Glucocorticoids for remission induction in incident ANCA-Associated Vasculitis (AAV) patients in real world practice – high exposure and temporal relationship to adverse events

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INTRODUCTION

ANCA-associated vasculitis (AAV) is a severe systemic vasculitis and rapid induction of remission is essential to reduce tissue and organ damage.

High dose glucocorticoids (GC) are part of current treatment but current EULAR/EDTA-ERA stress the importance of reducing GC dose as the disease activity comes under control. The adverse events associated with GCs are well known and in AAV the high first year mortality is due to infection, believed to link to the high GC exposure.

This retrospective study aimed to examine GC prescribing patterns, AAV response and possible GC related adverse events (AEs) in incident AAV patients managed 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).

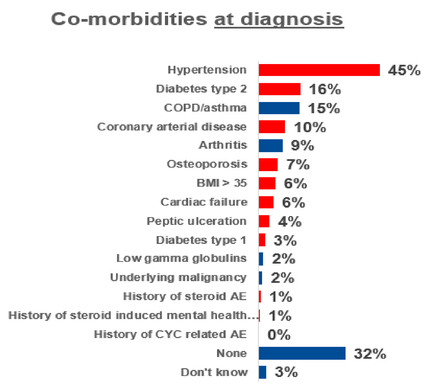
INCLUSION & EXCLUSION CRITERIA. Physicians selected incident adult patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) who had initiated remission induction therapy between November 2014 and February 2017. Patients had at least 6 months of therapy and continuous care 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.

RESULTS

Figure 1 – Comorbidities at diagnosis. Most incident AAV patients had comorbidities with only 32% having none. Many patients had comorbidities which could be potentially exacerbated with high dose GCs



RESULTS

Figure 2. Patients received a variety of different remission induction treatment regimes and the majority of patients received high dose GCs – often IV. Cyclophosphamide was the most common accompanying therapy

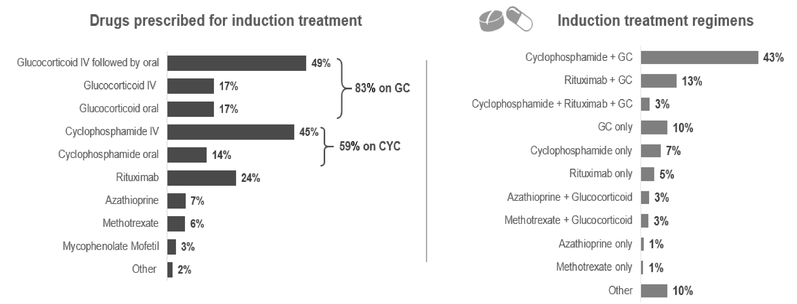


Table 1 – Response to induction therapy. Response to induction therapy was variable and even at 12 months many patients were not in full remission and most patients still were taking GCs.

Since only a minority of physicians used BVAS in routine clinical practice, response was characterised as:

Full response – no AAV activity and GC taper on track

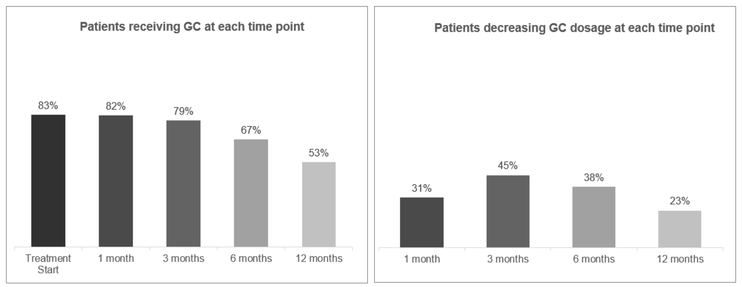
Partial response – reduction in AAV activity and major organ damage arrested

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
Taking GCs	82	79	67	53

Figure 3 – Many patients still take GCs over the first 12 months of therapy and dose titration varies in extent and over time Even at 12 months, over half of incident AAV patients are receiving GCs

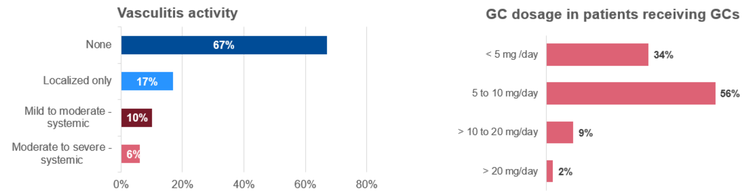


RESULTS

Table 2 - Adverse events and infection are common in the first 12 month of therapy. Detailed analysis shows the high frequency of GC related AEs and how some AEs eg new onset of diabetes are highest when GC dose is high vs others eg cataract formation which occur later in exposure

	Percent of patients with AE or infection at each time point (months)			
	1	3	6	12
Adverse events				
Cataract formation	0.5%	1.9%	2.9%	3.3%
New onset diabetes	5.3%	2.3%	1.4%	1.2%
Worsening of diabetes	5.3%	5.9%	5.1%	3.4%
Bone related events	1.8%	2.6%	1.9%	2.9%
Peptic Ulceration	3.4%	3.0%	2.2%	1.6%
Hypertension	19.5%	17.1%	14.9%	11.4%
Cardiac failure	3.7%	3.3%	2.4%	1.7%
Kidney disease	8.7%	6.7%	6/6%	5.5%
Bladder symptoms	2.2%	1.6%	1.2%	0.8%
Leucopaenia	12.9%	9.4%	5.7%	4.0%
Anemia	21.5%	17.2%	12.7%	10.2%
Allergic reaction	1.3%	1.2%	0.6%	0.3%
Low γ-globulins (<3g/L)	2.0%	2.4%	2.5%	1.9%
Change in viral infection status	0.6%	0.8%	0.3%	0.3%
Other	2.2%	3.2%	3.1%	2.0%
None	36.0%	57.7%	64.9%	57.4%
No data	19.1%	0	0	12.9%
Infections				
Upper Respiratory	10.9%	11.1%	9.0%	9.0%
Lower Respiratory	9.5%	8.3%	6.2%	4.8%
Urine	11.1%	10.5%	7.4%	6.7%
No infections	53.5%	72.3%	76.9%	67.2%
No data	19.1%	0	0	12.9%

Figure 4 – At 12 months some patients still had vasculitis activity and GC dose varied. 53% of patients still received GCs and the dose varied with the majority > 5mg per day



CONCLUSIONS

This study has examined real world outcomes in incident AAV patients in Europe and demonstrated there are unmet needs relating to gaining remission from disease while still avoiding harm. Over 80% of incident patients received high dose GCs, most commonly IV and over 50% still remained on GCs at 12 months following diagnosis. Full response to therapy at 12 months was still associated with need for continuing GCs.

Therapy related adverse events and infections are common, especially when the GC dose is highest in the first months of therapy. Detailed examination of these AEs demonstrated many are likely to be GC related and associated with either high dose AND/OR duration of GC exposure.

New therapeutic approaches are needed to address these unmet needs in AAV.

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