Real world clinical outcomes in ANCA associated vasculitis (AAV) – unmet needs in achieving and sustaining remission and avoiding cumulative organ damage

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INTRODUCTION

ANCA-associated vasculitis (AAV) is now a relapsing remitting long term condition but which still is associated with a significantly raised long term mortality risk. Patients are at risk from long term organ damage which is due to both recurrent active vasculitis and treatment related adverse events, in particular, glucocorticoids.

Achieving and sustaining remission are critical steps in clinical therapy and patients are at risk from acute and long term morbidity and mortality risks.

This retrospective study of AAV patients managed in real world clinical practice in Europe aimed to examine remission and relapse rates and adverse events in incident and maintenance AAV patients.

METHODS

STUDY DESIGN. Retrospective clinical audit of healthcare records from 2 separate cohorts of AAV patients managed in routine practice in Europe (France, Germany, Italy, Spain and UK).

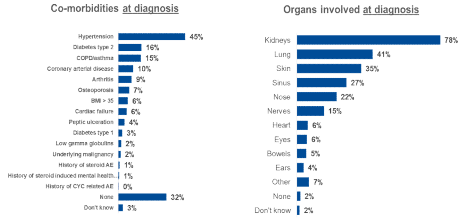
REMISSION INDUCTION PATIENTS - INCLUSION & EXCLUSION CRITERIA AND DATA COLLECTION. Physicians selected incident adult patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) who had initiated remission induction therapy between November 2014 and February 2017. Patients 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. 399 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

MAINTENANCE PATIENTS - INCLUSION & EXCLUSION CRITERIA AND DATA COLLECTION. Physicians selected adult patients with GPA or MPA who had received a full course of remission induction therapy for organ or life threatening AAV. They had to have received this induction course between 2013 to 2016. Patients could be included with a first induction treatment or at the time of a relapse. In addition patients who relapsed or died in the maintenance phase could be included. Physicians had to have access to the patients entire treatment record for the period. 493 physicians (293 nephrologists, 178 rheumatologists and 22 internal medicine physicians) completed up to 3 programmed patient record forms (PRF) - this online data collection tool was designed to gather clinical outcome data over the maintenance therapy phase from the point this was defined by the physician. . Data were collected relating to induction treatment of AAV then outcomes at 6, 12, 18 ad 36 months following maintenance start. Descriptive statistics were used to analyze the data

RESULTS

Remission induction Results 1. Definition of maintenance phase of AAV therapy – 929 incident 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.

Comorbidity at the time of original diagnosis was common, renal disease was often observed



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

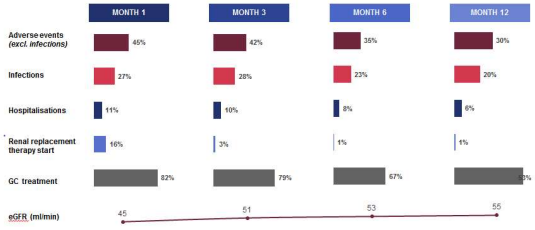
Partial response – reduction in AAV activity and major organ damage arrested

No response – no improvement in AAV activity

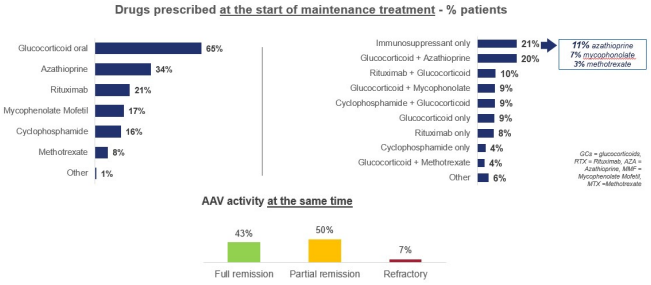
Results are shown as % of all incident patients at each time following start of induction therapy.

	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 1 - 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**

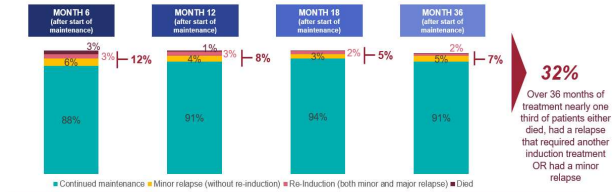


Maintenance Results 1 – Patient demographics and remission induction therapy - 1478 AAV patients were studied – 49% GPA and 51% MPA. Mean age was 54.2 years with 56% male. BVAS was reported in only 21% of PRF but 44% had severe progressive disease, 56% moderate systemic disease and 0% mild localized disease. 49% of patients received remission induction therapy for incident disease and 51% at relapse. Maintenance was defined as starting at mean 4.7 months (incident) and 6.5 months (relapsing).



RESULTS

Figure 1 – Clinical outcomes over 36 months of remission – Major and minor relapses remain a clinical problem with current maintenance therapy



At 3 years of continued maintenance therapy:

- 81% are still on maintenance, i.e. not relapsed to the extent they required re-induction or deceased
- 4% Died (≥ 2/3rds due to AAV relapse)
- 10% dropped out of study due to relapse requiring re-induction
- **18% minor relapses requiring either / or: an adjustment to / switch of maintenance regime**

Figure 2 – Active AAV symptoms and signs are still observed in the maintenance phase. Physicians report many patients are in only partial remission (reduced AAV activity with arrest of major organ damage).

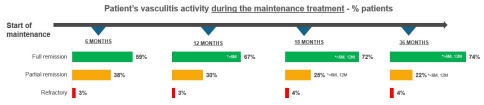
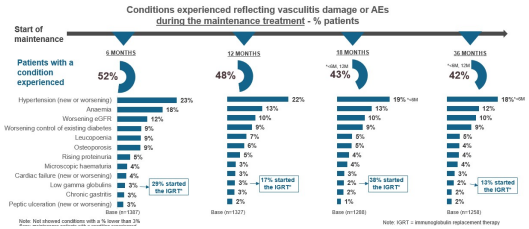


Figure 3 – Many patients experienced conditions reflecting vasculitis damage/AEs and loss of functional status occurred - After 36 months, 13% had reduced working hours, 13% restricted social life, 6% had to leave employment, 5% were registered as disabled and 2% had to leave full time education



CONCLUSIONS

Response to remission induction therapy in AAV patients is variable and many patients do not achieve a full response at 12 months. In addition infections and treatment related adverse events are common.

The maintenance phase of AAV treatment is variably defined but typically commences around 6 months – but at that point many patients are not in full remission and the majority are still receiving GCs. Minor and major relapse are still common over 3 years follow up and patients are faced with treatment AE burden and cumulative organ damage.

Clinical unmet need in AAV remains high and patients experience a significant burden of disease throughout their journey.

There is a need for new therapeutic options to improve clinical outcomes in AAV.

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