Clinical Profile and Healthcare Resource Use of Anca-Associated Vasculitis: A Real-World Analysis in Italy

Perrone V[1], Dovizio M[1], Veronesi C[1], Andretta M[2], Bacca M[3], Barbieri A[4], Bartolini F[5], Cavaliere A[6], Chinellato A[7], Ciaccia A[8], Cillo MR[9], Citraro R[10], Costantini A[11], Dell'Orco S[12], Ferrante F[13], Gentile S[14], Grego S[15], Lavalle A[16], Mancini D[3], Moscogiuri R[16], Mosele E[17], Pagliaro R[18], Procacci C[19], Re D[20], Santoleri F[11], Ubertazzo L[21], Vercellone A[22], Ramirez de Arellano Serna A[23], Degli Esposti L[1]

[1]CliCon S.r.l. Società Benefit Health, Economics & Outcomes Research, Bologna, BO, Italy; [2]Azienda ULSS 8 Berica, Vicenza, Italy; [3]ASL Brindisi, Brindisi, Italy; [4]ASL Vercelli, Vercelli, Italy; [5]USL Umbria 2, Terni, Italy; [6]ASL Viterbo, Viterbo, Italy; [7]Azienda ULSS 3 Serenissima, Mestre (VE), Italy; [8]Servizio Farmaceutico Territoriale ASL Foggia, Foggia, Italy; [9]ASL Salerno, Salerno, Italy; [10]Azienda ospedaliero-universitaria Mater Domini, Catanzaro, Italy; [11]ASL Pescara, Pescara, Italy; [12]ASL Roma 6, Albano Laziale, Italy; [13]ASL Frosinone, Frosinone, Italy; [14]Direzione Generale per la Salute Regione Molise, Campobasso, Italy; [15]ASL 3 Genovese, Genova, Italy; [16]ASL Taranto, Taranto, Italy; [17]UOC Assistenza Farmaceutica Territoriale Azienda ULSS 7 Pedemontana, Bassano del Grappa (VI), Italy; [18]ASL Roma 5,Tivoli, Italy; [19]Dipartimento Farmaceutico ASL BAT, Trani, Italy; [20]ASL Teramo, Teramo, Italy; [21]U.O.C.Farmacia Territoriale, ASL Roma 4, Civitavecchia (RM), Italy; [22]ASL Napoli 3 SUD, Torre del Greco, Italy;[23]CSL Vifor, Glattbrugg, ZH, Switzerland.

INTRODUCTION

ANCA-associated vasculitis (AAV) is a rare severe inflammatory disease associated with adverse outcomes damaging vital organs, including kidneys often resulting in end-stage renal disease (ESRD) [1]. While the majority of patients achieve remission with current standard of care, however, the extended treatments are associated with significant complications, causing organ damage and morbidity, which is the case of glucocorticoid (GC) treatment [2]. Therefore, AAV shows a high patient and healthcare burden with an increased risk of hospitalization [3,4].

The analysis aimed to estimate demographic and clinical characteristics of AAV patients, their therapeutic management, outcomes, and healthcare resource use and related costs in an Italian real-world setting.

METHODS

STUDY DESIGN. An observational study was conducted using Italian entities' administrative databases, covering about 12 million health-assisted individuals.

PARTICIPANTS. All adult patients with a diagnosis of **Granulomatosis with Polyangiitis (GPA)** or **Microscopic Polyangiitis (MPA),** between January 2010 and December 2020 (inclusion period) were identified.

INCLUSION & EXCLUSION CRITERIA. Adult (≥18 years) patients with AAV were identified based on the following criteria: at least one payment waiver code (RG0050/RG0070) or hospitalization (day hospital or regular admission) with primary or secondary discharge diagnosis of GPA (ICD-9-CM code: 446.4), or at least one payment waiver code (RG0020) for MPA, in association or not with hospitalization discharge diagnosis of MPA (ICD-9-CM code 446.0). Patients with no continuous inclusion during study were excluded from the analysis. As shown in Figure 1, the included patients were assigned to one of the two mutually exclusive cohorts: GPA and MPA.

GPA cohort

All patients who met one of these inclusion criteria were included in GPA cohort:
- payment waiver code (RG0050/RG0070) for GPA,

OR
- hospitalization (day hospital or regular admission) with primary or secondary discharge diagnosis of GPA (ICD-9-CM code: 446.4), *during inclusion period.*

MPA cohort

All patients who met this inclusion criterion were included in MPA cohort:
- payment waiver code (RG0020) for MPA*, *during inclusion period.*

**MPA patients were identified by the presence of the active payment waiver code (in association or not with hospitalization diagnosis code ICD-9-CM code 446.0).*

Figure 1. Study cohorts compared in the analysis: GPA vs MPA patients.

DATA COLLECTION & ANALYSIS. In the one-year period prior the index-date (first AAV-detection), demographic and clinical characteristics (Charlson Comorbidity-Index, CCI) were recorded. During one-year follow-up, oral GC prescriptions (ATC code: H02AB) and clinical outcomes (hospitalizations, end-stage renal disease-ESRD, and mortality) were collected. Annual healthcare resource use/patient (all-drugs, all-outpatient specialist services-OSS, all-hospital stays) and the related costs were evaluated.

All the statistical analyses were performed using STATA SE, version 17.0 (StataCorp LLC, College Station,TX, USA). Continuous variables are given as mean ± standard deviation (SD), categorical variables as numbers and percentages. In some subgroups composed of less than four patients, data were not issuable (N.I.) for data privacy, since the results might be potentially referrable to single individuals, in compliance with the "Codice in materia di protezione dei dati personali [Code for protection of personal data] (D. Lgs. 196/2003)".

RESULTS

Study population. Total 859 AAV patients were included, 713 (83%) of them with GPA and 146 (17%) MPA and then assigned to the one of the two mutually exclusive cohorts. Each cohort was further stratified according to the presence/absence of GCs therapy. A synthetic scheme of patients' selection and subgroup numbers are depicted in Figure 2.

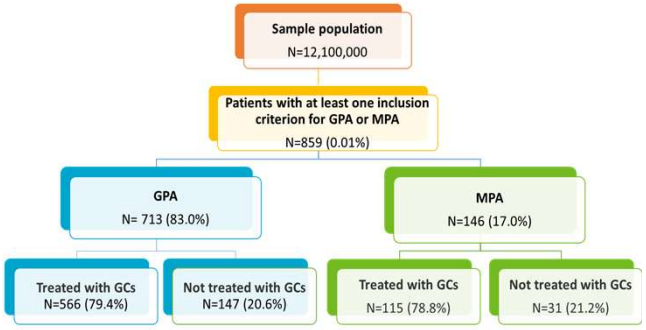

Figure 2. Flowchart of the patients' selection and subgroup numerosity.

Outcomes during follow up period. The clinical outcomes in the overall AAV patients, and in those divided according to the disease form, MPA and GPA were evaluated in terms of mortality, AAV-related hospitalization and onset of ESRD. Both occurrence of the event (number and percentage) and days-to-events (expressed as mean ± standard deviation) were considered. GPA accounts for a more severe phenotype. Worse results were observed in GPA patients, with the exception of ESRD where MPA showed a higher incidence, as expected (Table 1).

Table 1. Clinical outcomes in AAV patients, overall and by phenotype.

	GPA (N=713)	MPA (N=146)	Overall AAV (N=859)
Event occurrence, n (%)			
AAV hospitalizations	203 (28.5%)	19 (13.0%)	222 (25.8%)
ESRD	73 (10.2%)	23 (15.8%)	96 (11.2%)
Death	133 (18.7%)	20 (13.7%)	153 (17.8%)
Time to event, days (mean ± SD)			
Days to AAV hospitalization	445.0 ± 600.4	724.1 ± 685.8	468.9 ± 611.5
Days to ESRD	265.0 ± 616.5	748.7 ± 856.2	380.9 ± 707.7
Days to death	784.8 ± 933.9	1622.6 ± 1244.6	894.3 ± 1015.5

Healthcare resources during first year of follow up. As Table 2 shows, in total AAV patients, the number of drugs prescribed averaged 22.1 ± 13.8, those of hospitalizations averaged 0.7 ± 1.2 (ordinary) and 0.3 ± 0.6 (day-hospital), and 10.1 ±1 2.0 outpatient specialist services were erogated. Consistently with previously mentioned results, GPA was associated with a higher healthcare resource use, especially in terms of hospitalization expenditures (both day hospital and ordinary).

Table 2. Healthcare resource consumptions at 1-year follow up in AAV patients, overall and by disease

	GPA (N=713)	MPA (N=146)	Overall AAV (N=859)
Drugs (prescriptions)	21.4 ± 13.5	24.9 ± 14.8	22.1 ± 13.8
Ordinary hospitalizations	0.7 ± 1.3	0.3 ± 0.7	0.7 ± 1.2
Day hospital hospitalizations	0.3 ± 0.6	0.1 ± 0.4	0.3 ± 0.6
Outpatient Specialist Services (erogations)	9.9 ± 12.0	11.0 ± 12.0	10.1 ± 12.0

Direct healthcare costs. Figure 3 details total mean annual cost during follow up period, by presence of GC treatment (at least one prescription), by type of enrollment (payment waiver code or hospitalization). The overall healthcare direct costs tended to be increased in GC-treated patients, in the overall AAV population, as well as in each cohort, and regardless of the inclusion criteria (payment waiver code or hospitalization). The cost items that in GC-treated subjects had the most impactful burden on total expenditure were hospitalizations and drug expenses.

Figure 3. Total mean annual cost in GC-treated (red bar) and untreated (grey bar) patients during follow-up period, by type of enrollment (payment waiver code or hospitalization), in AAV patients, overall and by disease,

KEY MESSAGES

- Overall, 859 subjects met AAV inclusion criteria: 83% were GPA and 17% MPA.
- Among baseline characteristics, the mean age was 57.2 years (57 for GPA and 58 for MPA), and Charlson Comorbidity Index averaged 1.2 (1.3 for GPA and 1.0 for MPA).
- During the first year of follow-up, 79% AAV patients were treated with GCs, 18% died, 25.8% underwent AAV-related hospitalization and 11.2% developed ESRD.
- The healthcare resource consumption analysis during the first year of follow-up showed, among AAV patients, a mean of 22.1 prescribed drugs, 0.7 and 0.3 hospitalizations in ordinary and day hospital setting, respectively, and 10.1 outpatient specialist services**.** During all available follow-up, the overall healthcare direct costs averaged 4,806 € in AAV patients included by payment waiver code and 16,949 € in those hospitalized. In GC-treated patients, a higher trend of direct healthcare cost was found, especially related to drug and hospitalization expenditures.

CONCLUSIONS

AAV is associated with short-term unfavorable outcomes. GPA is more frequent and resulted in a worse phenotype. The elevated healthcare resource use were mainly due to drug and outpatient service erogations and ordinary hospitalizations. In this setting, the use of prolonged or life-long aspecific immunosuppression for AAV could reveal the clinical complexity of GC-treated patients which results in a great burden for healthcare consumptions and expenditures, above all due to hospitalizations. Further efforts are needed to optimize AAV treatment interventions with the goal of ameliorating the clinical outcomes of AAV patients.

REFERENCES

1. Trivioli G, Marquez A, Martorana D, et al. Genetics of ANCA-associated vasculitis: role in pathogenesis, classification and management. Nat Rev Rheumatol. 2022;10.1038/s41584-022-00819-y. doi:10.1038/s41584-022-00819-y
2. Floyd L, Morris A, Joshi M, Dhaygude A. Glucocorticoid Therapy in ANCA Vasculitis: Using the Glucocorticoid Toxicity Index as an Outcome Measure. Kidney360. 2021;2(6):1002-1010. doi:10.34067/KID.0000502021
3. Quartuccio L, Treppo E, Valent F, De Vita S. Healthcare and economic burden of ANCA-associated vasculitis in Italy: an integrated analysis from clinical and administrative databases. Intern Emerg Med. 2021;16(3):581-589. doi:10.1007/s11739-020-02431-y
4. Raimundo K, Farr AM, Kim G, Duna G. Clinical and Economic Burden of Antineutrophil Cytoplasmic Antibody-associated Vasculitis in the United States. J Rheumatol. 2015;42(12):2383-2391. doi:10.3899/jrheum.150479

DISCLOSURES. Vifor Pharma Group purchased the study report that is the basis for this poster presentation. This poster was developed with Vifor Pharma Group and CliCon S.r.l. Società Benefit. The views expressed here are those of the authors and not necessarily those of the supporters. Perrone V, Dovizio M, Veronesi C, Andretta M, Bacca M, Barbieri A, Bartolini F, Cavaliere A, Chinellato A, Ciaccia A, Cillo MR, Citraro R, Costantini A, Dell'Orco S, Ferrante F, Gentile S, Grego S, Lavalle A, Mancini D, Moscogiuri R, Mosele E, Pagliaro R, Procacci C, Re D, Santoleri F, Ubertazzo L, Vercellone A, Degli Esposti L report no conflicts of interest in this work. The agreement signed by Clicon S.r.l. and Vifor Pharma Group does not create any entity, joint venture or any similar relationship between parties. Clicon S.r.l. is an independent company. Neither CliCon S.r.l. nor any of their representatives are employees of Vifor Pharma Group for any purpose. Ramirez de Arellano Serna A is employee of Vifor Pharma Group.