Table 1. Demographic, clinical and laboratory characteristics of patients with Schnitzler's syndrome

Pts	The age (y)	The age at onset (y)	Diagnosis delay (y)	ESR (<15 mm/h)	CRP (<6g/l)	M-gradient (g/l)	Anakinra	Canakinumab	The treatment duration (y)
1	51	40	4	31	107	7,1	0	1	5
2	53	28	22	40	29	5,7	0	0	0
3	36	29	3	140	44	7,8	0	1	3
4	58	53	3	100	192	7,6	1	1	0,5
5	69	66	2	49	96	5,1	1	1	0,5

Abbreviations: Pts – patients, y- years, ESR – erythrocyte sedimentation rate, CRP – C-reactive protein

monoclonal IgMk secretion was revealed in 5 pts, IgMκ and IgMλ – in 1 and IgGκ and IgGλ - 1. No *NLRP3, TNFRSF1A* gene mutations were identified. Prior to the diagnosis, all pts were treated with glucocorticoids with a transient partial clinical response and a disease relapse after reducing the dose or stopping the treatment. 2 pts failed to respond to methotrexate and 1 – to hydroxychloroquine. 4 pts were prescribed with 150 mg canakinumab, a monoclonal antibody targeting IL-1, subcutaneously once every 8 weeks. The treatment duration varied from 6 months to 5 years. 2 pts, who initially received daily 100 mg anakinra subcutaneously for 2 to 3 months with a positive response, were further treated with canakinumab. During the treatment with canakinumab, all pts rapidly responded with a complete resolution of fever, rash, arthralgias and bone pains, an overall health improvement and a normalization in ESR and CRP levels. The therapy was well tolerated. In 1 patient, the intervals between canakinumab injections were prolonged to 5 months without any evidence of relapse. During this period, the male patient became a parent to a healthy child.

Conclusion: In rheumatology practice SchS can be misdiagnosed with AOSD. AOSD patients should be tested for monoclonal gammopathy. IL-1 inhibitors are a highly effective and well-tolerated treatment option for SchS. In SchS patients with a complete response to canakinumab, injection intervals can be individualized.

Disclosure of Interests: None declared

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AB1058 JOINT HYPERMOBILITY SYNDROME AND PRIMARY OPEN-ANGLE GLAUCOMA

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Background: Eye symptoms: myopia, prolapse of the upper eyelid, epiblepharon in the upper eyelid are small diagnostic criteria for joint hypermobility syndrome (JHS).

There are few publications in the literature on the relationship between JHS and primary open-angle glaucoma (POAG).

It is known that in the development of JHS, the distribution of collagen of types I and III with the predominance of collagen of type III is important, the latter is encoded by the COL3A1 gene. When using POAG in the connective tissue of the middle and deep layers of the sclera by the immunohistochemical method, intense focal accumulation of type I and III collagen was previously revealed, and in the layers of the sclera's own substance, type III collagen, unusual for it.

Objectives: To study articular and extraarticular clinical manifestations, instrumental, laboratory signs, as well as to conduct molecular genetic studies on the carriage of the Col3Al gene in patients with a diagnosis of POAG and compare them.

Methods: Nine consecutive patients with an established diagnosis of POAG (burdened heredity by glaucoma) with arthralgia were sent for consultation to the V.A. Nasonova Research Institute of Rheumatology from the Moscow Helmholtz Research Institute of Eye Diseases. All patients are women, the average age is 56.7 ± 10.5 years, the average Beighton score - 4.86 ± 1.7, the mean value of the Westergren ESR - 11,8 ± 5.1 mm/h, CRP_{hs} - 4.9 ± 9.4 mg / 1, all of them were seronegative for rheumatoid factor (RE) and ACCP. All patients responded to the JHS diagnosis according to the 1998 Brighton diagnostic criteria. DNA was isolated from the leukocyte fraction of venous blood using the Wizard DNA Purification Kit (Promega) according to the manufacturer's instructions. The study of gene polymorphisms was performed by the method of minisequencing with subsequent time-of-flight mass spectrometry of a sample on a matrix (MALDI-TOF) in the clinical diagnostic laboratory of NPF L1TEX LLC using a standard protocol (Wise C.A., 2003).

Results: 9 patients had arthralgia, 8 - vertebralgia, 3 - myalgia. 2 had a history of wrist joint dislocation, 7 had flat feet (3 of them had Hallucis valgus), 5 had spondylosis and spondylolisthesis (protrusions and disc herniation according to MRI of the spine), and 4 had excessive skin and / or striate atrophy of skin. Extraarticular manifestations: mitral valve prolapse was detected in 3 patients (in 1 of them + atrial septal defect) with ultrasound of the heart, in 3 - descent of the internal organs (nephroptosis, uterine prolapse), in 4 - pronounced varicose veins of the lower extremities. All patients had a carrier state of the A allele identified by marker C.2092G> A and C allele c.2244T> C of the COL3A1 gene, and a family history of glaucoma. Identification of compliance with JHS diagnostic criteria and the presence of genetic factors (COL3A1 gene) in patients with POAG is of great scientific importance, since it confirms not only clinical associations, but also the genetic proximity of these two conditions. It is also difficult to overestimate the practical value, since patients with POAG need the help of a doctor in the treatment of their articular and other non-ophthalmological manifestations of JHS, and establishing a diagnosis of JHS will require a more thorough examination of the eyes in terms of detecting POAG, its treatment or prevention.

Conclusion: The association of JHS, POAG and COL3A1 gene necessitates further study of the association of JHS and POAG: POAG as a clinical manifestation of JHS, on the one hand, and the role of JHS as a possible risk factor for the development of POAG - on the other hand.

Disclosure of Interests: None declared

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AB1059 A RANDOMIZED, PLACEBO-CONTROLLED STUDY OF ANAKINRA IN PATIENTS WITH STILL´S DISEASE

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Background: Adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (SJIA) are rare autoinflammatory disorders associated with an activated IL-1 pathway, characterized by spiking fever, rash, arthritis, lymphadenopathy, hepatosplenomegaly and serositis. There is a growing understanding that SJIA and AOSD are one disease with different ages of onset, i.e. Still's disease. The anaSTILLs study (anakinra in Still´s disease) was designed to further evaluate efficacy and safety of anakinra in patients with Still´s disease across all age groups.

Objectives: The primary objective was to demonstrate efficacy of anakinra versus placebo as assessed by ACR30 response with absence of fever at Week 2. Secondary objectives included: early onset of efficacy, sustained efficacy, time to study drug discontinuation, safety, pharmacokinetics, clinical signs and biomarkers.

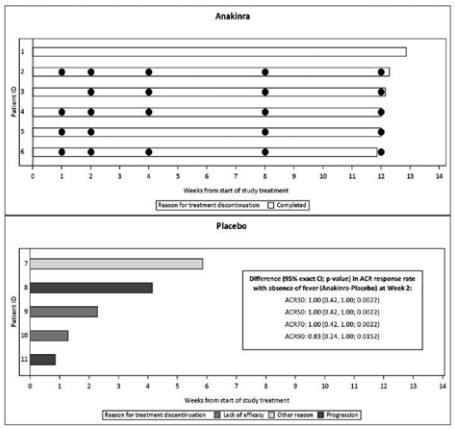
Methods: 'anaSTILLs' was a randomized, double-blind, placebo-controlled, 12-week study including patients with active and newly diagnosed (6 months) Still´s disease according to adapted ILAR criteria if <16, or Yamaguchi criteria, if ≥16 years of age at disease onset. Patients were randomized to anakinra 2 mg/kg (max 100 mg/day), 4 mg/kg (max 200 mg/day) or placebo.

Results: 12 patients were randomized and received study drug: 6 anakinra (2 mg/kg n=2, 4 mg/kg n=4) and 6 placebo, the study was terminated early due to slow recruitment. 1 patient on placebo had lymphoma, not Still's disease, and was excluded; thus in total 11 patients were analyzed for efficacy, 8 were children [median (range) age=4.0 (1-11) years] and 3 were adults [median (range) age=32.0 (25-51) years]. 55% were male and the mean symptom duration was 74.2 days. All patients on anakinra but none on placebo achieved ACR30 response with absence of fever at Week 2 (p-value=0.0022). The efficacy of anakinra was further demonstrated by superiority to placebo in ACR50/70/90 responses with absence of fever at Week 2. All placebo patients discontinued the study within 6 weeks, 2 due to progressive disease, 2 due to lack of efficacy and 1 due to withdrawal by patient. There was a numerically higher proportion with early onset of efficacy (Week 1) in the anakinra group compared to placebo. The

ACR30/50/70/90 responses in the anakinra group were sustained throughout the study period. Patients in the anakinra group had a prompt and persistent decrease in CRP and ferritin levels at Week 1, which was not observed in the placebo group. There were no unexpected safety findings. All anakinra patients developed anti-drug antibodies (ADAs) at some timepoint during the study. ADAs were persistent throughout the treatment period, except in one patient. Titers were low to moderate. One placebo patient had low ADA titers at one occasion. No neutralizing antibodies were observed and the ADAs did not appear to impact clinical efficacy or safety.

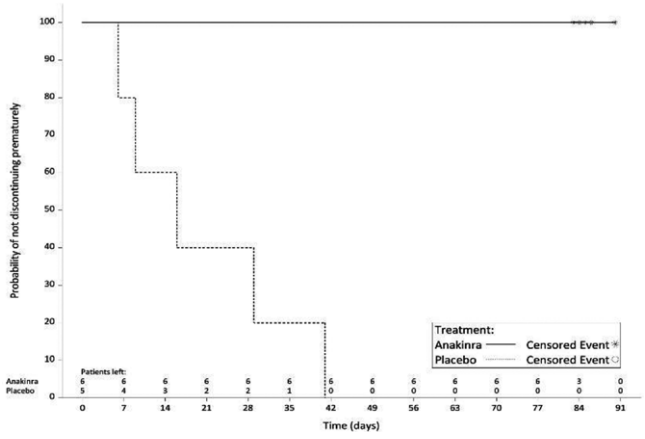
Conclusion: Anakinra is superior to placebo in the treatment of Still's disease. ADAs occur frequently but do not appear to adversely impact efficacy or safety. These results confirm the benefits of anakinra treatment in patients with active, newly diagnosed Still´s disease across ages.

Figure 1: Individual ACR90 response with absence of fever and treatment duration over time and ACR30/50/70 at week 2



Bars indicate time on study drug. Bullets indicate ACR90 response at the particular week.
Patient 1 had sustained ACR70 response but not ACR90.

Figure 2: Time to study drug discontinuation, Kaplan-Meier plot



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AB1060 A RARE IGG4-REALTED DISEASE PHENOTYPE WITH BONE DESTRUCTIVE LESIONS

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Background: IgG4-related disease (IgG4-RD) is an immunomediated fibroinflammatory condition with systemic course that can affect almost any organ in the body. In the majority of cases it is a benign condition with slow progression. The clinical symptoms are usually determined by compression of nearby anatomic structures by tumefective lesions, but not by invasive growth of the pseudotumor with the destruction of the organs. Bone destruction always raises suspicion of malignant tumor, but it should be considered in the course of IgG4-RD as well.

Objectives: To report a very rare bone destructive phenotype of IgG4-RD.

Methods: We report 5 cases of biopsy proven IgG4-RD with bone destructive lesions.

Results: In our cohort of patients there were 3 patients with multiple fascial bones destruction due to maxillary sinus pseudotumor expansion and 2 patient with vertebral destruction lesions.

Patients 1, 2 and 3 with facial bone destruction were young men aged 42, 36 and 28 years. In all cases the primary lesion was located in the maxillary sinus with expansion to the fascial soft tissues and orbit. Two patients had probable and 1 possible IgG4-RD diagnosis according to consensus diagnostic criteria, 2011. All patients were treated with rituximab and low doses of glucocorticoids with improvement of clinical symptoms (fascial edema, eye pain and/or headache), but lacking in radiologic improvement.

Patient 4 is a 51-year-old man who developed retrosternal pain, mimicking angina pectoris. Chest CT showed a tumor of posterior mediastinum, infiltrating the right lung and Th6-Th8 bodies destruction. Biopsy of the lesion revealed lymphoplasmatic infiltrate with lymph follicles formation, few eosinophils, significant diffuse fibrosis. Immunohistochemical study, showed IgG:IgG4 ratio >40%. The serum IgG4 concentration was 1.94 g/l (normal range below 2.0 g/l). Combined treatment was administered: rituximab 500 mg weekly #4 and cyclophosphamide 1000 mg + methylprednisolone 250 mg IV every 2 weeks #6. After that - cyclophosphamide 200 mg per week intramuscularly, methylprednisolone 4 mg daily per os. Due to spinal instability the patient undergone surgery. Six months later at check-up examination CT has shown a dramatic decrease of the mediastinal infiltrate. The treatment with cyclophosphamide and oral metylprednisolone was tapered gradually during 2 years due to no sites of pathological hypermetabolic activity were found on PET.

Patient 5 is a 60-year-old woman who had spinal surgery for C2 odontoid destruction. Biopsy revealed chronic inflammatory with massive fibrosis. 1,5 years later she developed salivary glands enlargement. During evaluation she had elevated serum IgG4 4.9 g/l and IgM 4.1 g/l (normal range below 0.6-3.7 g/l), serum protein electrophoresis with immunofixation showed monoclonal IgMκ 3.2 g/l. Left submandibular salivary gland biopsy revealed significant fibrosis, dense lymphoplasmatic infiltrate forming lymph follicle with IgG:IgG4 ratio 50-80% and no pathological signs of lymphoma. The patient was treated with rituximab 500 mg per week #2 and cyclophosphamide 1000 mg + methylprednisolone 250 mg IV every 2 weeks #3. The treatment was discontinued because of toxic hepatitis. Unfortunately, no follow-up was available. The tissue specimens after spinal surgery were also unavailable.

Conclusion: IgG4-RD can manifest by bone, including vertebral, destructive lesions and thus should be included when considering differential diagnosis in patients with bone destruction.

Disclosure of Interests: None declared

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AB1061 2019 ACR/EULAR CLASSIFICATION CRITERIA FOR IGG4-RELATED DISEASE IN RUSSIAN COHORT OF PATIENTS.

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Background: IgG4-related disease (IgG4-RD) is a systemic immunomediated fibroinflammatory condition that can affect almost any organ in the body. This is the reason for dramatic variety of clinical symptoms and complexity of diagnostics. 2011 Comprehensive diagnostic criteria (CDC) for IgG4-RD are used to establish the diagnosis for all lesions (except autoimmune pancreatitis type 1). In 2019 the new ACR/EULAR classification criteria for IgG4-RD were proposed to facilitate the formation of more homogenous groups of patients primarily for clinical trials inclusion purpose. They also provide a framework for clinicians considering diagnosis of IgG4-RD.

Objectives: To evaluate 2019 ACR/EULAR classification criteria for IgG4-RD in Russian cohort of patients with IgG4-RD.