Response to: Correspondence on 'Call for action in ANCA-associated vasculitis and lupus nephritis: promises and challenges of SGLT-2 inhibitors' by Säemann and Kronbichler

We thank our colleague Dr Patoulias[1] for pointing out that sodium glucose transporter (SGLT)-2 inhibition (SGLT-2i) could mediate nephroprotection in patients with lupus nephritis (LN) and ANCA-associated vasculitis (AAV) via specific mechanisms within the tubular cell compartment independent of the presence of diabetes mellitus.[2] As discussed by Dr Patoulias, kidney injury molecule-1 (KIM-1) is affected by SGLT-2i correlating with improvements in albuminuria, a hallmark of chronic kidney damage. KIM-1, however, is not only a mere marker of tubular injury, but it is actively involved in diverse pathogenic actions. Hence, its expression, for example, in diabetic kidney disease accelerates kidney injury via fatty acid uptake coupled with tubular glucose reabsorption in renal proximal tubular cells, resulting in various detrimental stress responses.[3] Upregulation of KIM-1 and the ensuing tubular cell responses illustrate the close relationship between diseased glomeruli and subsequent tubulointerstitial fibrosis in response to increased tubular workload, thereby diseases traditionally considered primarily of glomerular origin such as diabetic kidney disease, and also inflammatory diseases such as LN and AAV, illustrate the therapeutic potential of innovative therapies such as SGLT-2i by limiting permanent and progressive damage especially to the tubulointerstitial tissue. The concept of nephron overload has been very recently proposed to be the final result of various and diverse pathogenic insults in most forms of chronic kidney disease.[4] Since SGLT-2i substantially reduce tubular workload, they belong to the most efficient therapeutic interventions impacting nephron overload, suggesting also significant nephroprotective effects in LN and AAV.

Marcus Säemann [1,2] **Andreas Kronbichler** [3]

[1]6th Medical Department, Nephrology and Dialysis, Clinic Ottakring, Vienna, Austria
[2]Medical School, Sigmund Freud University, Vienna, Austria
[3]Department of Medicine, University of Cambridge, Cambridge, UK

Correspondence to Dr Marcus Säemann, 6th Medical Department, Nephrology and Dialysis, Clinic Ottakring, VIENNA, Austria; SAEMANNMARCUS@GMAIL.COM

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ORCID iDs
Marcus Säemann http://orcid.org/0000-0003-2316-449X
Andreas Kronbichler http://orcid.org/0000-0002-2945-2946

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