The evolving role of mepolizumab in EGPA

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There is overwhelming evidence that eosinophiles play a key role in the pathogenesis of EGPA. Il-5 is the central cytokine for eosinophil maturation, eosinophil release from the bone marrow and eosinophil survival. Mepolizumab is an antibody neutralising IL-5, which proved efficient in the hypereosinophilic syndrome and eosinophilic asthma, amongst other conditions. Targeting this cytokine in EGPA therefore seemed plausible. Two small uncontrolled trials demonstrated the safety of mepolizumab in EGPA and indicated the potential for induction of remission, maintenance and steroid sparing. A randomised controlled trial (MIRRA) confirmed those findings and showed higher rates of accrued remission for mepolizumab when given as ad-on medication to conventional immunosuppressants and/or glucocorticoids. Steroid sparing properties were also confirmed. MIRRA and previous trials in different indications indicated no major safety concerns. Based on this trial drug approval for EGPA might be feasible.

To date the major problems in the treatment of EGPA are 1) refractory disease 2) a high frequency of relapses and 3) the need for high glucocorticoid doses in many patients.

Mepolizumab could be used for induction of remission in addition to glucocorticoids. However, its not yet clear, which subgroup of patients might profit most. Especially patients with severe disease have not been investigated. For patients with refractors non-severe disease mepolizumab is a potential option. Mepolizumab also was efficient in preventing relapses and therefore may also be used for maintenance of remission, especially in patients suffering from prevalent relapses. Finally, patients with high need for glucocorticoids could profit from mepolizumab, particularly in case of steroid-sensitive comorbidities or steroid-induced complications.

Disclosure of Interest: F. Moosig Consultant for: Chugai, GSK

CURRENT CONTROVERSIES IN THE USE OF RITUXIMAB FOR INDUCTION AND MAINTENANCE OF AAV DISEASE

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Rituximab has now taken one of the first places in induction remission treatment of ANCA-associated vasculitides (AAVs) and is challenging cyclophosphamide. Rituximab is an anti-CD20 IgG1 mouse–human chimeric antibody that selectively depletes mature and memory B-cells.

Use of rituximab for induction

In AAVs, rituximab non-inferiority to cyclophosphamide as induction agent was clearly established. In the RAVE trial, which compared oral cyclophosphamide to rituximab as induction regimen, the remission rate at 6 months was 64% in the rituximab group and 53% in the cyclophosphamide group. Consequently, rituximab has revolutionised AAVs’ standard-of-care and is now recommended as first-line therapy for many patients with granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).

The RAVE trial prospectively compared two arms: induction with glucocorticoids, rituximab or placebo. Rituximab recipients vs. 28% of azathioprine-treated patients had relapsed. Prolonged follow-up of those patients showed that, at 60 months, although relapses had occurred in both groups, rituximab remained superior to azathioprine for sustaining remission. Although the results highlighted rituximab superiority in maintaining remission, it also became clear that relapses still occurred, frequently 18 to 24 months after the last rituximab infusion.

An answer to the optimal rituximab duration will be partially obtained with the MAINRITSAN3 trial (ongoing), which is comparing, after randomization, four additional semester rituximab infusions (500 mg) to placebo, after patients had previously received rituximab during 18 months. It seems reasonable that, in the future treatment duration will be adapted to prognostic factors and predictors of relapses.

Also, the impact of using higher dose of rituximab during maintenance will be addressed by the RITAZAREM trial (ongoing). This protocol evaluates rituximab infusions of 1 gram every 4 months for 20 months compared to oral azathioprine.

Use of rituximab for EGPA

Data on rituximab’s clinical benefits for eosinophilic granulomatosis with polyangiitis (EGPA) patients is currently restricted to low-evidence–based open-label studies and case reports. The main findings of these studies indicate a potential benefit in severe refractory/relapsing EGPA, especially in patients with positive ANCA. Two ongoing prospective studies in France are comparing rituximab to conventional immunosuppressants as induction (REOVAS trial) and maintenance phase (MAINRITSEG trial). It will help to define more precisely the indication of rituximab in EGPA patients and eventually highlight which patients would benefit from the treatment.

Disclosure of Interest: None declared

Tapering and flaring in PsA

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This talk will discuss the current evidence regarding tapering or drug withdrawal in patients with psoriatic arthritis. With increasing numbers of patients achieving good outcomes such as remission, the issue of how long to continue treatment for has been raised. Given the cost of some of the newer therapies, this question also has significant cost effectiveness implications.

There is a limited amount of evidence but data from randomised and observational studies will be discussed as well as key research questions that remain outstanding.

Disclosure of Interest: None declared

Tapering in axial spondyloarthritis – to do or not to do?

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According to the current version of the ASAS-EULAR management recommendations for axial spondyloarthritis, tapering of a biological disease modifying anti-rheumatic drug (bDMARD) can be considered once a remission is achieved. Tapering is opposed to a complete discontinuation that is associated with a very high disease flare risk (70%–100%) in axial spondyloarthritis. The question of tapering in axial spondyloarthritis has been addressed in a number of small clinical trials: in the majority of the them, tapering (either dose reduction or increase of the injection/infusion interval) could be done without a disease flare. It is, however, not clear, whether the tapering has any beneficial effect for a patient (i.e., in terms of safety) in addition to a cost-saving effect. Further, a number of questions related to tapering still requires an evidence-based answer: a) what is the optimal time-point of the initiation of tapering (e.g., 3, 6 or 12 months after remission achievement)? b) what is the optimal tapering regimen? c) are there reliable predictors of sustained remission/disease flare during tapering? The question of a bDMARD tapering after remission achievement will be at least partially answered in ongoing