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ANCA-associated Vasculitis Management in the United States: Data From the Rheumatology Informatics System for Effectiveness (RISE) Registry

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ABSTRACT. ***Objective.*** The management of antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis (AAV) has evolved substantially over the last 2 decades. We sought to characterize AAV treatment patterns in the United States.

Methods. We identified patients with AAV in the Rheumatology Informatics System for Effectiveness (RISE) registry who had at least 2 rheumatology clinician visits between January 1, 2015, and December 31, 2017. Demographics, medications, laboratory test results, and billing codes were extracted from the medical record. Demographic and prescription trends were assessed overall and across US regions.

Results. We identified 1462 patients with AAV, 259 (18%) with new or relapsing AAV. The majority were classified as having granulomatosis with polyangiitis (75%). The mean age was 59.8 years and 59% were female. The majority of patients were in the South (45%) followed by the Mid-West (32%), West (12%), and Northeast (8%). Patients had a median of 3 visits and follow-up of 579 days. The most commonly prescribed medications during the study period were glucocorticoids (86%) followed by rituximab (45%), methotrexate (33%), azathioprine (32%), and mycophenolate mofetil (18%); cyclophosphamide (CYC) was rarely used (7%). At the most recent visits in RISE, 47% of patients were on glucocorticoids. Prescription trends were similar across regions.

Conclusion. To our knowledge, this is the first study to evaluate the demographics and management of AAV by rheumatologists outside of major referral centers. Management strategies vary widely, but CYC is rarely used. These observations can be used to inform future research priorities. Additional studies are needed to characterize AAV severity in RISE as well as patient and provider treatment preferences.

Key Indexing Terms: ANCA-associated vasculitis, epidemiology, practice patterns, registry

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Antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis (AAV) is a small-to-medium vessel vasculitis associated with excess morbidity and mortality when compared to the general population.[1,2] The management of AAV has evolved substantially over the last 2 decades in the context of many randomized controlled trials.[3] Today, providers can choose from a variety of steroid-sparing treatments, which have been found to have efficacy in randomized controlled trials, including cyclophosphamide (CYC), rituximab (RTX), methotrexate (MTX), and mycophenolate mofetil (MMF).

The treatment approach is often guided by provider experience, patient preference, comorbidities, and disease severity, as well as formulary restrictions. Some AAV treatments have been compared in head-to-head studies (e.g., CYC vs RTX) but many have not (e.g., RTX vs MTX), leaving providers uncertain about the comparative effectiveness of these options.[3] RTX and CYC were found to be noninferior to one another for remission induction in a randomized controlled trial but their use in real-world practice is unknown.[3] Society recommendations leave treatment decisions up to providers and their patients.[4,5] In this context, there is scant data regarding contemporary management of AAV, particularly in the community setting. Understanding practice patterns can help guide future trial development,

inform cost-effectiveness study design, and establish important benchmarks.

To address this uncertainty, we analyzed practice trends in the Rheumatology Informatics System for Effectiveness (RISE) registry, which includes patients cared for by rheumatologists mostly located in the community setting.

METHODS

Data source. RISE is an electronic health record (EHR)-enabled registry that practices in the United States can voluntarily join to facilitate collecting data from their practices regarding value and quality of care; these data can then be used to fulfill quality reporting requirements. RISE automatically extracts data from a practice's EHR and is maintained by the American College of Rheumatology (ACR). The methods underlying database assembly and operation have been previously reported.[6]

Ethics. The ACR has received approval from the Western Institutional Review Board to allow deidentified data collected through RISE to be used for research. The current study was approved by the Mass General Brigham IRB (protocol number 2020P003390). Informed consent was not required as the current study was not deemed to be human subjects research by the Mass General Brigham IRB.

Cohort identification. Within the RISE cohort, we identified patients with AAV who were seen between January 1, 2015, and December 31, 2017, based on an adaptation of a previously validated vasculitis algorithm.[7] Specifically, AAV cases were defined as those in which at least 2 International Statistical Classification of Diseases, 10th revision (ICD-10) diagnosis codes for AAV (M31.3, M31.31, M31.7, M30.1) were used at least 3 months apart. In addition, cases had to have received treatment with immunosuppression (glucocorticoids [GCs], RTX, CYC, MTX, MMF, or azathioprine [AZA]) ± 90 days prior to or ± 180 days after the first diagnosis code appearing in the data. In an exploratory analysis, we classified cases as new or relapsing if the Current Procedural Terminology (CPT) code associated with the visit indicated that it was a new patient (99201-99205) or consultation (99241-99245) visit with the rheumatologist.

Immunosuppressive use. The medications of interest in this study included those commonly prescribed for AAV treatment: GCs, RTX, CYC, MTX, MMF, AZA, and combinations of these treatments. Mepolizumab was not approved by the Food and Drug Administration for the treatment of eosinophilic granulomatosis with polyangiitis (EGPA) until December 2017 (the end of the study period), so it was excluded from these analyses. We assessed the use of these medications at 2 timepoints during the study period: (1) the patient's first rheumatology visit in RISE; and (2) the patient's most recently available rheumatology visit in RISE. We also assessed whether each patient had ever received treatment with these medications during the study period.

Covariates of interest. We extracted demographic details, including age, sex, the location of the practice, race, and ethnicity, as well as relevant lab results (e.g., ANCA test, creatinine), medications (e.g., statins, diabetes medication), and diagnosis codes for other conditions (e.g., diabetes, hypertension, hyperlipidemia) from RISE. We defined diabetes by the use of a diagnosis code for diabetes (Clinical Classifications Software [CCS] category 49 or 50), or a prescription for a medication used to treat diabetes.[8] We defined hyperlipidemia by the use of a diagnosis code for hyperlipidemia (CCS category 53) or a prescription for a medication used to treat hyperlipidemia (e.g., statins). We defined hypertension by the use of a diagnosis code for hypertension (CCS category 98 or 99) or ≥ 2 blood pressure (BP) measures with systolic BP > 130 mmHg or diastolic BP > 80 mmHg. Definitions of these comorbidities were based on data available prior to the second occurrence of the ICD-10 diagnosis code that was used to identify AAV cases. Estimated glomerular filtration rate (eGFR) was determined using the Chronic Kidney Disease Epidemiology Collaboration formula and the first available creatinine.[9]

Statistical analysis. Continuous variables are reported as mean ± SD or median and IQR, where appropriate. Categorical variables are reported as n (%). Demographic and prescription trends were assessed overall and across US regions.

RESULTS

Cohort characteristics. From 236 practice sites and 1.1 million patients that participated in RISE during the study period, we identified 1462 patients with AAV with a visit during the study period (Table 1). AAV patients were seen at 126 practice sites by 398 unique providers. The mean age was 59.8 (± 15.3) years. The majority were female (864, 59%), White (824, 56%), and non-Hispanic (1044, 71%). Race was missing or unknown in 594 (41%) cases and ethnicity was undefined in 288 (20%) cases. During the study period, patients had a median of 3 (IQR 0–9) rheumatologist visits and 579 (IQR 328–715) days of follow-up from the first rheumatology visit. Of the 1462 patients, 259 (18%) were classified as new or relapsing patients.

Disease features. The majority of patients had granulomatosis with polyangiitis (GPA; 1097, 75%), followed by microscopic polyangiitis (MPA; 235, 16%) and EGPA (139, 10%). A minority ever had a proteinase 3 (PR3)- or myeloperoxidase (MPO)-ANCA test (221, 15%) available in the data during the study period; among these, a positive PR3- or MPO-ANCA test was present in 137 (62%) cases. The mean eGFR at baseline was 69 (± 42) mL/min/1.73m^2. At baseline, 367 (25%) patients had hyperlipidemia, 223 (15%) had hypertension, and 174 (12%) had diabetes mellitus.

AAV management. Table 2 includes the frequency with which treatments were used at each patient's first visit in RISE and the most recently available visit in RISE (during the study period), as well as the frequency with which treatments were used at any point during a patient's follow-up. GCs were used in the vast majority of cases at some point during the study period (1252, 86%). With regard to steroid-sparing agents, RTX was the most commonly used medication during the study period (652, 45%). MTX, AZA, and MMF were also commonly used (484 [33%], 470 [32%], and 256 [18%], respectively). In contrast to these treatments, CYC was used least often (97, 7%).

The most commonly used medications at the first visit during the study period were RTX (286, 20%) and MTX (290, 20%), followed by AZA (242, 17%), MMF (123, 8%), and CYC (30, 2%). At their first visit during the study period, 531 (36%) patients were prescribed GCs. Trends were nearly identical when the medications used at the most recently available visit during the study period were assessed; RTX (434, 30%) and MTX (345, 24%) were the most frequently used medications at this timepoint, along with GCs (684, 47%).

In the subgroup of patients identified as possibly having new or relapsing disease (n = 259), RTX (80, 31%) and MTX (48, 19%) were also the most commonly used medications. MMF was used in 18 (7%) cases and CYC was used in 11 (4%) cases.

Trends in the use of medications for AAV treatment at the various timepoints in care were similar across US geographic regions.

Table 1. Demographics of subjects with AAV in RISE Registry (2015–2017).

	Overall	Northeast	South	Mid-West	West	Unknown
N	1462	122	658	470	174	38
Age, yrs, mean (SD)	59.8 (15.3)	60.7 (16.2)	59.5 (15.4)	59.9 (15.3)	59.3 (14.4)	61.0 (14.9)
Female	864 (59)	67 (55)	396 (60)	283 (60)	98 (56)	20 (53)
Race						
White	824 (56)	90 (74)	359 (55)	255 (54)	93 (54)	27 (71)
Black	44 (3)	3 (3)	31 (5)	9 (2)	1 (1)	0 (0)
Other/Unspecified	594 (41)	29 (24)	268 (41)	206 (44)	80 (46)	11 (29)
Hispanic	130 (9)	3 (3)	90 (14)	12 (3)	23 (13)	2 (5)
No. encounters, median (IQR)	3 (0–9)	4.5 (1–13)	4 (0–11)	2 (0–6)	4 (1–8)	4.5 (0–11)
New visit	259 (18)	18 (15)	124 (19)	76 (16)	33 (19)	8 (21)
Follow-up, days, median (IQR)	579 (328–715)	507 (287–729)	573 (324–713)	594 (336–714)	595 (357–720)	623 (344–779)
AAV type						
GPA	1097 (75)	93 (76)	505 (77)	333 (71)	134 (77)	32 (84)
MPA	235 (16)	16 (13)	101 (15)	90 (19)	26 (15)	2 (5)
EGPA	139 (10)	13 (11)	57 (9)	49 (10)	16 (9)	4 (11)
ANCA testing						
Ever performed	221 (15)	12 (10)	87 (13)	68 (15)	53 (31)	1 (3)
Test ever positive	137 (62)	6 (50)	49 (56)	49 (72)	32 (60)	1 (100)

Values are expressed in n (%) unless otherwise indicated. AAV: ANCA-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody; EGPA: eosinophilic granulomatosis with polyangiitis; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; RISE: Rheumatology Informatics System for Effectiveness registry.

DISCUSSION

To our knowledge, this is the first study to characterize AAV cases and their management in the RISE registry, an increasingly utilized resource for rheumatology providers and researchers in the US. RTX, MTX, AZA, and GCs were the most commonly used medications to treat AAV in RISE; in contrast, CYC was rarely used. AAV management patterns were similar across geographic regions. In addition to characterizing the demographics and treatment of AAV in a novel data source, this study also highlights some of the opportunities and challenges associated with using RISE to study AAV.

The Rituximab in ANCA-Associated Vasculitis (RAVE) trial found that RTX was noninferior to CYC for remission induction.[10] However, the use of CYC, even in new or relapsing cases, was quite rare in RISE. This may reflect a less severe AAV phenotype that may be captured in RISE and/or patient or provider preferences. CYC has been associated with certain toxicities, including infertility, hemorrhagic cystitis, and secondary malignancy, so it requires careful monitoring and may make its use less appealing compared to RTX.[3] However, RTX is indicated for moderate-to-severe disease and was frequently used in the RISE cohort. Some intravenous CYC and RTX exposure may occur in the inpatient setting, which would not be captured in RISE, but we would expect oral regimens and subsequent infusions to be captured. Indeed, treatment with RTX was common in RISE so we would anticipate any CYC infusions to be similarly well captured. Given the rare use of CYC in RISE, comparative effectiveness and cost-effectiveness studies might focus on assessing non-CYC–based alternative regimens. Similar studies conducted outside of the US would also be useful to provide perspective on how practice varies internationally, especially given the cost of RTX therapy.[11]

In comparison with CYC use, we observed that MTX was more commonly used to treat AAV at various timepoints in the clinical course of this cohort. This may reflect that patients with AAV in RISE have less severe disease and/or that providers and patients prefer MTX over alternative options because of different side effect profiles or comfort level. The frequency of MTX and RTX use suggests that additional studies are needed to understand the comparative effectiveness of these treatments for AAV remission induction and maintenance, especially in less severe disease. We hypothesize that RTX may be commonly used in nonsevere AAV. Of note, MTX was found to be associated with a higher risk of relapse compared to CYC when used for remission induction[12] and was noninferior with regard to adverse events when compared to AZA for remission maintenance.[13]

AZA was commonly prescribed during the study period (2015–2017), although the MAINRITSAN trial, published in 2014, found RTX to be superior to AZA for remission maintenance.[14] Moreover, a subsequent follow-up study found RTX to have a survival benefit compared to AZA.[15] However, because of limitations associated with the RISE data source, which lacks comprehensive data prior to 2015, we are unable to assess whether patients had been stable on AZA prior to the publication in MAINRITSAN and were therefore continuing a treatment that had previously been effective for them during the study period. Reassessment of temporal trends in the use of RTX for remission maintenance in RISE as more follow-up time accrues will therefore be informative. Similarly, GC use was common in this cohort, likely reflecting the varied practice with regard to GC continuation or discontinuation once disease remission is achieved. As additional trials provide an evidence base to guide the long-term use of GCs in AAV, RISE may be used to understand how these results inform real-world practice.

Table 2. AAV treatment in the RISE Registry (2015–2017).

	Overall	Northeast	South	Mid-West	West	Unknown
Ever treated, n	1462	122	658	470	174	38
RTX	652 (45)	67 (55)	313 (48)	201 (43)	56 (32)	15 (40)
CYC	97 (7)	10 (8)	52 (8)	26 (5)	7 (4)	2 (5)
MTX	484 (33)	36 (30)	223 (34)	168 (36)	47 (27)	10 (26)
AZA	470 (32)	34 (28)	199 (30)	159 (34)	63 (36)	15 (40)
MMF	256 (18)	18 (15)	130 (20)	69 (15)	34 (20)	5 (13)
GC	1252 (86)	104 (85)	576 (88)	397 (85)	143 (82)	32 (84)
Induction treatment[a], n	259	18	124	76	33	8
RTX	80 (31)	4 (22)	37 (30)	25 (33)	12 (36)	2 (25)
CYC	11 (4)	1 (6)	4 (3)	3 (4)	1 (3)	2 (25)
RTX + CYC	8 (3)	1 (6)	5 (4)	1 (1)	1 (3)	0 (0)
MTX	48 (19)	2 (11)	24 (19)	17 (22)	4 (12)	1 (13)
MMF	18 (7)	0 (0)	11 (9)	4 (5)	3 (9)	0 (0)
Other/combination therapy	34 (13)	4 (22)	15 (12)	8 (11)	4 (12)	3 (38)
GC	39 (15)	5 (28)	20 (16)	9 (12)	5 (15)	0 (0)
None associated with visit	21 (8)	1 (5)	8 (7)	9 (12)	3 (9)	0 (0)
First treatment in study period, n	1462	122	658	470	174	38
RTX	286 (20)	34 (28)	141 (21)	77 (16)	27 (16)	7 (18)
CYC	30 (2)	1 (1)	11 (2)	12 (3)	5 (3)	1 (3)
MTX	290 (20)	18 (15)	125 (19)	110 (23)	34 (20)	3 (8)
AZA	242 (17)	16 (13)	99 (15)	81 (17)	40 (23)	6 (16)
MMF	123 (8)	5 (4)	60 (9)	32 (7)	26 (15)	0 (0)
GC	531 (36)	48 (39)	244 (37)	169 (36)	49 (28)	21 (55)
More recent treatment in study period, n	1462	122	658	470	174	38
RTX	434 (30)	46 (38)	213 (32)	125 (27)	40 (23)	10 (26)
CYC	19 (1)	0 (0)	10 (2)	5 (1)	4 (2)	0 (0)
MTX	345 (24)	22 (18)	149 (23)	125 (27)	41 (24)	8 (21)
AZA	315 (22)	22 (18)	129 (20)	104 (22)	50 (29)	10 (26)
MMF	170 (12)	10 (8)	78 (12)	48 (10)	29 (17)	5 (13)
GC	684 (47)	48 (39)	309 (50)	210 (45)	98 (56)	19 (50)

Values are expressed as n (%) unless otherwise indicated. [a] Induction regimen refers to a medication associated with an encounter with a CPT code indicating a new (99201–99205) or consultation (99241–99245) visit within XX days. AAV: antineutrophil cytoplasmic antibody–associated vasculitis; AZA: azathioprine; CPT: Current Procedural Terminology; CYC: cyclophosphamide; GC: glucocorticoid; MMF: mycophenolate mofetil; MTX: methotrexate; RISE: Rheumatology Informatics System for Effectiveness registry; RTX: rituximab.

Future studies are needed to understand how the RISE registry may be leveraged to conduct comparative effectiveness studies in AAV. RISE data might, for example, be used to identify patients with vasculitis to assist in recruitment for a new prospective trial or research study. Opportunities to leverage RISE in AAV research will be enhanced by the incorporation of quantitative (e.g., Birmingham Vasculitis Activity Score) or semi-quantitative (e.g., new, relapsing, remission) assessments of disease activity as structured data fields. Moreover, linkage of RISE with external databases, such as Medicare, would ensure more complete data capture to assess events that occur outside of the rheumatologist's office, such as during nephrology visits or hospitalizations.

Strengths of our study include the large number of patients with a rare condition that we were able to identify from across the US, many of whom were cared for in community-based rheumatology practices. To date, most studies describing the characteristics and management of AAV have derived from experiences at academic referral centers or within large referral networks. Despite these strengths, our study has certain limitations. First, we were unable to assess the validity of the algorithm we used for case identification. However, we adapted our methods from 1 previously validated, which had a positive predictive value of over 90% for identifying cases of GPA[7]; indeed, the vast majority of cases we identified were classified as GPA. Similarly, in exploratory analyses, we used new or consult CPT codes as a surrogate for new or relapsing disease, which has not been previously validated and may misclassify patients according to disease status. Second, because of the nature of the RISE registry, we did not have details regarding disease-specific characteristics and manifestations, including disease duration and organ involvement. However, unstructured data is likely to be available soon within RISE, facilitating at least a narrative review of physician notes. With respect to laboratory test results, even when available, ANCA test results were often uninterpretable because of missing reference ranges. Moreover, some laboratory tests (e.g., ANCA) may only be performed at the time of diagnosis but not repeated, such that those laboratory test results are not available for patients with preexisting disease who were diagnosed and tested prior to the registry's initiation of data capture. As current patients with AAV in RISE flare and as new patients with AAV establish care at practices participating in RISE, we

expect the proportion of patients with ANCA tests to increase. Third, patients who are racial/ethnic minorities, have more severe disease, and/or are enrolled in Medicaid insurance may not be well represented in RISE. Similarly, since this cohort was assembled from rheumatology practices, it may be less likely to include patients with more severe renal involvement or MPA. Additional studies are needed to understand whether our observations are true in those subgroups that are more likely to be cared for in academic medical centers or by other specialists (e.g., nephrologists).

In conclusion, this is the first US-based study to characterize the demographics and management of AAV in the rheumatology community using the ACR's RISE registry, to our knowledge. We found significant variation in the management of AAV at various timepoints in care and that CYC is rarely used in contrast to other options such as RTX and MTX. Some of the treatments commonly used have not been compared in head-to-head studies and/or have been found to be inferior to alternative treatments. Additional studies are needed to assess the comparative effectiveness of these treatments in routine care settings, to characterize AAV disease features in RISE, and to understand patient and provider AAV treatment preferences.

REFERENCES

1. Tan JA, Dehghan N, Chen W, Xie H, Esdaile JM, Avina-Zubieta JA. Mortality in ANCA-associated vasculitis: a meta-analysis of observational studies. Ann Rheum Dis 2017;76:1566-74.
2. Wallace ZS, Fu X, Harkness T, Stone JH, Zhang Y, Choi H. All-cause and cause-specific mortality in ANCA-associated vasculitis: overall and according to ANCA type. Rheumatology 2019;59:2308-15.
3. Wallace ZS, Miloslavsky EM. Management of ANCA-associated vasculitis. BMJ 2020;368:m421.
4. Ntatsaki E, Carruthers DM, Chakravarty K, D'Cruz DP, Harper L, Jayne D, et al. BSR and BHPR guideline for the management of adults with ANCA-associated vasculitis. Rheumatology 2014;53:2306-9.
5. Yates M, Watts RA, Bajema IM, Cid MC, Crestani B, Hauser T, et al; BSR and BHPR Standards, Guidelines and Audit Working Group. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. Ann Rheum Dis 2016;75:1583-94.
6. Yazdany J, Bansback N, Clowse M, Collier D, Law K, Liao KP, et al. Rheumatology Informatics System for Effectiveness: a national informatics-enabled registry for quality improvement. Arthritis Care Res 2016;68:1866-73.
7. Sreih AG, Annapureddy N, Springer J, Casey G, Byram K, Cruz A, et al; Vasculitis Patient-Powered Research Network. Development and validation of case-finding algorithms for the identification of patients with anti-neutrophil cytoplasmic antibody-associated vasculitis in large healthcare administrative databases. Pharmacoepidemiol Drug Saf 2016;25:1368-74.
8. Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project (HCUP). Clinical Classifications Software (CCS) for ICD-10-PCS (beta version). [Internet. Accessed March 25, 2021.] Available from: www.hcup-us.ahrq.gov/toolssoftware/ccs10/ccs10.jsp
9. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604-12.
10. Stone JH, Merkel PA, Spiera R, Seo P, Langford CA, Hoffman GS, et al; RAVE-ITN Research Group. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. N Engl J Med 2010;363:221-32.
11. Wallace ZS, Harkness T, Blumenthal KG, Choi HK, Stone JH, Walensky RP. Increasing operational capacity and reducing costs of rituximab administration: a costi ng analysis. ACR Open Rheumatol 2020;2:261-8.
12. de Groot K, Rasmussen N, Bacon PA, Tervaert JW, Feighery C, Gregorini G, et al. Randomized trial of cyclophosphamide versus methotrexate for induction of remission in early systemic antineutrophil cytoplasmic antibody-associated vasculitis. Arthritis Rheum 2005;52:2461-9.
13. Pagnoux C, Mahr A, Hamidou MA, Boffa JJ, Ruivard M, Ducroix JP, et al; French Vasculitis Study Group. Azathioprine or methotrexate maintenance for ANCA-associated vasculitis. N Engl J Med 2008;359:2790-803.
14. Guillevin L, Pagnoux C, Karras A, Khouatra C, Aumaitre O, Cohen P, et al; French Vasculitis Study Group. Rituximab versus azathioprine for maintenance in ANCA-associated vasculitis. N Engl J Med 2014;371:1771-80.
15. Terrier B, Pagnoux C, Perrodeau É, Karras A, Khouatra C, Aumaître O, et al; French Vasculitis Study Group. Long-term efficacy of remission-maintenance regimens for ANCA-associated vasculitides. Ann Rheum Dis 2018;77:1150-6.