-1, max 12); and the median interval between cycles was 14.81 months (6–15.75, min 6, max 120).
The EAS included SLE with 23 (43.4%) cases, systemic sclerosis with 7 (13.2%) cases, Sjögren's syndrome with 6 (11.3%) cases, vasculitis with 5 (9.4%) cases, Still disease with 3 (5.7%) cases, autoinmune cytopenias with 3 (5.7%) cases, dermatomyositis with 2 (3.8%) cases, Behçet's disease with 2 (3.8%) cases, IgG4 disease with 1 (1.9%) case and sarcoidosis with 1 case (1.9%).
A partial response was observed in 27 patients (50.9%) and complete in 20 patients (37.7%). There was no response in 6 of the 53 patients (11.3%). The response by disease groups is detailed in Table 1.

| SAD | Partial response | Complete response | No response |
|---|---|---|---|
| SLE (n=23) | 9 (39,1%) | 12 (52,2%) | 2 (8,7%) |
| Systemic Sclerosis (n=7) | 5 (71,4%) | 2 (28,6%) | 0 |
| Vasculitis (n=5) | 5 (100%) | 0 | 0 |
| Sjögren (n=6) | 3 (50%) | 3 (50%) | 0 |
| AI cytopenias (n=3) | 1 (33,3%) | 1 (33,3%) | 1 (33,3%) |
| Dermatomyositis (n=2) | 1 (50%) | 1 (50%) | 0 |
| Behçet's disease (n=2) | 0 | 0 | 2 (100%) |
| IgG4 related disease (n=1) | 0 | 1 (100%) | 0 |
| Sarcoidosis (n=1) | 1 (100%) | 0 | 0 |

**Conclusions:** In our study, patients treated with RTX achieved response in 88.7%; similar than some experiences of RTX off-label use.
Remision of the disease occurs in 50% of the patients.
The best results are observed in SLE, especially in lupus nephritis, and Sjögren disease.
The results in SS are promising due to the limited therapeutic resources for this disease.
**References:**
[1] Ramos-Casals M, García-Hernández FJ, de Ramón E, Callejas JL, Martínez-Berriotxoa A, Pallarés L, et al. Off-label use of rituximab in 196 patients with severe, refractory systemic autoimmune diseases. Clinical and experimental rheumatology 2010; 28 (4): 468–76.
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## AB0459 TREATMENT OF SYSTEMIC AUTOIMMUNE DISEASES WITH RITUXIMAB: SAFETY DATA

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**Background:** Systemic autoimmune diseases (SAD) have traditionally been treated with steroids and immunosuppressants, but not all patients respond to this strategy. Rituximab (RTX) has been used in several SAD with favorable efficacy and safety results; there are only reports of isolated clinical experiences of small series of patients. The description of this drug safety data in daily clinical practice may be relevant.
**Objectives:** To describe the adverse events and the hospital admissions during the treatment of a series of patients with SAD with RTX.
**Methods:** Demographic data, related to disease and treatment, response and safety variables were included. We use the EULAR definitions of partial response (improvement of at least 50% of the main manifestations) and complete response (disappearance of the manifestations), because of the heterogeneity of the SAD.
**Results:** We included 53 patients, 90.6% were women; the mean age at diagnosis was 31.42±14.33 years; and the median duration of disease at the onset of RTX 1.99 (0–7.5) years. Patients received a median of 2 cycles (1–3; min -1, max 12); and the median interval between cycles was 14.81 months (6–15.75;min 6, max 120).
The SAD were SLE with 23 cases (43.4%), systemic sclerosis with 7 cases (13.2%), Sjögren's syndrome with 6 cases (11.3%), vasculitis with 5 cases (9.4%), Still disease with 3 cases (5.7%), autoinmune cytopenias with 3 cases (5.7%), dermatomyositis with 2 cases (3.8%), Behçet's disease with 2 cases (3.8%), IgG4 disease with 1 case (1.9%) and sarcoidosis with 1 case (1.9%).
A partial response was observed in 27 patients (50.9%) and complete in 20 patients (37.7%). There was no response in 6 of the 53 patients (11.3%).
Adverse events were detected in 15 of the 53 patients (28.3%) and 20 were hospitalized (37.7%) during the treatment with RTX (Table 1).

| Infecctions (9) | Disease activity (8) | Others (3) |
|---|---|---|
| Respiratory: 7 | LES: 8 | Acute coronary syndrome: 1 |
| Pyelonephritis: 1 | | Vertebral fracture: 1 |
| Stomach flu: 1 | | Metrorrhagia: 1 |

Three patients developed hypogammaglobulinemia, only one of them was associated with recurrent respiratory infections and even hospitalized in one occasion. Febrile neutropenia was detected in 2 patients, and one of them required admission. Three patients were diagnosed with pneumonia and admitted for supportive and antibiotic treatment. Three other patients suffered gastroenteritis requiring admission in one of them. In two cases, low respiratory infections were repeated requiring admission on 7 occasions. There was also recurrent otitis and a severe hypersensitivity reaction.
**Conclusions:** The most frequent adverse event were the infectious, mainly respiratory tract infections followed by an infusion reaction. No patient developed opportunistic diseases. This findings are similar than observed in other studies on patients with SAD treated with RTX. Infusion reactions are becoming less frequent, due in part to premedication.
We are dealing with a large number of patients with refractory EAS treated with RTX, so the data obtained from this study show an acceptable safety profile.
**References:**
[1] Ramos-Casals M, García-Hernández FJ, de Ramón E, Callejas JL, Martínez-Berriotxoa A, Pallarés L, et al. Off-label use of rituximab in 196 patients with severe, refractory systemic autoimmune diseases. Clinical and experimental rheumatology 2010;28(4):468–76.
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## AB0460 USE OF INTRAVENOUS IMMUNOGLOBULIN (IVIG) IN AUTOIMMUNE RHEUMATIC DISEASES: EXPERIENCE IN A THIRD LEVEL MEDICAL CENTER

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**Background:** IGIV therapy in rheumatology has been used as an alternative treatment for patients with refractory, severe disease, or with contraindication to the use of conventional immunosuppressive therapy as serious infections; it has recently been increased its use to treat multiple autoimmune diseases, however with a limited number of precise indications as there are not enough studies to increase the level of evidence for the administration of IVIG
**Objectives:** To describe the experience gained with the use of IVIG in autoimmune rheumatic diseases in a third level medical center
**Methods:** This is an observational, descriptive and retrospective study. We report the use of IVIG in our clinical practice, efficacy and adverse effects. We included consecutive patients with autoimmune rheumatic diseases that received IVIG between 2012 and 2015. The information was extracted from clinical records
**Results:** We included 35 patients: 19 women, 16 men, 18 with systemic lupus erythematosus (SLE), 15 with autoimmune inflammatory myopathy, 1 with primary Sjögren's syndrome (SSp) and 1 with polyarteritis nodosa (PAN).
The most common indication was active disease associated with severe infection that contraindicated the use of immunosuppressants in 24 patients and in 11 patients refractory activity disease to conventional therapy. The most frequent indications in patients with SLE were: 6 thrombocytopenias, 5 lupus nephritis, 4 pulmonary hemorrhage and 3 neurolupus; of the group of inflammatory myopathy the indications were: 6 dysphagia, 5 respiratory insufficiency and 4 refractory myopathy. In patients with SSp and PAN the indication was peripheral neuropathy.
The mean number of IVIG applications was 3.3 (range 1–15). Activity scales were decreased in all patients with IVIG: mean SLEDAI at baseline 15.6 and in the follow up 4.5; in inflammatory myopathies remission was reached in 86% of the cases.
The steroid dose was significantly reduced in most patients in the follow up.
Four patients had adverse effects associated with IGIV: 2 with tachycardia and hypertension, one with acute pulmonary edema and one with hemolytic anemia.
**Conclusions:** In our experience, IGIV administration was effective in controlling the activity of the autoimmune rheumatic disease, mainly in patients with concomitant infection, and with a good safety profile.
**Discussion:** IGIV was an effective alternative treatment in patients with contraindication of conventional treatment or in refractory disease, however it is a high cost treatment and should be used in well selected cases
**References:**
[1] Erwin W. Gelfand, M.D. Intravenous Immune Globulin in Autoimmune and Inflammatory Diseases. N Engl J Med 2012;367:2015–25.
[2] Bem Mulhearn I, and Ian N. Bruce. Indications for IVIG in rheumatic disease. Rheumatology 2015; 54: 383–391.
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## AB0461 BENEFITS OF VITAMIN D IN SLE DEPEND ON THE ORGAN SYSTEM

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**Background:** Low 25-OH Vitamin D is associated with SLE. Both a randomized clinical trial and a longitudinal cohort study proved that supplementation reduced SLE disease activity.
**Objectives:** We examined whether Vitamin D benefits in SLE are dependent on the organ system.
**Methods:** Vitamin D and SLEDAI components were measured at each cohort visit starting in 2010 and 16,519 visits of 1,345 different patients were included. The patients were 92% female, 50% Caucasian, 41% African American.
Organ-specific disease activity was defined as a set of binary variables based on SLEDAI. If the patient received any score for any component, then the patient was defined as having that type of activity.
Interestingly, after adjustment for repeated measures and covariates, the relationship between vitamin D and immunologic disease activity totally disappeared.

Table 1. Estimated association between vitamin D levels and odds of organ-specific lupus disease activity, adjusting for age, race, sex, calendar year, prednisone use and plaquenil use

| Vitamin D Level (ng/mL) | Immunologic Disease Activity | | Skin Disease Activity | | Renal Disease Activity | |
|---|---|---|---|---|---|---|
| | OR (95% CI) | P-value | OR (95% CI) | P-value | OR (95% CI) | P-value |
| <10 (n=163) | 1.0 (0.7, 1.5) | 0.88 | 1.4 (1.0, 2.1) | 0.049 | 3.1 (2.0, 4.9) | <0.0001 |
| 10–20 (n=1039) | 1.0 (0.9, 1.1) | 0.93 | 0.9 (0.8, 1.1) | 0.41 | 2.2 (1.5, 3.1) | <0.0001 |
| 20–30 (n=2760) | 1.0 (0.9, 1.1) | 0.97 | 1.0 (0.9, 1.2) | 0.53 | 1.6 (1.2, 2.0) | 0.0008 |
| 30–40 (n=3959) | 1.0 (0.9, 1.1) | 0.78 | 1.1 (1.0, 1.2) | 0.13 | 1.2 (0.9, 1.5) | 0.23 |
| 40–50 (n=3578) | 1.0 (Ref Grp) | | 1.0 (Ref Grp) | | 1.0 (Ref Grp) | |
| 50–60 (n=2308) | 1.0 (0.9, 1.1) | 0.78 | 1.1 (0.9, 1.3) | 0.19 | 1.0 (0.7, 1.3) | 0.91 |
| 60–70 (n=929) | 1.0 (0.9, 1.2) | 0.98 | 1.0 (0.8, 1.3) | 0.74 | 0.8 (0.5, 1.3) | 0.33 |
| 70–80 (n=504) | 1.1 (0.8, 1.2) | 0.92 | 1.3 (1.0, 1.7) | 0.072 | 0.8 (0.4, 1.4) | 0.41 |
| 80+ (n=356) | (1.1 (0.9, 1.4) | 0.42 | 1.4 (1.0, 1.9) | 0.072 | 0.6 (0.3, 1.6) | 0.32 |

However, for skin activity, there was a significantly elevated risk among those in the very extreme levels of vitamin D. For Renal Disease Activity, there was a significantly higher rate of renal disease activity among those with low levels of vitamin D. In addition, there was a clear trend such that the higher the vitamin D, the lower the risk of renal disease activity.

We then conducted a "within person" analysis. In this analysis, each person serves as his own control, and the question is: "When a person has a vitamin D level lower than his/her average, are they more likely to have renal disease activity". Note, this analysis implicitly adjusts for race, sex, and all variables (measured and unmeasured) that are invariant within a person. The results are shown in Table 2.

Table 2. Within-person analysis of the relationship between vitamin D levels and renal activity adjusting for prednisone use, plaquenil use, and implicitly for all time-invariant characteristics

| Vitamin D Level | Odds Ratio | P-value |
|---|---|---|
| 10 ng/mL or more lower than personal average | 1.5 (1.3, 1.8) | <0.0001 |
| Within 10 ng/mL of the personal average | 1.0 (Ref Grp) | |
| 10 ng/mL or more higher than personal average | 0.8 (0.7, 1.0) | 0.080 |

For Renal, it appears (based on the within-person analysis), that increasing vitamin D results in a reduction in renal activity. Based on other analyses, it is clear this drop was mostly among those in the vitamin D deficiency range.

**Conclusions:** Low vitamin D is associated with cutaneous and renal SLE activity, but not with immunologic (low C3 or high anti-DNA) activity, in adjusted analyses.

**Disclosure of Interest:** None declared

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## AB0462 VITAMIN D SUPPLEMENTATION SIGNIFICANTLY REDUCES CHOLESTEROL IN SLE

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**Background:** The benefit of vitamin D on SLE global and renal activity have now been proven by both cohort studies and a clinical trial. The benefits on cardiovascular risk factors, however, are less well understood.

**Objectives:** We present the first longitudinal study on hyperlipidemia.

**Methods:** A within-person aanalysis addressed the question of whether a person tends to have higher cholesterol when her vitamin D is lower than her average vitamin D. To assess this, for each visit, we calculated the difference between the vitamin D level at that visit and the person's average of vitamin D. Differences in the range of vitamin D <50 ng/mL were distinguished from differences in the range above 50 ng/mL. Then we modelled the relationship between these differences in vitamin D and the difference between the person's cholesterol at each visit and the person's average cholesterol.

**Results:**

Table 1. Difference in Cholesterol at each visit per 10 ng/mL difference in between the patient's vitamin D at that visit and the patient's average vitamin D

| Range of Vitamin D | Estimated difference in cholesterol (relative to a patient's average cholesterol) as a function of differences in a patient's Vitamin D levels (relative to her average Vitamin D levels) | | | |
|---|---|---|---|---|
| | Unadjusted | P-value | Adjusted[1] | P-value |
| 0–50 ng/mL | -3.4 (-3.9, -2.9) | <0.0001 | -3.1 (-3.6, -2.6) | <0.0001 |
| 50+ ng/mL | -1.1 (-1.7, -0.5) | 0.0003 | -1.0 (-1.7, -0.4) | 0.0016 |

[1]Adjusted for age, age-squared, sex, race, proportion of time on Plaquenil, mean prednisone dose, mean BM and systolic blood pressure.

Table 2. Difference in Cholesterol per 10 ng/mL Difference in Vitamin D

| Range of mean Vitamin D | Estimated difference in cholesterol per 10 ng/mL difference in Vitamin D (95% CI) | | | |
|---|---|---|---|---|
| | Unadjusted | P-value | Adjusted[1] | P-value |
| 0–50 ng/mL | -3.7 (-4.2, -3.2) | <0.0001 | -3.0 (-3.5, -2.4) | <0.0001 |
| 50+ ng/mL | -0.9 (-1.5, -0.2) | 0.014 | -1.1 (-1.8, -0.3) | 0.0037 |

[1]Adjusted for age, age-squared, sex, race, proportion of time on Plaquenil, mean prednisone dose, mean BMI and SBP.

This means that at a particular clinic visit, if a person's vitamin D is higher than the person's mean vitamin D by 10 ng/mL and the person has vitamin D below 40 ng/mL, then the expected cholesterol will decrease by 3.4 mg/dL. There is no significant effect of higher vitamin D among those whose mean vitamin D exceeds 50.

**Conclusions:** Vitamin D supplementation (in those whose level is below 40 ng/mL) has a significant benefit on total cholesterol that is independent of age, sex, ethnicity, Plaquenil, prednisone and body mass index. Vitamin D supplementation - as it also helps systolic blood pressure - is both important for SLE activity and for reduction of cardiovascular disease.

**Disclosure of Interest:** None declared

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## AB0463 THERAPEUTIC PLASMA EXCHANGE (TPE) FOR REFRACTORY SLE: A COMPARISON OF OUTCOMES BETWEEN DIFFERENT SUB-PHENOTYPES?

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**Background:** Therapeutic plasma exchange (TPE) offers an alternative therapeutic modality for patients with systemic lupus erythematosus (SLE) and primary antiphospholipid syndrome (APS). However, there is conflicting evidence regarding its efficacy in different sub-phenotypes.

**Objectives:** This study aims to investigate the main clinical characteristics and outcomes of patients with different phenotypes of SLE and APS treated with TPE at a tertiary care centre.

**Methods:** Database of Blood and Apheresis Unit between 2001–2013 was screened for patients with SLE and primary APS. SLE disease activity index (SELENA-SLEDAI), the indications for treatment, complications and outcomes were obtained from review of medical records and phone calls. A total of 24 patients (SLE: 20, APS: 4) were recruited for the study.

**Results:** Mean ages of SLE (M/F: 1/19) and primary APS (PAPS) patients (M/F: 2/2) were 32.4±12.89 and 52.0±10.7, respectively. The main indications for TPE were haematologic, neurologic, pulmonary involvement and APS-related. TPE was preferred in 8 patients because of leukopenia, and co-infection. SLEDAI was significantly decreased after TPE (16.7±8.3 vs. 8.8±3.1, p=0.001). Both primary APS and SLE related CAPS patients had completely responded to TPE. Success rate of TPE in patients with thrombocytopenia were lower than patients with haemolytic anaemia. Median (IQR 25%>75%) TPE sessions were 6.5 (5–10.5).

Table 1. Clinical, disease activity, treatment findings and TPE outcomes of SLE patients

| Patient number | Major TPE Indication | Age/ Sex | H/o Nephr itis | Pre-TPE Drugs | preTPE SLEDAI | Concomitant problem, synchronous treatment/ procedures | PostTPE SLEDAI | Outcome | Follow-up |
|---|---|---|---|---|---|---|---|---|---|
| 1 | TTP | 29 | no | MP, CYC | 13 | | 13 | CR | 144 months |
| 2 | Thrombocytopenia, bleeding | 59 | no | MP | 5 | | 4 | PR | 5 months |
| 3 | Thrombocytopenia, cerebral hematoma | 24 | yes | MP, CYC, MG | 37 | L, MP, HD | NA | Exitus | |
| 4 | Thrombocytopenia, bleeding | 22 | yes | MP, CYC | 31 | MP, RTX, HD | 14 | PR, HD | 58 months |
| 5 | Thrombocytopenia, bleeding | 15 | no | MG | 9 | L | 9 | TF | 12 months |
| 6 | Renal Failure, Cytopenia | 54 | yes | MP, CYC, MMF | 27 | L, MP, CYC, HD | 5 | CR | 31 months |
| 7 | Renal Failure | 22 | yes | MP, CYC, MMF, RTX, IVIG | 16 | PR, HD | 8 | CR | 3 months |
| 8 | Alveolar hemorrhage | 30 | yes | MP, CYC, MG | 16 | MP, CYC, HD, MV | NA | Exitus | |
| 9 | Alveolar hemorrhage | 18 | yes | MP, CYC | 38 | MP, CYC, RTX, HD, MV | NA | Exitus | |
| 10 | Pulmonary Fibrosis, Dyspnea, Skin | 33 | no | MP, CYC, MG | 13 | MP, CYC | 7 | PR, pulm HT | 21 months |
| 11 | Psychosis, Active Disease | 26 | no | MP, CYC | 23 | L, MP, CYC | 11 | CR | 48 months |
| 12 | Neuromyelitis optica, vision loss, paraplegia | 32 | no | MP, CYC, MG | 20 | MP, CYC | 10 | CR | 96 months, |
| 13 | Myasthenia Gravis, generalized weakness | 32 | no | AZA | 12 | L | 12 | CR | 132 months |
| 14 | Myasthenia Gravis, generalized weakness | 30 | no | MG | 11 | | NA | Exitus | |
| 15 | Longitudinal myelitis, quadriplegia | 23 | yes | | 29 | PR, MP, CYC, RTX | 10 | PR, paraplegia | 16 months |
| 16 | CAPS | 25 | no | | 24 | MP, CYC | 10 | CR | 84 months |
| 17 | APS-widespread thrombosis | 60 | no | MP, CYC, MG | 11 | | 8 | CR | 4 months |
| 18 | Evans syndrome | 33 | no | | 9 | | 8 | CR | 36 months |
| 19 | Hemolytic anemia | 47-M | yes | MP, CYC, MG | 28 | MP, CYC | NA | Give up TPE | 12 months |
| 20 | Hemolytic anemia | 34 | no | MP, CYC | 8 | | 3 | CR | 73 months |

Abbreviations: L, leukopenia, PN: Pneumonia, MP: Pulse methyl prednisolone, CYC: Cyclophosphamide, AZA: Azathioprine, RTX:Rituximab, HD: Hemodialysis, MV: Mechanical Ventilation, CR: complete Response, PR: partial response, TF: Treatment Failure

**Conclusions:** This study suggests catastrophic antiphospholipid syndrome (CAPS) and other APS related problems respond well to the TPE treatment. TPE should be kept in mind for the treatment of patients with other features of SLE, especially those resistant to other agents and in the presence of leukopenia and psychosis

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## AB0464 AZATHIOPRIONE METABOLITES IN CONNECTIVE TISSUE DISEASE

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**Background:** Azathioprine (AZA) is a common treatment for connective tissue diseases (CTD). AZA is a pro-drug which is metabolised to active moieties of