

**Disclosure of Interest:** J. Stone Grant/research support from: Genentech/Roche, Xencor, Consultant for: Genentech/Roche, Xencor, Z. Wallace: None declared, C. Perugino: None declared, A. Fernandes: None declared, P. Patel: None declared, P. Foster Shareholder of: Full time employee of Xencor, Employee of: Full time employee of Xencor, D. Zack Shareholder of: Full time employee of Xencor, Employee of: Full time employee of Xencor  
**DOI:** 10.1136/annrheumdis-2017-eular.3301

# FRI0589 CANCER IS FREQUENT IN PATIENTS WITH ANTICENTROMERE PATTERN

C. Vázquez-Triñanes<sup>1</sup>, V. Alende<sup>2</sup>, E. González<sup>3</sup>, R. Lorenzo<sup>4</sup>, T. Caínzos<sup>5</sup>, L. González<sup>6</sup>, S. Rodríguez<sup>6</sup>, B. Sopena<sup>2</sup> on behalf of Círculo de estudio de las enfermedades autoinmunes de Galicia (CEAG). <sup>1</sup>Systemic Autoimmune Diseases and Thrombosis Unit, H. Álvaro Cunqueiro, Vigo; <sup>2</sup>Hospital Clínico Universitario de Santiago, Santiago; <sup>3</sup>Complejo Hospitalario de Ourense, Ourense; <sup>4</sup>H. Álvaro Cunqueiro, Vigo; <sup>5</sup>Hospital Arquitecto Marcide, Ferrol; <sup>6</sup>H. Povisa SA, Vigo, Spain

**Background:** Anti-centromere pattern (ACA) is infrequently seen among antinuclear antibodies (ANA) detected by indirect immunofluorescence (IFI). ACA is associated with systemic autoimmune diseases (SAD), especially systemic sclerosis (SSc). Some studies had recently related ACA with cancer, mostly with breast and lung cancer [1]. However, most published series of patients with ACA lack information about cancer occurrence. A prevalence of cancer of 11.1% was the only reported data, on a series of 45 unselected patients with ACA [2]

**Objectives:** Our aim was to study the prevalence of cancer in the largest series of patients with ACA, with a long follow-up. Our second objective was to make a cohort to calculate the incidence of cancer and to try to identify risk markers of cancer in these patients

**Methods:** We included consecutive patients with at least 2 positive determinations of ANA with ACA by IFI on Hep2 cells between January 1st of 2011 and June 30th of 2015 in 6 Galician hospitals. The authors reviewed each patient's chart to determine the presence of cancer and its type among numerous variables. Then, patients with cancer at the moment of the first positive determination of ANA with ACA were excluded. We checked the presence of any tumour in patients of this cohort at the end of follow-up to calculate the incidence of cancer. Finally, we compared patients with and without cancer by multivariate analysis, with the SPSS 20.0. The ethics committees of each hospital approved the study and patients gave their consent

**Results:** 369 patients with ACA were studied, of which 333 were women (90.2%), with a mean age of 64.7 years (range: 22–92). The mean follow-up from the first positive ACA determination was 67.6 months. 283 patients (76.7%) had a SAD: 46.3% SSc (79% of whom were lc-SSc), 8.13% primary biliary cholangitis, 7.05% Sjögren's syndrome, 4.6% autoimmune hepatitis and 11 other SAD (polyarthritis, SLE, Raynaud phenomenon, sarcoidosis, mixed connective tissue disease, etc). 45 of these patients (15.9%) had any overlap syndrome. 39 patients had cancer at some time (10.6%), 3 of them with 2 types of cancer. The most frequent were: breast in 9 (23.1%), lung in 5 (11%), NHL in 5 (11%) and colorectal in 4 (10.3%). Cancer preceded the diagnosis of ACA in 19 patients (48.7%), with a mean time to diagnosis of 9.1 years (range 1–18). In the cohort of 350 patients with ACA the incidence was 1.14 per 100 patients per year (n 20). The mean time to diagnosis of cancer was 7.3 years (range 1–27). The oldest age was the only risk marker of cancer identified (70.8±13.29 years vs. 63.9±14.32, p 0.005). There were no differences in the other variables analysed including sex, tobacco, diagnosis of SAD, capillaroscopy pattern, ANA titrations and mortality

**Conclusions:** Cancer was frequent in patients with ACA, with a prevalence of 10.6% and incidence of 1.14 per 100 patients per year. The only risk marker of cancer identified in this population was the oldest age

## References:

- [1] Briasoulis E, Kamposioras K, Tzouvas V et al. CENP-B specific anti-centromere autoantibodies heralding small-cell lung cancer. A case study and review of the literature. Lung cancer 2008;60:302–306.
- [2] Zuber M, Gotzen R, Filler I. Clinical correlation of anticentromere antibodies. Clinical rheumatology 1994;13(3):427–432.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4455

# FRI0590 SOLUBLE INTERLEUKIN-2 RECEPTOR LEVELS REFLECT DISEASE ACTIVITY IN IGG4-RELATED DISEASE AND PRIMARY SJÖGREN'S SYNDROME

M. Akiyama, T. Sasaki, Y. Kaneko, H. Yasuoka, K. Suzuki, K. Yamaoka, T. Takeuchi. Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan

**Background:** Soluble interleukin-2 receptor (sIL-2R) is known as an indicator for activation status of lymphocytes and could be a potential biomarker for disease activity of lymphoproliferative disorders and autoimmune diseases.

**Objectives:** The aim of this study was to examine the association of sIL-2R with disease activity in patients with IgG4-related disease (IgG4-RD) and primary Sjögren's syndrome (pSS).

**Methods:** Consecutive 45 patients with active, untreated IgG4-RD, 117 patients

with pSS, and 10 patients with sicca syndrome (subjects with xerostomia with neither anti-SSA/SSB antibodies nor lymphocytic infiltration by lip biopsy) were enrolled. Disease activity of IgG4-RD and pSS was determined based on the IgG4-RD responder index (IgG4-RD RI) score and the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) score, respectively. The association of sIL-2R with disease activity was analyzed.

**Results:** The levels of sIL-2R and serum IgG were significantly higher in both IgG4-RD (709U/mL, and 1988mg/dL) and pSS (464U/mL, and 1851mg/dL) compared to sicca syndrome (276U/mL, and 1255mg/dL). Serum levels of IgG4, IgE, and circulating eosinophil counts were significantly higher in IgG4-RD (552mg/dL, 732IU/mL, and 366/mm<sup>3</sup>) compared to pSS (37mg/dL, 216IU/mL, and 157/mm<sup>3</sup>) and sicca syndrome (45mg/dL, 132IU/mL, and 137/mm<sup>3</sup>). On the other hand, the levels of serum IgA and IgM were significantly higher in pSS (312mg/dL, and 112mg/dL) compared to IgG4-RD (182mg/dL and 81mg/dL) and sicca syndrome (228mg/dL and 78mg/dL). The levels of serum C-reactive protein, lactate dehydrogenase, CH50, CC chemokine ligand (CCL17)/thymus and activation-regulated chemokines (TARC) were not different among the three groups. In patients with IgG4-RD, the baseline IgG4-RD RI scores significantly correlated with the levels of sIL-2R ( $\rho=0.715$ ,  $p<0.0001$ ), serum IgG ( $\rho=0.672$ ,  $p<0.0001$ ) and IgG4 ( $\rho=0.632$ ,  $p<0.0001$ ), but not serum IgE levels ( $\rho=0.290$ ,  $p=0.082$ ) and circulating eosinophil counts ( $\rho=0.149$ ,  $p=0.335$ ). In patients with pSS, the ESSDAI scores significantly correlated with the levels of sIL-2R ( $\rho=0.615$ ,  $p<0.0001$ ) and serum IgG ( $\rho=0.627$ ,  $p<0.0001$ ), but not the levels of serum IgA ( $\rho=0.169$ ,  $p=0.073$ ) and IgM ( $\rho=0.133$ ,  $p=0.157$ ). Furthermore, the number of affected organs positively correlated with sIL-2R levels in both IgG4-RD ( $\rho=0.725$ ,  $p<0.0001$ ) and pSS ( $\rho=0.559$ ,  $p<0.0001$ ). Receiver operating characteristic curve analysis demonstrated that sIL-2R was the most distinguishable biomarker for the presence of extra-dacryosialadenitis lesions in patients with IgG4-RD, compared to serum IgG and IgG4, with a cut-off value of 424 U/mL (AUC=0.917,  $p<0.0001$ ), and in patients with pSS with 513 U/mL (AUC=0.894,  $p<0.0001$ ). The sIL-2R levels in patients with IgG4-RD decreased significantly after glucocorticoid treatment. Notably, the cases which could be followed up at disease relapse or exacerbation showed the re-elevation of sIL-2R levels.

**Conclusions:** Soluble IL-2R level is a biomarker for disease activity, in particular for the extent of organ involvements and extra-dacryosialadenitis lesions in patients with IgG4-RD and pSS. Furthermore, sIL-2R level could be useful for longitudinal disease monitoring in patients with IgG4-RD.

**Acknowledgements:** We sincerely thank all the physicians and others caring for the patients enrolled in this study.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2017-eular.4220

# FRI0591 RISK FACTORS FOR DISEASE RELAPSE IN IGG4-RELATED DISEASE FOLLOWING GLUCOCORTICOID TREATMENT

T. Sasaki, M. Akiyama, Y. Kaneko, H. Yasuoka, K. Suzuki, K. Yamaoka, T. Takeuchi. Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan

**Background:** IgG4-related disease (IgG4-RD) is a fibroinflammatory disease characterized by elevated serum IgG4 and infiltration of IgG4<sup>+</sup> plasma cells at affected sites. The patients with IgG4-RD respond well to glucocorticoids (GCs), but one-third of the patients experience disease relapse during tapering of GCs (1). The risk factors for disease relapse following treatment are unclear.

**Objectives:** The aim of this study was to identify the risk factors of disease relapse following reduction of GCs therapy.

**Methods:** Consecutive, newly diagnosed patients with IgG4-RD who were followed over 6 months after treatment with GCs in our department were enrolled. The patients were divided into two groups according to the presence or absence of disease relapse. Disease relapse was defined as the appearance of new lesions or the re-enlargement of involved organs that required dose-increase of GCs. Patient characteristics and laboratory findings at diagnosis were compared and receiver operating characteristic curve analysis was performed to identify the relevant predictive factors of disease relapse.

**Results:** A total of 34 patients were included and all patients were treated with GCs alone as initial treatment. Ten patients (29.4%) experienced relapses during GCs dose tapering which was at 16.0 months (median) after GCs initiation. No difference was found in age, sex, body weight, and disease duration between the two groups. The observation periods and the initial/last GCs dose were also not different. However, serum IgG4 (939 vs 450 mg/dl,  $p=0.008$ ), serum IgG4/IgG ratio (0.35 vs 0.24  $p=0.046$ ), soluble IL-2 receptor (907 vs 677 U/ml,  $p=0.032$ ) and number of organ involvement (4.3 vs 3.0,  $p=0.028$ ) were significantly higher in patients with relapse than those without, while the level of IgA (135 vs 205 mg/dl,  $p=0.015$ ) and IgM (60 vs 91 mg/dl,  $p=0.038$ ) were significantly lower in the patients with relapse. IgG4 decreased to a comparable level in both groups after GCs treatment (200 vs 91 mg/dl,  $p=0.124$ ), but increased in the relapse group afterward (387 vs 115 mg/dl at last observation,  $p=0.048$ ). The predictive values (sensitivity, specificity) at IgG4-RD diagnosis for relapse were as follows: serum IgG4 570 mg/dl (90.0%, 75.0%), IgG4/IgG 0.31 (70.0%, 79.2%), soluble IL-2 receptor 470 IU/ml (100.0%, 54.5%), the number of affected organs of four (80.0%, 70.8%), IgA 100 mg/dl (50.0%, 100.0%) and IgM 60 mg/dl (80.0%, 75.0%) (Figure 1).

**Conclusions:** Higher serum IgG4, soluble IL-2 receptor, and the number of affected organs and lower levels of serum IgA and IgM at baseline indicate

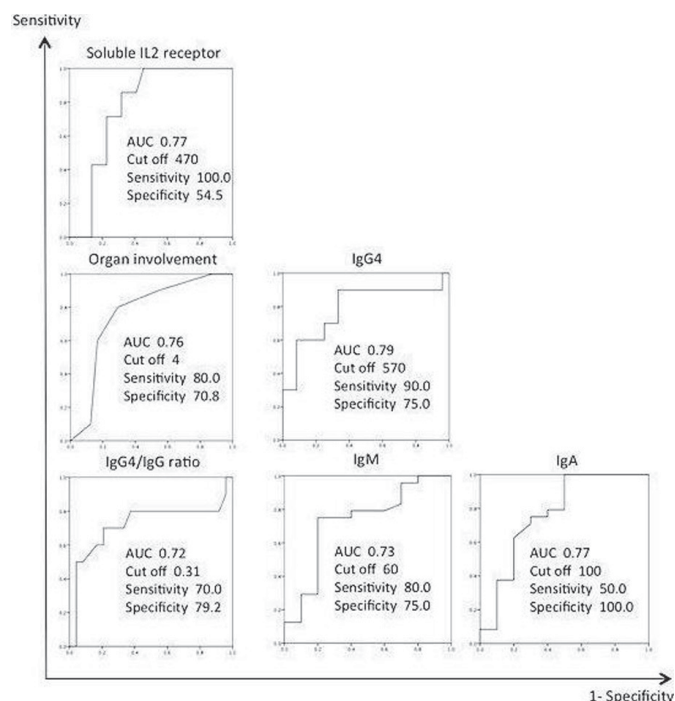


Figure 1

the higher likelihood of disease relapse following GCs therapy in patients with IgG4-RD.

#### References:

- [1] Brito-Zerón P, Kostov B, Bosch X, Acar-Denizli N, Ramos-Casals M, Stone JH. Therapeutic approach to IgG4-related disease: A systematic review. *Medicine (Baltimore)*. 2016;95:e4002.

**Acknowledgements:** We sincerely thank all the physicians and others caring for the patients enrolled in this study.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.4190

#### FRI0592 CLINICAL, ANALYTICAL AND RADIOLOGICAL CHARACTERISTICS IN A COHORT OF PATIENTS WITH SARCOIDOSIS

A. Ruiz Román<sup>1</sup>, C. Aguilera Cros<sup>1</sup>, M. Arcila Durán<sup>1</sup>, M. León Luque<sup>1</sup>, M. Lisbona Muñoz<sup>1</sup>, J.P. Sanchez Serrano<sup>2</sup>, J.A. Rodríguez Portal<sup>3</sup>, J. Povedano Gomez<sup>1</sup>. <sup>1</sup>Rheumatology, Hospital Virgen del Rocío, Sevilla; <sup>2</sup>Breeding and Genetics, Irla, Caldas de Montbui; <sup>3</sup>Pneumology, Hospital Virgen del Rocío, Sevilla, Spain

**Background:** Sarcoidosis is a systemic granulomatous disease, frequently affecting lungs, eyes and skin, although it may damage other organs, among them the musculoskeletal system

**Objectives:** To describe the clinical characteristics and radiological pattern in a cohort with predominantly pulmonary sarcoidosis, and to determine the relationship between the levels of angiotensin converting enzyme (ACE), pulmonary radiological stage and sarcoidosis course (chronification or remission)

**Methods:** Data from 2328 patients in an Interstitial Lung Diseases consultation during the first half of 2016 were analyzed. Out of these, 50 had sarcoidosis. The delay in the diagnosis of sarcoidosis was defined as the difference in years between the diagnostic suspicion and diagnosis of sarcoidosis.

Chi square tests were used, assuming an error of the first species not higher than 0.05, in order to: 1. Study the association between angiotensin converting enzyme (ACE) levels and binary variables (extrapulmonary symptoms, radiological stage and evolution of S) 2. Determine the association between evolution, the radiological stage and the presence of extrapulmonary symptoms.

**Results:** We included 29 (58%) women and 21 (42%) men, (mean age of 44±11.7 years). Initial diagnosis: 88% S, 8% lymphoma and 4% tuberculosis. Of the 44 diagnosed cases of S, 24 were on the first visit, 11 the following year and 1 seven years later. Of the 4 lymphomas, 2 were diagnosed of S that same year and the other 2 were diagnosed the following year. Of the 2 tuberculosis, one was diagnosed of S in one year and the other at 4 years.

The most frequent extrapulmonary manifestations were cutaneous 24%, followed by the articular, cardiac and ocular in 10%, neurological 8% and renal 4%. In 6% of patients, the first clinical manifestation of the disease was bilateral arthritis of the ankles. The ACE title is increased in 62% of patients, normal in 34%. The mean and standard deviation of the title of patients with an increased ACE value was 150.5 and 53.4 IU/L, respectively. In all patients, x-ray and high resolution tomography were performed, with stage 2 being the most frequent (44%), followed

by 3 (20%), 0 and 1 (14%) and 4 (8%). Histological confirmation was obtained by transbronchial biopsy (66%), cutaneous (12%) or lymph node biopsy (12%) in 90% of the patients. 90% of patients have been treated with oral glucocorticoids and 42% associate immunosuppressive therapy.

The ACE levels showed no statistical association with any of the variables studied, although a very clear association (p=0.04754) was observed between the course of the disease and the presence of extrapulmonary symptoms: from the 25 patients without extrapulmonary symptoms, only in 35% of cases the process become chronic.

**Conclusions:** Our results, in general, coincide with what is published in the literature. In our cohort, initial diagnosis of S was relatively high (28/50 =56%), while misdiagnosis was relatively low (6/50 =12%). The level of ACE does not seem to be clearly associated with the presence of extrapulmonary symptoms, nor with the course of S. However, the presence of extra-pulmonary symptoms seems to lead to a chronification

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.5480

#### FRI0593 ASSOCIATION OF THYMOMA WITH AUTOIMMUNE DISEASES IN A SERIES OF 83 CASES

A. González García<sup>1</sup>, W.A. Sifuentes Giraldo<sup>2</sup>, J.L. Morell Hita<sup>2</sup>, J.L. Patier de la Peña<sup>1</sup>. <sup>1</sup>Internal Medicine; <sup>2</sup>Rheumatology, Ramon y Cajal University Hospital, Madrid, Spain

**Background:** Thymoma is the most common neoplasm originated from the thymus gland and accounting for 50% of anterior mediastinal tumors. Within its clinical manifestations are included the loss of self-tolerance and the development of autoimmunity.

**Objectives:** To study the frequency of autoimmune diseases (AD) in patients with thymoma and to describe their clinical characteristics and outcome.

**Methods:** We performed a retrospective observational study of a cohort of patients diagnosed with thymoma and followed-up in our center between January 1985 and September 2016. The variables evaluated included demographics, thymoma characteristics, clinical and analytical manifestations of autoimmunity, treatment and outcome.

**Results:** A total of 83 patients were included, 56.6% of them women, with a mean age at diagnosis of the thymoma of 58.4±15.8 years (range: 16–94), 31.3% of which corresponded to type I The classification of Masaoka, 39.1% to II, 17.2% to III and 10.9% to IV. There were one or more AD associated in 41 cases (49.4%). The most frequent diagnoses were myasthenia gravis (19), systemic lupus erythematosus (SLE) (4), subacute cutaneous lupus erythematosus (1), Sjögren's syndrome (1), rheumatoid arthritis (1), spondyloarthritis (1), sarcoidosis (1), hemolytic anemia (2), pernicious anemia (1), aplastic anemia (1), cutaneous limited systemic sclerosis (1), urticaria-vasculitis, erythroblastopenia (1), recurrent pericarditis (1), thyroid disease (2) and lichen planus (1). The diagnosis of AD preceded to thymoma in 38.2% of cases and was later in the remaining cases. In 4 cases there was also a concomitant primary immunodeficiency (variable common immunodeficiency 3, CD4 immunodeficiency 1). The most frequently identified autoantibodies were anti-acetylcholine receptor (14/41, 34.1%), anti-striated muscle (3/41, 7.3%), ANA (11/41, 26.8%), (3/41, 7.3%), rheumatoid factor (3/41, 7.3%), anti-thyroid (3/41, 7.3%), antiphospholipids (2/41, 9%) and anticentromere (1/41, 2.4%). In the comparison of patients with and without associated AD, no significant differences were found regarding age, sex or Masaoka classification. There were 6 deaths, 4 in group with associated AD and 2 in the group without AD, but without significant difference (p=0.3797).

**Conclusions:** In the analyzed population of patients with thymoma of our center, almost half of them developed AD, which in a major group preceded the diagnosis of neoplasia. The spectrum of autoimmunity associated with thymoma was quite broad, including organ-specific AD such as myasthenia gravis (which is most frequently described in the literature) and autoimmune cytopenias, but also to systemic AD, the most common being SLE. The autoimmunity study should be included in the assessment of the patient with thymoma as it could contribute to the early diagnosis of associated AD.

**Disclosure of Interest:** None declared

DOI: 10.1136/annrheumdis-2017-eular.6992

#### FRI0594 A CASE OF MOSAICISM IN TNF ASSOCIATED PERIODIC SYNDROME (TRAPS)

A. Kontzias<sup>1</sup>, C. Calabrese<sup>1</sup>, Y.-W. Cheng<sup>2</sup>. <sup>1</sup>Rheumatology and Immunology; <sup>2</sup>Laboratory Medicine, Cleveland Clinic, Cleveland, United States

**Background:** Tumor necrosis factor receptor (TNFR)-associated periodic syndrome (TRAPS) is an autosomal-dominant disease caused by gain-of-function mutations in the TNFRSF1A gene, which encodes the 55-kd TNFR type I (TNFRI) protein. Mosaicism has been recently identified in a single patient.<sup>1</sup> A 60 year old male presented with a 6 year history of intermittent fever as high as 103.5, lasting 3–4 weeks with associated peritoneal symptoms, arthralgias, myalgias, lymphadenopathy, bilateral episcleritis, erythematous rash in his torso. Prednisone up to 60 mg daily only partially alleviated his symptoms and colchicine was ineffective.

**Objectives:** To explore the role of mosaicism in a patient with adult onset TRAPS phenotype.