Introduction and Aims: Calciphylaxis or calcific uremic arteriolopathy (CUA), is a rare, but potentially life-threatening syndrome characterized by progressive and painful skin ulcerations associated with media calcification of medium-size and small cutaneous arterial vessels. Calciphylaxis primarily affects patients on dialysis or after renal transplantation. Clinical manifestation of calciphylaxis is associated with high mortality, superinfection of necrotic skin lesions with subsequent sepsis significantly contributing to this poor outcome. The aim of our observational cross-sectional study was to identify genetic risk factors of CUA.

Methods: In a candidate gene approach we looked at genes associated with arterial calcification and CKD-MBD in 372 end-stage kidney disease patients without a history of CUA (control group) and 161 CUA patients from the German calciphylaxis register. We used a tagging SNP approach for the following genes analyzed: CaSR, FGF23, KL, VDR, STC1, Nt5E, MGP, AHSG, BGLAP and VKORC1.

Results: In a preliminary analysis the SNP rs9527033 within an intron of the Klotho (KL) gene was found to be significantly associated with CUA (p<10^{-5}).

Conclusions: Our Caucasian CUA cohort is the largest one ever studied for genetic risk factors of this syndrome. The identification of an association between rs9527033 and CUA supports an early intervention in patient sub-groups identified to be at high risk, and it will prompt further studies on the pathomechanisms of CUA.