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The European Vasculitis Society 2016 Meeting Report

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In June 2016, a meeting of the European Vasculitis Society (EUVAS) was held in Leiden, the Netherlands. For the first time, the meeting was structured around parallel meetings of the EUVAS petals as part of the EUVAS Research Council, which was formed in 2011 to enhance scientific research in systemic vasculitis. The petals consist of the following fields of interest: disease assessment, biomarker studies, epidemiology and etiology, clinical trials, registries, genetics, toxicity and infection, database, and histology (Figure 1). The theme of the meeting was phenotypic subtyping. In this report, we give an overview of the state-of-the art issues arising from the petal meetings. The goal of EUVAS is to stimulate ongoing research in clinical, serological, and histological management, and techniques for patients with systemic vasculitis, with an outlook on the applicability for clinical trials.

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Disease Assessment

The careful definition and classification of different forms of antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis (AAV) requires consideration of clinical, serological, and histological evidence. There is considerable overlap among the disease entities. A major study is underway to improve our ability to discriminate among different forms of vasculitis by using data from >5000 individuals with different forms of vasculitis or disease mimics. The diagnostic and classification study in vasculitis (DCVAS)[1] will report preliminary criteria for ANCA vasculitis in the near future. These criteria will assist in separating granulomatosis with polyangiitis (GPA) from microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA), and other forms of less well-defined vasculitis (which may or may not have ANCA present). The emphasis for the DCVAS project is on characterizing patients for future clinical and epidemiological studies.

Further phenotypic characterization of disease severity is facilitated by using clinical evaluation tools such as the Birmingham Vasculitis Activity Score (BVAS)[2–4] and the Vasculitis Damage Index (VDI).[5,6]

Figure 1. European Vasculitis Society (EUVAS) petals. Fields of interest in systemic vasculitis: disease assessment, biomarker studies, epidemiology and etiology, clinical trials, registries, genetics, toxicity and infection, database, and histology.

These clinical tools are increasingly important in characterizing disease status in terms of activity and damage; this facilitates the distinction among different diseases states. Terms such as active disease, response to therapy, partial response to therapy, relapse, or low-grade disease activity can be defined on the basis of the BVAS assessment. This has already been applied to clinical studies for defining patients with active disease who are eligible for inclusion in studies and in defining a response to the therapy, remission, and relapse. BVAS and VDI also allow more detailed phenotyping of patients with more or less severe end-organ involvement within individual diagnoses (e.g., patients with GPA may have relatively limited disease, whereas other patients with GPA may have much more extensive disease). Defining organ involvement dictates the need for treatment, but may also be a reflection of the underlying pathophysiology and genetic predisposition to severity, as well as susceptibility to disease. Once the classification criteria are established, we need to use them in combination with disease evaluation tools to explore how the different phenotypes behave and respond to therapy, and also to discover whether the phenotypic characterization corresponds to better understanding of underlying pathophysiology.

Database and Long-term Follow-up

The survival of patients with AAV improved dramatically after the introduction of corticosteroids and cyclophosphamide (CYP) in the 1970s.[7] After this, treatment modalities improved with greater safety and outcome. Since the 1990s, EUVAS has designed and accomplished several prospective randomized clinical trials (RCTs), mostly without pharmaceutical companies. The first 4 RCTs revealed new information on how to best treat patients with AAV, according to disease extension and severity.[8–11] However, because AAV is chronic (i.e., relapsing) in at least 50% of patients, it is difficult to draw firm conclusions solely from the results of an RCT that lasts 18 months. Thus, we performed a 5-year follow-up of patients in the first 4 RCTs, and several reports were published from these studies.[12] We obtained more robust information on actual patient and kidney survival, complications due to treatment, and complications due to disease. The longer term follow-up revealed that the initial results were not always robust in the longer term. For example, patients with proteinase 3 (PR3)-AAV appeared to be more prone to relapse if they received pulse CYP compared with continuous oral CYP.[13] Patients treated with methotrexate as induction therapy in the NORAM study, most of whom had PR3-ANCA, were exposed to more CYP and corticosteroids in the 5-year follow-up than those who had received CYP as induction. In the short-term perspective, it seems that relapses may not be harmful with regard to the long-term outcome of renal function. However, this may not be true for the longer term perspective. From the 5-year follow-up, we learned that the incidence of malignancies was not higher in this population compared with a matched background population, with the exception of nonmelanoma skin cancer.[14] If this finding reflects an improvement in the treatment strategies, or is a result of a too short a follow-up, we can only tell if the study period is prolonged. Thus, we aimed for a longer follow-up of patients who participated not only in the first 4 RCTs, but also those included in the later IMPROVE and RITUXVAS studies. We would then have a cohort that consisted of approximately 700 European patients followed-up for at least 10 years. The 10-year follow-up has been launched, and we are working on retrieving data on patient and renal survival, relapse rate, cumulative incidence of malignancies, and possibly comorbidities. A larger cohort of patients makes it possible to try to place patients into subgroups with similar clinical presentations and/or phenotypes, in an attempt to identify those with a particular high risk for poor outcome, as Mahr *et al.* did in a cluster analysis.[15]

Registries

Patient registries and databases play an important role in clinical research, patient care, and healthcare

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