

Patients with relapsing ANCA-Associated Vasculitis (AAV) experience unmet needs around remission induction and therapy related adverse events

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INTRODUCTION

There are still significant unmet medical needs in AAV even though overall patient survival improved with induction therapy. There are still challenges around the rapidity and completeness of remission induction as well as the adverse long term morbidity and mortality risks. Relapse in AAV remains a major clinical challenge with 10% or more AAV patients experiencing relapses of varying severity each year following diagnosis. Relapsing patients are at high risk of cumulative organ damage from both acute vasculitis and drug related adverse events. Long term organ damage from vasculitis and glucocorticoid (GC) toxicity are a particular concern. This study aimed to measure clinical outcomes and adverse events in relapsing AAV patients in routine clinical practice in Europe.

METHODS

STUDY DESIGN. Retrospective clinical audit of healthcare records from 268 relapsing AAV patients in a cohort of over 1100 new and relapsing AAV patients managed by 399 physicians (240 nephrologists, 120 rheumatologists and 20 internal medicine physicians) who routinely manage incident AAV patients (France, Germany, Italy and UK).

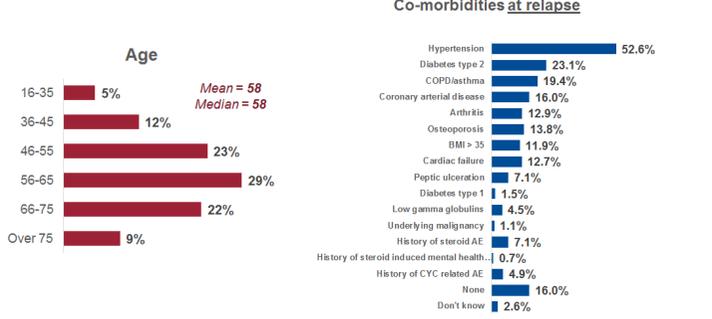
INCLUSION & EXCLUSION CRITERIA. Physicians selected relapsing adult patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) who had initiated remission induction therapy between November 2014 and February 2017. Patients had at least 6 months of therapy and continuous care by the physician over the time of follow, were over 18 years, had a confirmed diagnosis of AAV.

DATA COLLECTION AND ANALYSIS. Physicians completed up to 3 programmed patient record forms (PRF) - this online data collection tool was designed to gather clinical outcome data over the first 12 months of remission induction therapy. Data were collected relating to time of relapse of AAV then outcomes at 1, 3, 6 and 12 months. Descriptive statistics were used to analyze the data

PARTICIPANTS. 268 relapsing AAV patients were studied - 54% GPA and 46% MPA with 60.1% male. BVAS was reported in only 21% of PRFs. 69% of patients were hospitalized for induction treatment and 23% received plasma exchange. Induction therapy varied with 35.1% receiving cyclophosphamide (CYC), 44% Rituximab (RTX), and 76.5% received GCs.

RESULTS

Figure 1 - Age and comorbidities at diagnosis. Relapsing patients were typically over 55 years old and the majority of relapsing AAV patients had comorbidities with only 16% having none. Most patients had more than 1 comorbidity (mean 1.9). 7.1% of patients had experienced a GC related adverse event in the past and many of the comorbidities were likely to be impacted by high dose GCs used for induction.



RESULTS

Figure 2 - Organ involvement and severity of vasculitis at relapse Major organ involvement at relapse was common and as BVAS was measured in only a minority of patients a qualitative scale was used to demonstrate most patients had systemic disease of moderate or severe nature.

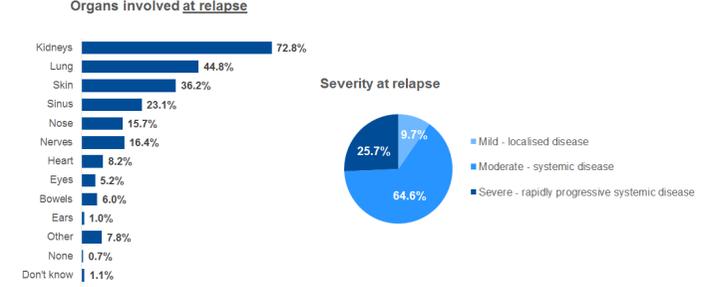
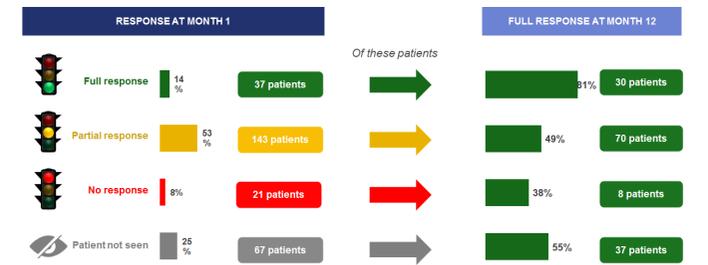


Table 1 - Response to induction therapy. Response was variable and at 12 months many patients had not responded fully. Since only a minority of patients used BVAS in routine clinical practice, response was characterised as:
 Full response - no AAV activity and GC taper on track
 Partial response - reduction in AAV activity and major organ damage arrested
 No response - no improvement in AAV activity
 Results are shown as % of all relapsing patients at each time following start of induction therapy.

	1 month	3 months	6 months	12 months
Full response	13.8	39.9	57.1	54.1
Partial response	53.4	53.0	36.6	29.1
No response	7.8	7.1	6.3	4.5
Not recorded	25.0	-	-	12.3

Figure 3. Response to induction therapy 14% patients responded fully by month 1 and most (81%) still had a full response at month 12. Over 50% of AAV patients had only partially responded at month 1 and 49% of them later achieved a full response at 12 months. A small group of patients had no response at each point over the 12 month follow up.



RESULTS

Figure 4 - Adverse events and infection are common and healthcare resource utilisation is significant. These events are most frequently observed in the first 3 months of therapy when many patients are using glucocorticoids.

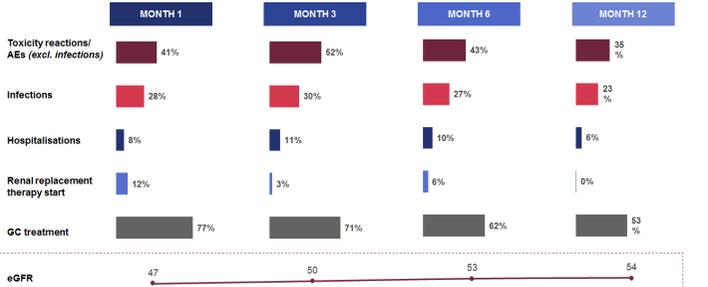
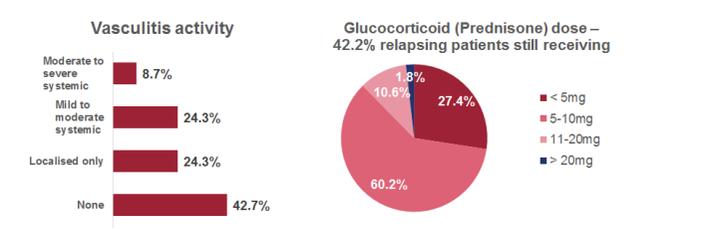


Figure 5 - End of follow up in 268 relapsing AAV patients The total AAV duration was 47.4 months (Standard deviation 35.6 months) and 13.4% patients were receiving chronic renal replacement therapy. 62.7% had relapsed once, 23.1% twice and 14.2% three times. Current vasculitis activity and GC use are reported below.



CONCLUSIONS

This study has examined real world clinical outcomes in a group of 268 relapsing AAV patients who required remission induction therapy. At the time of relapse, these patients had significant comorbidity and many of these clinical conditions would be impacted by induction therapy, in particular high dose glucocorticoids. Indeed approximately 15% of relapsing patient had a previous adverse event related to glucocorticoids, rituximab or cyclophosphamide. Response to therapy was variable with many patients taking several months to achieve adequate response. An early response at 1 month was associated with a good response at 12 month. In addition many patients experienced adverse events or infections especially in the first months of therapy. Relapsing AAV patients still face unmet medical needs and there is a need for new therapy options to achieve rapid and complete remission while preserving organs and avoiding adverse events and infections. **DISCLOSURES.** This study was supported by Vifor Fresenius Medical Care Renal Pharma a Vifor Pharma Group Company.