The impact of relapse on long-term kidney function in ANCA-associated vasculitis

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Lisa Uchida[1], Vanja Ivkovic[2], Anna Matyjek[3], Duvuru Geetha[4], Balazs Odler[5], Carmel Hawley[6], Zachary S. Wallace[7], Carol McAlear[8], Mats Junek[9], Peter A. Merkel[8,10], Michael Walsh[9,11], David R W Jayne[1], Andreas Kronbichler[12]; on behalf of the PEXIVAS investigators

1) Department of Medicine, University of Cambridge 2) Department of Health, Medicine and Caring Sciences, Linköping University Faculty of Medicine and Health Sciences 3) Department of Biostatistics and Translational Medicine, Medical University of Lodz 4) Division of Nephrology and Division of Rheumatology, Johns Hopkins University 5) Division of Nephrology, Department of Internal Medicine, Medical University of Graz 6) The Australasian Kidney Trials Network (AKTN), University of Queensland 7) Division of Rheumatology, Allergy and Immunology; Mongan Institute, Massachusetts General Hospital, Harvard medical school 8) Division of Rheumatology, Department of Medicine, University of Pennsylvania 9) Department of Medicine, McMaster University 10) Division of Epidemiology, Department of Biostatics, Epidemiology, and Informatics, University of Pennsylvania 11) Population Health Research Institute, Hamilton Health Sciences, McMaster University 12) Department of Internal Medicine IV, Nephrology and Hypertension, Medical University of Innsbruck

Introduction

- ANCA-associated vasculitis (AAV) causes chronic and end stage kidney disease (CKD/ESKD).
- The long-term trajectory of kidney function on AAV is not well defined.
- The impact of kidney relapse on long-term trajectories of glomerular filtration rate (GFR) also remains unclear.

Objective

We evaluated long-term kidney function, and the impact of relapse on GFR trajectory, in a *post hoc* analysis of data from the PEXIVAS trial.

Methods

Study design
- *Post-hoc* analysis of the PEXIVAS trial
- Inclusion criteria: Patients with kidney involvement at baseline who achieved remission prior to 12 months and had at least two subsequent GFR assessments
- Patients who reached ESKD before month 12 and those without GFR data beyond month12 were excluded

Definitions
- Kidney relapse: the recurrence of new or worsening BVAS renal items that required a change in treatment: 'haematuria' and/or 'increase in serum creatinine' and/or 'red cell casts and/or glomerulonephritis'.

Primary Endpoints
1. GFR slope after month 12 before/after kidney relapse
2. Mean GFR after month 12, comparing the kidney relapse group and the non kidney relapse group over the observational period

Statistical methods
- **Time 0** was defined as:
  1. **For relapsers : Time of relapse**
  2. For non-relapsers: The time corresponding to the month of relapse of their matched relapsers.
- Patients were matched using propensity scores based on sex, ANCA subtype, GFR at randomisation and time of enrolment.
- GFR data was repositioned along the x-axis, with Time 0 aligned to the same time point.
- A **linear mixed-effects model** was used to estimate GFR slope, adjusting for the main effects of age, sex, ANCA subtype, GFR at randomisation, and their interactions with time.
- Mean GFR at specific time points was compared between groups by using a **generalized estimation equation.**

Results

Table 1. Baseline characteristics of AAV patients from the PEXIVAS trial with and without kidney relapse after month 12 (n=459)

	Patients without kidney relapse* (N=408)	Patients with kidney relapse* (N=51)	p-value
Age, median (IQR)	64 (56-72)	67 (56-72)	0.60
Female sex, n (%)	175 (42.9)	21 (41.2)	0.93
Baseline BVAS/GPA, median (IQR)	8 (6-11)	8 (7-10)	0.84
History of vasculitis, n (%)	36 (8.8)	4 (7.8)	1.00
ANCA serotype			0.43
Anti-PR3, n (%)	172 (42.2)	25 (49.0)	
Anti-MPO, n (%)	236 (57.8)	26 (51.0)	
Comorbidities			
Hypertension, n (%)	198 (48.5)	21 (41.2)	0.40
Diabetes, n (%)	53 (13.0)	2 (3.9)	0.10
Pulmonary haemorrhage			0.46
Not severe, n (%)	77 (18.9)	6 (11.8)	
Severe, n (%)	30 (7.4)	4 (7.8)	
Dialysis, n (%)	40 (9.8)	5 (9.8)	1.00
PLEX regimen			0.68
PLEX, n (%)	209 (51.2)	24 (47.1)	
No PLEX, n (%)	199 (48.8)	27 (52.9)	
Glucocorticoid dose regimen			0.44
Standard, n (%)	196 (48.0)	28 (54.9)	
Reduced, n (%)	212 (52.0)	23 (45.1)	
Planned immunosuppressive therapy			0.53
Intravenous cyclophosphamide, n (%)	194 (47.5)	28 (54.9)	
Oral cyclophosphamide, n (%)	152 (37.3)	15 (29.4)	
Rituximab, n (%)	62 (15.2)	8 (15.7)	
Laboratory results			
Creatinine at randomization, µmol/L median (IQR)	286 (190-415)	270 (182-426)	0.75
Creatinine ≥500 µmol/L or on dialysis, n (%)	72 (17.6)	10 (19.6)	0.88
eGFR at randomization, ml/min/1.73 m2 median (IQR)	17.2 (11.3-29.6)	19.2 (11.0-30.1)	0.76
eGFR at month 12, ml/min/1.73 m2 median (IQR)	41.3 (28.4-58.3)	42.7 (30.8-62.6)	0.37

Values are reported as number (percentage) or median (interquartile range).
*Six patients (11.8%) in the kidney relapse group and 20 patients (4.9%) in the non-kidney relapse group had a kidney relapse before month 12.

Baseline characteristics were similar between patients with and without kidney relapse, including GFR at 12 months.

Primary outcome 1

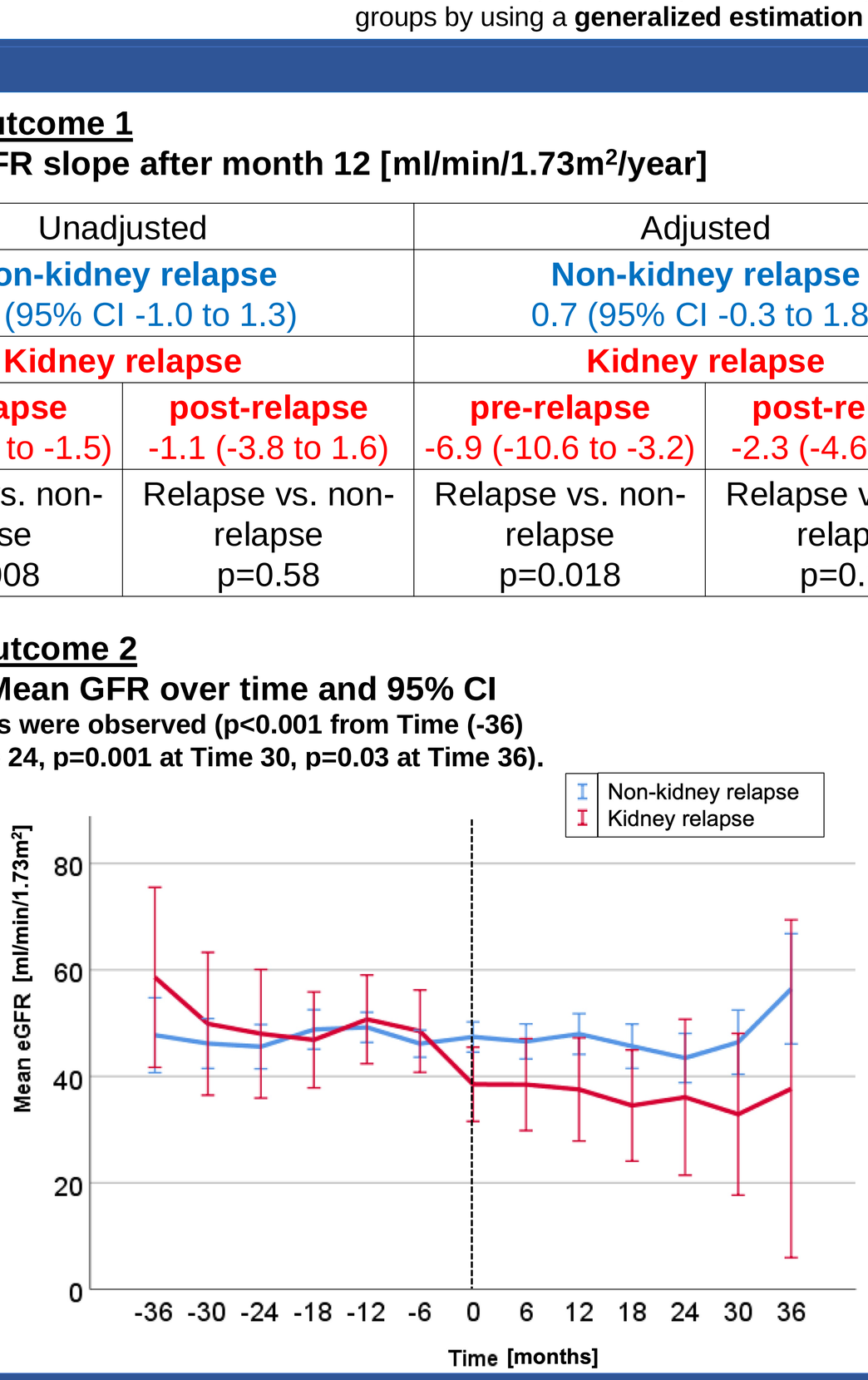
Table 2. GFR slope after month 12 [ml/min/1.73m^2/year]

Unadjusted		Adjusted	
Non-kidney relapse 0.2 (95% CI -1.0 to 1.3)		**Non-kidney relapse** 0.7 (95% CI -0.3 to 1.8)	
Kidney relapse		**Kidney relapse**	
pre-relapse -5.9 (-10.2 to -1.5)	**post-relapse** -1.1 (-3.8 to 1.6)	**pre-relapse** -6.9 (-10.6 to -3.2)	**post-relapse** -2.3 (-4.6 to 0.1)
Relapse vs. non-relapse P=0.008	Relapse vs. non-relapse p=0.58	Relapse vs. non-relapse p=0.018	Relapse vs. non-relapse p=0.10

Primary outcome 2

Figure 1. Mean GFR over time and 95% CI

Differences were observed (p<0.001 from Time (-36) up to Time 24, p=0.001 at Time 30, p=0.03 at Time 36).



Conclusion

- Kidney relapse in AAV occurring after 12 months of treatment initiation was associated with a marked decline in GFR prior to relapse, which persisted at a slower rate post-relapse. In contrast, patients without relapse demonstrated stable GFR trajectories over time. (**Figure 1, Table 2**)
- The GFR slope differed between relapse and non-relapse groups during the pre-T0 period (p=0.018). (**Table 2**)
- The underlying reasons for the preceding decline in GFR prior to relapse remains unclear, although this may indicate persisting vasculitis activity and delayed relapse diagnosis.
- Early identification and treatment of kidney relapse in AAV may improve long-term kidney function.

References:
Walsh M, et al; PEXIVAS Investigators. Plasma Exchange and Glucocorticoids in Severe ANCA-Associated Vasculitis. *N Engl J Med*. 2020 Feb 13;382(7):622-631.

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Contact: lrk33@cam.ac.uk