Variable response to induction therapy and significant burden of treatment adverse events over the first 12 months of remission induction treatment in ANCA Associated Vasculitis (AAV) Patients – a study of routine clinical practice

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INTRODUCTION

The aims of therapy in ANCA-associated vasculitis (AAV) patients with active disease 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 reality of clinical outcomes and adverse events in AAV patients over the first 12 months of remission induction therapy in routine clinical practice in the UK

METHODS

STUDY DESIGN. Retrospective clinical audit of healthcare records from incident AAV patients managed by 100 physicians (60 nephrologists, 40 rheumatologists) who routinely manage AAV patients in the 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. 297 AAV patients were studied – 37% GPA and 63% MPA reflecting the case mix of the physicians taking part. 79.5% of patients were incident patients and 20.5% were relapsing. Mean age was 58.17 years (SD 15.6) with 49.5% male.

BVAS was reported in under 10% of PRF but 38.4% had severe life threatening disease, 52.5% moderate systemic disease and 9.1% mild localized disease.

RESULTS

Figure 1 – Renal parameters, CRP and BVAS at diagnosis (incident or time of relapse). Most patients had evidence of renal involvment and a significant proportion had severe disease with low eGFR or high protein excretion.

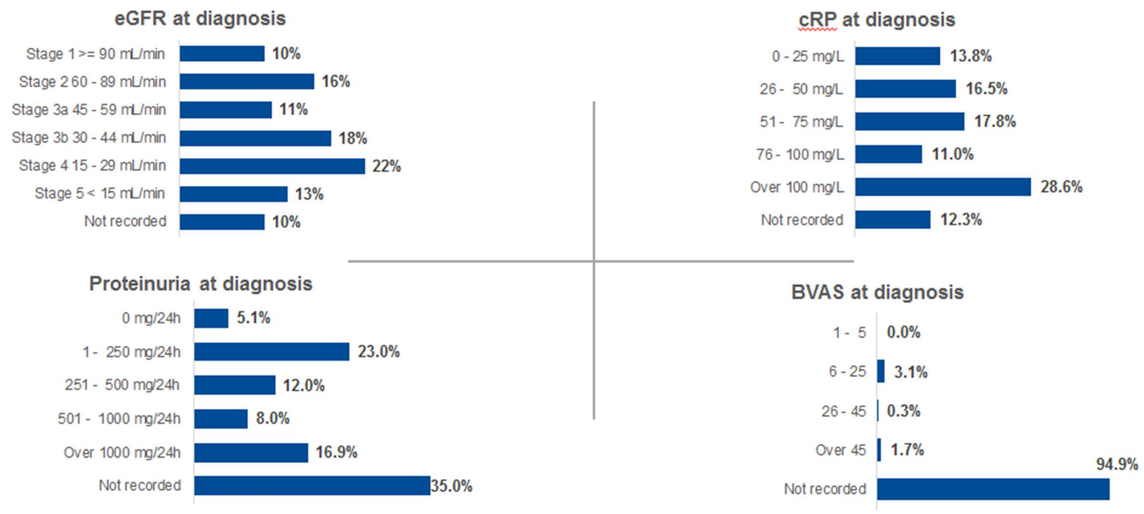
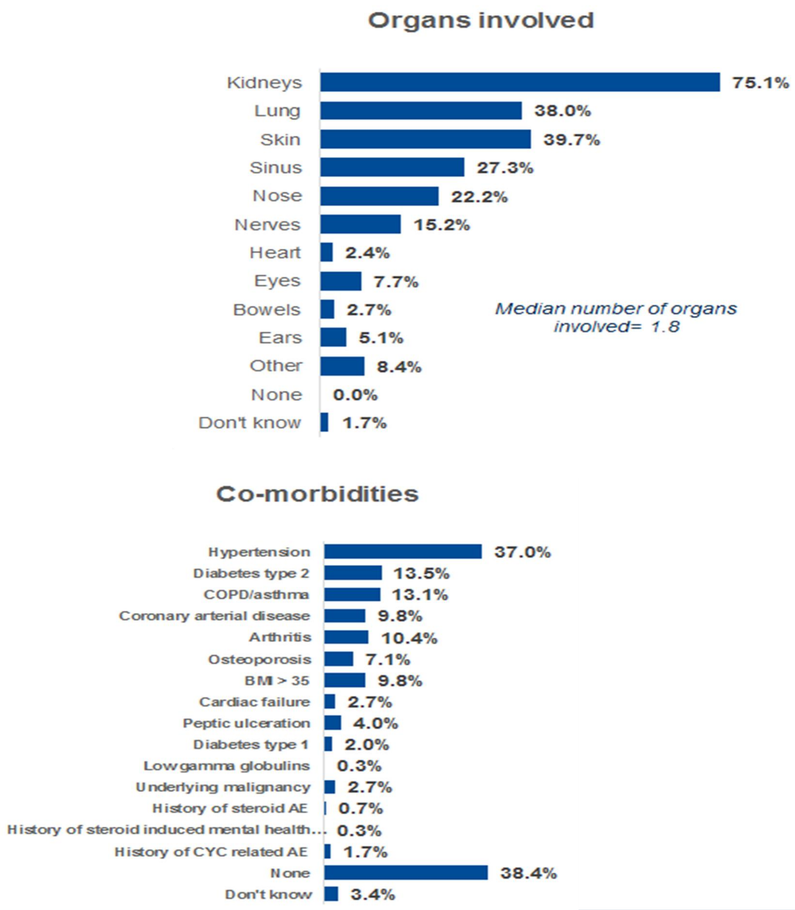


Figure 2 - Organ involvement and comorbidities at diagnosis (incident or time of remission). Most incident AAV patients had comorbidities with only 38.4% having none (3.4% missing data). Organ/tissue involvement showed a typical distribution with renal and lung involvement being commonly observed and most patients having more than one organ involved (median 1.8).



RESULTS

Table 1 – Response to induction therapy. Remission induction therapy varied with most patients receiving a combination of glucocorticoids (GCs) and either cyclophosphamide or rituximab.

Cyclophosphamide - 63.3%
Rituximab – 22.9%
Glucocorticoids – 83.5%

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	18.5	48.5	67.3	67.0
Partial response	51.9	43.8	26.3	19.2
No response	8.1	7.7	6.4	4.0
Not recorded	21.5	-	-	9.1

Figure 3 - 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).

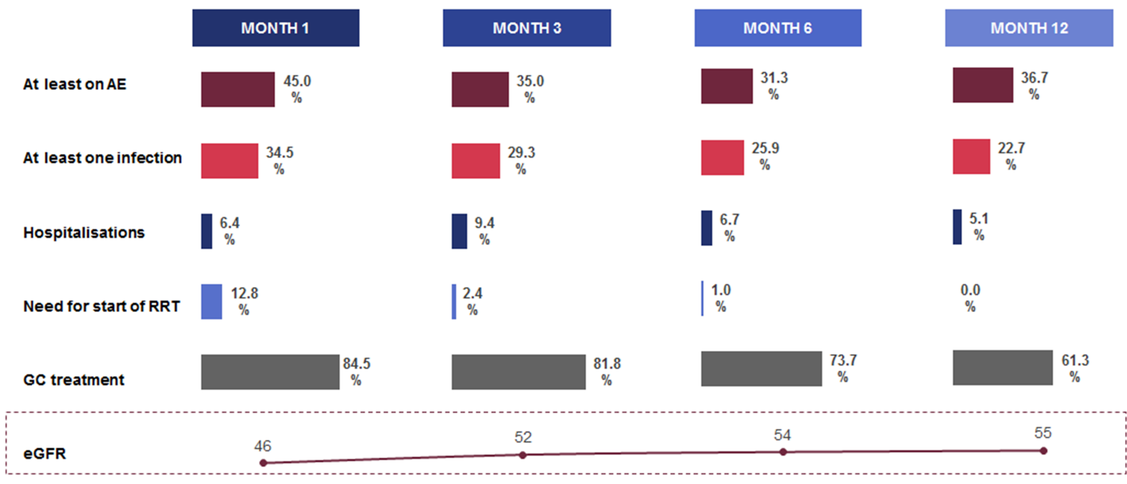
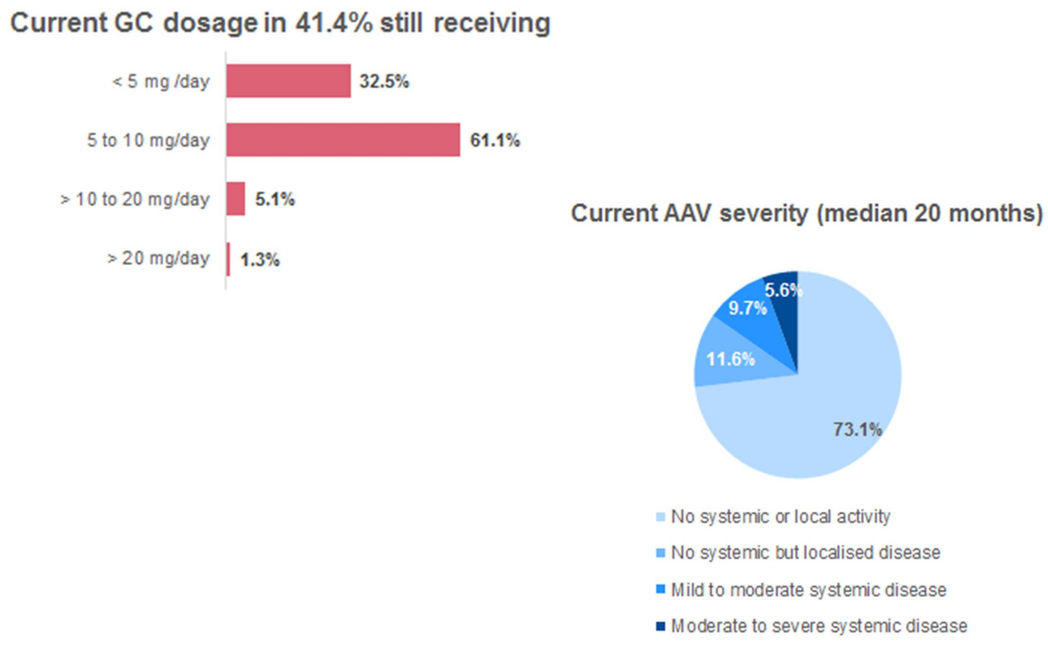


Figure 4 – Current clinical situation at last follow up appointment. At last follow up appointment (median 20 months follow up), some patients still had vasculitis activity and many were still taking glucocorticoids.



CONCLUSIONS

This study has examined real world outcomes after starting remission induction therapy in the UK AAV patients and demonstrated significant unmet medical needs.

Incident patients frequently have comorbidity at start of therapy and 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 and this can take several 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. Many AAV patients remain on glucorticoids for significant periods.

There is unmet medical need with current therapies for AAV related to achieving improved full response rates and reducing the toxicity of therapy.

DISCLOSURES. **This study was supported by Vifor Fresenius Medical Care Renal Pharma a Vifor Pharma Group Company.**

Poster presented at the UK Renal Week, Brighton, June 2019