |
| Low disease activity states, n(%) | Baseline | 3 months | 6 months | 9 months | 12 months | 18 months | |
| LLDAS | 0 (0) | 10 (17.9) | 15 (31.9) | 10 (34.5) | 5 (21.7) | 4 (40) | |
| Remission | 0 (0) | 3 (5.4) | 4 (7.1) | 3 (5.4) | 4 (7.1) | 2 (3.6) | |

**Conclusions:** In real-life clinical settings, belimumab is efficacious in controlling disease activity of SLE and permitting tapering of glucocorticoid dose. Similar to data from RCTs, this effect seems to be more pronounced in serologically active patients.

**Disclosure of Interest:** None declared

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## AB0443 INFUSION REACTIONS TO RITUXIMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE ANALYSIS

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**Background:** B-cell depletion with Rituximab (RTX) has been used since since 2000 in the treatment of Systemic Lupus Erythematosus (SLE). An issue with the use of RTX is the attrition rate due reactions during of following infusions. This can prevent re-treatment with RTX in patients with a good initial response to RTX and in whom other treatments had failed, this is especially important in SLE patients with limited biologic options.

**Objectives:** To identify the rates and patient characteristics of infusion reactions to RTX in patients with SLE.

**Methods:** A retrospective analysis of the SLE patient cohort receiving RTX at University College London Hospitals via examination of patient records was used to determine if there was a clinically significant reaction (from clinic letters or discharge summary) for each RTX infusion. One cycle of RTX refers to 2 infusions given 2 weeks apart. A descriptive analysis of the reaction was recorded as was the decision making surrounding the infusions.

**Results:** Records from 151 RTX-treated patients were reviewed with 13 excluded due to missing data. 138 remaining patients (130 females and 8 males, mean age (1st infusion) =33 years; range: 16–73) received a total of 478 individual RTX infusions (between 1–9 cycles). Prior to 2007, standard of care was to receive Cyclophosphamide (CYC) with each cycle. The total rate of infusion reactions was 5.85% (23 patients had 28 reactions). Of these 4 (50%) were males, 19 females (14.6%; *p*=0.009, Chi square). Average number of cycles in those without, compared to with a reaction was 1.61 vs 1.64. With 1st dose, 7 patients (25%) had reactions, 19 with 2nd (67.9%). 3 patients were retreated (1 twice); 2/3 had further reactions and the 3rd two further cycles without issues. Most were not retreated. Reactions ranged from mild to severe (Table 1). A total of 24 RTX reactions were categorized into: Immediate- unlikely immune mediated 4; likely cytokine release 7; IgE mediated 5; and bone pain reactions 2. Delayed-early (24–48hours) 1; and late (>48hours) 5; by a Clinical Allergist. 4 reactions were excluded from this analysis; 1 death as likely CYC induced (but occurred within 24 hours of RTX) and 3 due to lack of data.

Table 1. Severity of Infusion Reactions

| Severity of reaction | Number of patients | % of total infusion reactions | Retreated? |
|---|---|---|---|
| Death | 1 | 3.6% | N |
| Severe | 3 | 10.7% | Y – 1 (had further reaction) |
| Moderate | 7 | 25.0% | Y – 1 (2 further cycles) |
| Mild | 8 | 28.6% | Y – 1 (2 further cycles) |
| Delayed | 5 | 17.9% | Y – 1 (1 further cycle) |
| Unclassified | 4 | 14.3% | N |

Mild (infusion resumed/completed), Moderate (had to cease infusion reaction), Severe (hospital admission), Delayed/serum sickness.

**Conclusions:** The number of previous cycles was similar in patients who reacted versus those who did not. Patients were most likely to experience a clinically significant reaction with the second infusion. Males had higher incidence of reactions. Most (19%) were immediate and the majority (79%) of immediate and delayed reactions occurred during 1st (10) and 2nd (9) cycles. The total rate of infusion reactions in this cohort was lower than previously reported however this is likely contributed to by the limitations of a retrospective review. However 64% of reactions (11/17) in this cohort were significant, necessitating cessation of infusion or hospital admission.

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## AB0444 EFFECT OF RITUXIMAB ON A SALIVARY GLAND ULTRASOUND SCORE IN PRIMARY SJÖGREN'S SYNDROME: RESULTS OF THE TRACTISS MULTICENTRE RANDOMISED TRIAL SUB-STUDY

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**Background:** B lymphocytes are important in the pathogenesis of primary Sjögren's syndrome (PSS), but two phase III trials (TEARS and TRACTISS) of the B cell depleting agent rituximab (RTX) failed to show an effect on their primary endpoints in PSS. Whilst RTX may lack efficacy in a non-stratified PSS population, other possible explanations for these negative results include the choice and timing of primary outcome. In a small single-site salivary gland ultrasound (SGUS) substudy in TEARS, more subjects in the RTX arm demonstrated improvement in parotid gland echostructure. Importantly, SGUS is an operator-dependent technique.

**Objectives:** To compare the effects of RTX versus placebo on SGUS in PSS, in a multicentre, multiobserver substudy of TRACTISS.

**Methods:** Subjects consenting to SGUS were randomised to 1000mg RTX or placebo given at weeks 0, 2, 24 and 26, and scanned at baseline and weeks 16 and 48. Sonographers completed a 0–11 total ultrasound score (TUS) comprising domains of echogenicity, homogeneity, glandular definition, glands involved, and size of hypoechoic foci. Baseline-adjusted values of TUS were analysed over time, modelling change from baseline at each time point. For each TUS domain we fitted a repeated measures logistic regression model to model the odds of a response in the RTX arm (defined as a 1 point improvement) as a function of the baseline score, age category, disease duration and time point.

**Results:** 66 patients (49.6% of the total study population) consented to SGUS, and 52 (39.1%; n=26 RTX and n=26 placebo) completed the baseline and at least one follow-up visit. Estimated baseline-adjusted TUS at week 16 was 6.2 (95% CI 5.4–7.0) for placebo and 5.0 (95% CI 4.4–5.6) for RTX, and at week 48, 6.1 (95% CI 5.5–6.6) and 4.8 (95% CI 4.2–5.4) respectively. Estimated between group differences (RTX-placebo) in baseline adjusted TUS were -1.2 (95% CI -2.1 to -0.3; p=0.0099) and -1.2 (95% CI -2.0 to –0.5; p=0.0023) at weeks 16 and 48. Glandular definition was the only domain to show statistically significant improvement with an OR of 6.8 (95% CI 1.1–43.0; p=0.043) at week 16 and 10.3 (95% CI 1.0–105.9; p=0.050) at week 48. Improvement of $\geq$1 point in TUS was associated with improvement in oral dryness VAS at week 16 (diff=15.9; CI 1.5 to 30.3; p=0.030) but not week 48 in the RTX arm.