Conclusions: Pneumococcal vaccines, unlike other vaccines, frequently trigger severe local and systemic inflammation in CAPS patients. Clinicians must balance potential benefits of pneumococcal immunisation against safety concerns.

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FRI0586 INTERLEUKIN (IL)-1 INHIBITION WITH ANAKINRA AND CANAKINUMAB IN BEHÇET'S DISEASE RELATED UVEITIS: A MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY

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Objectives: To evaluate the role of interleukin (IL)-1 inhibitors anakinra (ANA) and canakinumab (CAN) in the treatment of Behçet disease (BD)-related uveitis

Methods: multicenter retrospective observational study including 19 consecutive BD patients (31 affected eyes) receiving treatment with anti-IL-1 agents. Data were analyzed at baseline, at 3 and 12 months. Primary end-point: reduction of ocular inflammatory flares (OIF). Secondary end-points: improvement of Best Corrected Visual Acuity (BCVA); reduction of macular thickness defined by optical coherence tomography (OCT) and of vasculitis identified with fluorescein angiography (FA); evaluation of statistically significant differences between patients treated with IL-1 inhibitors as monotherapy, subjects also administered with disease modifying anti-rheumatic drugs (DMARDs) and/or corticosteroids as well as between patients administered with IL-1 inhibitors as first line biologic treatment and those previously treated with TNF- α inhibitors

Results: at 12 months OIF significantly decreased from 200/100 patients/year to 48.87/100 patients/year ($p < 0.0001$). The frequency of retinal vasculitis identified by FA significantly decreased between baseline, 3-month and 12-month follow-up visits ($p < 0.0001$ and $p = 0.001$, respectively). OIF rate was significantly higher in patients co-administered with DMARDs (81.8/100 patients/year) than in patients undergoing IL-1 inhibitors as monotherapy (0.0/100 patients/year) ($p = 0.03$). No differences were identified on the basis of corticosteroid use and between patients administered with IL-1 inhibitors as first-line biologic approach or second-line. Steroid dosage was significantly decreased at 12-month visit compared to baseline ($p = 0.02$).

Conclusions: treatment with IL-1 inhibitors is effective in the management of BD-related uveitis and provides a long-term control of ocular inflammation in refractory and long-lasting cases.

Disclosure of Interest: None declared

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FRI0587 DIFFERENT FACTORS ARE RELATED TO RECURRENCE OF EXISTING ORGAN INVOLVEMENT AND NEW DEVELOPMENT OF ORGAN INVOLVEMENT IN IGG4-RELATED DISEASE

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Background: IgG4-related disease (IgG4-RD) is a recently recognized systemic inflammatory disorder that can affect many organs [1]. In IgG4-RD, relapse including recurrence of existing organ involvement (REOI) and new development of organ involvement (NDOI) easily occurs during the clinical course, and its predictors have been suggested [2, 3]. However, differences between risk factors of REOI and those of NDOI have not been clarified.

Objectives: This study aimed to clarify the respective risk factors of REOI and NDOI in IgG4-RD.

Methods: We retrospectively investigated factors related to REOI and NDOI in 86 IgG4-RD patients whose follow-up period was more than 12 months. For assessment of factors related to REOI and NDOI, we performed uni- and multivariate Cox regression analysis. On stepwise multivariate analysis, we applied the variables with $P < 0.1$ in univariate analysis and the predictors of relapse suggested in past reports (age, sex, serum IgG4, IgG, and IgE levels, eosinophil counts, and RF positivity) [2, 3], and used the forward selection method (including factors presenting with $P < 0.05$).

Results: The patients comprised 57 men and 29 women (mean age 65.9 years). Mean follow-up period was 63.1 months (range 14–150). At diagnosis, their mean serum IgG4 level was 718 mg/dL (range 10.7–3,610). Seventy-one patients were treated with glucocorticoid (GC). REOI was detected at 52.3 months (range 1.0–120) after the diagnosis in 20 patients, including 4 not receiving GC at that time. On the other hand, NDOI was detected at 37.6 months (range 5.0–120) after the diagnosis in 15 patients, including 8 not receiving GC then. In multivariate Cox regression analysis, blood eosinophil counts [per 100/ μ L, hazard ratio (HR) 1.072, 95% confidence interval (CI) 1.018–1.129, $P = 0.008$] and continuation of GC (vs discontinuation or observation without GC, HR 0.245, 95% CI 0.076–0.793, $P = 0.019$) had a significant impact on the time to NDOI, whereas age (per year, HR 0.942, 95% CI 0.899–0.986, $P = 0.011$) and ANA positivity (vs negativity, HR 6.632, 95% CI 1.892–23.255, $P = 0.003$) had a significant impact on the time to REOI.

Conclusions: The present study suggests that the risk factors of REOI and NDOI in IgG4-RD are different.

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FRI0588 INTERIM RESULTS OF A PHASE 2 STUDY OF XMAB®5871, A REVERSIBLE B CELL INHIBITOR, IN IGG4-RELATED DISEASE

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Background: IgG4-related disease (IgG4-RD) is an immune-mediated condition causing fibro-inflammatory lesions that can lead to irreversible organ damage. No approved therapies for IgG4-RD exist. We report the use of a novel monoclonal antibody, XmAb5871, in IgG4-RD. XmAb5871 is a humanized anti-CD19 antibody with an Fc portion engineered for increased affinity (up to 400-fold over native IgG₁) to Fc γ RIIb, the only Fc receptor on B cells. Co-ligation of CD19 and Fc γ RIIb leads to inhibition of B lineage cells bearing these targets. Reversible inhibition of B cell function without B cell ablation is one potential advantage of this approach.

Methods: The trial is an open-label investigation of XmAb5871 in active IgG4-RD, defined by an IgG4-RD Responder Index (RI) of ≥ 3 . XmAb5871 (5 mg/kg) is administered IV every 14 days for 12 doses. The primary outcome measure is the proportion of patients on day 169 (2 weeks following the last dose) with a decrease in the IgG4-RD RI of 2 or more points compared to baseline. Glucocorticoids are permitted but not required at entry and must be discontinued by two months. Other immunosuppressive medications are not allowed. Imaging and mechanistic studies are performed at baseline and at selected intervals.

Results: Fifteen patients were enrolled between March 2016 and January 2017. As of October 31, 2016, 12 patients had received at least one infusion of XmAb5871. The median age of the 12 patients is 58 years (range: 43 to 78 years). Two-thirds of the patients are male. Nine of the 12 patients had elevated serum IgG4 concentrations at baseline with a mean serum IgG4 of 499 mg/dL (range: 25–2415; normal < 86 mg/dL). The median baseline IgG4-RD RI score was 10 (range: 2–30), with active inflammatory disease in at least one organ system (median 4, range: 1–10). The organs most commonly affected were lymph nodes (75% of patients), submandibular glands (67%), parotid glands (58%), and lacrimal glands (50%). Four patients (33%) had kidney involvement and 3 (25%) had heart/pericardium findings. Nine of 11 patients (82%) have had an initial response to XmAb5871 therapy of at least a three-point reduction in the IgG4-RD RI within two weeks of the first dose. As of Oct 31st, 2016, five patients attained disease remission (an IgG4-RD RI of 0 and no prednisone treatment after 2 months) during the study. Efficacy outcomes will be updated as more patients complete the study. One patient had been on glucocorticoid treatment for 2 years and was on prednisone of 15 mg/day at baseline, but was able to discontinue prednisone by 2 months after starting treatment. Three patients experienced minor, transient gastrointestinal side-effects during the 1st infusion. One patient had infusion-related GI symptoms on the 5th infusion and subsequently developed rash and arthritis. She was found to have anti-drug antibodies and has discontinued the study. Mechanistic studies show that both peripheral B cells and plasmablasts decrease substantially following therapy in the majority of patients. Studies of the mechanism of this decrease and functional B cell assays are under way.

Conclusions: XmAb5871 is tolerated well in patients with active IgG4-RD and is a promising treatment approach for IgG4-RD.

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FRI0589 CANCER IS FREQUENT IN PATIENTS WITH ANTICENTROMERE PATTERN

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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

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

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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/mm³) compared to pSS (37mg/dL, 216IU/mL, and 157/mm³) and sicca syndrome (45mg/dL, 132IU/mL, and 137/mm³). 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.

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

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Background: IgG4-related disease (IgG4-RD) is a fibroinflammatory disease characterized by elevated serum IgG4 and infiltration of IgG4⁺ 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