Conclusion: In a population-based study we found an overall increased SMR. The risk of CV comorbidity and of CV death among patients with a register diagnosis of GPA was increased.

There was a striking temporal relation between a high HR of CV morbidity and mortality during the first year after the diagnosis of GPA. Nevertheless, the HR of CV morbidity and mortality was albeit lower still increased after 10 years with a diagnosis of GPA.

The result indicates a strong association between systemic vascular inflammatory disease and CV involvement. At the time of diagnosis of GPA systemic inflammatory activity usually is present and the results point towards an association of inflammation with CV risk-factors probably including premature and pronounced atherosclerosis. The persistence of increased HR of CV involvement after 10 years indicates a permanent influence on the risk factors.

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FRI0264

ADVERSE EVENTS DUE TO HIGH DOSE GLUCOCORTICOIDS – LESSONS FROM ANCA-ASSOCIATED VASCULITIS AND OTHER INFLAMMATORY DISEASES

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Background: High dose glucocorticoids (GCs) are a component of induction remission and maintenance regimes in ANCA-associated vasculitis (AAV) and are used in other inflammatory disorders. The adverse event (AE) profile of GC is well known and in AAV is believed to link to early mortality risk from infection as well as long term organ/tissue damage. However, it is known GC AE reporting is incomplete and EULAR made specific recommendations for such reporting in clinical trials (Van der Goes 2010).

Objectives: This systematic literature review aimed to examine AE rates and outcomes related to high dose GC use in AAV and to quantify AE risk in terms of GC dose and duration.

Methods: A systematic literature review was performed of studies published between 1 Jan 2007 and 30 January 2018. Data on GC-related AEs (defined as any untoward medical occurrence) and serious AEs (defined in European Medicines Agency CPMP/ICH/377/95) which threaten life or function were extracted from identified trials. The initial AAV search demonstrated incomplete GC data collection compared to EULAR recommendations in most AAV studies so the search strategy was extended to include other inflammatory disorders in which similar GC regimes and doses are used namely systemic lupus erythematosus, glomerulonephritis, pemphigus and giant cell arteritis.

Results: Three hundred and eleven studies of these 5 conditions were identified in which GC-related AEs were published. 38 studies were selected for a detailed AE analysis on the basis of their inclusion of full description of GC regime, actual delivered GC dose and patient exposure. Of the 62,630 patients enrolled in the 38 studies, 35,587 were exposed to GCs. 21 studies reported serious AEs, while 17 studies reported AEs only. The most common serious AEs related to specific organ damage - particularly musculoskeletal, ocular and neuropsychiatric - but mortality and infection were also observed. The most common AEs were metabolic conditions, with diabetes related events comprising 72% of the metabolic AEs, and weight gain comprising 15%.

	Serious adverse events	Adverse events
Number of patients in studies reporting GC-related events	2340	9602
Events reported (n)/%	840/36%	2479/26%
Most common events%	Mortality 14%	Metabolic 50%
	Infection 7%	Musculoskeletal 16%
	Organ damage 49%	Ocular 14%
		Infections 12%

Correlation analysis demonstrated mean total GC dose was positively related to risk of death ($r = 0.51$) and infection ($r = 0.49$) while GC therapy duration was related to risk of infection ($r = 0.62$).

Conclusion: GC-related AE reporting in clinical studies of high dose GCs could be improved. Serious AEs including organ damage, infection and mortality were reported and both total GC dose and therapy duration are important risk factors mortality and infection. Metabolic and musculoskeletal events are a particular patient burden. New therapeutic options for AAV and other disorders should aim to reduce this AE profile.

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FRI0265

ANTI-IGE AND ANTI-IL5 THERAPY FOR EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA), formerly Churg-Strauss syndrome, is a rare type of anti-neutrophil cytoplasm antibody-associated vasculitis, associated with asthma, nasal poliposis and rinosinusitis, in which eosinophils play a key role.

Eosinophil targeted therapies alone or associated to conventional treatment with corticosteroids and immunosuppressant drugs may be useful in patients with refractory disease or asthma difficult to treat.

Objectives: To describe the efficacy and safety of eosinophil targeted therapies in patients with relapsing or refractory EGPA

Methods: Retrospective study including all patients with EGPA included at the REVAS Registry, who were treated with omalizumab, mepolizumab or reslizumab. Complete response (CR) was defined as the absence of asthma and/or sinonasal exacerbations with a prednisone dosage of ≤ 7.5 mg/day, and partial response (PR) when the prednisone dosage was ≥ 7.5 mg/day. Statistical analysis was performed using SPSS 20 package.

Results: Seventeen patients (median age 49 years) received omalizumab (n=9) for a mean period of 53.4 (5-91) months, mepolizumab (n=7) for a mean period of 13.6 (5-16) months, or reslizumab (n=1) for a mean period of 7 months, for severe steroid-dependent asthma (94.1%) and/or sinonasal involvement (82.4%). ANCA were positive in 8 (47.1%) cases with MPO specificity in 7 cases. All patients were receiving corticosteroids with a mean dosage of 15 mg/day prior to eosinophil targeted therapies institution. Four (57.1%) patients treated with omalizumab achieved a CR, 1 a PR, and 2 had no improvement. The median dosage of prednisone 6 months after omalizumab initiation was 10 (2.5-10) mg/day and the median dosage after 12 months 5 (0-10) mg/day. The median number of exacerbations decreased from 4 over the 6 months previous to therapy startment to 2 in the following 12 months. Both patients refractory to omalizumab were treated with mepolizumab with CR at 6 months in 1 case. Treatment with mepolizumab was also started in 4 patients treated with omalizumab after a prolonged period of treatment (72.4 months), due to recurrence of asthma and/or sinusitis, and peripheral blood eosinophilia $>10\%$. Three (75%) patients achieved a CR, and 1 patient experienced a major vasculitis relapse needing immunosuppressant drugs. Six (85.7%) patients initially treated with mepolizumab achieved a complete remission after 6-12 months of treatment. One patient achieved a PR. The median dosage of prednisone 6 months after mepolizumab initiation was 5 (3.1-6.8) mg/day and the median dosage after 12 months 3.5 (0-5) mg/day. The median number of exacerbations decreased from 2.5 over the 6 months previous to therapy startment to 1 in the following 12 months. The patient treated with reslizumab achieved a CR at 6 months of therapy. All 3 drugs were safe and well tolerated.

Conclusion: The results of the present study suggest that eosinophil targeted therapies have a corticosteroid-sparing effect in EGPA patients with asthmatic and/or sinonasal manifestations, and that may be used sequentially in refractory cases. However, reducing the corticosteroid dosage may also increase the risk of severe EGPA flares. More data are needed to widely recommend this therapy in EGPA patients.

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FRI0266 ABERRANT PD-1 AND VISTA EXPRESSION ON CD4+ TH-CELLS IN GIANT CELL ARTERITIS

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Background: The immune system controls immune responses by balancing positive and negative immune checkpoint (IC) molecules in cell-cell interactions. These co-stimulatory and co-inhibitory molecules allow complete T-cell activation and T-cell effector functions giving rise to an optimal immune response while preventing autoimmunity (1). Failure of tolerance results in the initiation and propagation of pathogenic T-cell responses leading to the development of autoimmune diseases such as Giant Cell Arteritis (GCA). The latter is a complex illness of multiple pathogenic factors with important contributions of both innate and adaptive immunity in its initiation and perpetuation (2,3). Recently, a loss of inhibitory checkpoints on immune cells has been implicated in the immunopathology of GCA (4,5). The possible contribution of IC pathways to the dysregulation of Th-cells in GCA could aid in our understanding of GCA immunopathology.

Objectives: In this study, we aimed to investigate the expression of different IC molecules and their ligands by circulating monocytes, and functionally distinct populations of CD4+T-cells in peripheral blood samples from GCA-patients in comparison to healthy controls (HCs).

Methods: In a cross-sectional study, fresh blood samples were obtained from 30 GCA-patients with/without immunosuppressive treatment (glucocorticoids) and 18 sex and age-matched HCs. The frequency of the expression of different IC including CD80/86, PD-L1, PDL2 and V-domain Ig suppressor of T-cell activation (VISTA) were determined on total monocytes and subsets (classical, intermediate and non-classical). In parallel, expression of the corresponding receptors CD28, Cytotoxic T-Lymphocyte-associated antigen-4 (CTLA-4), Programmed death-1 (PD-1), and VISTA were determined on total CD4+ and subsets of Th-cells defined by CD45RA and CD25 expression of GCA-patients and HCs by flow cytometry.

Results: The frequencies of CD80/CD86+ and VISTA+ monocytes were decreased in GCA-patients compared to HCs. Proportions of circulating CD4+ Th-cells in GCA-patients were not different when compared to HCs. The frequencies of CD28 and CTLA-4 expressing CD4+Th-cells did not differ between GCA-patients and HCs. In contrast, proportions of PD-1 and VISTA expressing Th-cells were significantly decreased in GCA patients. Memory T-cells showed decreased expression of IC molecules. Interestingly, naïve T-cell populations already demonstrated loss of PD-1 and VISTA.

Conclusion: In GCA, lower frequencies of CD80/CD86+ and VISTA+ circulating monocytes were found. Likewise, decreased proportions of PD-1+CD4+ and VISTA+CD4+ Th-cells were noted. Decrease of negative IC on the surface of immune cells could add to the persistent activation of CD4+T-cells seen in GCA.

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FRI0267 DIAGNOSING POLYMYALGIA RHEUMATICA: THE IMPACT OF FAST-TRACK CLINIC AT HOSPITALIZATION RATES

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Background: Polymyalgia Rheumatica (PMR) is a common inflammatory autoimmune rheumatic disease, with the highest incidence rates seen in Scandinavia.

One of the challenges in the diagnosis of PMR is the lack of diagnostic tests specific for the disease. The diagnosis may require exclusion of other conditions that can present with polymyalgia symptoms and may lead to hospitalization. Only limited data on hospitalization rates among patients with PMR exists (1).

Ultrasound (US) may be useful in differentiating PMR from non-inflammatory conditions and can also be used for the diagnosis of concomitant Giant Cell Arteritis (GCA)

GCA Fast Track Clinics (FT) using US as the main diagnostic tool have shown both improvement in patient outcomes and decrease in the cost of care(2)

Objectives: To investigate the admission rates of patients diagnosed with PMR and the impact of the FT on these rates.

Methods: A FT clinic for patients suspected to have PMR was established at rheumatological outpatient clinic of South-West Jutland Hospital (serving 250.000inhabitants) in January 2018. Collaboration with the Emergency Medical department was established and patients with PMR symptoms referred to the hospital were examined at FT within 0-1 days, thereby avoiding hospitalization. Similarly, patients referred with PMR symptoms to the outpatient clinic by a GP, were examined at FT within 1-2 days. At FT a thorough history and clinical examination were performed including musculoskeletal and vascular US. Retrospectively data from patients diagnosed with PMR from 2013-2018 was analyzed.

Results: In a 6 years' period, 336 patients were diagnosed with PMR. 54 patients were diagnosed during hospitalization. Hospitalized patients were older (mean values $\pm$ standart deviaton-sd) 73,61 $\pm$ 8,96 vs 70,94 $\pm$ 7,97 years, p=0,024, with significantly higher initial C-reactive protein (CRP, mg/l) levels 99 $\pm$ 58,8 vs 43,9 $\pm$ 37,p<0,0001 and a shorter duration of symptoms(6,92 $\pm$ 5,5 vs 13,6 $\pm$ 13,7 weeks, p=0,0018). No differences were found regarding gender, PMR related symptoms, initial prednisolone dose and response to treatment. An equal annual distribution of the number of new diagnosed cases and hospitalizations rates during the first 5 years was found. After the implementation of the FT at January 2018 a significant decrease in hospitalization rates (19,4% vs 3,5% p=0,001) and inpatient days of care (4,15 $\pm$ 3,1 vs 1 $\pm$ 0, p<0,0001) was observed. The time from symptoms debut to diagnosis was also significantly decreased from 13, 74 to 6, 79 weeks (Table)

	Diagnosed at 2013-2017 N 268	Diagnosed at 2018 N 56	P values
Age (years) mean $\pm$ sd	71,3 $\pm$ 8,5	71,79 $\pm$ 6,6	n.s*
Gender (female)	58,2%	48,2%	n.s
Duration of symptoms (weeks) mean $\pm$ sd	13,74 $\pm$ 13,74	6,79 $\pm$ 4,72	0,001
Bilateral shoulder pain	95,9%	98,2%	n.s
Abnormal CRP and/or SR at debut	91,8%	100%	0,03
CRP (mg/l) mean $\pm$ sd	52,82 $\pm$ 48,3	56,5 $\pm$ 37,2	n.s
Morning stiffness	90,3%	92,7%	n.s
Hip pain or limited range of motion	71,4%	61,8%	n.s
RF and aCCP negative	95,1%	100%	n.s
Absence of other joint involvement	72%	75%	n.s
Initial prednisolone dose (mg) mean $\pm$ sd	18,44 $\pm$ 8,41	19,2 $\pm$ 9,25	n.s
Hospitalized n(%)	52 (19,4%)	2 (3,5%)	0.01
Inpatient days of care mean $\pm$ sd	4,15 $\pm$ 3,1	1 $\pm$ 0	0,0001

*n.s=non-significant