TK1

Detection of GATA3 Copy Number Variants Using Bespoke Read-Depth Analysis in the Genomics England 100,000 Genomes Cohort

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TUESDAY - Moderated Poster Session, HALL Q, March 10, 2026, 16:00 - 17:00

Introduction: Mutations in GATA3 are associated with hypoparathyroidism, sensorineural deafness, and renal dysplasia (HDR syndrome). While single nucleotide variants are well recognized, larger copy number variants (CNVs) may be underdetected by standard variant calling approaches.

Methods: We interrogated the Genomics England 100,000 Genomes Project dataset to identify structural variants affecting GATA3. A bespoke read-depth analysis tool was applied to whole genome sequencing data, with candidate CNVs visualised in the Integrative Genomics Viewer (IGV) and validated by read-depth plotting. Clinical features were reviewed from patient records.
Results: We identified a patient with a heterozygous read-depth loss spanning the GATA3 locus. This CNV was confirmed using IGV inspection and quantitative read-depth profiling. Clinically, the patient exhibited cystic kidney disease, sensorineural deafness, and disturbances of calcium homeostasis—consistent with HDR syndrome but with an atypical renal presentation. There was a positive family history of chronic kidney disease and hypoparathyroidism

Discussion: Our findings demonstrate that GATA3 mutations present with a wide spectrum of renal phenotypes, including cystic kidney disease. Importantly, CNV losses across GATA3 represent a rare cause of HDR syndrome that may be easily missed using routine genomic pipelines. Incorporation of tailored read-depth analysis into diagnostic workflows could improve detection of these clinically relevant variants.

TK2

Ravulizumab in atypical haemolytic uremic syndrome: time-to-treatment analysis from a phase 3 trial

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TUESDAY - Moderated Poster Session, HALL Q, March 10, 2026, 16:00 - 17:00

Introduction: Atypical hemolytic uremic syndrome (aHUS) is a rare thrombotic microangiopathy (TMA) caused by complement dysregulation. Previous studies have demonstrated that earlier diagnosis and treatment initiation lead to better outcomes. There is limited data demonstrating this with ravulizumab, a complement C5 inhibitor (C5i) approved for the treatment of aHUS.

Methods: This analysis reports data from the 4.5-year extension period of a phase 3, single-arm clinical trial of C5i-naive adult patients with aHUS (NCT02949128). Patients received body-weight–based intravenous ravulizumab every 4–8 weeks. The primary endpoint was complete TMA response at Week 26. A time-to-treatment post hoc analysis was performed and grouped by ≤7 days or >7 days from time of first aHUS symptom to initiating ravulizumab.

Results: Overall, 56 patients were analyzed: 24 in the ≤7 days group and 32 in the >7 days group. There were no substantial differences between the groups according to age at first infusion and sex. Complete TMA response was observed in the ≤7 days group in 16/24 patients (67%) at Week 26 and 18/24 (75%) by end of study; in the >7 days group in 14/32 patients (44%) at Week 26 and 18/32 (56%) by end of study. Mean change in estimated glomerular filtration rate (eGFR) from baseline was higher for patients in the ≤7 days group than in the >7 days group (Figure). In the ≤7 days group, 15/24 patients (63%) were on dialysis at baseline and 4/22 (18%) at Week 26; in the >7 days group, 14/32 patients (44%) were on dialysis at baseline and 8/27 (30%) at Week 26.

Conclusions: Earlier ravulizumab initiation led to improved outcomes, including reduced dialysis requirements, which demonstrates the importance of rapid diagnosis and treatment of patients with aHUS.

TK3

Harmonizing Predictive Metrics: Evaluating the Clinical Birmingham Vasculitis Activity Score (BVAS) in Predicting Outcomes of ANCA-Associated Vasculitis (AAV)

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TUESDAY - Moderated Poster Session, HALL Q, March 10, 2026, 16:00 - 17:00

Background:
Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) encompasses a group of severe autoimmune disorders characterised by necrotising granulomatous inflammation of small blood vessels, frequently involving the kidneys. Renal involvement is present in over 75% of patients and is strongly associated with long-term morbidity, end-stage renal disease (ESRD), and mortality. Accurate assessment of vasculitic activity at presentation is essential to guide treatment and predict outcomes. The Birmingham Vasculitis Activity Score (BVAS-3) is widely used for quantifying disease activity in AAV, and while its prognostic role in short-term outcomes is recognized, its value in predicting long-term renal and survival outcomes remains uncertain. We hypothesised that higher BVAS scores at presentation would independently predict ESRD, relapse, and mortality in AAV patients with renal involvement.

Methods:
We conducted a retrospective longitudinal study of 75 biopsy-confirmed AAV patients diagnosed between 2010 and 2022. Patients fulfilled the Chapel Hill Consensus Conference (CHCC2012) classification for granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA), or renal-limited vasculitis (RLV). Clinical parameters at presentation, including ANCA serology (PR3/MPO), serum creatinine, estimated glomerular filtration rate (eGFR), urine protein:creatinine ratio (UPCR), haemoglobin levels, and systemic manifestations from clinical letters were recorded. BVAS-3 was retrospectively calculated from clinical documentation. Induction and maintenance therapies, including glucocorticoids, cyclophosphamide, rituximab, and azathioprine, were documented. The outcomes assessed were ESRD, relapse, and mortality. Statistical analyses included independent samples t-tests and binary logistic regression to evaluate the predictive capacity of BVAS.

Results:
The cohort had a mean age of 66.2 years, with 56% male patients. PR3-ANCA positivity was identified in 41.3%, while 58.7% were MPO-ANCA positive. Subtype distribution included GPA (46.7%), MPA (45.3%), EGPA (2.7%), and RLV (5.3%). Mean BVAS at diagnosis was 17.9, with GPA patients demonstrating the highest mean score (19.7). At presentation, advanced renal impairment was common, reflected by mean eGFR <30 mL/min/1.73m², high UPCR, and significant proteinuria and haematuria. Over the follow-up period, 29.3% developed ESRD, 21.3% experienced relapse, and 38.7% died, with infection and malignancy as leading causes of mortality. Despite the appearance of higher mean BVAS scores observed in patients who developed adverse outcomes, neither t-tests nor logistic regression

demonstrated statistically significant associations between BVAS and ESRD (OR=1.024, p=0.620), relapse (OR=1.063, p=0.208), or mortality (OR=1.032, p=0.463).

Conclusion:
Our findings suggest that while BVAS is a valuable tool for assessing disease activity at presentation, its prognostic value for long-term renal and survival outcomes in AAV with renal involvement appears limited when considered in isolation. The absence of a significant association highlights the heterogeneity of AAV and the influence of other factors, including immunosuppressive regimens, comorbidities, and additional biochemical markers, on patient trajectories. Future multicentre studies with larger cohorts are required to confirm these findings and explore integrated prognostic models combining BVAS with emerging biomarkers such as urine immunoglobulin excretion or neutrophil-to-lymphocyte ratio. Developing multivariable indices may enable more precise risk stratification and improve clinical decision-making for patients with AAV.

Keywords: ANCA, BVAS, vasculitis, end-stage renal disease, relapse, mortality

TK4

One Drug, Multiple Approaches: A Multiple Case Study Exploring Variation in Tolvaptan Prescribing Across UK Kidney Units

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TUESDAY - Moderated Poster Session, HALL Q, March 10, 2026, 16:00 - 17:00

Introduction:
Tolvaptan is the only approved disease-modifying treatment for ADPKD, slowing disease progression but requiring lifestyle adaptations for aquaretic effects and intensive monitoring. Despite national guidance, prescribing rates vary across UK kidney units, raising concerns about equitable access and appropriate use. Understanding the factors driving this variation could support strategies for more consistent, evidence-based care.

Methods:
A multiple case study was conducted across three kidney units, purposively selected based on tolvaptan use in eligible and ineligible individuals. Between December 2024 and August 2025, data were collected through semi-structured interviews, clinic observations and review of local documents. Data were analysed thematically using a structured framework, with iterative coding and cross-case comparison.

Results:
Four interrelated themes were identified across the cases, capturing the factors associated with variation in tolvaptan prescribing.

Clinic structures and patient pathways: One unit delivered all ADPKD care through a dedicated service overseeing all patients. In the other two units, some or all patients were managed in general nephrology clinics and required referrals to access tolvaptan. General nephrologists reported limited experience with tolvaptan, which was not always “top-of-mind”, creating uncertainty about whether all eligible patients were identified. Although numbers on tolvaptan were comparable across sites, limited capacity at one unit caused months-long delays for some patients. Different staff compositions were thought to shape eligibility assessment and prescribing rates. Clinic structures were developed iteratively based on tolvaptan trial participation, geography, GIRFT feedback, and available staff.

Informal networks: Peer-to-peer learning, particularly early in service development, was considered important. Informal discussions with other units via email or messaging apps, and interactions at manufacturer-led events were more valued than formal training. Not all units had access to these networks. It is possible that limited access to these networks contributed to differences in service development and prescribing across units.

Eligibility criteria and guidelines: All sites referenced the UKKA commentary as the primary source of guidance, but eligibility criteria used varied. Decline in eGFR was the most consistently used, but the use of genomic testing and imaging criteria varied depending on

local resources and practice norms. Units also drew on supplementary resources, including individual reference documents, local protocols, guidance from other units and experience gained during tolvaptan clinical trials.

Patient information and counselling: One unit provided the manufacturer's patient information leaflet, while the other two considered it potentially fear-inducing and provided self-developed materials. Clinicians' perceptions of tolvaptan's efficacy, alongside it being the only disease-modifying therapy available, shaped the extent of advocacy and how information was presented. Prescribing approaches ranged from proactive "give it a go" approaches to more conservative models guided by clinicians' judgements of likely tolerance.

Discussion:
Variation in tolvaptan prescribing across UK kidney units reflects local structures, staff capacity, informal networks and access to expertise. Differences in eligibility criteria used, patient information and clinician judgement influences therapy initiation and likelihood of patient acceptance. Mechanisms for shared learning, standardised approaches or automated eligibility assessment may reduce unnecessary variation. Insights from this study may inform the implementation of therapies in other rare or single-disease contexts.

TK5

Real-World Outcomes of Patients with Monoclonal Gammopathy of Renal Significance

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TUESDAY - Moderated Poster Session, HALL Q, March 10, 2026, 16:00 - 17:00

Background: Monoclonal Gammopathy of Renal Significance (MGRS) comprises rare renal disorders caused by monoclonal immunoglobulins from non-malignant B-cell or plasma cell clones. Subtypes include amyloid (MGRS-A) and non-amyloid (MGRS-NA), such as light chain deposition disease and MGUS-associated nephropathy. Clinical presentation is variable and often occurs without overt haematological malignancy, necessitating high suspicion. Renal outcomes are poorly characterised, with many patients progressing to end-stage kidney disease (ESKD). Diagnosis typically follows renal biopsy for proteinuria, haematuria, or unexplained renal decline. Treatment, led by haematologists, targets the underlying clone, but real-world data are needed to define trajectories and subgroup-specific outcomes.

Methods: This retrospective single-centre evaluation included 17 patients with biopsy-proven MGRS (10 MGRS-A, 7 MGRS-NA) managed between January 2022 and October 2024. Patients with multiple myeloma or other B-cell malignancies were excluded. Data were extracted from electronic records, including demographics, renal parameters (eGFR, proteinuria), haematologic markers (paraprotein, free light chains, kappa/lambda ratio), treatments, toxicities, and survival. Assessments occurred at key clinical milestones: first renal decline, pre-treatment, on-treatment, post-treatment, and last follow-up. Renal response was defined as ≥25% eGFR improvement; haematologic response followed IMWG criteria (≥VGPR: >90% paraprotein reduction or immunofixation-only). Longitudinal eGFR trajectories were modelled using age-adjusted linear mixed-effects regression, with subgroup and interaction terms plus random patient intercepts. Survival and time-to-event outcomes were analysed with Kaplan-Meier curves and log-rank testing. Univariate associations used Mann-Whitney U tests. Analyses were performed in R (v4.3.1), with $p<0.05$ considered significant.

Results: Median age was 65 years (MGRS-A) and 62 years (MGRS-NA); MGRS-NA showed worse function (18.0 vs median eGFR 49.0 in MGRS-A, $p<0.05$). Care intervals included 1.1 months to renal review, 1.6 to biopsy, 4.1 to haematology consultation. Once patients were under haematology care, the initiation of treatment was at a median of 1.0 month. Most patients (88.2%) received bortezomib-based chemotherapy (median 4 cycles); toxicities affected 94.1% (fatigue 23.5%, renal decline 17.6%, neuropathy 17.6%). Hematologic ≥VGPR: 57.1% MGRS-NA, 50% MGRS-A. Longitudinal modelling revealed a significant 'time' & 'subgroup' interaction ($p<0.01$), with steeper decline in eGFR in MGRS-NA (last follow-up eGFR: 9.0 vs. 42.0 mL/min in MGRS-NA). Median time to dialysis was 29.35 months in MGRS-NA vs. none reaching ESKD in MGRS-A ($p<0.01$). Haematologic responses ≥VGPR occurred in 4/7 (57.1%) MGRS-NA and 5/10 (50.0%) MGRS-A. Renal response, defined as

≥25% eGFR increase, occurred in 3/17 (17.6%) overall but all within the MGRS-A subgroup (3/10, 30.0%) and in none of the MGRS-NA subgroup (0/7, Fisher's exact p=0.23). Higher creatinine predicted poorer renal response (p<0.05); in MGRS-NA, lower eGFR was linked to death (p<0.05), higher eGFR to hematologic response (p<0.05). Relapse occurred in 8/17 (47.1%). The median time to relapse was 51 months for MGRS-NA versus 69 months for MGRS-A (p=0.25).

Conclusions: In routine practice, MGRS-NA exhibits accelerated renal decline and earlier dialysis despite comparable patient survival to MGRS-A. Haematologic responses do not reliably translate into renal recovery. Preservation of kidney function may therefore be a more realistic goal. These data support early recognition, expedited biopsy, and an integrated renal-haematology service to reduce irreversible renal injury and optimise outcomes.

TK6

Autosomal dominant tubulointerstitial kidney disease (ADTKD) due to a pathogenic GATA3 variant: a case report

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TUESDAY - Moderated Poster Session, HALL Q, March 10, 2026, 16:00 - 17:00

Introduction

Autosomal dominant tubulointerstitial kidney disease (ADTKD) is a rare genetic disorder most frequently caused by mutations in UMOD, MUC1, REN or HNF1B. However, increasing use of genomic testing is expanding the spectrum of causal genes. Variants in GATA3 are classically associated with HDR syndrome (hypoparathyroidism, deafness, renal dysplasia), but no reports of GATA3-associated ADTKD exist to our knowledge. We present a case of a 59-year-old man with progressive chronic kidney disease, bland urine sediment, normal kidneys, deafness, and gout who was found to have a pathogenic GATA3 variant.

Methods

Clinical data were obtained from patient records, family history, and laboratory investigations. Genetic analysis included a tubulointerstitial kidney disease panel (R202, PanelApp v1.3), targeted MUC1 VNTR sequencing, and whole genome sequencing (R257, PanelApp v12.12) with variant confirmation.

Results

The patient developed gout at age 35 and progressive bilateral deafness in early adulthood. He presented with chronic kidney disease (CKD 3b, eGFR 35 ml/min/1.73m²), hypertension and bland urinary sediment. Renal ultrasound and CT showed two structurally normal kidneys. Biochemistry showed normal calcium and low-normal parathyroid hormone (2.4 pmol/L), without features of salt-wasting. Genetic testing identified a heterozygous GATA3 c.896G>A, p.(Arg299Gln) variant, classified as pathogenic. The tubulointerstitial kidney disease gene panel and MUC1 testing were negative.

Family history revealed multiple affected relatives: the patient's mother died with end-stage kidney disease in her late 50s and had gout; one brother died in his 60s with kidney failure and stones; another brother and a sister developed gout and CKD in midlife. A strong history of early-onset deafness was reported across the family.

Discussion

This case expands the phenotypic spectrum of ADTKD to include pathogenic GATA3 variants. Unlike classical HDR syndrome, this patient had normal calcium, no clinical hypoparathyroidism, no proteinuria and no renal dysplasia. However, exhibited bland urine, normal kidneys, gout, and progressive CKD consistent with ADTKD but with a strong personal and family history of adolescent-onset deafness. The strong family history of kidney disease and deafness supports autosomal dominant inheritance. Recognition of GATA3 as a rare cause of ADTKD has important implications for diagnosis, counselling, and family screening. Broader use of genomic testing in CKDx may uncover additional atypical presentations of GATA3-associated disease, revealing further genetic heterogeneity of ADTKD. We suggest that GATA3 should be considered in the differential diagnosis of ADTKD, even in the absence of hypoparathyroidism or renal dysplasia. Incorporating broad genomic

testing into CKDx and ADTKD pathways will help identify atypical genetic causes and refine counselling for affected families.

TK7

When the graft carries a hidden disease: donor-derived polycystic kidney disease in a kidney transplant

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TUESDAY - Moderated Poster Session, HALL Q, March 10, 2026, 16:00 - 17:00

Introduction

Kidney transplantation remains the optimal treatment for kidney failure, but donor organs occasionally harbour unrecognised disease. Autosomal dominant polycystic kidney disease (ADPKD) affects approximately 1 in 1,000 individuals in the UK and is the most common inherited cause of kidney failure. Intracranial aneurysms occur in 8–12% of ADPKD patients, compared with ~2% in the general population, and account for up to 22% in those with a family history. Subarachnoid haemorrhage (SAH) is therefore disproportionately common in ADPKD and may be the sentinel event revealing disease. Current UK donor characterisation requires structured history, GP records, family interview, laboratory investigations and imaging, but inherited renal disease is not systematically excluded or considered when SAH is the cause of death.

Methods

We reviewed the clinical course of a transplant recipient whose deceased donor kidney was subsequently found to harbour polycystic kidney disease (PKD). Data were collected from clinical records, laboratory investigations, imaging and follow-up over 15 years. Findings were considered in the context of epidemiological data on PKD prevalence, aneurysm risk and current NHS Blood and Transplant donor characterisation standards.

Results

The recipient was transplanted in 2009 from a young adult donor who died suddenly of SAH, with no suspicion of inherited disease at retrieval. The graft functioned well initially, with serum creatinine 58 µmol/L at implantation. From 2021 onwards, progressive decline in kidney function was observed, with eGFR falling by ~5 ml/min/1.73m² per year and rising albuminuria (albumin:creatinine ratio 51 to 176 mg/mmol). Ultrasound demonstrated multiple cortical cysts typical of ADPKD. No viral reactivation, rejection, or donor-specific antibodies were identified. The patient developed progressive graft dysfunction consistent with donor-derived polycystic kidney disease.

Discussion

This case provides evidence of probable ADPKD transmission via kidney transplantation, leading to progressive graft failure. It highlights SAH in young donors as a clinical red flag for inherited renal disease, warranting systematic assessment. Incorporating targeted family history could prevent transmission of unrecognised ADPKD. In the future, artificial intelligence tools to predict donor organ quality and rapid molecular diagnostics may further mitigate risk. Balancing these safeguards with ongoing organ shortage will require nuanced risk–benefit conversations, particularly for younger recipients. Ensuring public trust in organ allocation demands transparent recognition and minimisation of donor-derived disease risk.

TK8

Efficacy of Tolvaptan in the treatment of Autosomal Dominant Polycystic Kidney disease in maintaining residual renal funtion– a single centre experience

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TUESDAY - Moderated Poster Session, HALL Q, March 10, 2026, 16:00 - 17:00

Introduction

Polycystic kidney disease (PKD) causes an irreversible decline in kidney function, with the majority of patients requiring renal replacement therapy during their lifetime [1]. The most common form of PKD is autosomal dominant polycystic kidney disease [ADPKD], which is also the most common genetic cause of chronic kidney disease [CKD].

In the TEMPO trial, Tolvaptan slowed the annual rate of kidney growth (Total kidney volume (TKV)) and reduced the rate of decline of kidney function [2]. Following this, the REPRISE trial also showed a slower decline in eGFR versus placebo in ADPKD with later stage disease [3].

NICE therefore recommends Tolvaptan for patients who have stage 2 or 3 kidney disease with evidence of rapid disease progression [4].

This project is aimed at evaluating the efficacy of tolvaptan in a single nephrology department to assess whether the benefits of tolvaptan, which had been identified in the previously published literature [2, 3], were reproduced in our patient population and assess whether tolvaptan can delay progression and maintain residual renal function in our ADPKD population.

Method

We identified all patients with a diagnosis of ADPKD that had been treated with tolvaptan in a tertiary centre ADPKD clinic. Baseline characteristics were identified. A total of 81 patients were started on Tolvaptan over the last 9 years. 35 patients had Tolvaptan discontinued due to either side effects, intolerance or worsening renal function. 3 patients moved to different health boards and 2 patients sadly died. Currently 41 patients continue on Tolvapan therapy. Among them, 37 patients that had been on tolvaptan for over 6 months were included for efficacy analysis.

Data was collected from the ADPKD clinic database, clinic attendances and letters, blood results and imaging reports. Data was collected at onset of therapy then at 12 monthly intervals from the following January accepting results within 3 months either side of the follow-up interval. Most up-to-date results were also collected.

Results

Of the 37 patients who have been on Tolvaptan for over 6 months, commenced over the last 9 years, mean age is 53.8 years old with M : F – 17 : 20.

Baseline eGFR prior to commencing tolvaptan ranged from 26 - >90 ml/min/1.73m2 (mean 52.4).

Time of therapy ranged from 6months to 9 years with a mean treatment time of 4.2 years.

Average change in eGFR per year ranged from -24ml/min/1.73m2/year to +4 ml/min/1.73m2/year with a median change of -1.7 ml/min/1.73m2/year

Discussion

In this small study looking at the efficacy of tolvaptan in patients with ADPKD, tolvaptan was tolerated well by the majority of patients. 15 patients discontinued treatment due to symptoms associated with tolvaptan including increased thirst and frequency of micturition. 5 patients stopped due to a drop in eGFR and 3 for a rise in eGFR >90. 3 patients were stopped due to non adherence with clinic review/monitoring.

ADPKD is often associated with progression of CKD and decline in kidney function. This is a retrospective study analyzing patient kidney function at the time of study irrespective of their duration on tolvaptan or the dose of tolvaptan. The study shows a slowing of decline in kidney function with a median decline in eGFR of -1.7ml/min/1.73m2 per year.

This study, however, does not look at other parameters including the slowing of the increase in TKV, which may be associated with slowing of kidney function decline.

Conclusion

Our study suggests of those who have tolerated Tolvaptan, there is evidence of benefit with stabilisation and slower rate of progression. The slowing of kidney function decline reflects that of the TEMPO study, albeit at much smaller sample size.

We plan to analyse our data further by plotting eGFR trends pre and during therapy to predict time to RRT and ascertain Tolvaptan's impact on this.

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TK9

Anti-GBM Disease Post-Transplant in Alport Syndrome: Historical Concern or Ongoing Clinical Risk?

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TUESDAY - Moderated Poster Session, HALL Q, March 10, 2026, 16:00 - 17:00

Introduction

Anti–glomerular basement membrane (anti-GBM) disease following renal transplantation in patients with Alport syndrome is a well-recognised phenomenon, historically reported in approximately 3% of cases. It typically occurs in the first year post-transplant, and can result in a rapid, irreversible decline in graft function over weeks to months. The condition arises because the transplanted kidney expresses collagen IV epitopes not previously encountered by the recipient's immune system. With the advent of modern immunosuppressive regimens, it remains uncertain whether this clinical entity continues to occur, and whether clinicians should remain vigilant to this theoretical risk.

Methods

We reviewed the case notes of 16 patients with Alport syndrome (11 male) who underwent renal transplantation over the past 30 years at the Freeman Hospital, a regional tertiary centre. Two male patients received two renal allografts. Clinical, serological, and histological data were examined, with particular attention to evidence of anti-GBM disease.

Results

No cases of overt anti-GBM disease were identified. Specifically, no patients demonstrated elevated anti-GBM titres or biopsy evidence of linear IgG and C3 deposition along the GBM in the transplanted kidney. Several episodes of rejection were documented, but none were attributable to anti-GBM disease. The median graft survival time was 15 years with a range of 3 to 37 years. Molecular genentic diagnoses included COL4A3, COL4A4 and COL4A5 variants but no large gene deletions.

Conclusions

Although renal transplantation in Alport syndrome carries a theoretical risk of anti-GBM disease, this was not observed in our cohort. This risk may depend on the underlying genetic variation. For example, it has been noted that those with X-linked Alport carrying a truncating variant in COL4A5 or a large deletion have been overrepresented in previous case series. Furthermore, anti-GBM antibody assays may be misleading in this setting due to reduced sensitivity and specificity. This may be because post-transplant alloantibodies in Alport patient's often target a different collagen IV epitope to autoantibodies seen in Goodpasture's syndrome. Histological confirmation thus remains the diagnostic gold standard. Our findings suggest that anti-GBM disease may represent a largely historical complication in the era of modern immunosuppression, though clinical vigilance should be maintained.

TK10

Onto Newer (Good)pastures: A Review of Anti-GBM Disease Post-Renal Transplant in Alport Syndrome Patients

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TUESDAY - Moderated Poster Session, HALL Q, March 10, 2026, 16:00 - 17:00

Introduction
Alport syndrome (AS) is a hereditary condition characterised by progressive chronic kidney disease leading to kidney failure, sensorineural hearing loss and eye abnormalities. AS patients have reduced or no expression of the α3α4α5 triple helix, a major component of the kidney glomerular basement membrane (GBM), due to pathogenic variants in COL4A3, COL4A4 and COL4A5 genes. Post-transplant anti-GBM disease is an immune phenomenon which continues to be seen in Alport's patients, and is immunologically distinct from 'traditional' Goodpasture's disease.

Methods
A literature search was conducted using PubMed followed by thorough examination of published case reports and case series on this immune phenomenon.

Results
The pathophysiology of anti-GBM disease post-renal transplant follows that of any non-tolerised antigen presented to the immune system. The donor kidney expresses normal α3α4α5(IV) in the GBM, which leads to an alloimmune reaction in the AS recipient on transplantation. There is activation of GBM-specific B cells in the recipient producing highly specific anti-GBM antibodies against the donor graft, targeting the non-collagenous domains of type IV collagen. These alloantibodies can initiate a highly destructive complement cascade, leading to an aggressive and rapidly crescentic anti-GBM glomerulonephritis and acute rejection of the donor kidney. If patients with AS undergo re-transplantation, with their first graft rejected due to post-transplant anti-GBM disease, we see an accelerated and often more aggressive rejection of the second renal transplant. Post-transplant anti-GBM disease is reported in the literature to affect only a small proportion of patients with AS, with up to 5% as the most widely quoted figure. Interestingly, anti-GBM disease can also be an isolated 'immunological' disease, without the patient ever developing clinical nephritis. The fact that alloantibody production in AS does not invariably culminate in post-transplant anti-GBM nephritis mirrors a wider phenomenon in glomerular disease.

The target alloantigen within the GBM that mediates post-transplant anti-GBM disease in AS patients is a subject of debate, varying between publications and subtypes of AS (based on genetic inheritance). The target alloantigen is thought by some to be α3(IV) in both X-linked and autosomal recessive AS but most identify the culprit alloantigen in X-linked AS as α5(IV).

Discussion

Post-transplant anti-GBM nephritis in AS remains a rare but devastating complication. It is difficult to comment on whether its incidence has reduced with the advent of more potent immunosuppressants in recent decades, as the available literature is mostly in the form of case reports or case series with retransplantation. Due to the paucity of available literature, especially recent large-centre data, there needs to be more active surveillance and documentation of these cases.

Genetic testing is essential not only to confirm the diagnosis in recipients but also to identify at-risk related donors and may also help to stratify risk of alloimmunity by mutation type and inheritance pattern. More sophisticated immunological assays are needed to detect AS-specific alloantibodies that commercial anti-GBM tests (targeting only the Goodpasture antigen, α3(IV)) often miss. Together, these advances would enable earlier identification of patients at greatest risk and inform donor selection.