A Retrospective Analysis of Cardiovascular Disease (CVD) Events and All-cause Mortality in Prevalent Patients with Focal Segmental Glomerulosclerosis (FSGS) in the US

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Poster #: SA-PO702

RESULTS

Baseline characteristics

- The cohort consisted of 7,974 adult patients (age ≥18 years) (Table 1)
- Mean age was 51.1 years, 43.5% were female and 60.1% Caucasian
- Median proteinuria was 2.3 g/g and evidence of nephrotic range proteinuria* was observed in 15.1% of patients
- Median estimated glomerular filtration rate (eGFR) was 33.3 mL/min/1.73 m^2 and among patients with available eGFR or CKD stage diagnosis codes, 80.2% had CKD stage 3–5

Table 1. Baseline characteristics

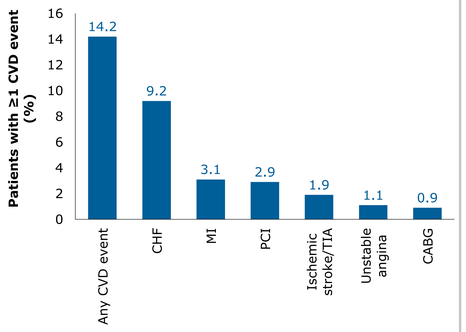
	N=7,974
Age, Mean (SD), years	51.1 (16.5)
Age, n (%)	
18–45 years	2,950 (37.0)
46–65 years	3,282 (41.2)
>65 years	1,742 (21.8)
Gender, n (%), Female	3,471 (43.5)
Ethnicity, n (%), Hispanic	683 (8.6)
Race, n (%)	
Caucasian	4,793 (60.1)
African American	2,130 (26.7)
Asian	253 (3.2)
Insurance type, n (%)	
Commercial	3,515 (44.1)
Medicare	2,719 (34.1)
Medicaid	1,312 (16.5)
Proteinuria, g/g, median (Q1,Q3)	2.3 (0.8,4.8)
Nephrotic range proteinuria,* n (%)	1,203 (15.1)
eGFR, mL/min/1.73 m^2, median (Q1,Q3)	33.3 (16.4,60.2)
CKD stage, n (%)	
Stage 1	536 (6.7)
Stage 2	744 (9.3)
Stage 3	1,887 (23.7)
Stage 4	1,340 (16.8)
Stage 5/KF	1,945 (24.4)
Unknown	1,522 (19.1)
Charlson Comorbidity Index, mean (SD)	1.7 (1.8)
Any pre-index CVD event, n (%)	239 (3.0)

*Urinary protein-creatinine ration (UP/C) >3.0 g/g or 24-hour urine protein >3.5 g/day. Denominator includes patients without proteinuria data

Post-index CVD events in the overall cohort

- Post-index CVD events were observed for 14.2% of patients in the overall cohort (N=7,974). The most common CVD events were CHF (9.2%), MI (3.1%), and PCI (2.9%) (Figure 1)

Figure 1. Patients with ≥1 CVD event in the overall cohort



Post-index CVD events by baseline proteinuria

- Elevated baseline proteinuria (≥3.5 g/g vs. >1.5–<3.5 g/g vs. ≤1.5 g/g) was associated with a significantly higher proportion of patients experiencing ≥1 CVD event. The proportion of patients experiencing individual CVD events, including MI, ischemic stroke/TIA, or CHF, were significantly higher with higher levels of baseline proteinuria (Figure 2)

Post-index CVD events by KF status

- Progression to KF was associated with a significantly higher proportion of patients experiencing ≥1 CVD event overall and all individual components within our definition (Figure 3)

Post-index all-cause mortality

- Risk of all-cause mortality was significantly higher with higher levels of baseline proteinuria (≥3.5 g/g vs. >1.5–<3.5 g/g vs. ≤1.5 g/g) or after progression to KF (Figure 4)
- Among patients who died, higher baseline proteinuria was associated with significantly shorter (p=0.001) median time to death (Figure 5)

Figure 2. Patients with ≥1 CVD event by baseline proteinuria level

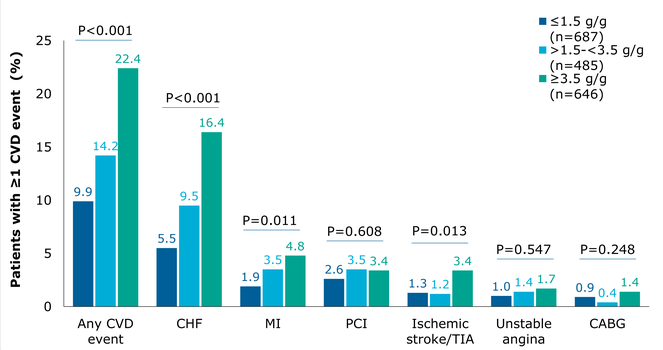
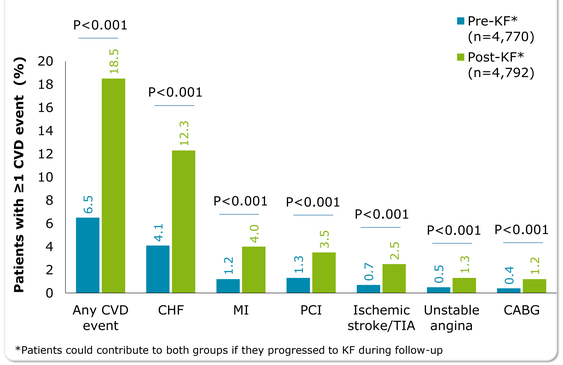
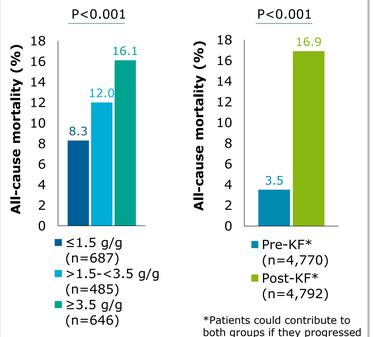


Figure 3. Patients with ≥1 CVD event by KF status



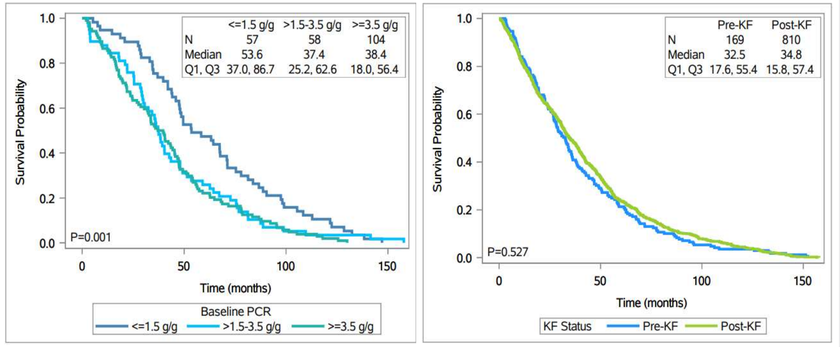
*Patients could contribute to both groups if they progressed to KF during follow-up

Figure 4. All-cause mortality



*Patients could contribute to both groups if they progressed to KF during follow-up

Figure 5. Time to all-cause mortality



INTRODUCTION

- If not controlled, FSGS-associated glomerular lesions often follow a progressive course to kidney failure (KF), and FSGS is a leading cause of glomerular KF in the US[1-3]
- Persistent podocyte injury leads to proteinuria and a progressive decline in glomerular filtration rate[3-5]
- Chronic kidney disease is known to be associated with an increased risk of CVD but there is limited direct evidence of this association in FSGS[6]

Objectives

- Estimate the rate of CVD events in patients with FSGS
- Estimate the association between baseline proteinuria (≤1.5 g/g vs >1.5-<3.5 g/g vs ≥3.5 g/g) and CVD events
- Estimate the relationship between KF and CVD events
- Estimate the relationship between baseline proteinuria or KF with all-cause mortality

METHODS

Study design and data source

- Descriptive, retrospective analysis based on Optum's de-identified Market Clarity and proprietary natural language processed (NLP) data. The Optum® de-identified Market Clarity Dataset deterministically links medical and pharmacy claims with electronic health record (EHR) data from providers across the care continuum.
- Study period: January 01, 2007 – March 31, 2021
- Identification period: July 01, 2007 – March 31, 2021 (index identification period)
- Baseline period: 6 months prior to index date
- Index date: first FSGS ICD-10 diagnosis code or NLP term within the identification period
- KF defined as: first evidence of CKD stage 5 (eGFR<15 mL/min/1.73 m^2 or ICD-10: N18.5), kidney transplant procedure, dialysis. Patients could transition from pre- to post-KF status during follow-up, upon meeting this definition

Statistical analysis

- Categorical and continuous variables were summarized using descriptive statistics. Differences between groups were assessed using Fisher's exact test (CVD event rates) or the Jonckheere-Terpstra test (time to mortality).

Inclusion criteria

- Patients with at least two NLP term entries with "focal_segmental_glomerulosclerosis" or "segmental glomerulosclerosis" AND/OR FSGS-associated ICD-10 diagnosis codes (N03.1, N04.1, N05.1, N06.1, N07.1), within 180 days at least 30 days apart
- Patients with negation terms in relation to the FSGS NLP term were excluded (negation terms: 'deny', 'failed', 'ignore', 'n/a', 'negative', 'question', 'reject', 'rule out', 'uncertain', 'unspecified')
- Age ≥18 years
- ≥6 months pre-index activity (baseline)

Exclusion criteria

- COVID-19 pre- or post-index

Outcomes

- CVD events: Hospital admission with a primary diagnosis of myocardial infarction (MI), ischemic stroke/transient ischemic attack (TIA), unstable angina, or congestive heart failure (CHF); inpatient or outpatient revascularization procedure (percutaneous coronary intervention [PCI] or coronary artery bypass graft [CABG])
- All-cause mortality: death date recorded

Methods updates since abstract submission

- Additional inpatient CVD events identified from EHR
- Historical revascularization procedures removed from event definition

DISCUSSION

- A substantial proportion of FSGS patients experienced CVD events
- Elevated proteinuria was associated with significant increases in the proportion of patients who experienced CVD events, risk of all-cause mortality and shorter time to death among those who died
- Progression to KF was also associated with significant increases in the proportion of patients who experienced CVD events and risk of all-cause mortality

Limitations

- This study was limited to patient data in Optum® Market Clarity and may not be representative of the broader US population with FSGS
- Missing data or errors in detection of FSGS-related terms and codes in patient records may introduce bias into the analyses
- Included patients with FSGS-related NLP terms may have more severe disease and bias the study results
- All events which occur post-KF may not have been captured because some patients transition from commercial to traditional Medicare coverage. This may cause underestimation of event numbers post-KF
- Time to all-cause mortality analyses are limited by the small number of events in the baseline proteinuria stratifications

CONCLUSIONS

- Higher severity of proteinuria (>1.5 g/g or >3.5 g/g) was associated with a higher risk of CVD events, a higher risk of all-cause mortality and shorter time to death among those who died
- Progression to KF was associated with a higher risk of CVD events, and a higher risk of all-cause mortality
- New therapies for FSGS that reduce proteinuria and delay progression to KF may reduce CVD events and improve overall survival
- Earlier diagnosis and treatment are key to delaying disease progression and improving outcomes

DISCLOSURES

Juan Carlos Velez received consulting fees from Travere Therapeutics, Inc.; **Kamlesh M Thakker** has a consulting contract with Travere Therapeutics, Inc. and does not have any equity interest in Travere Therapeutics, Inc.; **Mark Bensink** is the Managing Director of BenofitConsulting which received consulting fees from Travere Therapeutics, Inc.; **Edgar Lerma** received consulting fees from Travere Therapeutics, Inc.; **Richard Lieblich** received consulting fees from Travere Therapeutics, Inc.; **Martin Bunke** is a consultant for Travere Therapeutics, Inc.; **Kaijun Wang** is an employee and stockholder of Travere Therapeutics, Inc.; **David Oliveri, Andrew Rava, Diana Amari, and David Cork** are employees of Genesis Research which received compensation from Travere Therapeutics, Inc. for conducting this study

ACKNOWLEDGMENTS

This study was funded by Travere Therapeutics, Inc.

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ABBREVIATIONS

CABG, coronary artery bypass graft; CHF, congestive heart failure; CI, confidence interval; CKD, chronic kidney disease; CVD, cardiovascular disease; KF, kidney failure; eGFR, estimated glomerular filtration rate; EHR, electronic health record; FSGS, focal segmental glomerulosclerosis; MI, myocardial infarction; NLP, natural language processed; PCI, percutaneous coronary intervention; SD, standard deviation; TIA, transient ischemic attack; US, United States

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Presented at ASN Kidney Week 2022; November 03 – November 05, 2022; Orlando, Florida