A Retrospective Cohort Study of Veteran's Affairs Data: Epidemiology, Treatments, Clinical Outcomes, and Burden of Focal Segmental Glomerulosclerosis

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

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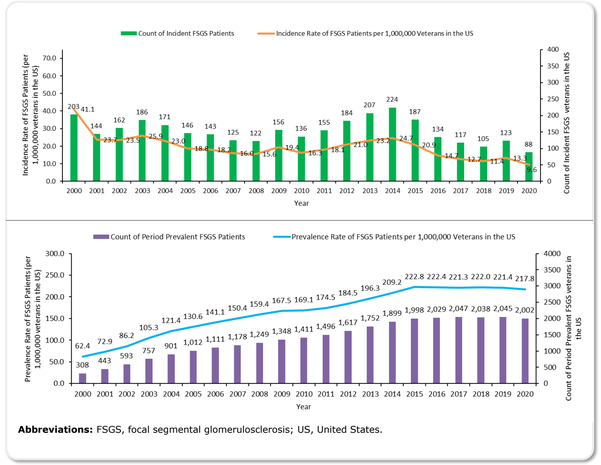
RESULTS

Epidemiology Results

- Average annual incidence during 2000-2020 was 19.6 per million, decreasing over time from 41.1 in 2000 to 9.6 in 2020
- Average annual period prevalence of FSGS was 164.7 per million VA-enrolled veterans over the 2000-2020 time period

Figure 1. Incidence and Prevalence of FSGS veterans



Abbreviations: FSGS, focal segmental glomerulosclerosis; US, United States.

Patient Characteristics

- 2,515 patients with FSGS were included in the analyses
- At the index date, median age was 59 years, and 95% were male. The majority of patients were White (46.4%) or Black (38.1%)
- Patients had an average of 8.9 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 hypertension (87.0%) and hyperlipidemia (56.0%)
  - The most common medications were statins (55.1%), ACE inhibitors (53.1%), and calcium channel blockers (47.0%)
  - Among patients with available lab values, mean UP/C was 2.8 g/g and mean eGFR level was 43.9 mL/min/1.73m^2
  - 12.3% of patients had KF
  - CKD stage during baseline was unknown for 36.4% of patients; the most commonly identified stages were 4 (16.4%) and 3b (11.6%)

Table 1. Patient Characteristics

Patient Characteristics	FSGS Patients (N=2,515)
Age as of the index date, mean (SD) [median]	57.5 (13.2) [58.7]
Female, n (%)	135 (5.4%)
Race (top 3), n (%)	
White	1,168 (46.4%)
Black	957 (38.1%)
Hispanic	122 (4.9%)
Employment status, n (%)	
Employed	842 (33.5%)
Unemployed	791 (31.5%)
Retired	816 (32.4%)
Unknown	66 (2.6%)
Geographic region, n (%)	
Northeast	815 (32.4%)
Midwest	774 (30.8%)
South	680 (27.0%)
West	246 (9.8%)
Length of follow-up, years, mean (SD) [median]	8.9 (5.6) [7.7]
CCI excluding renal disease and KF, mean (SD) [median]	1.1 (1.5) [0.0]
Comorbidities (top 3), n (%)	
Hypertension	2,188 (87.0%)
Hyperlipidemia	1,408 (56.0%)
Anemia	652 (25.9%)
Medication use (top 5), n (%)	
Statins	1,387 (55.1%)
ACE inhibitors	1,336 (53.1%)
Calcium channel blockers	1,183 (47.0%)
Diuretics	676 (26.9%)
Glucocorticoids	587 (23.3%)
Urine protein levels (UP/C), n (%)	1,541 (61.3%)
g/g, mean (SD) [median]	2.8 (4.8) [0.4]
eGFR, n (%)	1,505 (59.8%)
mL/min/1.73m^2, mean (SD) [median]	43.9 (26.6) [38.0]
KF, n (%)	310 (12.3%)
CKD stage, n (%)	
Stage 1	94 (3.7%)
Stage 2	242 (9.6%)
Stage 3	603 (24.0%)
Stage 4	412 (16.4%)
Stage 5/KF	249 (9.9%)

Abbreviations: ACE, angiotensin-converting enzyme; CCI, Charlson comorbidity index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; KF, kidney failure; SD, standard deviation.
Notes: Baseline characteristics (CCI excluding renal disease and KF, comorbidities, medication use) were assessed during the 6-month baseline period. Disease characteristics (urine protein, eGFR, KF, and CKD stage) were measured as close as possible to the index date during the baseline period. CKD stage was identified by eGFR level or diagnosis codes.

Treatment Use

- The most commonly used treatments during the first year of follow-up included statins (65.9%), ACE inhibitors (59.9%), and calcium channel blockers (54.2%)

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

Medication	FSGS Patients (N=2,515)
Medication use, n (%)	
ACE inhibitors	1,506 (59.9%)
ARB	338 (13.4%)
Beta blockers	707 (28.1%)
CNIs	285 (11.3%)
Calcium channel blockers	1,364 (54.2%)
Diuretics	846 (33.6%)
GLP-1 receptor agonist	3 (0.1%)
Glucocorticoids	1,049 (41.7%)
MRAs	200 (8.0%)
Potassium binders	134 (5.3%)
SGLT2 inhibitor	7 (0.3%)
Statins	1,658 (65.9%)

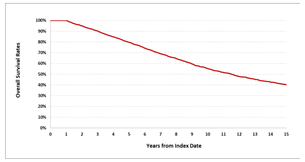
Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; CNIs, calcineurin inhibitors; GLP, glucagon-like peptide; FSGS, focal segmental glomerulosclerosis; MRAs, mineralocorticoid receptor antagonists; SGLT2, sodium-glucose transport protein 2.

Clinical Outcomes

- 51.5% of patients died during the follow-up period, with the median time to death being 11.6 years. The KM survival rate (95% CI) at 5 years was 79.7% (78.0%; 81.2%) and at 10 years was 55.3% (53.1%; 57.5%)
- 76.9% of patients experienced a KF event during follow-up, with the median time to first KF event being 4.1 years. The KM rate (95% CI) at 1 year was 23.1% (21.5%; 24.8%), at 5 years was 54.8% (52.9%; 56.8%) and at 10 years was 73.7% (71.8%; 75.6%)

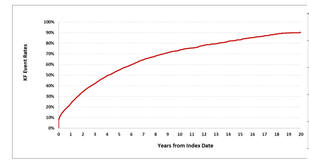
Figure 2. Clinical Outcomes (KM analysis)

A. Overall Survival



Number of Deaths	1,296 (51.5%)
Median Time to Death in Years	11.6
Proportion Alive at 1 Year (95% CI)	-
Proportion Alive at 5 Years (95% CI)	79.7 (78.0, 81.2)
Proportion Alive at 10 Years (95% CI)	55.3 (53.1, 57.5)

B. Time to First KF Event



Number of patients with a KF event	1,934 (76.9%)
Median Time to KF event in Years (95% CI)	4.1
Proportion with KF event at 1 Year (95% CI)	23.1 (21.5, 24.8)
Proportion with KF event at 5 Years (95% CI)	54.8 (52.9, 56.8)
Proportion with KF event at 10 Years (95% CI)	73.7 (71.8, 75.6)

Abbreviations: CI, confidence interval; KM, Kaplan-Meier.
Note: Median time to death and to first KF event were calculated across all patients using KM analyses.

HRU

- 39.8% of patients had an inpatient admission during the year following the index date, with an average of 0.9 admissions per patient and an average length of stay of 19.1 days among patients with at least one admission
- Nearly all patients had an outpatient visit (99.8%) during the first year post-index, with an average of 33.6 visits per patient. 33.0% of patients had an emergency room visit, with an average of 0.7 visits

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

HRU During the First Year Post-Index	FSGS Patients (N=2,515)
All-cause visits	
Inpatient admissions, n (%)	1,001 (39.8%)
Number of visits, mean (SD) [median]	0.9 (1.5) [0.0]
Number of inpatient days*, mean (SD) [median]	19.1 (36.8) [8.0]
Outpatient admissions, n (%)	2,510 (99.8%)
Number of visits, mean (SD) [median]	33.6 (30.8) [25.0]
Emergency room visits, n (%)	830 (33.0%)
Number of visits, mean (SD) [median]	0.7 (1.4) [0.0]

Abbreviations: HRU, healthcare resource use; FSGS, focal segmental glomerulosclerosis; SD, standard deviation.
Notes: *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 $36,543, with medical costs of $31,141 and pharmacy costs of $5,402, on average
- Medical costs were driven by outpatient ($16,072) costs, followed by inpatient costs ($13,655)

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

Healthcare Costs During the First Year Post-Index	FSGS Patients (N=2,515)
All-cause costs (in 2021 USD)	
Total costs per patient, mean (SD) [median]	36,543 (88,858) [12,354]
Pharmacy costs per patient	5,402 (15,499) [1,505]
Total medical costs per patient	31,141 (80,422) [10,004]
Inpatient admission costs per patient	13,655 (72,132) [0]
Outpatient visit costs per patient	16,072 (24,463) [8,501]
Emergency room visit costs per patient	1,415 (3,630) [0]

Abbreviations: FSGS, focal segmental glomerulosclerosis; SD, standard deviation.

DISCUSSION

- This study found evidence that patients with FSGS in the VA data experienced considerable clinical burden, with three fourths experiencing a KF event during follow-up
- Resource use was also high, with a third of patients having an inpatient admission and emergency room visit during the first year following the index date
- Costs to the VA were substantial, with average direct healthcare costs of $36,543 per patient during the first year following FSGS diagnosis
- This study adds to the limited research on the clinical and economic burden on patients with FSGS in the US
  - A 2021 retrospective study of FSGS patients in the US with commercial or Medicare Advantage insurance also found substantial medical costs of almost $60,000 in the year following initial FSGS diagnosis[4]
  - A 2017 study of commercially-insured patients with FSGS also found high resource burden in the year following diagnosis, including 29% of patients with emergency room visits, 21% with inpatient stays, and average total costs of almost $45,000[5]

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 the general FSGS population
- Identifying patients via diagnosis codes may mis-identify patients or omit relevant patients and cannot distinguish primary vs secondary FSGS. In particular, the change to ICD-10-CM codes in late 2015 may have impacted incidence in 2015-2020.
- The lab data is not well populated, making interpretation of disease severity challenging
- Administrative databases may be subject to data omissions or coding inaccuracies

CONCLUSIONS

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

DISCLOSURES

Mark Bensink is the managing director of BenoftConsulting, 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.

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INTRODUCTION

Background

- Focal segmental glomerulosclerosis (FSGS) is a glomerular disease characterized by proteinuria, reduced renal function, and progression to kidney failure (KF)[1]
- The incidence of FSGS in the US has been estimated at approximately 3.2 per 100,000 person-years (2004-2013)[2]
- As FSGS progresses, more widespread glomerulosclerosis occurs resulting in the loss of integrity of the glomerular filtration barrier and reduction in renal function;[1] among nephrotic patients, progression to KF typically occurs over 5-10 years[3]
- Real-world evidence on prevalence and incidence rates, patient characteristics, treatments, clinical outcomes, healthcare resource utilization (HRU), and direct healthcare costs related to FSGS is lacking

Objectives

- This retrospective observational study aimed to:
  - Describe the prevalence and incidence rates of FSGS in the Veteran's Affairs (VA) databases
  - Describe patient characteristics, treatment use, clinical burden, HRU, and costs of patients diagnosed with FSGS 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 FSGS (ICD-9-CM: 581.1, 582.1; ICD-10-CM: N03.1, N04.1, N05.1, N06.1, N07.1) 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 FSGS
- 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 FSGS 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 FSGS 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 FSGS 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
- 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)

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

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