Porcine kidney xenotransplantation as a bridge to allotransplantation: a first-in-human study

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Summary

Background Kidney xenotransplantation offers a potential solution to the organ shortage, but questions remain regarding durability, zoonotic infection risk, and whether the immunological response to the xenograft elicits sensitisation that could complicate subsequent allotransplantation. We report outcomes from a porcine kidney xenograft in a living recipient followed by human allotransplantation.

Methods A patient with end-stage kidney disease, a prolonged anticipated waiting time for deceased donor transplantation, and with no suitable living donor underwent transplantation at Massachusetts General Hospital (Boston, MA, USA) with a gene-edited porcine kidney (EGEN-2784; eGenesis [Cambridge, MA, USA]) incorporating the deletion of major glycan xenoantigens, inactivation of porcine endogenous retroviruses, and insertion of seven human transgenes. The recipient received costimulation blockade-based immunosuppression with complement inhibition. Monitoring included renal function, flow cytometric crossmatch, anti-HLA antibodies, and porcine microbial surveillance, including metagenomic sequencing. This report describes the first recipient in a planned three-patient study conducted under a US Food and Drug Administration Expanded Access Investigational New Drug application.

Findings The xenograft functioned immediately after transplantation on Jan 25, 2025, and sustained dialysis independence for 271 days. A biopsy on day 14 showed T-cell-mediated rejection, which resolved with treatment. Graft function remained stable for approximately 6 months until immunosuppression was reduced in the setting of non-zoonotic bacterial infection. Microvascular inflammation with endothelial injury subsequently emerged, progressing to thrombotic microangiopathy despite persistently negative donor-specific crossmatch, leading to graft failure and nephrectomy. Tissue analysis showed a macrophage and natural-killer-cell-predominant infiltrate with minimal T-cell involvement. No porcine pathogen transmission was detected. Anti-HLA antibodies remained unchanged. 82 days after explantation, the patient underwent human kidney allotransplantation with immediate graft function and no evidence of sensitisation during 231 days of follow-up.

Interpretation This case shows that porcine kidney xenotransplantation can provide prolonged renal support and be discontinued without clinically significant allosensitisation or zoonotic infection. Early cellular rejection resolved with treatment, whereas later graft failure was associated with microvascular injury progressing to thrombotic microangiopathy despite a negative donor-specific crossmatch, supporting the possibility that mechanisms beyond conventional antibody-mediated rejection contributed to late graft injury. Kidney xenotransplantation has the potential to provide prolonged dialysis-free support while also serving as a bridge to subsequent human allotransplantation.

Funding Massachusetts General Hospital and eGenesis.

Introduction

Kidney transplantation provides the best survival and quality of life for patients with end-stage kidney disease, but organ demand far exceeds supply, meaning many patients die while awaiting transplantation.[1,2] Xenotransplantation using genetically engineered porcine organs has been proposed as a solution to the organ shortage.[3] Early attempts were limited by profound interspecies incompatibilities, including natural antibodies to carbohydrate xenoantigens and dysregulation of complement and coagulation pathways, leading to rapid graft loss. Advances in genome engineering have enabled the development of pigs with multiple targeted genetic modifications designed to overcome these barriers.[4–12] These modifications include deletion of major carbohydrate xenoantigens, insertion of human transgenes regulating complement, inflammation, and coagulation, and CRISPR–Cas-mediated inactivation of porcine endogenous retroviruses.[11]

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Research in context

Evidence before this study

Kidney transplantation remains the optimum therapy for end-stage kidney disease; however, organ shortage is a global challenge. Worldwide, hundreds of thousands of patients await kidney transplantation, and many die each year while on waiting lists or without access to transplantation. In the USA alone, more than 100 000 patients are currently on waiting lists. Genetically engineered porcine kidneys have emerged as a promising strategy to address this shortage. We searched PubMed on April 14, 2026, for studies published from Jan 1, 2016, to April 14, 2026, and available in English, using the terms "xenotransplantation AND kidney AND (human OR clinical)". We included peer-reviewed original research describing porcine-to-human xenotransplantation in decedent or living recipients, with or without subsequent transition to human allotransplantation. Early studies in decedent models established technical feasibility. We reported the first porcine kidney xenotransplantation in a living human recipient in March, 2024, with survival of 52 days before death from cardiac causes unrelated to the xenograft. To our knowledge, no previous report has documented xenograft survival beyond 2 months, successful transition to human allotransplantation, or detailed mechanisms of late xenograft failure in living recipients.

Added value of this study

In this Article, we describe, to our knowledge, the longest dialysis-free survival (9 months) following porcine kidney xenotransplantation in a living human and the first transition to human kidney allotransplantation. The allograft functioned immediately, and no allosensitisation was detected following xenograft explantation. Longitudinal immunological and pathological analyses identified a distinct phenotype of macrophage and natural-killer-cell-mediated microvascular injury leading to thrombotic microangiopathy, despite persistently negative donor-specific crossmatch. No porcine pathogen transmission was detected post-transplantation.

Implications of all the available evidence

Porcine kidney xenotransplantation can provide sustained renal function and could serve as a reversible bridge to allotransplantation without evidence of allosensitisation or zoonotic infection during follow-up. Identification of innate immune-mediated microvascular injury as a mechanism of late xenograft failure has important implications for immunosuppressive strategies, donor genetic engineering, and monitoring in future clinical xenotransplantation studies.

In non-human primates, these genetic modifications, combined with immunosuppressive strategies, particularly CD40–CD154 costimulation blockade, have enabled prolonged survival of porcine kidney xenografts.[11,13,14] In the past 5 years, genetically engineered porcine kidneys have been transplanted into deceased human recipients, showing technical feasibility and providing important translational insights into human xenotransplantation.[4,12] Building on these preclinical and translational studies, a genetically engineered porcine kidney was subsequently transplanted into a living patient with end-stage kidney disease.[7,9,15] Although the recipient survived for 52 days before death due to cardiac causes unrelated to xenotransplantation, the graft showed early renal function without evidence of rejection.[7] However, key questions remain regarding durability, zoonotic risk, immunological consequences, and whether xenotransplantation might compromise subsequent human transplantation.[16]

We report outcomes from the first living human recipient in a planned three-patient study, who underwent transplantation with a gene-edited porcine kidney xenograft followed by human kidney transplantation.

Methods

Study design

This study was conducted under a US Food and Drug Administration (FDA) Expanded Access Investigational New Drug application, allowing transplantation of EGEN-2784 (eGenesis; Cambridge, MA, USA) genetically modified porcine kidneys[11] into patients lacking timely access to human donor organs. The transplantation, recovery, and follow-up were done at Massachusetts General Hospital (Boston, MA, USA). The protocol was approved on Jan 13, 2025, by the Institutional Review Board (IRB) at Massachusetts General Hospital (IRB number 2024P003475) and conducted in accordance with the Declaration of Helsinki and applicable regulatory guidance for xenotransplantation. Key protocol details are provided in the appendix (pp 18–22). An independent data safety monitoring process was implemented.[17]

Patient selection

Potential participants were patients with end-stage kidney disease who were actively listed for kidney transplantation at Massacheusetts General Hospital, had a prolonged anticipated waiting time for deceased donor transplantation, and had no suitable living donor. The selected patient provided written informed consent. Princpial eligibility criteria included age 50–70 years, maintenance dialysis for at least 6 months, and an estimated probability of less than 20% of receiving a deceased donor kidney within 5 years based on the Kidney Transplant Decision Tool from the Scientific Registry of Transplant Recipients. Eligibility required multidisciplinary evaluation of medical suitability, psychosocial readiness, and ability to comply with

See Online for appendix

For more on the **Kidney Transplant Decision Tool** see https://srtr.hrsa.gov/decision-tools/kidney-transplant-decision-tool/"

intensive post-transplant monitoring, including assessments by transplant nephrology, transplant surgery, infectious disease, immunology, cardiology, and psychiatry, and assessments of physical performance and frailty. Full eligibility criteria are provided in the appendix (p 18). Sex and ethnicity data were taken from hospital records. An implantable loop recorder was placed before transplantation for continuous cardiac rhythm monitoring.

Gene-edited porcine donor organs

The transplanted porcine kidney (EGEN-2784) was obtained from a pig raised in a designated pathogen-free facility and engineered with genomic modifications intended to enhance compatibility with the human immune system (table). These modifications included deletion of three major carbohydrate xenoantigens, insertion of seven human transgenes regulating complement, inflammation, and coagulation, and inactivation of porcine endogenous retrovirus sequences using CRISPR–Cas genome editing.[11] Donor animals were screened in accordance with regulatory guidance (appendix p 13).

Transplantation procedure and immunosuppression

The porcine donor kidney was procured under sterile conditions, preserved by cold static storage, and transplanted heterotopically with vascular anastomosis to the iliac vessels and ureteral implantation into the bladder (table).

Induction immunosuppression for the patient consisted of rituximab (1000 mg on day –3 before transplantation), rabbit antithymocyte globulin (1·5 mg/kg intravenously on days –1 and 0 before transplantation, and postoperative day 1), intravenous corticosteroids followed by a prednisone taper, and pegcetacoplan (1080 mg intravenously on preoperative days –3, –2, and –1, followed by 1080 mg subcutaneously three times weekly for 3–6 months). Maintenance immunosuppression consisted of tegoprubart (20 mg/kg intravenously with dosing adjusted to maintain trough concentrations of >800 µg/mL), tacrolimus (adjusted to target trough concentrations), mycophenolic acid (540 mg orally twice daily), and prednisone (table; appendix pp 2, 17).

Patient monitoring

Longitudinal monitoring was done by immunological assessment (flow cytometric crossmatch and anti-HLA antibody testing), per-protocol and for-cause biopsies with histological and molecular assessment (appendix p 14), microbiological surveillance including metagenomic sequencing (appendix p 13), and serial clinical assessment of graft function, all done at varying timepoints based on the protocol and in the setting of clinical events. Detailed methods are provided in the appendix (pp 18–22).

The objective of the FDA-authorised Expanded Access protocol was to evaluate the safety and feasibility of transplantation with the EGEN-2784 porcine kidney under tegoprubart-based immunosuppression. Prospective clinical assessments included dialysis-free survival, graft function, patient survival, infection surveillance, and immunological monitoring.

	Characteristics and details
Recipient	
Age, sex	66 years, male
End-stage kidney disease cause	Type 2 diabetes
Blood group	O
Weight	90 kg
5-year transplant probability	~9% (SRTR)
5-year waiting list mortality risk	>40% (SRTR)
Expected wait time (blood group O)	>5 years
Porcine donor	
Species	Yucatan miniature pig
Total modifications	69 genomic modifications
Knockouts	GGTA1, CMAH, and B4GALNT2
Transgenes	CD46, CD55, THBD, EPCR, CD47, HMOX1, and TNFAIP3
PERV inactivation	CRISPR-Cas genome editing
Facility	Designated pathogen-free
Kidney weight	170 g
Surgical parameters	
Transplantation date	Jan 25, 2025
Cold ischaemia time	2 h 39 min
Warm ischaemia time	25 min
Duration of the surgery	2 h 15 min
Vascular anastomosis	Iliac vessels (heterotopic)
Immunosuppression	
Induction	rATG, corticosteroids, rituximab, and pegcetacoplan
Mantainance	Tegoprubart (anti-CD154), tacrolimus, MPA, and prednisone

Clinical, genomic, surgical, and immunosuppressive characteristics of the recipient and porcine donor, and details of surgical parameters and immunosuppression. The gene-edited porcine kidney (EGEN-2784) incorporated three xenoantigen knockouts, seven human transgenes, and CRISPR–Cas-mediated PERV inactivation. Immunosuppression comprised costimulation blockade-based maintenance therapy with complement inhibition at induction. MPA=mycophenolic acid. PERV=porcine endogenous retrovirus. rATG=rabbit antithymocyte globulin. SRTR=Scientific Registry of Transplant Recipients.

Table: **Xenotransplantation characteristics and details**

Role of the funding source

Massachusetts General Hospital and eGenesis funded the study. eGenesis provided the genetically engineered porcine donor organ, Eledon Pharmaceuticals supplied tegoprubart, and Apellis Pharmaceuticals supplied pegcetacoplan for use in the Expanded Access protocol. Representatives of eGenesis contributed to protocol development, study design, and generation of specified donor-related data but had no role in the independent clinical data analysis, overall data interpretation, or writing of the manuscript.

Results

The transplant recipient was a 66-year-old, non-Hispanic, White man with end-stage kidney disease secondary to long-standing type 2 diabetes, who had been receiving maintenance haemodialysis for 2 years before transplantation (table). His medical history included diabetic complications (retinopathy and peripheral neuropathy), hypertension, hyperlipidaemia, obesity, and secondary hyperparathyroidism. He also had coronary artery disease with previous myocardial infarction requiring percutaneous coronary intervention to the left anterior descending and the left circumflex arteries, with preserved left ventricular function on subsequent evaluation.

Despite adequate dialysis clearance, the patient had progressive functional decline after initiating haemodialysis, including fatigue, poor appetite, and reduced activity tolerance. He required a cane and reported frequent post-dialysis exhaustion. At a separate outpatient unit (Concord, MA, USA), he underwent in-centre haemodialysis three times per week and had previously discontinued home haemodialysis following a bleeding complication from his arteriovenous fistula.

The patient had no available living donor and was actively listed for deceased donor kidney transplantation. As a blood group O candidate, the expected waiting time exceeded 5 years. Based on the Kidney Transplant Decision Tool, the estimated probability of receiving a deceased donor kidney within 5 years for the region and transplant centre was approximately 9%, whereas the estimated risk of death or removal from the waiting list exceeded 40% (table).

Given his progressive clinical decline on dialysis, low likelihood of timely human transplantation, preserved lower extremity physical performance on Short Physical Performance Battery assessment, and absence of frailty on formal screening assessment, the patient was considered a candidate for investigational xenotransplantation under an Expanded Access protocol. Given his history of coronary artery disease, and an unexpected cardiac event in our first xenotransplant recipient,[7] an implantable loop recorder was placed for cardiac rhythm surveillance.

Transplantation was done on Jan 25, 2025. The xenograft showed immediate function following transplantation (figure 1). Urine production began intraoperatively and reached approximately 6 L in the first 24 h, stabilising at 4–5 L per day during the first postoperative week (figure 2A). Serum creatinine declined from 7·0 mg/dL before transplantation to approximately 1·5 mg/dL within 1 week (figure 2B) with stable electrolyte parameters (figure 2C, 2D; appendix p 3). The post-transplantation course evolved into two distinct phases of graft injury: early T-cell-mediated rejection (TCMR) followed by delayed microvascular injury after a period of stable graft function (figure 1).

Serum creatinine had increased to 1·9 mg/dL on postoperative day 14, and kidney biopsy showed Banff grade IIA TCMR, with interstitial inflammation, tubulitis, and vascular involvement (figure 3; appendix p 15). Multiplex immunofluorescence showed a predominantly T-cell and macrophage infiltrate with local cellular proliferation (appendix p 4). Treatment with pulse corticosteroids (500 mg intravenously on each of postoperative days 15, 16, and 17) and two doses of rabbit antithymocyte globulin (150 mg on each of postoperative days 15 and 16) resulted in rapid recovery of graft function and complete histological resolution on repeat biopsy at postoperative day 25 (figure 3; appendix p 4). Targeted gene expression profiling of the day 14 biopsy supported a TCMR signature, which was attenuated on follow-up assessment at day 25 (appendix p 5). Despite a positive

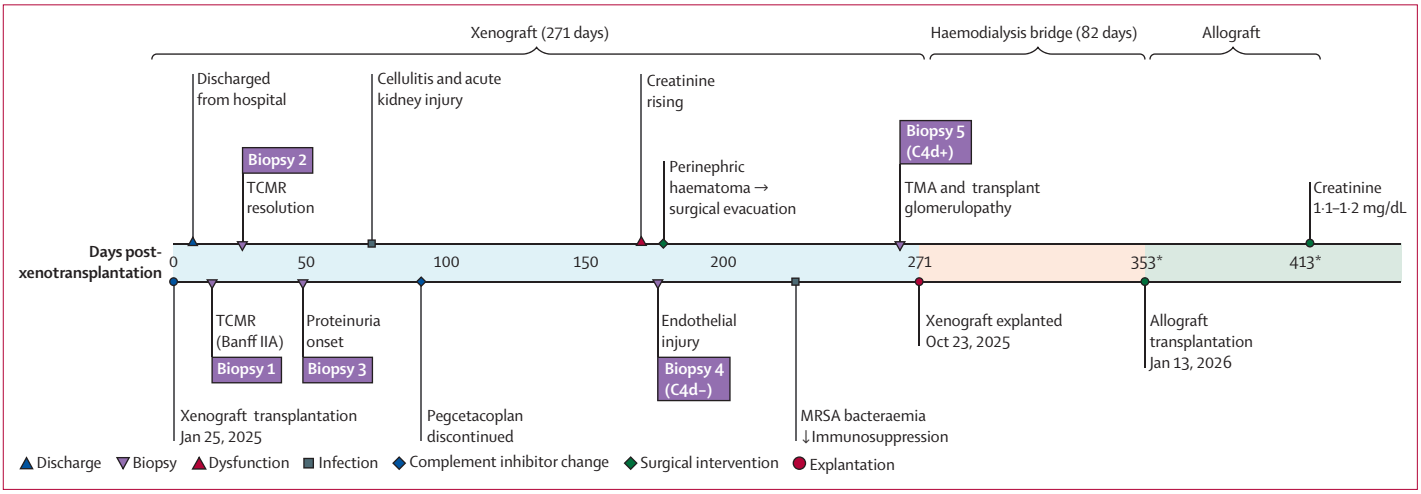


Figure 1: **Clinical course**

Timeline of clinical events following porcine kidney xenotransplantation in a living human recipient. The xenograft survived for 271 days (blue), followed by a haemodialysis bridge (82 days, pink), and human kidney allotransplantation (green). MRSA=meticillin-resistant *Staphylococcus aureus*. TMA=thrombotic microangiopathy. TCMR=T-cell-mediated rejection. *Days calculated from the xenograft transplantation date.

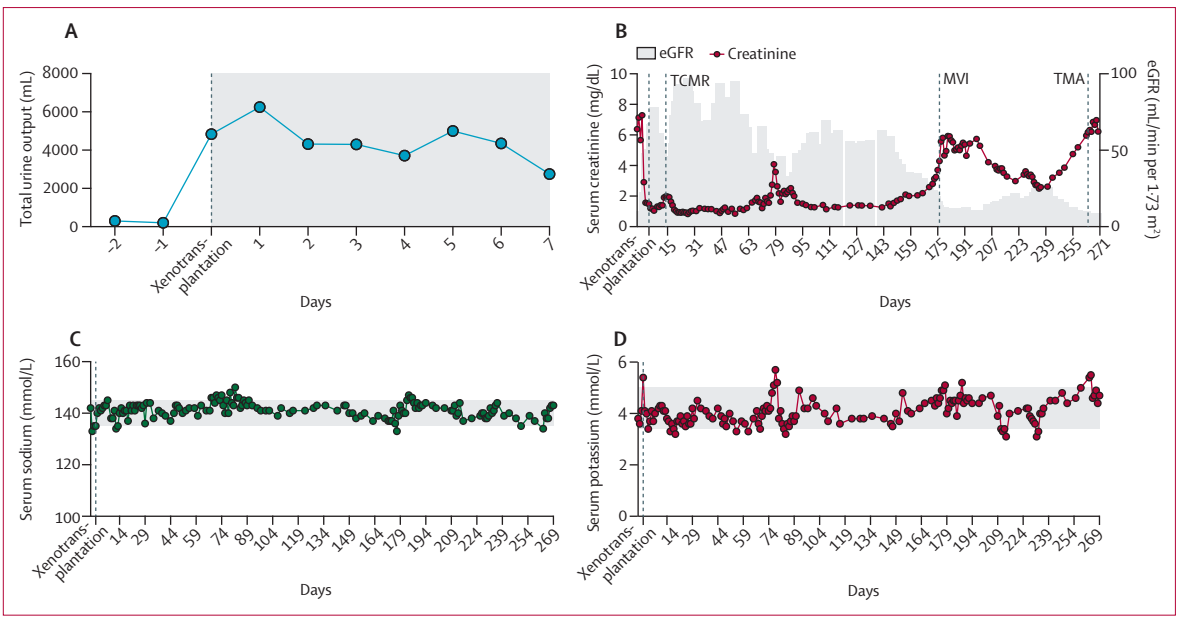


Figure 2: **Longitudinal renal function and biochemical parameters before and after porcine kidney xenotransplantation**
(A) Total daily urine output (mL) during the first week after xenotransplantation. (B) Serum creatinine and eGFR throughout the xenograft period. Note that scales on y axes differ between plots. Vertical dashed lines indicate for-cause kidney biopsies—key histopathological findings are annotated: day 14, Banff IIA TCMR; day 176, MVI with endothelial injury; day 264, TMA with transplant glomerulopathy. (C) Serum sodium. (D) Serum potassium. All panels share a common x-axis representing days relative to xenotransplantation (day 0). eGFR=estimated glomerular filtration rate. MVI=microvascular inflammation. TCMR=T-cell-mediated rejection. TMA=thrombotic microangiopathy.

C4d stain (figure 3C; appendix p 6), glomerulitis was not present, flow cytometry crossmatch against donor kidney endothelial cells and donor peripheral blood mononuclear cells were negative (figure 4A, 4B; appendix p 7), and transcript analysis showed minimal evidence of antibody-mediated rejection (appendix p 5).

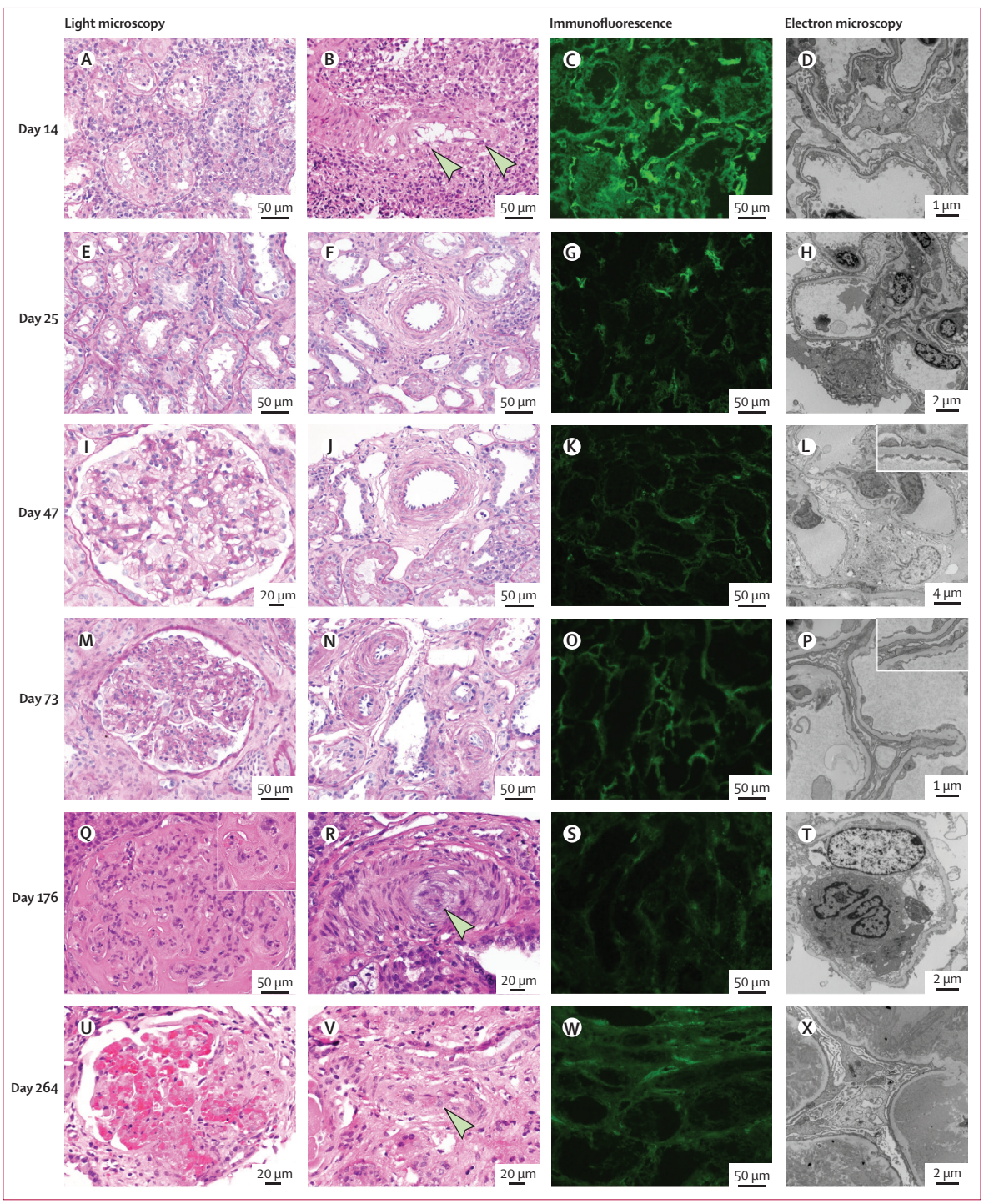
At postoperative day 47, new-onset proteinuria was detected despite stable kidney function (figure 1; appendix p 3). Biopsy showed no evidence of rejection but did show podocyte injury with foot process effacement without membranous deposits or endothelial injury (figure 3). Mild mesangial expansion (mm1) was present in a subset of glomeruli and was accompanied by transient mesangial immunoglobulin staining, predominantly IgM and IgA, with only minimal mesangial electron-dense deposits detected by electron microscopy (appendix p 16). The patient was treated with corticosteroids (250 mg intravenously on each of days 47 and 48), tocilizumab (780 mg intravenously on day 60), and renin-angiotensin system blockade with subsequent escalation to plasmapheresis (3 sessions on days 67, 69, and 70), obinutuzumab (1000 mg intravenously on day 70), and daratumumab (1800 mg subcutaneously on 92) for persistent proteinuria.

On postoperative day 72, the patient developed lower-extremity cellulitis (figure 1). A per-protocol kidney biopsy on day 73 showed no evidence of rejection (figure 3). Intravenous vancomycin (dosed according to serum concentrations) was initiated on day 74, and intravenous meropenem (1 g daily) was added on day 76. During this period, serum creatinine increased, peaking at 4·0 mg/dL on day 78, consistent with acute kidney injury. Kidney function improved after discontinuation of vancomycin and initiation of supportive management. Complement inhibition with pegcetacoplan (1080 mg subcutaneously three times per week, started 3 days before xenotransplantation) was discontinued on postoperative day 90 because of concern for over-immunosuppression.

On postoperative day 146, the patient developed atypical chest pain and underwent coronary angiography, which showed restenosis of a previously stented left anterior descending artery. Repeat percutaneous coronary intervention was performed successfully with initiation of dual antiplatelet therapy. Continuous rhythm surveillance through the implantable loop recorder did not detect clinically significant arrhythmias during follow-up. Kidney function remained stable, and no graft-related complications were observed.

After approximately 5 months of stable graft function, a progressive rise in serum creatinine was observed around postoperative day 170 (figure 2B). A clinically indicated kidney biopsy taken on postoperative day 176 showed microvascular inflammation characterised by glomerulitis and endothelial injury, indicative of thrombotic microangiopathy without histological evidence of T-cell or antibody-mediated rejection (figure 3; appendix p 15). C4d staining was negative

(figure 3S), and flow cytometry crossmatch against donor-matched porcine kidney endothelial cells and peripheral blood mononuclear cells remained negative throughout the xenograft course (figure 4A, 4B; appendix p 7). Complement activation products (C5b-9) were detected in glomeruli and arterioles with trace-to-1+ mesangial immunoglobulin deposits at days 47 and 73 that subsequently decreased (appendix pp 6, 8). By contrast to the early rejection biopsy, multiplex immunofluorescence imaging showed sparse T-cell infiltration with predominance of macrophages, natural killer (NK) cells, and CD11b-positive myeloid populations within and around the glomerular microvasculature (figure 5; appendix p 9),



including close spatial localisation of NK cells and macrophages within glomerular capillary loops. This pattern of injury was accompanied by an increase in porcine-derived cell-free DNA levels, coinciding with the onset of graft dysfunction (figure 4C).

The patient was treated empirically with pulse corticosteroids, plasmapheresis, complement inhibition with eculizumab, and re-initiation of pegcetacoplan, together with a single dose of tocilizumab (780 mg intravenously on day 187) for IL-6 receptor blockade (appendix pp 2, 10, 17). The biopsy procedure was complicated by a perinephric haematoma, resulting in graft compression, which required surgical evacuation. Following management of both the presumed immune-mediated injury and the procedural complication, kidney function improved, and serum creatinine declined without the need for dialysis.

Approximately 50 days later, on postoperative day 226, the patient was admitted to hospital with a fever and was found to have a meticillin-resistant *Staphylococcus aureus* urinary tract infection with associated bacteraemia (figure 1). Mycophenolic acid was temporarily withheld, and subsequently resumed at 180 mg orally twice daily, and complement inhibition was again discontinued. The patient was treated with intravenous daptomycin (775 mg once daily) for 4 weeks, with resolution of the infection, and was discharged with stable kidney function. This reduction in immunosuppression preceded subsequent progression of graft dysfunction.

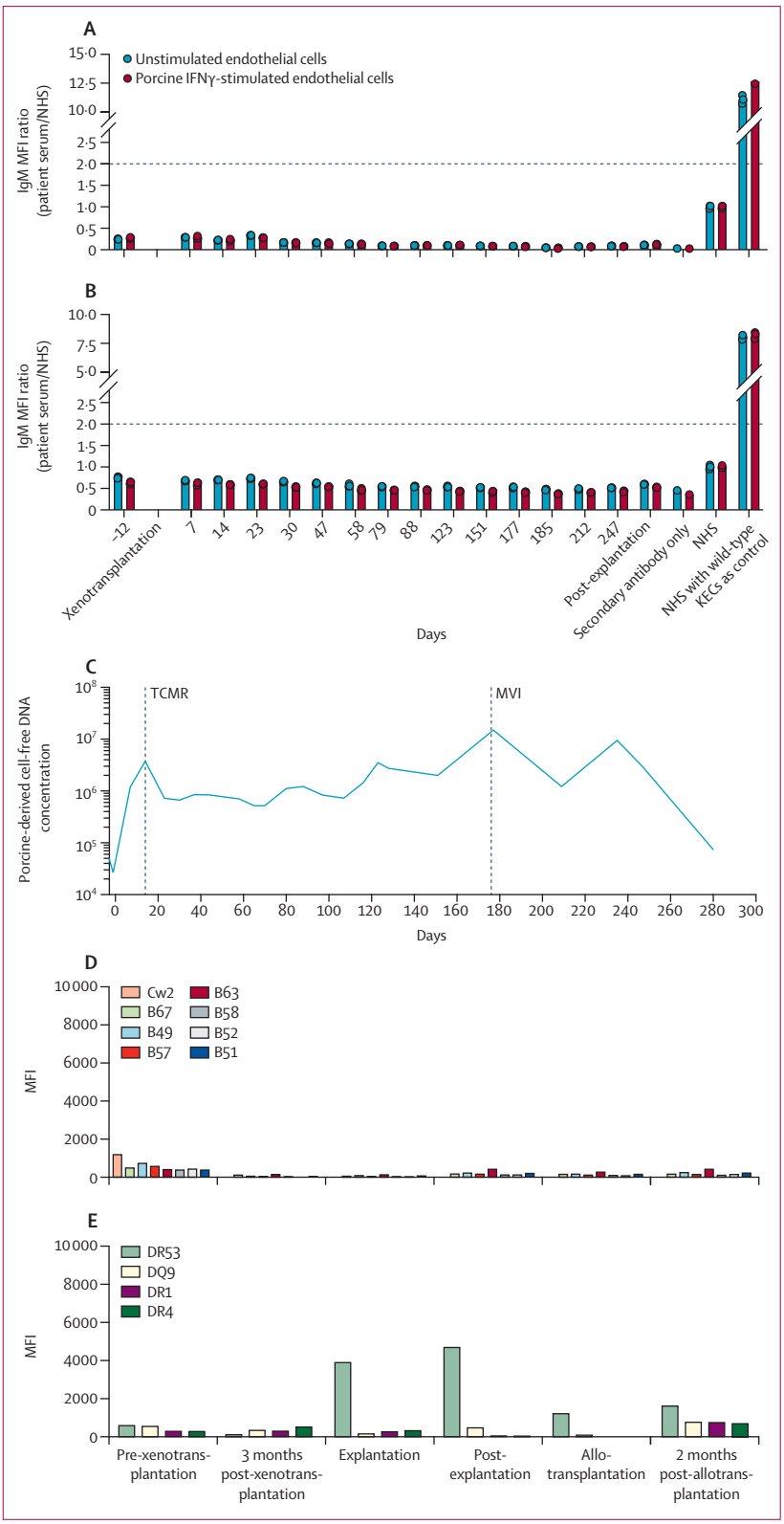
On postoperative day 264, a recurrent rise in serum creatinine (to 6·18 mg/dL) prompted repeat biopsy. Histopathology showed thrombotic microangiopathy with chronic microvascular injury, including transplant glomerulopathy, interstitial fibrosis, and tubular atrophy (figure 3; appendix p 15). C4d staining was positive in peritubular capillaries (figure 3W). There was no clinical or laboratory evidence of systemic thrombotic microangiopathy (appendix p 3).

Despite supportive management, kidney function continued to decline. Given the extent of irreversible microvascular injury and progressive graft dysfunction, the xenograft was surgically explanted on postoperative day 271. Histopathological analysis of the explanted graft showed features similar to those of the day 264 biopsy, with severe arterial and glomerular thrombotic microangiopathy (figure 3).

In regard to systemic immune correlates of microvascular injury, peripheral blood mononuclear cell stimulation assays showed increased cytokines, including IL-6, TNF-α, IL-8, MCP-1, and IL-1β, in association with microvascular endothelial injury observed at day 176 (appendix p 11). Longitudinal proteomics identified a distinct transition, with enrichment of innate immune and inflammatory pathways and increased markers of endothelial stress, matrix remodelling, acute phase response, and neutrophil activation (appendix p 11). Together, these findings were consistent with systemic innate immune activation and endothelial stress temporally associated with the onset of microvascular injury.

82 days after xenograft nephrectomy, the patient underwent kidney transplantation from a deceased donor. Serial anti-HLA antibody monitoring by single-antigen bead assay across the xenograft period, at the time of allotransplantation, and during post-transplantation follow-up showed no emergence of persistent de novo antibodies (figure 4D, 4E). The donor kidney was a fortuitous zero HLA mismatch—an uncommon and largely unpredictable event that, under standard Organ Procurement and Transplantation Network allocation policies, confers substantial priority because of the favourable immunological match; cold ischaemia time was 15 h 38 min. Induction immunosuppression consisted of basiliximab (20 mg intravenously on days 0 and 3 after allotransplantation). Maintenance immunosuppression consisted of oral tacrolimus (4 mg twice daily, subsequently adjusted to standard-to-low target trough concentrations), mycophenolic acid (540 mg orally twice daily), and corticosteroids (intravenous methylprednisolone, followed by an oral prednisone taper according to protocol), given the favourable zero HLA mismatch. At the time of transplantation, the patient's serum creatinine was 6·8 mg/dL. The allograft showed

Figure 3: **Histopathological evolution of xenograft injury**
(A–D) Day 14. Biopsy shows widespread mononuclear interstitial infiltrate with tubulitis (PAS, ×400; A) and moderate endarteritis (arrows), diagnostic of Banff IIA TCMR (haematoxylin and eosin, ×400; B). C4d immunofluorescence is present despite a negative flow cytometric crossmatch against donor cells (×400; C). Electron microscopy shows intact glomerular endothelium and podocyte foot processes (×7100; D). (E–H) Day 25. Follow-up biopsy shows resolution of TCMR with no tubulitis or endarteritis (PAS, ×400; E–F). C4d staining shows weak peritubular capillary positivity (×400; G). Electron microscopy is unremarkable (×3500; H). (I–L) Day 47. Glomeruli show reactive podocytes with no tubulointerstitial or microvascular inflammation (PAS, ×400; I). Arteries are unremarkable (PAS, ×400; J). C4d is negative (×400; K). Electron microscopy shows podocyte injury with swelling and segmental foot process effacement (×2200) without appreciable endothelial injury (inset; L). (M–P) Day 73. Persistent reactive podocytes without evidence of rejection or endothelial injury (PAS, ×400; M). Arteries and arterioles are unremarkable (PAS, ×400; N). C4d is negative (×400; O). Electron microscopy shows extensive podocyte foot process effacement (×7100) with intact endothelium (inset; P). (Q–T) Day 176. Glomerulitis with endothelial injury and segmental intracapillary mononuclear cells, with evidence of early TMA; inset shows red cell fragmentation in glomerular capillaries (haematoxylin and eosin, ×400; Q). Arteriolar involvement with early fibrin deposition and intimal mucoid change (arrow; haematoxylin and eosin, ×400; R). C4d is negative, consistent with the absence of antibody-mediated rejection (×400; S). Electron microscopy of a glomerular capillary showing an intracapillary monocyte, swollen endothelial cell, and podocyte injury (×5600; T). (U–X) Day 264. Progressive TMA with multiple intracapillary thrombi, fibrin deposition, and red cell fragmentation in glomeruli (haematoxylin and eosin, ×400; U). Similar findings in arterioles (arrow; haematoxylin and eosin, ×400; V). C4d is positive in peritubular capillaries (×400; W). Electron microscopy of a glomerular capillary showing endothelial loss and intracapillary thrombi with fibrin tactoids (×5600; X). PAS=periodic acid–Schiff. TCMR=T-cell-mediated rejection. TMA=thrombotic microangiopathy.



immediate function, with serum creatinine declining to approximately 1 mg/dL (appendix p 12).

Longitudinal infectious disease surveillance during the xenograft period and after explantation revealed no evidence of zoonotic infection (appendix p 13). Metagenomic plasma sequencing and targeted pathogen screening detected no porcine-derived pathogens throughout the observation period, including after allotransplantation.

As of Sept 1, 2026, the patient is 231 days post-kidney allotransplantation with stable graft function (creatinine 1·0–1·1 mg/dL; appendix p 12). Post-allotransplantation complications have included transient hyperglycaemia requiring adjustment of insulin therapy in the setting of diabetes and corticosteroid use, and transient BK viraemia that resolved following reduction of immunosuppression without impairment of allograft function.

Discussion

This study shows that porcine kidney xenotransplantation can achieve prolonged, life-sustaining renal function in a living human recipient and supports further clinical investigation under intensive regulatory oversight. To our knowledge, it represents the longest reported period of dialysis-free xenograft function, with subsequent human kidney transplantation without evidence of allosensitisation. The clinical course was characterised by two distinct phases of graft injury, with early TCMR that was responsive to immunosuppression, followed by later microvascular and endothelial injury progressing to thrombotic microangiopathy. Notably, this later phase occurred despite persistently negative donor-specific crossmatch, suggesting mechanisms distinct from conventional antibody-mediated rejection. Importantly, the absence of allosensitisation and the favourable early course of subsequent human kidney transplantation support xenotransplantation as a reversible bridging strategy for some patients. This evolving clinical

Figure 4: **Immunological monitoring throughout the xenograft period and following allotransplantation**

(A) FCXM showing IgM binding against donor porcine kidney endothelial cells, expressed as MFI ratio relative to pooled NHS (>100 donors) at serial timepoints in days post-xenotransplantation. (B) FCXM showing IgG binding against donor porcine kidney endothelial cells, expressed as MFI ratio relative to pooled NHS at serial timepoints in days post-xenotransplantation. Endothelial cells derived from the donor's contralateral kidney were used as target cells. The dashed horizontal line indicates the positivity threshold. Wild-type Yucatan porcine KECs were additionally tested against pooled NHS as a control. (C) Porcine-derived cell-free DNA measured serially during the xenograft period in days post-xenotransplantation; vertical dashed lines indicate biopsy-confirmed graft injury events (TCMR, day 14; microvascular inflammation with endothelial injury, day 176). (D) Anti-HLA class I antibody MFI by single-antigen bead assay, shown for specificities with peak MFI ≥500. (E) Anti-HLA class II antibody MFI by single-antigen bead assay, shown for specificities with peak MFI ≥500. FCXM=flow cytometric crossmatch. IFN-γ=interferon-gamma. KECs=kidney endothelial cells. MFI=mean fluorescence intensity. MPM=molecules of pig-derived cell-free DNA per µL of plasma. MVI=microvascular inflammation. NHS=normal human serum. TCMR=T-cell-mediated rejection.

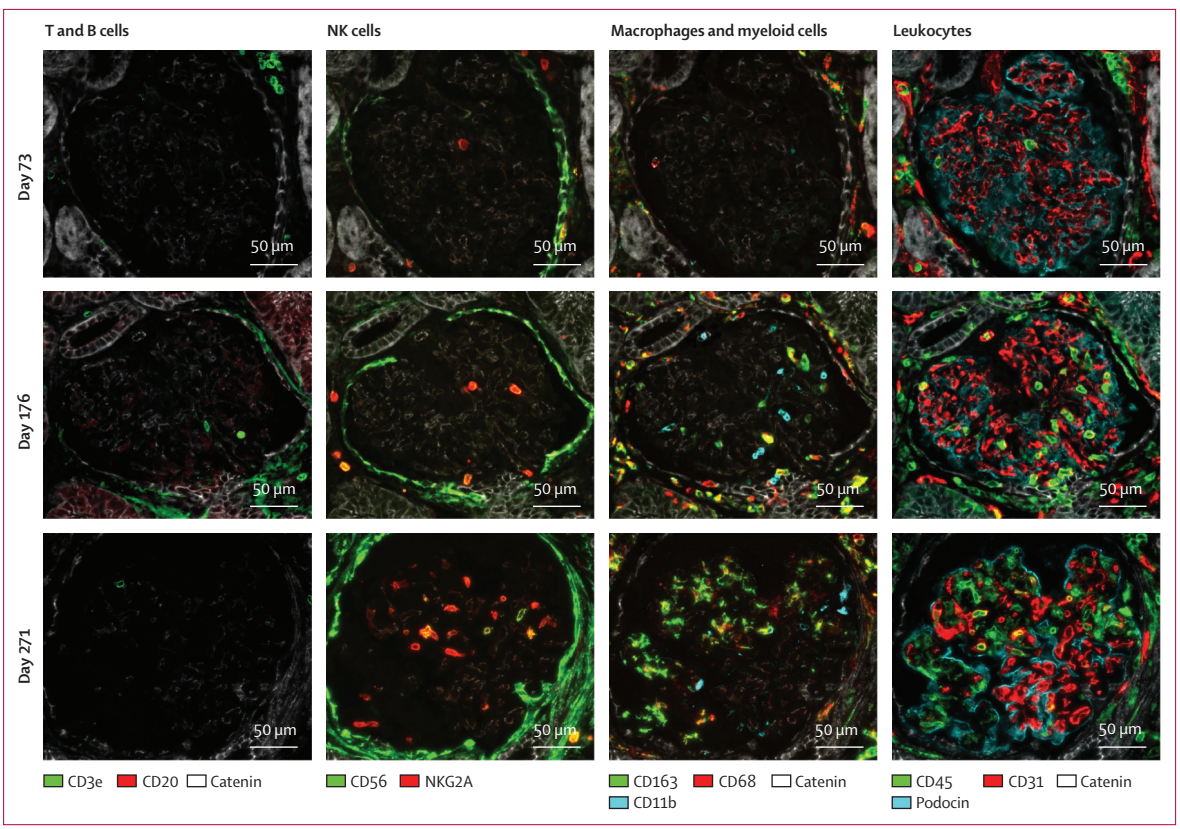


Figure 5: **Multiplex immunofluorescence characterisation of the xenograft immune microenvironment during late graft injury**
Representative multiplex immunofluorescence images of glomerular regions from xenograft kidney biopsies obtained at postoperative days 73 and 176, and from the explant specimen (day 271). Panels depict immune cell populations. Structural markers include endothelium (CD31), podocytes (podocin), and tubular epithelium (β-catenin). NK=natural killer.

framework should also be considered in xenotransplantation alongside emerging data on recipient perspectives and lived experience.[18]

The xenograft showed immediate function, with rapid creatinine clearance and robust urine output after transplantation, consistent with effective filtration and tubular function. Dialysis independence was maintained for more than 9 months, with stable electrolyte balance, blood pressure control, and volume homoeostasis. Notably, phosphate levels remained within normal range in the setting of an intact parathyroid axis, by contrast to a previously reported recipient with hyperphosphataemia and absent parathyroid hormone,[15] suggesting that the recipient's endocrine factors could influence xenograft tubular handling of electrolytes. Collectively, these observations extend previous observations showing that genetically engineered porcine kidneys have potential to support key physiological functions in humans.[12,15,19] Given the sudden cardiac death observed in the first xenotransplant recipient treated at our centre,[7] this patient underwent continuous rhythm monitoring with an implantable loop recorder, and no clinically significant arrhythmias were detected.

The early rejection episode at postoperative day 14 showed Banff grade IIA TCMR, with interstitial inflammation, tubulitis, and vascular involvement, accompanied by a predominantly T-cell and macrophage infiltrate, consistent with recent immune profiling data from another clinical kidney xenotransplant recipient.[9] Although C4d staining was positive during ongoing pegcetacoplan therapy, donor-reactive antibodies were not detected, and transcriptomic analysis showed minimal evidence of antibody-mediated rejection, suggesting proximal complement activation in the absence of detectable circulating antibodies or overt antibody-mediated injury. This pattern might reflect non-injurious antibody binding consistent with accommodation,[20,21] activation of non-classic complement pathways, particularly the lectin pathway,[22] or persistent C4d deposition despite ongoing complement inhibition. Treatment with corticosteroids and rabbit antithymocyte globulin resulted in rapid recovery of graft function, complete histological resolution by day 25, and attenuation of TCMR-associated gene expression signatures. These findings indicate that early cellular rejection of a xenograft is reversible with conventional immunosuppressive therapy. The occurrence of early TCMR in the first

reported living porcine kidney xenotransplant recipient and in the recipient described here was somewhat unexpected and suggests that early xenogeneic cellular immune responses might be more robust than previously appreciated, prompting modifications of induction strategy in subsequent recipients.

The later phase of graft dysfunction in this patient was characterised by progressive microvascular endothelial injury with complement activation and a distinct immune profile enriched in macrophages, myeloid populations, NK cells with phenotypic features suggestive of chronic activation,[23] and with minimal T-cell involvement. Histologically, this phase was marked by glomerulitis and progression to thrombotic microangiopathy. This pattern differs from classic alloimmune rejection and supports a prominent role for innate immune pathways in xenograft injury. The absence of detectable donor-reactive antibodies by flow cytometric crossmatch supports mechanisms distinct from conventional antibody-mediated rejection. However, contributions from antibody-dependent processes below the limits of detection or mediated through non-classic pathways cannot be excluded. In addition, currently available molecular classifiers and rejection-associated transcript signatures were developed in human allotransplantation and might not fully capture the unique biology of xenograft injury.

These findings are consistent with recent clinical and translational reports on xenotransplantation showing persistent activation of innate immune and endothelial pathways, suggesting that microvascular injury could arise even in the absence of detectable donor-specific antibodies.[9,12,13,24–26] A similar pattern of late glomerular thrombotic microangiopathy has also been described in long-term pig-to-non-human primate kidney xenografts, in which graft failure was associated with macrophage-predominant injury and reduced glomerular VEGFA expression, supporting the relevance of these findings across preclinical and clinical xenotransplantation models.[27] Rapid progression of interstitial and intimal fibrosis in our case further suggests that chronic fibrotic remodelling could represent an important downstream consequence of persistent endothelial and innate immune activation in xenografts.

The mechanism of the late microvascular injury is likely multifactorial. Complement inhibition with pegcetacoplan was discontinued approximately 3 months after transplantation, after which endothelial injury became apparent, suggesting that sustained complement blockade could be required to protect the graft microvasculature.[24,25,28] In addition, immunosuppression was reduced during episodes of infection, potentially permitting breakthrough immune activation. In the context of known and potentially unrecognised species-specific incompatibilities in endothelial regulation and innate immune signalling, these factors could have contributed to progressive microvascular injury and thrombotic microangiopathy.

More broadly, recent work in transplantation has emphasised that T-cell or antibody-mediated mechanisms do not always explain microvascular inflammation and could also reflect innate allorecognition, including NK-cell activation through missing-self pathways and monocyte activation through the SIRPα–CD47 axis[29] or dysregulation of the complement system. These observations suggest that endothelial compatibility between porcine grafts and the human recipient is a central determinant of xenograft durability and that sustained control of complement-mediated and innate immune pathways will be critical to improving long-term outcomes.

An additional important observation concerns infectious safety. Intensive surveillance throughout the xenograft course and after explantation identified no evidence of zoonotic transmission. Serial monitoring using metagenomic plasma sequencing and conventional microbiological testing did not detect porcine-derived pathogens, including common infectious agents such as porcine cytomegalovirus. These findings are consistent with previous preclinical and early clinical studies suggesting that the risk of cross-species pathogen transmission can be mitigated by using designated pathogen-free donor herds, inactivating porcine endogenous retroviruses, rigorous donor screening, and longitudinal recipient surveillance.[7,30] Although continued vigilance remains essential, these data further support the infectious safety of genetically engineered porcine donors raised in biosecure facilities and transplanted into carefully monitored recipients.

This study has some limitations. Interpretation of our findings is limited by the single-patient nature of this experience, the absence of a comparison group, and the complexity of clinical factors that might have influenced graft outcomes, all of which restrict definitive conclusions regarding efficacy, durability, and generalisability. The observed outcomes likely also reflect careful patient selection, intensive multidisciplinary management, and highly specialised institutional expertise that might not be generalisable to broader clinical settings. Reductions in immunosuppression during infectious complications make mechanistic interpretation challenging, and the discontinuation of complement inhibition before the onset of microvascular injury prevents definitive conclusions regarding its protective role. Exploratory biomarker analyses were constrained by sample availability and prioritised at timepoints surrounding the first detection of microvascular injury and thrombotic microangiopathy. Although all biopsies underwent comprehensive clinical histopathological assessment and multiple biopsies underwent multiplex immunofluorescence analysis, a shortage of residual tissue precluded transcriptomic profiling across all timepoints.

This case illustrates both the promise and the remaining challenges of clinical kidney xenotransplantation. The xenograft provided sustained dialysis-free kidney function while maintaining key physiological functions, supporting the feasibility of porcine kidneys as a bridging or alternative strategy for patients who lack timely access to human donor organs. The development of progressive microvascular injury also underscores the need for improved strategies to protect the graft endothelium, including optimised immunosuppression, complement inhibition, and further donor genetic engineering. Such advances are particularly important given that current therapies for xenograft-associated microvascular injury and thrombotic microangiopathy might not always be effective and carry substantial infectious risk, treatment burden, and financial cost. The economic sustainability of xenotransplantation as either destination therapy or a bridge strategy also remains uncertain and will require formal evaluation as clinical experience expands. Scaling these regimens beyond carefully selected recipients will be challenging without parallel efforts to simplify monitoring and reduce adjunctive therapy requirements, although these challenges must be weighed against the substantial health-care burden and poor long-term outcomes associated with maintenance dialysis. The absence of zoonotic infection and the transition to a subsequent human kidney transplant in this case further reinforce the potential role of xenotransplantation as a bridge or long-term strategy in selected patients. Importantly, this approach will require continued attention to ethical patient selection, preservation of equitable organ allocation practices, and integration within existing transplant systems.

Early clinical application of kidney xenotransplantation will likely focus on individuals with low access to timely human transplantation but sufficient physiological reserve to tolerate intensive monitoring and immunosuppression.[17] Longer-term follow-up and systematic analyses will be essential to define durability, safety, and the optimal clinical role of kidney xenotransplantation as a scalable approach to address the global shortage of transplantable organs.

Contributors

LVR and TJB directly accessed and verified the underlying data. LVR conceived and led the study, designed the protocol, oversaw all aspects of the work, interpreted the data, and wrote the first draft of the manuscript. TK contributed substantially to study conception and protocol design, clinical care of the recipient, data interpretation, and critical revision of the manuscript. TJB conducted and contributed to the design, performance, and interpretation of immunological assays. IAR, CTA, AG, RNS, and RBC performed pathological analyses, interpreted histologic findings, and contributed to manuscript revision. J-YC and SSa contributed to multiplex tissue imaging and spatial profiling of xenograft tissue. RPa, HNL, RPi, JCM, JAF, and JE-K contributed to clinical care of the recipient and clinical data interpretation. FH and RV contributed to immunological profiling, multiomics sample processing, and coordination between clinical and laboratory teams. AP contributed to data collection, sample processing, and data curation. JAB, SCL, KG, MC, and SP contributed to protocol development and study design. MK, SB, and MSL contributed to data interpretation and critical revision of the manuscript. GTR performed bioinformatic analyses and contributed to data interpretation. VKT contributed to cardiac clinical care and interpretation of cardiovascular data. ACB contributed to electrophysiological evaluation and clinical management. VP performed crossmatch and immunologic compatibility testing. AL, MD, SSh, and NE contributed to surgical procedures and perioperative management. LVR is the guarantor of the study. All authors reviewed the manuscript, had access to the data, take responsibility for the integrity of the work and the accuracy of the analyses, approved the final manuscript, and had final responsibility for the decision to submit for publication.

Declaration of interests

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Data sharing

Data supporting the findings of this study are available on reasonable request from the corresponding author via email, subject to applicable institutional and proprietary data sharing agreements.

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References

1 Schold J, Srinivas TR, Sehgal AR, Meier-Kriesche HU. Half of kidney transplant candidates who are older than 60 years now placed on the waiting list will die before receiving a deceased-donor transplant. *Clin J Am Soc Nephrol* 2009; **4:** 1239–45.

2 Zambeli-Ljepović A, Tungsanga S, Ghimire A, et al. The potential of kidney transplantation to reduce mortality from chronic kidney disease: a global, cross-sectional, modelling study. *Lancet Glob Health* 2025; **13:** e1691–700.

3 Riella LV, Madsen JC, Pierson RN, et al. Advancing hope through science: The Inaugural Richard Slayman International Workshop on Xenotransplantation. *Transplantation* 2026; published online Feb 17. https://doi.org/10.1097/tp.0000000000005652.

4 Porrett PM, Orandi BJ, Kumar V, et al. First clinical-grade porcine kidney xenotransplant using a human decedent model. *Am J Transplant* 2022; **22:** 1037–53.

5 Adams AB, Lovasik BP, Faber DA, et al. Anti-C5 antibody tesidolumab reduces early antibody-mediated rejection and prolongs survival in renal xenotransplantation. *Ann Surg* 2021; **274:** 473–80.

6 Griffith BP, Goerlich CE, Singh AK, et al. Genetically modified porcine-to-human cardiac xenotransplantation. *N Engl J Med* 2022; **387:** 35–44.

7 Kawai T, Williams WW, Elias N, et al. Xenotransplantation of a porcine kidney for end-stage kidney disease. *N Engl J Med* 2025; **392:** 1933–40.

8 Montgomery RA, Stern JM, Lonze BE, et al. Results of two cases of pig-to-human kidney xenotransplantation. *N Engl J Med* 2022; **386:** 1889–98.

9 Ribas GT, Cunha AF, Avila JP, et al. Immune profiling in a living human recipient of a gene-edited pig kidney. *Nat Med* 2026; **32:** 270–80.

10 Yamada K, Yazawa K, Shimizu A, et al. Marked prolongation of porcine renal xenograft survival in baboons through the use of α1,3-galactosyltransferase gene-knockout donors and the cotransplantation of vascularized thymic tissue. *Nat Med* 2005; **11:** 32–34.

11 Anand RP, Layer JV, Heja D, et al. Design and testing of a humanized porcine donor for xenotransplantation. *Nature* 2023; **622:** 393–401.

12 Montgomery RA, Stern JM, Fathi F, et al. Physiology and immunology of a pig-to-human decedent kidney xenotransplant. *Nature* 2025; **650:** 218–29.

13 Adams AB, Faber D, Lovasik BP, et al. Iscalimab combined with transient tesidolumab prolongs survival in pig-to-rhesus monkey renal xenografts. *Xenotransplantation* 2024; **31:** e12880.

14 Eisenson D, Hisadome Y, Santillan M, et al. Consistent survival in consecutive cases of life-supporting porcine kidney xenotransplantation using 10GE source pigs. *Nat Commun* 2024; **15:** 3361.

15 Lee SA, Lafargue MC, Williams WW, et al. Physiologic homeostasis in a living human after pig kidney xenotransplantation. *Nat Commun* 2025; **16:** 8453.

16 Redfield RR, Scalea JR, Zens TJ, et al. The mode of sensitization and its influence on allograft outcomes in highly sensitized kidney transplant recipients. *Nephrol Dial Transplant* 2016; **31:** 1746–53.

17 Pierson RN 3rd, Allan JS, Cooper DKC, et al. Expert opinion special feature: patient selection for initial clinical trials of pig organ transplantation. *Transplantation* 2022; **106:** 1720–23.

18 Levan ML, Ahuja HK, Reed RD, et al. Beyond theory and into practice: a qualitative study of the experiences of xenotransplant recipients. *Am J Transplant* 2025; **26:** 349–58.

19 Firl DJ, Lassiter G, Hirose T, et al. Clinical and molecular correlation defines activity of physiological pathways in life-sustaining kidney xenotransplantation. *Nat Commun* 2023; **14:** 3022.

20 Park WD, Grande JP, Ninova D, et al. Accommodation in ABO-incompatible kidney allografts, a novel mechanism of self-protection against antibody-mediated injury. *Am J Transplant* 2003; **3:** 952–60.

21 Haas M, Segev DL, Racusen LC, et al. C4d deposition without rejection correlates with reduced early scarring in ABO-incompatible renal allografts. *J Am Soc Nephrol* 2009; **20:** 197–204.

22 Cohen D, Colvin RB, Daha MR, et al. Pros and cons for C4d as a biomarker. *Kidney Int* 2012; **81:** 628–39.

23 Ishiyama KI, Kitawaki T, Otsuka Y, Takaori-Kondo A, Kadowaki N. Programmed cell death 1-expressing CD56-negative natural killer (NK) cell expansion is a hallmark of chronic NK cell activation during dasatinib treatment. *Cancer Sci* 2021; **112:** 523–36.

24 Jones-Carr ME, Fatima H, Kumar V, et al. C5 inhibition with eculizumab prevents thrombotic microangiopathy in a case series of pig-to-human kidney xenotransplantation. *J Clin Invest* 2024; **134:** e175996.

25 Loupy A, Goutaudier V, Giarraputo A, et al. Immune response after pig-to-human kidney xenotransplantation: a multimodal phenotyping study. *Lancet* 2023; **402:** 1158–69.

26 Schmauch E, Piening BD, Dowdell AK, et al. Multi-omics analysis of a pig-to-human decedent kidney xenotransplant. *Nature* 2025; **650:** 205–17.

27 Rosales IA, Giarraputo A, Trivin-Avillach C, et al. Mechanistic insights from transcript analysis of long-term pig to non-human primate kidney xenografts. *Kidney Int* 2026; **109:** 506–24.

28 Mohiuddin MM, Singh AK, Scobie L, et al. Graft dysfunction in compassionate use of genetically engineered pig-to-human cardiac xenotransplantation: a case report. *Lancet* 2023; **402:** 397–410.

29 Thaunat O, Lakkis FG, Kosmoliaptsis V, et al. Sensitization in transplantation assessment of risk 2025 innate working group: the potential role of innate allorecognition in kidney allograft damage. *Am J Transplant* 2025; **25:** 2038–47.

30 Fishman JA, El Khoury J, Kawai T, et al. Infectious disease surveillance and management in clinical xenotransplantation: experience with the first human porcine kidney transplant. *Am J Transplant* 2025; **25:** 2451–57.