A Retrospective Cohort Study of Veteran's Affairs Data: Epidemiology, Treatments, Clinical Outcomes, and Burden of Immunoglobulin A Nephropathy

Mark Bensink,[1] Deborah Goldschmidt,[2] Zheng-Yi Zhou,[2] Sherry Shi,[2] Yilu Yin,[3] Lizheng Shi[3]

[1]Travere Therapeutics, Inc., San Diego, CA, USA; [2]Analysis Group, Boston, MA, USA; [3]Tulane University, New Orleans, LA, USA

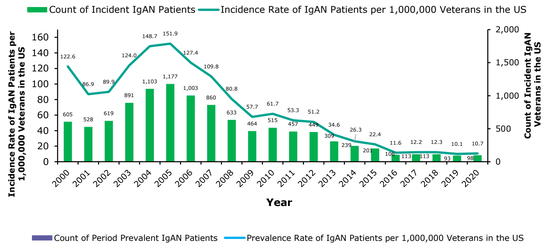
Poster# EPH40

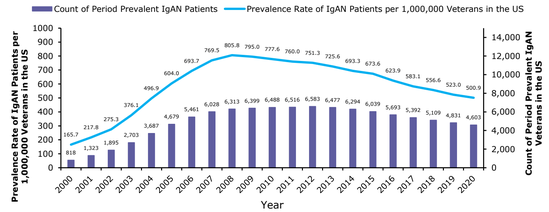
RESULTS

Epidemiology Results

- Average annual incidence during 2000-2020 was 67.0 per million but fluctuated substantially, ranging from a low of 10.1 in 2019 to a high of 152.0 in 2005
- Annual period prevalence of IgAN was an average of 589.0 per million VA-enrolled veterans over the 2000-2020 time period

Figure 1. Prevalence and Incidence of IgAN veterans





Abbreviations: IgAN, immunoglobulin A nephropathy; US, United States.

Patient Characteristics

- 8,243 patients with IgAN were included in the analyses
- At the index date, median age was 63 years, and 96% were male. The majority of patients were White (59.2%) or Black (19.7%)
- Patients had an average of 9.5 years of follow-up post-index
- During the 6-month baseline period:
  - Mean Charlson Comorbidity Index was 1.1 and the most common comorbidities were interstitial fibrosis and tubular atrophy (91.4%) and hypertension (80.6%)
  - The most common medications were statins (48.6%), ACE inhibitors (47.6%), and calcium channel blockers (38.1%)
  - Among patients with available lab values, mean (SD) [median] 24-hour urine protein was 1.8 g/day (3.5) [0.2] and mean (SD) [median] eGFR level was 47.5 mL/min/1.73m^2 (27.2) [45.0]
  - 7.1% of patients had KF
  - CKD stage during baseline was unknown for 56% of patients; the most commonly identified stages were 3b (9.4%) and 3a (9.2%)

Table 1. Patient Characteristics

Patient Characteristics	IgAN Patients (N=8,243)
Age as of the index date, mean (SD) [median]	62.3 (13.7) [62.7]
Female, n (%)	334 (4.1%)
Race (top 3), n (%)	
White	4,879 (59.2%)
Black	1,623 (19.7%)
Hispanic	423 (5.1%)
Employment status, n (%)	
Employed	2,110 (25.6%)
Unemployed	2,394 (29.0%)
Retired	3,556 (43.1%)
Unknown	183 (2.2%)
Geographic region, n (%)	
Northeast	900 (10.9%)
Midwest	2,272 (27.6%)
South	2,102 (25.5%)
West	2,969 (36.0%)
Length of follow-up, years, mean (SD) [median]	9.5 (5.5) [9.0]
CCI excluding renal disease and KF, mean (SD) [median]	1.1 (1.4) [0.0]
Comorbidities (top 3), n (%)	
Interstitial fibrosis and tubular atrophy	7,535 (91.4%)
Hypertension	6.641 (80.6%)
Hyperlipidemia	4,303 (52.2%)
Medication use (top 5), n (%)	
Statins	4,010 (48.6%)
ACE inhibitors	3,921 (47.6%)
Calcium channel blockers	3,137 (38.1%)
Beta blockers	1,904 (23.1%)
Diuretics	1,706 (20.7%)
24-hour urine protein, n (%)	2,581 (31.3%)
g/day, mean (SD) [median]	1.8 (3.5) [0.2]
eGFR, n (%)	3,515 (42.6%)
mL/min/1.73m^2, mean (SD) [median]	47.5 (27.2) [45.0]
KF, n (%)	583 (7.1%)
CKD stage, n (%)	
Stage 1	277 (3.4%)
Stage 2	691 (8.4%)
Stage 3	1605 (19.5%)
Stage 4	583 (7.1%)
Stage 5/KF	489 (5.9%)

Abbreviations: ACE, angiotensin-converting enzyme; CCI, Charlson comorbidity index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; IgAN, immunoglobulin A nephropathy; KF, kidney failure; SD, standard deviation.
Note: Baseline characteristics (CCI excluding renal disease and KF, comorbidities, medication use) were assessed during the 6-month baseline period. Disease characteristics (24-hour urine protein, eGFR, KF, and CKD stage) were measured as close as possible to the index date during the baseline period.

Treatment Use

- The most commonly used treatments during the first year of follow-up included statins (59.6%), ACE inhibitors (55.9%), and calcium channel blockers (46.9%)

Table 2. Medication Use During the First Year Following the Index Date

Medication	IgAN Patients (N=8,243)
Medication use, n (%)	
ACE inhibitors	4,610 (55.9%)
ARB	855 (10.4%)
Beta blockers	2,286 (27.7%)
CNIs	303 (3.7%)
Calcium channel blockers	3,868 (46.9%)
Diuretics	2,110 (25.6%)
GLP-1 receptor agonist	14 (0.2%)
Glucocorticoids	1,973 (23.9%)
MRAs	429 (5.2%)
Potassium binders	325 (3.9%)
SGLT2 inhibitor	4 (0.0%)
Statins	4,914 (59.6%)

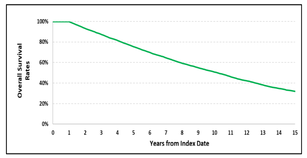
Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; CNIs, calcineurin inhibitors; GLP, glucagon-like peptide; IgAN, immunoglobulin A nephropathy; MRAs, mineralocorticoid receptor antagonists; SGLT2, sodium-glucose transport protein 2.

Clinical Outcomes

- 66% of patients died during the follow-up period, with the median time to death being 10.2 years. The KM survival rate (95% CI) at 5 years was 75.5% (74.5%; 76.4%) and at 10 years was 50.8% (49.7%; 51.9%)
- 76.5% of patients experienced a KF event during follow-up, with the median time to first KF event being 6.2 years. The KM rate (95% CI) at 1 year was 12.9% (12.2%; 13.6%), at 5 years was 43.5% (42.5%; 44.6%) and at 10 years was 64.8% (63.7%; 65.8%)

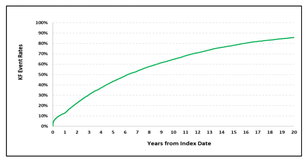
Figure 2. Clinical Outcomes (KM Analysis)

A. Overall Survival



Number of Deaths	5,440 (66%)
Median Time to Death in Years	10.2
Proportion Alive at 1 Year (95% CI)	-
Proportion Alive at 5 Years (95% CI)	75.5 (74.5, 76.4)
Proportion Alive at 10 Years (95% CI)	50.8 (49.7, 51.9)

B. Time to First KF Event



Number of patients with a KF event	6,305 (76.5%)
Median Time to KF event in Years (95% CI)	6.2
Proportion with KF event at 1 Year (95% CI)	12.9 (12.2, 13.6)
Proportion with KF event at 5 Years (95% CI)	43.5 (42.5, 44.6)
Proportion with KF event at 10 Years (95% CI)	64.8 (63.7, 65.8)

Abbreviations: CI, confidence interval; KF, kidney failure, KM, Kaplan-Meier.

HRU

- 31.3% of patients had an inpatient admission during the year following the index date, with an average of 0.7 admissions per patient and an average length of stay of 26.1 days among patients with at least one admission
- Nearly all patients had an outpatient visit (99.6%) during the first year post-index, with an average of 26.4 visits per patient. 22.7% of patients had an emergency room visit, with an average of 0.5 visits

Table 3. HRU During the First Year Following the Index Date

HRU During the First Year Post-Index	IgAN Patients (N=8,243)
All-cause visits	
Inpatient admissions, n (%)	2,577 (31.3%)
Number of visits, mean (SD) [median]	0.7 (1.4) [0.0]
Number of inpatient days*, mean (SD) [median]	26.1 (53.7) [8.0]
Outpatient admissions, n (%)	8,212 (99.6%)
Number of visits, mean (SD) [median]	26.4 (24.2) [20.0]
Emergency room visits, n (%)	1,872 (22.7%)
Number of visits, mean (SD) [median]	0.5 (1.4) [0.0]

Abbreviations: HRU, healthcare resource use; IgAN, immunoglobulin A nephropathy; SD, standard deviation.
Note: *Number of inpatient days is only calculated among patients with at least 1 inpatient admission.

Healthcare Costs

- During the first year of follow-up, the average total healthcare costs per patient were $30,754, with medical costs of $26,247 and pharmacy costs of $4,507, on average
- Medical costs were driven by inpatient ($12,824) and outpatient ($12,536) costs

Table 4. Healthcare Costs During the First Year After the Index Date

Healthcare Costs During the First Year Post-Index	IgAN Patients (N=8,243)
All-cause costs (in 2021 USD)	
Total costs per patient, mean (SD) [median]	30,745 (93,088) [8,172]
Pharmacy costs per patient	4,507 (13,996) [1,237]
Total medical costs per patient	26,247 (87,471) [6,396]
Inpatient admission costs per patient	12,824 (80,643) [0]
Outpatient visit costs per patient	12,536 (20,949) [5,800]
Emergency room visit costs per patient	887 (2,976) [0]

Abbreviations: IgAN, immunoglobulin A nephropathy; SD, standard deviation.

DISCUSSION

- This study found evidence that patients with IgAN in the VA data experienced considerable clinical burden, including three fourths experiencing a KF event during follow-up
- Resource use was also high, with a third of patients having an inpatient admission during the first year following the index date
- Costs to the VA were substantial, with average direct healthcare costs of $30,754 per patient during the first year following IgAN diagnosis
- This study adds to the limited research on the clinical and economic burden on patients with IgAN in the US
  - A 2018 literature review found no publications with evidence on economic or humanistic burden of IgAN[7]
  - A 2021 systematic review and meta-analysis found only 2 real-world retrospective studies assessing the economic burden of IgAN, one in British Columbia, Canada and one in China[8]

Limitations

- Medical services provided outside of the VA health system were not recorded in the database. Patients who progress to KF are eligible for Medicare, so their care may not be observable; therefore, some clinical outcomes, HRU, and costs would be underestimated for them.
- The VA includes a predominantly male population, which is not representative of general IgAN population
- Identifying patients via diagnosis codes, which are not specific to IgAN, may mis-identify patients or omit relevant patients. In particular, the change to ICD-10-CM codes in late 2015 may have impacted incidence in 2015-2020.
- The sample selection criteria required 1 year of VA coverage following index in order to calculate HRU and costs; however, this criteria excluded patients who died during the first year, leading to an overestimate of survival
- Administrative databases may be subject to data omissions or coding inaccuracies

CONCLUSIONS

- IgAN is associated with a substantial clinical and resource burden among patients in the VA
- There is a high unmet medical need for IgAN treatments that delay or prevent progression to KF, which necessitates dialysis or renal transplant, and reduce the HRU and cost burdens on patients and healthcare systems

DISCLOSURES

Mark Bensink is the managing director of BenofitConsulting, which received consulting fees from Travere Therapeutics, Inc.

Deborah Goldschmidt, Zheng-Yi Zhou, and Sherry Shi are employees of Analysis Group, which received consulting fees from Travere Therapeutics, Inc.

Yilu Li and Lizheng Shi are employees of Tulane University.

ACKNOWLEDGMENTS

Priscilla Lopez of Analysis Group provided assistance with the preparation of the poster content
This study was funded by Travere Therapeutics, Inc.

REFERENCES

1. Wyatt RJ, Julian BA. *N Engl J Med.* 2013; 368:2402-2414.
2. Suzuki H, Kiryluk K, Novak J, et al. *J Am Soc Nephrol.* 2011; 22(10): 1795-1803.
3. Penfold RS, Prendecki M, McAdoo S, Tam FW. *Nephrol Renovasc Dis.* 2018; 11:137-148.
4. Lafayette RA, Kelepouris A. *Am J Nephrol*. 2018; 47:S43-S52.
5. Barratt J, Feehally J. *J Am Soc Nephrol*. 2005; 16:2088-2097.
6. Xie J, Kiryluk K, Wang W, et al. *PLoS One.* 2012;7:e38904.
7. George AT, Zaour N, Nic Lochlainn EM. *Value in Health.* 2018; 21 (Supp 3).
8. Kwon CS, Daniele P, Forsythe A, Ngai C. *J of HEOR*. 2021; 8(2).

Scan the QR code to obtain a PDF of this poster.

Charges may apply.

No personal information is stored.

INTRODUCTION

Background

- Immunoglobulin A Nephropathy (IgAN) is characterized by the glomerular accumulation of immune complexes containing IgA, which leads to damage of the glomerular filtration barrier, resulting in proteinuria, hematuria, and progressive loss of glomerular filtration rate[1,2]
- Patients with IgAN usually remain undiagnosed until they present with symptoms of established kidney disease[3-5]
- The progression to kidney failure (KF) can be slow and varies among populations, with studies showing that 15% to 40% of patients with IgAN develop chronic kidney failure (CKF) within 10 to 20 years of diagnosis[5,6]
- Real-world evidence on prevalence and incidence rates, patient characteristics, treatments, clinical outcomes, healthcare resource utilization (HRU), and direct healthcare costs related to IgAN is lacking

Objectives

- This retrospective observational study aimed to:
  - Describe the prevalence and incidence rates of IgAN in the Veteran's Affairs (VA) databases
  - Describe patient characteristics, treatment use, clinical burden, HRU, and costs of patients diagnosed with IgAN in the VA databases

METHODS

Data Source

- This study used deidentified, retrospective data from the VA databases from October 1999 through February 2021
- The VA is the United States' largest integrated health care system with over 1,200 sites of care, serving over eight million veterans each year
- The VA Corporate Data Warehouse includes all medical encounter information in the VA, comprised of medical centers, community-based outpatient clinics, community-living centers, Veteran centers, and domiciliary care
- Only medical care administered at VA facilities was observable in the data, and only costs paid by the VA (and not other payers, such as Medicare or Medicaid) were observable

Sample Selection

- For prevalence and incidence estimation, patients were required to have:
  - ≥2 diagnoses associated with IgAN (ICD-9-CM: 581.89, 583.9; ICD-10-CM: N00.3-N00.9, N02.5, N02.7-N02.9) 30-180 days apart
  - For the rest of the analyses, patients were further required to have:
    - ≥6 months of continuous eligibility prior to the index date and ≥12 months of continuous eligibility following the index date
    - No evidence of COVID-19 during the baseline or follow-up periods (ICD-10-CM code U07.1)
- The *index date* was defined as the first diagnosis date of IgAN
- The *baseline period* was defined as the 6-month period before the index date
- The *follow-up period* was defined as the period from the index date until death, end of continuous eligibility, or end of data availability, whichever came first

Statistical Methods

Epidemiology

- Prevalence and incidence estimates for IgAN in the VA database were calculated on a per 1,000,000 persons per year basis from 2000-2020
- Incidence for a given year was estimated as the number of patients with ≥2 diagnoses for IgAN 30-180 days apart, with the first diagnosis in the given year, divided by the number of VA-enrolled veterans in that year
- Prevalence for a given year was estimated as the number of patients with follow-up during the given year, who had ≥2 diagnoses for IgAN 30-180 days apart with the first diagnosis in or before the given year, divided by the number of VA-enrolled veterans in that year

Statistical Methods (continued)

Patient Characteristics

- Demographics as of the index date, comorbidities and disease characteristics during the baseline period, and laboratory values during the baseline period and as close as possible to the index date were summarized using means, medians, and standard deviations (SDs) for continuous variables, and frequency counts and proportions for categorical variables
- 24-hour urine protein (24hUP) value was reported directly from the data, if available. If not, urine protein/creatinine ratio (UP/C) measurements were used (either directly from the data, or calculated using urine protein and creatinine measurements from the same day) and converted to 24hUP

Treatment use

- Treatment classes used during the first year following the index date were described using frequency counts and proportions

Statistical Methods (continued)

Clinical outcomes

- Overall survival and time to first KF event were assessed from the index date using Kaplan-Meier (KM) analyses, with patients censored at the end of the follow-up period
- Median times to first KF event and overall survival were reported, along with KM rates and associated 95% confidence intervals (CIs) at key time points

HRU and Healthcare Costs

- All-cause HRU during the first year after the index date was summarized, stratified by place of service
- Total direct healthcare costs (in 2021 USD) during the first year after the index date, including pharmacy costs and medical costs, were described
- Frequency counts and proportions of patients with ≥1 visit in each HRU category were reported; number of HRU visits and costs were described using means, medians, and SDs

Contact information: Mark Bensink, Mark.Bensink@travere.com

Presented at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Conference; May 7-10, 2023; Boston, MA