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.