Variable Response to Induction Therapy and Significant Burden of Treatment Adverse Events over the First 12 Months in Incident ANCA-Associated Vasculitis (AAV) Patients – a Study of Routine Clinical Practice in the EU

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INTRODUCTION

The aims of therapy in incident ANCA-associated vasculitis (AAV) patients are to ensure rapid diagnosis, quickly assess comorbidity and vasculitis activity before commencing remission induction therapy .

It is important to achieve control of active AAV as soon as possible to preserve organ function but also to avoid treatment related morbidity e.g. infection as well as to prevent longer term glucocorticoid (GC) damage. Prevention of relapse is also an important aim of therapy once remission is induced.

This study aimed to understand the unmet medical needs in AAV by examining key clinical outcomes as well as adverse events and infections in incident AAV patients in routine clinical practice in Europe.

METHODS

STUDY DESIGN. Retrospective clinical audit of healthcare records from incident 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).

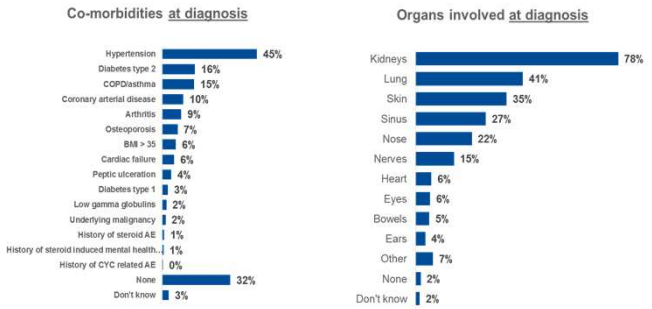
INCLUSION & EXCLUSION CRITERIA. Physicians selected incident adult patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) who had initiated remission induction therapy between November 2014 and February 2017. Patients had at least 6 months of therapy and continuous care by the physician over the time of follow, were over 18 years, had a confirmed diagnosis of AAV for at least 12 months, and had received at least one course of induction therapy to achieve remission.

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 AAV therapy. Data were collected relating to baseline presentation with AAV then outcomes at 1, 3, 6 and 12 months. Descriptive statistics were used to analyze the data

PARTICIPANTS. 929 AAV patients were studied – 54% GPA and 46% MPA. Mean age was 56.8 years (SD 14.2) with 53.7% male. BVAS was reported in only 12% of PRF but 34% had severe progressive disease, 54% moderate systemic disease and 12% mild localized disease. Median symptom duration before AAV diagnosis was 6 weeks but 16% had symptoms for more than 12 weeks. 69% of patients were hospitalized for induction treatment and 23% received plasma exchange. Induction therapy varied with 59% receiving cyclophosphamide (CYC), 24% Rituximab (24%), and 83% received GCs.

RESULTS

Figure 1 - Organ involvement and comorbidities at diagnosis. Most incident AAV patients had comorbidities with only 32% having none. Organ/tissue involvement showed a typical distribution with renal and lung involvement being commonly observed and most patients having more than one organ involved (median 1.8).



RESULTS

Table 1 – Response to induction therapy. Response to induction therapy was variable and even at 12 months many patients were not in full remission. 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 incident patients at each time following start of induction therapy.

	1 month	3 months	6 months	12 months
Full response	17.7	43.4	61.4	58.8
Partial response	55.8	49.4	31.6	23.5
No response	7.5	7.2	4	4.8
Not recorded	19.1	-	-	12.9

Figure 2. Patients who responded fully by month 1 were more likely to still have a full response at month 12.

Over 50% of AAV patients had only partially responded at month 1 and 58% 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.

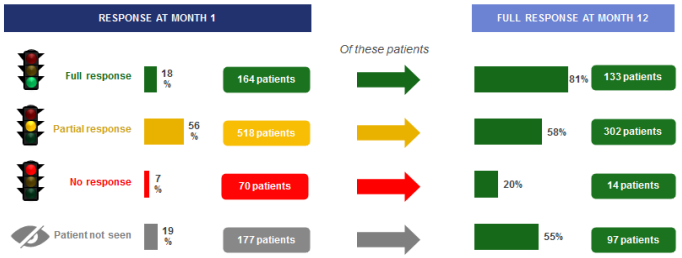
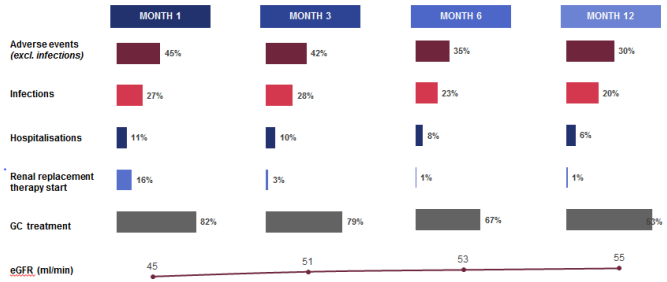


Figure 3 - Adverse events and infections are common and healthcare resource use is significant. Many incident AAV patients experience adverse events and infections and the majority remain on GCs over the first 12 months of therapy. **6% of patients relapsed over this time**



RESULTS

Figure 4 - Adverse events and infection are a particular problem at the start of induction therapy. These events are most frequently observed in the first 3 months of therapy but accumulate over time (# number).

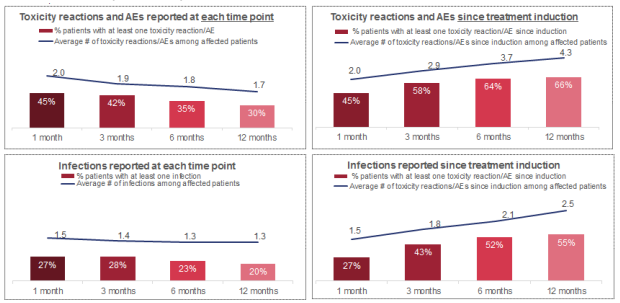
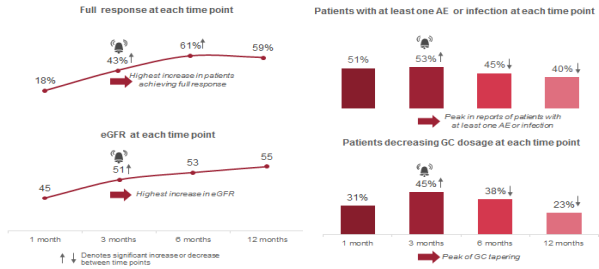


Figure 5 - 3 months into remission induction therapy is an important time for incident AAV patients. By 3 months more patients start to respond to treatment and show improved renal function. However, it is also the point when more patients experience side effects from induction treatment and physicians taper the GC dosage.



CONCLUSIONS

This study has examined real world outcomes in incident AAV patients in Europe and demonstrated significant unmet medical needs.

Incident patients frequently have comorbidity at diagnosis and some patients experienced signifcant delays until the diagnosis was made. Patients have a range of organ involvement at diagnosis but severity scores such as BVAS are infrequently used in clinical practice.

The response to remission induction therapy was variable and a signficant proportion of patients have a partial response only. Early response is associated with a better full response rate at 12 months.

Therapy related adverse events and infections are common, especially in the first 3 months and most patients will experience at least one of these problems in the first 12 months.

There is unmet medical need in incident AAV patients related to achieving improved full response rates and reducing the toxicity of therapy.

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