Maintenance treatment for ANCA associated vasculitis (AAV) in real world practice in Germany – reality of vasculitis remission and relapse and burden of disease

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ePoster 11

INTRODUCTION

ANCA-associated vasculitis (AAV) is associated with a more favorable long-term outcome today, since immediate survival has improved significantly due to introduction of immunosuppressive therapy [1]. However, patients with AAV have a mortality rate that is several times higher than that of the general population [1] and AAV remains still a relapsing remitting condition that can affect any organ [2, 3]. AAV treatment is now scheduled for a longer term, but patients are at risk from long-term organ damage, which is due to recurrent active vasculitis and iatrogenic side effects of the therapy, such as glucocorticoids in particular [4, 5]. Therefore, achieving and sustaining remission are critical steps in clinical therapy and improved long-term morbidity and mortality risks during the maintenance phase remain unmet medical needs.

This retrospective study of AAV patients managed in real world clinical practice in Germany aimed to examine the definition of the maintenance phase, the therapies used for maintenance and clinical outcomes including vasculitis control, adverse events and infections.

METHODS

STUDY DESIGN. Healthcare records from 300 patients who were diagnosed with GPA (granulomatosis with polyangiitis) or MPA (microscopic polyangiitis) and managed by 100 German physicians (45% rheumatologists) were available for evaluation.

INCLUSION CRITERIA. Patients who completed induction therapy for organ or life threatening AAV and then initiated maintenance therapy between 2014-16 were studied. In addition, patients who relapsed or died during the maintenance phase could be included. Physicians had to have access to the patients entire treatment record for the period.

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 maintenance therapy phase from the time point this was defined by the physician.

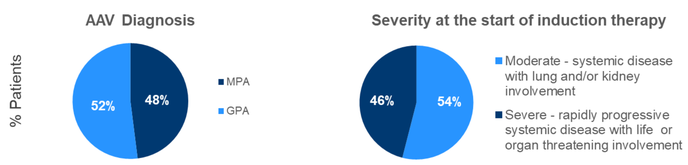
Data were collected at the start of maintenance therapy and then 6, 12, 18 and 36 months later. Descriptive statistics were used to analyze the data.

RESULTS

Patient demographics and remission induction therapy – Of the 300 AAV patients evaluated, 52% were diagnosed with GPA and 48% with MPA (Fig. 1). The mean age of the patients was 52.9 years (55% males). When asked about the severity of the disease at the start of the induction therapy, 54% of the patients had moderate (systemic disease with lung and/or kidney involvement) and 46% had severe disease (rapidly progressive systemic disease with life or organ threatening involvement) (Fig. 1). 51% had incident AAV and 49% suffered from a relapse.

The most commonly prescribed drugs for induction therapy included cyclophosphamide (69%) and rituximab (36%). The most prescribed drug combination at induction treatment was cyclophosphamide + glucocorticoid (46%).

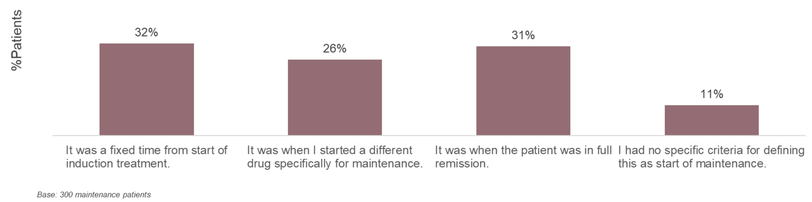
Figure 1 – Patient demographics of patient charts submitted



Base: 300 maintenance patients

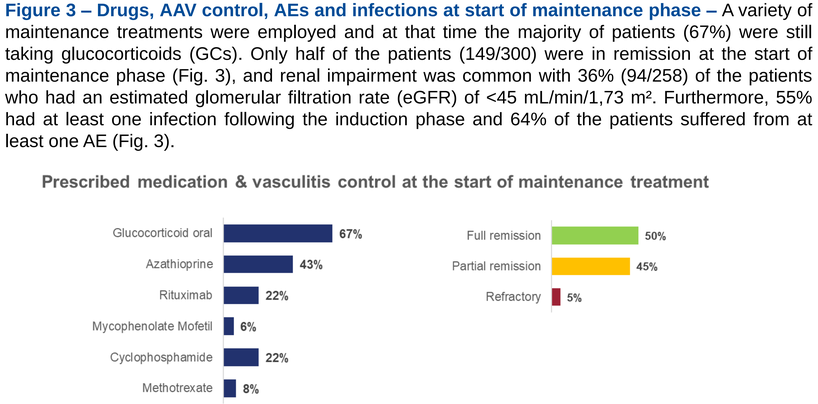
RESULTS

Figure 2 – Definition of AAV maintenance therapy – The starting time of maintenance therapy was inconsistently defined by the physicians or was missing (Fig. 2) – on average after 5.5 months after the induction therapy.

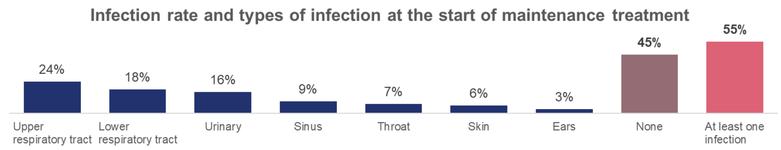


Base: 300 maintenance patients

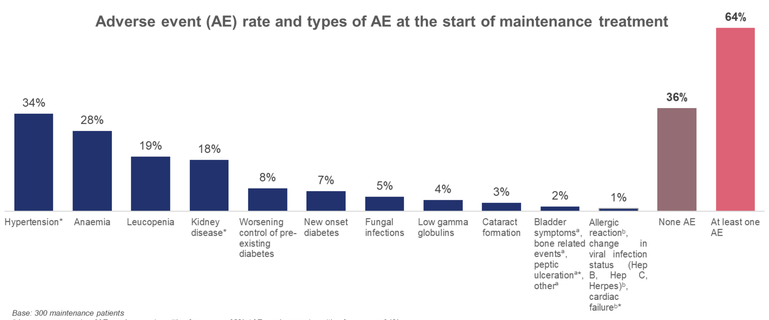
Figure 3 – Drugs, AAV control, AEs and infections at start of maintenance phase – A variety of maintenance treatments were employed and at that time the majority of patients (67%) were still taking glucocorticoids (GCs). Only half of the patients (149/300) were in remission at the start of maintenance phase (Fig. 3), and renal impairment was common with 36% (94/258) of the patients who had an estimated glomerular filtration rate (eGFR) of <45 mL/min/1,73 m². Furthermore, 55% had at least one infection following the induction phase and 64% of the patients suffered from at least one AE (Fig. 3).



Base: 300 maintenance patients



Base: 300 maintenance patients

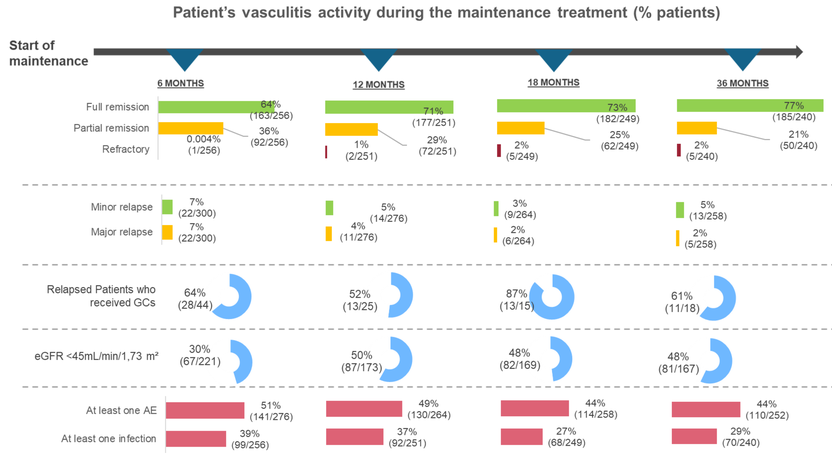


Base: 300 maintenance patients
**de novo or worsening; †AE, each occurring with a frequency of 2%; ‡AE, each occurring with a frequency of 1%*

RESULTS

Clinical outcomes over 36 months of maintenance treatment – AAV maintenance patients have been followed for an average of 51.8 months. Fourteen of 300 patients (5%) deceased, 61/252 patients (24%) relapsed at least once, and 11/252 patients (4%) had to start renal replacement therapy after 36 months. No systemic or local activity of the vasculitis was found in 106/203 patients (52%) at this time, while 40/203 patients (19%) were still experiencing active disease (localized or mild to moderate).

Figure 4 – Active vasculitis is still observed during the maintenance phase – As the physicians reported, many patients were only in partial remission (reduced AAV activity with arrest of major organ damage) during the maintenance phase. Major and minor relapses also remained a clinical concern under currently available maintenance therapy, with many relapses occurring during GC therapy (Fig. 4). Overall, 39% (98/252) were still receiving oral GCs at most recent review (26% of them receiving >5 mg per day). After 36 months of maintenance therapy, almost half of the patients (48%) had an eGFR of <45 mL/min/1,73 m², while 44% of the patients were still experiencing at least one AE and 29% at least one infection (Fig. 4).



CONCLUSIONS

In this study, real world outcomes of long-term maintenance treatment in German AAV patients were evaluated demonstrating a significant burden of disease and unmet medical needs.

In practice, there are currently different conceptions about the appropriate starting time of AAV maintenance therapy. Moreover, many patients are still not remitted when maintenance treatment is started. Even during maintenance phase, a significant proportion of AAV patients do not yet achieve a complete remission.

Relapses are still an unsolved clinical problem and a high proportion of patients require ongoing GC therapy in order to maintain remission. At the same time the real life data indicate that treatment-related adverse events represent a substantial burden on the patients.

References

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