Rate of Loss of eGFR and Time-Averaged Proteinuria in IgAN Patients Progressing From Early Stage Disease to Kidney Failure

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RESULTS

Patient Population

- Baseline characteristics and follow-up of the eGFR slope and TA-PU analysis populations are presented in **Table 1**

Table 1. Baseline Characteristics and Follow-Up of the eGFR and TA-PU Analysis Populations

	eGFR slope analysis population (n=184)	TA-PU analysis population (n=195)
Age, median (IQR), years	41 (32-48)	39 (29-47)
Female, n (%)	51 (28)	52 (27)
Ethnicity, n (%)		
Asian	19 (10)	21 (11)
Black, mixed, other	10 (5)	10 (5)
White	134 (73)	142 (73)
Not stated/missing	21 (11)	22 (11)
UPCR, median (IQR), g/g	1.04 (0.39-1.84)	1.11 (0.42-1.86)
eGFR, median (IQR), mL/min/1.73 m²	57 (48-69)*	59 (50-72)†

eGFR, estimated glomerular filtration rate; IQR, interquartile range; TA-PU, time-averaged proteinuria; UPCR, urine protein-creatinine ratio.
*n=158.
†n=155.

Comparison of eGFR Slopes Prior to and After Progressing Through the 45 mL/min/1.73 m² Threshold

- Mean eGFR decline was rapid and comparable in the early and late stages of CKD (ie, prior to and after patients progressed through an eGFR threshold of 45 mL/min/1.73 m²), whether unadjusted or adjusted for age and sex (**Table 2A; Figure 1**)

Comparison of TA-PU Prior to and After Progressing Through the 45 mL/min/1.73 m² Threshold

- Median TA-PU was 41% greater after patients progressed through the 45 mL/min/1.73 m² threshold than before reaching this mark (**Table 2B**)

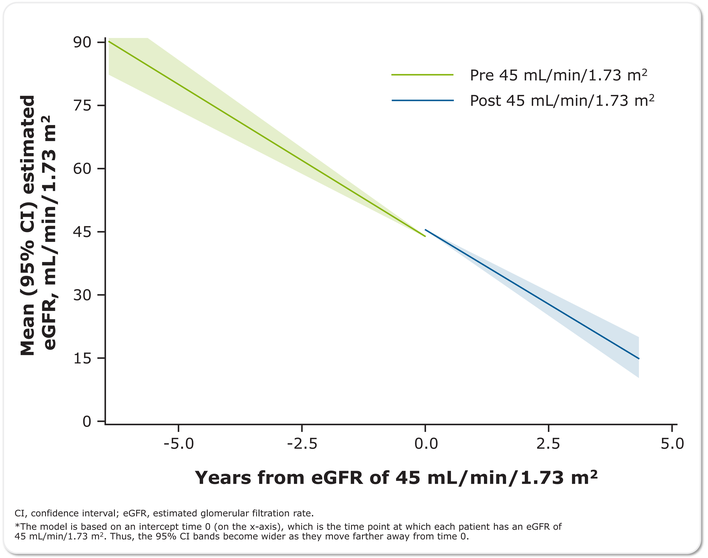
Table 2. (A) Mean Annualized eGFR Slopes and (B) Median TA-PU Prior to and After Progressing Through an eGFR Threshold of 45 mL/min/1.73 m²

A (n=184)	Early CKD stage*	Late CKD stage†	Difference (95% CI) after threshold
Mean annualized slope (95% CI)			
Unadjusted	−7.2 (−8.4 to −6.0)	−7.0 (−8.2 to −5.8)	0.13 (−0.19 to 0.45)
Age-sex adjusted	−7.2 (−8.4 to −6.0)	−7.0 (−8.2 to −5.8)	0.14 (−0.18 to 0.46)

B (n=195)	Early CKD stage*	Late CKD stage†	Difference, geometric mean (95% CI)
Median TA-PU (IQR), g/g	1.11 (0.64 to 1.89)	1.57 (0.95 to 2.67)	0.42 (0.08 to 0.76)

CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range; TA-PU, time-averaged proteinuria.
*Prior to eGFR threshold of 45 mL/min/1.73 m².
†After eGFR threshold of 45 mL/min/1.73 m².

Figure 1. Predicted Annualized eGFR Slope Prior to and After Progressing Through an eGFR Threshold of 45 mL/min/1.73 m²



CI, confidence interval; eGFR, estimated glomerular filtration rate.
*The model is based on an intercept time 0 (on the x-axis), which is the time point at which each patient has an eGFR of 45 mL/min/1.73 m². Thus, the 95% CI bands become wider as they move farther away from time 0.

Limitation

- This study population is enriched for patients with more rapid progressions by the requirement that they have eGFR data of <45 mL/min/1.73 m²

CONCLUSIONS

- Given the comparability of eGFR decline prior to and after progressing through an eGFR threshold of 45 mL/min/1.73 m², slope measurements in early disease stages may be useful in estimating future eGFR loss
- The comparability of eGFR slopes but differences in TA-PU suggest that patients with stable rates of eGFR loss experience increasing damage to the glomerular filtration barrier

DISCLOSURES

DP, FB, KO, RS, and **ANT** have nothing to disclose; **BH** and **WG** are employees and stockholders of Travere Therapeutics, Inc.; **AM, JB,** and **DPG** received consultancy fees from Travere Therapeutics, Inc.; **MAS** received consultancy fees from Travere Therapeutics, Inc., and Purespring Therapeutics.

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INTRODUCTION

- Cohort studies in immunoglobin A nephropathy (IgAN) have demonstrated the impact of time-averaged proteinuria (TA-PU) on estimated glomerular filtration rate (eGFR) decline over long-term follow-up[1,2]
- Randomized controlled trials typically measure proteinuria and eGFR over 1 to 2 years[3,4]
- However, none of these studies have compared disease progression in early vs later stages of disease

Objective

- To compare the extent of TA-PU and eGFR decline prior to and after entering chronic kidney disease (CKD) stage 3B in patients with IgAN

METHODS

Data Source

- This study used data from the UK National Registry of Rare Kidney Diseases (RaDaR)
- Since 2013, patients with biopsy-proven IgAN and eGFR of <60 mL/min/1.73 m² or proteinuria of ≥0.5 g/day at any time in their disease history have been enrolled into the RaDaR IgAN Cohort
- RaDaR contains data on patients with IgAN from 87 kidney units across the UK, with automated collection of retrospective and prospective laboratory data

Definitions and Clinical Measures

- Diagnosis was the earlier of either the primary kidney diagnosis date or the date of biopsy recorded in RaDaR
- eGFR was calculated via the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula[5] (adults) or the modified Schwartz formula[6] (pediatric)
- TA-PU was defined as the time-weighted averages for urine protein-creatinine ratio (UPCR), calculated from the area under the curve of serial measurements divided by the duration of follow-up

Eligibility Criteria

- Patients were included if they had:
  - A primary kidney diagnosis date or date of biopsy recorded in RaDaR
  - For eGFR slope analysis population, ≥3 eGFR values prior to and after the calculated date at which they progressed through an eGFR threshold of 45 mL/min/1.73 m²
  - For TA-PU analysis population, ≥2 UPCR values prior to and after the calculated date at which they progressed through an eGFR threshold of 45 mL/min/1.73 m²

Statistical Analyses

- Linear regression of eGFR values from baseline (first UPCR value ≥6 months after diagnosis) until kidney replacement therapy initiation or end of follow-up was used to define each patient's time 0 as the estimated date their eGFR progressed through the 45 mL/min/1.73 m² threshold
- Longitudinal proteinuria was assessed as TA-PU
- Differences in eGFR slope and TA-PU prior to and after time 0 were analyzed using a linear multilevel model and paired *t* test, respectively

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