ABSTRACT
The definition of remission in patients with systemic vasculitis must be distinguished from the term “cure,” which implies that patients are well and not requiring ongoing therapy. Remission should be defined using a standardised approach to measuring clinical disease activity, and the definition should be qualified by the duration of the remission and the type of maintenance therapy required to sustain remission. Remission is an important goal of management in the systemic vasculitides and is achievable in most patients. Maintenance of remission is a more difficult target, and evidence from studies of patients with antineutrophil cytoplasmic antibody (ANCA)–associated systemic vasculitis indicates that durable, lasting remission is unlikely to occur. Despite good disease control, damage or scarring from disease or its treatment is a common finding and is a separate outcome from remission. Future studies of vasculitis therapies should address the concept of rapid and sustained disease control, so that patients spend most of their time in a state of good health, with minimal damage.

Introduction
The natural history of untreated Wegener’s granulomatosis (WG) involves a mean survival of 5 months, with a mortality of 93% at 2 years (1). In the 1980s, cyclophosphamide and glucocorticoids became accepted as standard remission-induction therapy, and remission became a routine outcome measure. Antineutrophil cytoplasmic antibody (ANCA)–associated systemic vasculitis (AASV) is associated with a significant deterioration in the ability to perform activities of daily living and in the overall quality of life (QOL) (3-5). The QOL as measured by the short form 36 (SF-36) (6) for patients with AASV is lower than the population norms. Despite improvement in QOL as a result of current therapy, most patients have persistently reduced QOL, as measured by the SF-36 (7, 8).

Ideally, therapy should be aimed at curing a disease but this is rarely achieved in AASV. Despite initial good control, relapses are common in AASV; 14% to 70% of patients will suffer a relapse within 2 years of remission, depending upon the type of disease and immunosuppression (9, 10, 12-16). Since most patients ultimately relapse with current therapy, remission is an acceptable outcome state.

Over time, the goal of therapy has changed from increasing the likelihood of survival to lengthening and improving the quality of disease-free survival (9, 10). With evolving therapies, the understanding of the concept of remission has also shifted from a subjectively perceived clinico-pathological absence of disease to a quantifiable absence of disease activity. This paper discusses the evolving concept and definition of remission and its ramifications.

The concept and definition of remission
The extent, intensity, and duration of active inflammation in patients with vasculitis is not only correlated with symptoms related to acute disease, but is also highly predictive of long-term outcome and damage (11). Current therapies achieve disease control for only a limited period of time, making “cure” an unrealistic expectation. Therefore, absence of clinical symptoms has been the primary end point in a majority of therapeutic trials in AASV. There is limited evidence in Churg-Strauss syndrome (CSS) of treatment resulting in a permanently sustained remission without dependence on continuing immunosuppressive therapy (12). The terms “cure” or...
“complete recovery,” defined as disease control without treatment for an extended time period (e.g., 18 months), have been used in a few trials for treating CSS (12, 13). In contrast, patients with AASV often suffer disease relapse in the absence of maintenance immunosuppressive therapy. Therefore, a time-limited, rather than an indefinite, absence of disease activity can be regarded as a realistic outcome in AASV and, in analogy to the definition used in oncology, the term “remission” has been used to describe this disease state.

Definition of “remission”
The term remission, defined as the absence of disease activity attributable to active vasculitis, has been used to describe the outcome of patients with AASV in clinical practice and clinical trials. The majority of published randomised controlled trials and open-label studies in patients with AASV have used this definition of remission (7, 10, 14-19). Depending on the disease stage and the type and length of induction therapy, rates of remission in these studies ranged up to 93%, suggesting that the complete absence of clinical disease activity while receiving immunosuppressive therapy is a realistic and feasible end point. Thus, an international working group consisting of members of two collaborative research groups (the European Vasculitis Study Group and the Vasculitis Clinical Research Consortium) and regulatory agencies developed consensus definitions for disease states for use in clinical trials, which were incorporated into the European League Against Rheumatism (EULAR) recommendations for conducting clinical trials in systemic vasculitis (20). In the EULAR consensus document, the term “remission” has been defined as the complete absence of active clinical disease, and the use of this definition is recommended for clinical trials (Table I).

Use of the term remission implies that the absence of disease activity is being checked systematically. Typically this can be performed using a validated and published disease activity score like the Birmingham Vasculitis Activity Score (BVAS) (21) or its disease-specific variant, the Birmingham Vasculitis Activity Score for WG (BVAS/WG) (22). Despite the use of validated rating scales, reported rates of remission may nonetheless vary considerably, depending on how carefully patients are evaluated. For example, a patient with WG may be reported to be free of symptoms but may still have subclinical active disease in the nose or kidney. Therefore, differences in the intensity of evaluation (e.g., regular inspection by an otorhinolaryngologist and/or cranial magnetic resonance imaging vs patient-reported symptoms) can account for differences in rates of remission and should be specified in any study protocol.

Remission rates are affected by time and treatment
Patients with AASV suffer frequent flares. Randomised controlled trials (RCTs) in AASV with similar induction regimens have shown that the probability of relapse is significant (up to 70%) despite initial good control of disease activity (7, 8, 23). The number of patients who sustain remissions will therefore decrease with time. The EULAR guidelines recommend that a definition for remission should be qualified by a minimum duration spent in remission (20). Terms such as “sustained remission” have been used in the past to set time limits of remission, such as 6 months in the WG etanercept trial (WGET) (24). However, achieving remission should be differentiated from sustaining it. For example, in a trial comparing methotrexate (MTX) plus glucocorticoid with cyclophosphamide plus glucocorticoid for early or localised AASV, rates of remission were high (89% in the MTX arm, 94% in the cyclophosphamide arm), but relapses were frequent (70% in the MTX arm, 47% in the cyclophosphamide arm at 18 months) (8). If only sustained remission had been documented, the trial might have shown no benefit for MTX therapy.

There is evidence that continued immunosuppression following remission can reduce the risk of relapses in AASV. In all the studies mentioned above, patients remained on some form of immunosuppression at induction of remission (7, 8, 23). Furthermore, it has been documented in large cohort

<table>
<thead>
<tr>
<th>Activity state</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Remission</td>
<td>Absence of disease activity attributable to active disease qualified by the need for ongoing stable maintenance immunosuppressive therapy. The term “active disease” is not restricted to vasculitis only, but also includes other inflammatory features like granulomatous inflammation in WG or tissue eosinophilia in CSS.</td>
</tr>
<tr>
<td>Response</td>
<td>50% reduction of disease activity score and absence of new manifestations.</td>
</tr>
<tr>
<td>Relapse</td>
<td>Recurrence or new onset of disease attributable to active vasculitis.</td>
</tr>
<tr>
<td>Major relapse</td>
<td>Recurrence or new onset of potentially organ- or life-threatening disease.</td>
</tr>
<tr>
<td>Minor relapse</td>
<td>Recurrence or new onset of disease that is neither potentially organ threatening nor life threatening.</td>
</tr>
<tr>
<td>Refractory disease</td>
<td>Chronic, persistent disease defined as presence of at least one major or three minor items on the disease activity score list, after ≥12 weeks of treatment.</td>
</tr>
<tr>
<td>Low-activity disease</td>
<td>Persistence of minor symptoms (e.g., arthralgia, myalgia) that respond to a modest increase of the glucocorticoid dose and do not warrant an escalation of therapy beyond a modest dose increase of the current medication.</td>
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</tbody>
</table>

AASV: antibody-associated systemic vasculitis; CSS: Churg-Strauss Syndrome; WG: Wegener’s granulomatosis.
studies (10, 17) that many patients require low doses of glucocorticoid (≤7.5 mg) to control minor symptoms (e.g., arthralgia, nasal crusting) after attaining remission. Thus, given the potency of current induction therapies, complete withdrawal of glucocorticoid or other immunosuppressants is not necessarily required in order to define a patient as being in a state of remission. Therefore, EULAR recommendations propose that ‘remission’ should be qualified by the type, duration, and allowed maximum dosage of any immunosuppressive therapy, including glucocorticoid, at the time of induction of remission. To determine whether or not the absence of clinical symptoms is actually related to the effects of the experimental drug under study and not simply a result of high-dose glucocorticoid therapy, the EULAR recommendations propose that a patient should be taking a stable dose of ≤7.5 mg of prednisolone per day for a defined period in order to be considered in remission.

Is remission purely a clinical state, or should it be linked to biomarkers?

In AASV, remission is primarily a clinical state. However, some biomarkers that reflect organ function (e.g., renal or respiratory function) are an integral part of disease assessment tools such as BVAS. Proteinase 3 (PR3) ANCA and myeloperoxidase (MPO) ANCA are highly specific markers of AASV, and there is some evidence that high ANCA levels at diagnosis, their persistence at the time of induction of remission, and their subsequent reappearance are all associated with a higher risk of relapse, renal failure, and decreased survival (18, 25-28). However, a meta-analysis of 22 studies could not reach a conclusion about the value of serial ANCA testing because of varying methodologies in the papers. At present a definition of remission in AASV should not be linked to ANCA testing. If future long-term studies, particularly those applying genomics and proteomics, identify novel biomarkers with a higher prognostic value in AASV, they may be included in the definition of remission (e.g., absence of disease activity combined with presence of low or undetectable levels of the biomarker).

Remission is distinct from “grumbling” disease

The benefit of immunosuppressive therapy in AASV is usually seen within 6 weeks. By 3 months, remission is induced in most cases (8). Complete remission may not be possible in a subset of patients. The persistence of disease manifestations (at least 1 major or 3 minor items in the BVAS) beyond this length of time is defined as chronic persistent refractory disease (20). In these refractory patients, further reduction of disease activity is possible with continued immunosuppression to produce low-grade “grumbling” disease. For purposes of use in future trials, such a disease state has been termed a low-activity disease state by the EULAR consensus group (20). The symptoms of low-activity disease may be controlled by a modest increase in the glucocorticoid dose. Remission should be distinguished from such a state of partial response. This state is a potentially useful outcome measure in the treatment of patients with refractory disease. Persistent disease presents a difficult problem with regard to scoring disease activity. The original BVAS 1994 score sheet included only clinical features that were either new or worse in the month before the assessment. This meant that the score would be misleadingly low for patients suffering with chronic low-grade activity. For this reason, additional provision was made in the European Vasculitis Study Group (EUVAS) modification of the scoring sheet to record persistent disease items (29). In the latest version of the BVAS (BVAS 2003), there is a tick box to indicate that all the items on the sheet are attributable to low-level disease activity. In the presence of even a single item attributable to new or worse disease, all the items on the sheet are scored as due to active disease. This version is currently undergoing validation.

Rationale for defining remission

For the patient, remission may mean independence from medication, doctors, and hospital. For the clinician, it is a useful end point to target with current therapy. For the researcher, remission is an important end point for clinical trials and an opportunity to study the pathophysiology of the disease in its quiescent state. The recognition of relapse or low-activity states is facilitated by the definition of the zero state of disease activity.

The role of ‘remission’ in clinical trials

Clinical trials and cohort studies of AASV have defined remission, albeit inconsistently, in an attempt to set an unambiguous clinical end point. Remission has been used as a primary outcome measures in open pilot trials (30, 31) as well as in randomised controlled trials (8, 23). Another role for the definition of remission has been as an inclusion criterion in clinical trials to identify patients in a specific disease state. An obvious use is in clinical trials to test therapies for maintenance of remission in AASV (7, 32). The WGET has used the definition of remission more extensively by describing status at three different points in the trial to determine when to switch to maintenance therapy, when to taper maintenance therapy, and as an outcome measure (24).

Most clinical trials have set remission as a score of zero using the BVAS or the BVAS/WG. These widely accepted, validated scores rely on the zero state of disease activity to be able to score disease activity accurately. By contrast, in trials of rheumatoid arthritis (RA), the concept of remission has largely been replaced by measure of response. The American College of Rheumatology (ACR) defined a standardised state of improvement, the ACR20, in order to quantify improvement (33). More recently, the disease activity score based on a 28-joint count (DAS28) (34) has been used as an outcome measure in trials like TICORA (35). When remission in RA is not achieved, the ACR20 and the DAS28 make it possible to measure how much the patient has progressed towards the zero state of disease.
Clinical practice should be evidence-based. Practice guidelines convert outcome measures from clinical trials and/or cohort studies into clinically relevant targets. Remission can be ascertained reliably by measuring disease activity with a validated scoring index and demonstrating the absence of activity. Thus, the discussion of remission inevitably includes disease activity scores. The BVAS could be included in a practice guideline to assist standard management of systemic vasculitis. The WGET and TICORA trials were dependent on the use of disease activity scores. The WGET was a placebo-controlled trial of etanercept for remission maintenance in WG, which concluded that etanercept was not superior to placebo in maintaining remission and preventing relapses. Remission and relapse were defined using the BVAS/WG score. The TICORA was an open trial that showed that the effect of standard disease-modifying therapy for treating RA was greatly enhanced by the use of a protocol based on measurement of disease activity and the use of glucocorticoids for early disease. If the WGET trial had shown a positive outcome as in TICORA, that protocol could have been modified for use in clinical practice. In primary systemic vasculitis, current biomarkers are not sufficiently reliable to determine disease activity on their own. The importance of disease activity scores is therefore accentuated in helping the physician to identify remission, relapse, and low-disease activity states.

Disease activity scores and the concept of remission are also used in health economics. Biologic therapies are costly and their use must be justified both clinically and economically. Among other criteria, the increasing use of biologic therapy in vasculitis will require justification by an increased proportion of time spent in remission. It is conceivable that a threshold BVAS score could be used as a qualifying mark akin to the use of DAS28 in RA.

The evidence for remission induction in AASV
Remission in AASV is common. The remission rates from various studies are shown in Table II.

The choice of treatment for induction of remission depends on the type and intensity of disease. The combination of cyclophosphamide and glucocorticoid have been standard therapies since the 1980s (2). There has been debate over the length and method of administration of cyclophosphamide. In a meta-analysis of three trials (36), monthly pulses of IV cyclophosphamide resulted in more frequent relapses than daily oral cyclophosphamide, but the difference was not statistically significant (odds ratio [OR] 1.79; 95% confidence interval [CI] 0.85–3.75). In other trials, IV cyclophosphamide has been shown to be of equal efficacy as daily oral cyclophosphamide, resulting in similar control at a lower cumulative dose (37, 38). The use of <10 g of cyclophosphamide in the first 6 months is an independent risk factor for disease relapse (relative risk [RR] 2.83, 95% CI 1.33 – 6.02) (16). This favours the current consensus of 2 to 3 weekly pulses of cyclophosphamide for 6 months. This approach has been adopted by the EUVAS group in the conduct of the ANCA-associated Vasculitis European Randomised Trials (AVERT) (39).

In patients without critical organ involvement, MTX is an alternative option to cyclophosphamide for remission induction, but relapse rates are higher in patients initially treated with MTX, in the absence of continuing immunosuppression (hazard ratio [HR] 1.85, 95% CI 1.06 – 3.25) (8). In patients with CSS with a 5-factor score (FFS) of zero (40), glucocorticoids alone may be used successfully for remission induction (41). The addition of plasma exchange to standard therapy with cyclophosphamide and glucocorticoid resulted in improved renal survival at 1 year in patients with severe renal impairment in microscopic polyangiitis (MPA) and WG (42). However, in CSS with poor prognostic factors, this combination did not show any survival benefit at 5 years over standard therapy (12).

The presence of damage at diagnosis, represented by a single item on the Vasculitis Damage Index (VDI) (43) is associated with treatment resistance (OR 1.53, 95% CI 1.03 – 2.27) (16). Other factors imparting treatment resistance are female sex (OR 1.8, 95% CI 1.01 – 3.3, p = 0.048), African American origin as opposed to white American origin (OR 3.1, 95% CI 1.19 – 7.85, p = 0.013), and impaired renal function at diagnosis (OR for serum creatinine elevation per 100 μmol/l 1.28, 95% CI 1.16 – 1.39, p = < 0.001) (18).

Intravenous immunoglobulin (IVIG) infusions and biologic therapies have been used for remission induction in refractory AASV or, in the presence of contraindications to cyclophosphamide, in small open-label pilot trials. A single infusion of IVIG (2 g/kg) was effective at reducing disease activity by at least 50% of baseline in more than 80% of

<table>
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<tr>
<th>Citation</th>
<th>Disease – No. of patients</th>
<th>Remission rate, %</th>
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<tbody>
<tr>
<td>Rotten 1993 (14)</td>
<td>WG – 158</td>
<td>89</td>
</tr>
<tr>
<td>Aasarod 2000 (15)</td>
<td>WG – 108</td>
<td>81</td>
</tr>
<tr>
<td>Reinhold-Keller 2000 (10)</td>
<td>WG – 155</td>
<td>53</td>
</tr>
<tr>
<td>Koldingsoe 2003 (16)</td>
<td>WG – 56</td>
<td>85</td>
</tr>
<tr>
<td>Guillemin 1999 (17)</td>
<td>CSS – 96</td>
<td>91</td>
</tr>
<tr>
<td>Hogan 2005 (18)</td>
<td>WG – 59</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td>MPA – 202</td>
<td></td>
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<tr>
<td></td>
<td>RLV – 89</td>
<td></td>
</tr>
<tr>
<td>Rihova 2005 (19)</td>
<td>WG – 33</td>
<td>87</td>
</tr>
<tr>
<td></td>
<td>MPA – 10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CSS – 3</td>
<td></td>
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<tr>
<td></td>
<td>RLV – 14</td>
<td></td>
</tr>
</tbody>
</table>

CSS: Churg-Strauss Syndrome; MPA: microscopic polyangiitis; RLV: renal limited vasculitis; WG: Wegener’s granulomatosis.

Table II. Remission rates in AASV.
cases compared to 32% improvement in the placebo group, although the responses were not maintained after 3 months (44). In a pooled analysis of open-label trials, 81% of patients achieved remission with infliximab; 69% of those patients had been resistant to standard treatment (45). In another open-label pilot trial, rituximab induced remission in 11 patients with treatment-resistant WG (46). These results require validation in larger randomised trials. There has been limited success with antithymocyte globulin for the same purpose (31).

The evidence for remission maintenance in AASV
Sustained remission without pharmacotherapy for over 18 months has been used as a definition for cure in CSS and shown to be achievable even in patients with a poor prognostic factor (12). This is otherwise uncommon in the other AASV. Relapse rates in AASV are shown in Table III.

After induction of remission with cyclophosphamide and glucocorticoid, azathioprine (AZA) is the favoured drug for maintenance of remission. There is no difference in the rate of relapse as compared with cyclophosphamide (15.5% with AZA and 13.7% with cyclophosphamide; p = 0.65), but it is a safer alternative (7). Continuation of AZA for beyond 12 months has also been shown to reduce mortality (RR 0.390, 95%CI 0.202 – 0.752) (27). Co-trimoxazole used for the maintenance of remission in WG, with or without cyclophosphamide plus glucocorticoid, reduced the risk of relapse (RR 0.40; 95%CI 0.17 to 0.98) (25). Etanercept was no better than placebo in the maintenance of remission (23).

The treatment used for induction of remission plays an important role in its maintenance as well. The use of < 10 g of cyclophosphamide in the first 6 months and high dose prednisolone (> 20 mg/day) for less than 2.75 months are independently associated with an increased risk of relapse (RR 2.83, 95%CI 1.33 – 6.02 and RR 2.41, 95%CI 1.12 – 5.21, respectively) (16). The presence of ANCA at diagnosis (RR 2.89, 95%CI 1.12 – 7.45, and HR 1.87, 95%CI 1.11 – 3.14), its persistence at initiation of remission maintenance therapy, or its reappearance in the phase of remission (RR 2.6, 95%CI 1.1 – 8.0; p = 0.04) are all associated with an increased risk of relapse (18, 25, 47, 48). Specific organ involvement at diagnosis, in the form of cardiac (RR 2.87, 95%CI 1.09 – 7.58) (16), pulmonary (HR 1.71, 95%CI 1.04 – 2.81) (18), and otorhinolaryngologic involvement (HR 1.73, 95%CI 1.04 – 2.88) (18) also predict increased risk of relapse. Relapse increases the likelihood of a further relapse (RR 1.33, 95%CI 0.98 – 1.78) (49).

Damage assessment
Can anybody who has damage ever truly be considered to have remission? A vasculitic leg ulcer that does not otherwise hamper daily life is considered to be active disease, as it will be amenable to treatment, but end-stage renal failure that will require dialysis will be considered to be remission if there is no active urinary sediment and no other active manifestation. This represents an important limitation of the definition of remission. The term remission does not imply the absence of disease-related manifestations; it merely represents the absence of disease-related activity. It should be a specific term used to guide treatment of active inflammatory disease, not for holistic care. Damage from disease or its treatment may result in a poorer overall outcome despite good control of disease activity. Technically, such patients may be regarded as being in remission, but their perception may be contrary (4, 5). In a survey of patients with WG, more than two thirds of patients reported that they suffered with the ill effects of disease-related damage and thought that the effects would be permanent (50). Achieving an early state of remission would mean less time during which damage can accumulate.

Damage control as an outcome measure
If disease activity is effectively curtailed, damage should be limited. Should damage control then be an outcome measure in clinical trials? Damage as measured by the VDI has been recorded in RCTs but not as a primary outcome measure (7, 11). High disease activity at diagnosis is associated with more damage accrual (11, 51). There is also evidence that accumulation of even a single VDI item is associated

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**Table III. Relapse rates in AASV.**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Disease</th>
<th>No. of patients</th>
<th>Relapse rate, %</th>
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<tbody>
<tr>
<td>Booth 2003 (54)</td>
<td>WG – 82</td>
<td>MPA – 120</td>
<td>34 at 13 mo</td>
</tr>
<tr>
<td></td>
<td>CSS – 11</td>
<td>RLV – 33</td>
<td></td>
</tr>
<tr>
<td>Koldingsnes 2003</td>
<td>WG – 56</td>
<td>60 at 18 mo</td>
<td></td>
</tr>
<tr>
<td>Gordon 1993 (55)</td>
<td>WG – 15</td>
<td>52 at 18 mo</td>
<td></td>
</tr>
<tr>
<td>Jayne 2003 (7)</td>
<td>WG – 95</td>
<td>16 on AZA at 18 mo</td>
<td>14 on CYC at 18 mo</td>
</tr>
<tr>
<td>De Groot 2005 (8)</td>
<td>WG – 89</td>
<td>70 on MTX at 18 mo</td>
<td>47 on CYC at 18 mo</td>
</tr>
<tr>
<td>Reinhold-Keller 2002</td>
<td>WG – 71</td>
<td>37 at 19 mo</td>
<td></td>
</tr>
<tr>
<td>Aasarod 2000 (15)</td>
<td>WG – 108</td>
<td>55 at 22 mo</td>
<td></td>
</tr>
<tr>
<td>Gordon 1993 (55)</td>
<td>MPA – 95</td>
<td>25 at 24 mo</td>
<td></td>
</tr>
<tr>
<td>WGET 2005 (23)</td>
<td>WG – 179</td>
<td>57 at 27 mo</td>
<td></td>
</tr>
<tr>
<td>Gordon 1993 (55)</td>
<td>WG – 28</td>
<td>44 at 42 mo</td>
<td></td>
</tr>
<tr>
<td>Hoffman 1992 (9)</td>
<td>WG – 99</td>
<td>56 at 60 mo</td>
<td></td>
</tr>
<tr>
<td>Guillevin 1999 (17)</td>
<td>CSS – 96</td>
<td>25 at 69 mo</td>
<td></td>
</tr>
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</table>

AZA: azathioprine; CSS: Churg-Strauss Syndrome; CYC: cyclophosphamide; MPA: microscopic polyangiitis; MTX: methotrexate; RLV: renal limited vasculitis; WG: Wegener’s granulomatosis.
with reduced response to treatment (OR 1.53, 95% CI 1.03 – 2.27) (16), and reduced survival (HR 5.54, 95% CI 1.28 – 24.05; p = 0.022) (52). We also know that early accrual of damage is linked to a poor prognosis. A 6-month VDI score ≥ 4 has been shown to be associated with increased mortality rates (OR 12.4, 95% CI 4.2 – 36.9) (53). Thus, there is evidence that damage accrual has a prognostic significance and therefore should be an outcome measure in future clinical trials.

In longitudinal studies, a damage index may have an even more important role. We think that damage accrual is bimodal in distribution (53). There is an early phase, primarily due to activity, and a later phase due to ongoing therapy and disease flares. Comparing the results of various therapies on damage control over the long term would be of value, particularly for low-activity disease states. For example, a clinician may be tempted to increase the level of immunosuppression to combat a low-activity disease state, unless evidence indicated that treatment conferred greater damage and an adverse prognosis. In recent years, a number of large multicentre clinical trials of AASV have been conducted in the United States and Europe (7, 8, 23). For the first time we have large data sets of patients that we can follow longitudinally in accordance with the newly published EULAR guidelines (20). It would be desirable to observe those cohorts to answer this question.

The future
Defining the damage and activity related to AASV depends heavily on validated instruments for use in clinical trials. The use of these instruments should be encouraged in clinical practice as well. Although these instruments require training for their use, this can be incorporated into the education for health professionals caring for patients with vasculitis. These clinical tools need to be revalidated on a periodic basis to increase their value. Presently, projects are under way to validate a new version of the BVAS and the VDI. The refinement of the VDI has become an international initiative under the Outcome Measures in Rheumatology (OMERACT) process, merging it with the American initiative to build a similar damage assessment tool.

The absence of disease activity with continuing immunosuppression for a defined period of time is an acceptable definition of remission today. With availability of better therapies, this definition may cease to be an adequate outcome. With the onset of targeted therapies in rheumatology, it may be possible to achieve real cure in the future. Efforts to identify an appropriate biomarker may yield a sensitive and specific marker that can be used either in tandem with clinical instruments or by itself. These possibilities indicate that we will need to continue to revalidate the definitions of remission, the methodology of defining it, and the acceptability of remission itself as a satisfactory treatment goal.

References
Remission in ANCA positive vasculitis / C. Mukhtyar et al.