WK1

Scalable Urine Transcriptomics for Rare Kidney Disease

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WEDNESDAY - Moderated Poster Session, HALL Q, March 11, 2026, 13:45 - 14:45

Background: Kidney biopsies remain the standard source of native renal tissue for studying disease mechanisms, but they are invasive and often unsuitable for longitudinal follow-up. Urine offers a safe, repeatable alternative, containing kidney-derived epithelial and immune cells that can be studied directly. Human urine–derived renal epithelial cells (hURECs) can be cultured and used to investigate disease mechanisms and therapeutic responses. Bulk RNA sequencing (RNA-seq) of hURECs is practical and scalable, but interpretation is limited by variable mixtures of cell types. Single-cell RNA sequencing (scRNA-seq) can resolve this heterogeneity, but its cost and complexity restrict large-scale or routine use, especially in rare diseases. Computational deconvolution methods offer a potential solution, provided a suitable single-cell reference is available. Existing kidney atlases are inadequate, as they omit urinary tract cell types and exclude rare disease patients. The main aim of this project is to generate an appropriate reference for hURECs deconvolution.

Methods: We integrated >50 published urinary scRNA-seq datasets from five independent studies, including male donors with diabetic kidney disease (n=9), acute kidney injury (n=23), FSGS (n=14), and healthy controls (n=3), together with our own unpublished autosomal dominant polycystic kidney disease (ADPKD) pilot data (n=8). Integration was performed in Seurat (v4.4.0) with Harmony batch correction. Cell-type–specific quality-control thresholds were applied to maximise retention of biologically meaningful populations. As proof of principle, bulk RNA-seq from Fabry disease hURECs was deconvoluted using MuSiC (v0.1.1) with the Kidney Cell Atlas as reference.

Results: Integrated analysis recovered major kidney cell types, including rare populations such as podocytes, as well as additional urinary tract–derived populations. ADPKD pilot samples aligned to shared clusters, supporting feasibility of cross-disease integration. Cluster composition analysis showed representation of all datasets within major clusters, indicating limited study-specific bias. Deconvolution of Fabry bulk hURECs revealed baseline heterogeneity and a unique B-cell signature absent from the original analysis. However, the Kidney Cell Atlas reference forced urinary tract cells into kidney-only categories, underscoring the need for a urine-specific atlas.

Conclusion: This pilot study demonstrates feasibility but is limited to male-only cohorts. We are expanding this to include rare disease patients, women, and healthy controls. Planned next steps include benchmarking multiple deconvolution tools and experimentally validating predicted cell-type signals. Our ultimate goal is to build a Urine Transcriptomic Atlas and an hUREC deconvolution framework to enable scalable, cell-type–specific biomarker discovery in rare kidney disease

WK2

National genomic practices and attitudes towards KDIGO recommendations for the care of people with ADPKD

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Introduction:
Genetic information in individuals and first-degree relatives has the capacity for earlier diagnosis, individualised therapy, accurate risk stratification and earlier access to disease-modifying therapies. This new treatment paradigm needs to be considered in the context of recent KDIGO recommendations for the management of Autosomal Dominant Polycystic Kidney Disease (ADPKD).

Methods:
A cross-sectional survey of lead clinicians for ADPKD at UK kidney units was distributed between February and June 2025. Multiple choice and free text questions were used to assess agreement with KDIGO recommendations in those diagnosed with ADPKD, and genomic testing in them and their first-degree relatives. Quantitative data were summarised descriptively and free-text responses analysed thematically.

Results:
Of 68 kidney units, 47 (69.1%) responded with 41 (60.3%) fully completing the survey. General nephrology clinics were the most common location for genomic screening (Figure 1). Although most units (87.0%, 40/46) offered diagnostic genomic testing for individuals with a clinical diagnosis of ADPKD, the staff available across kidney units varied substantially (Figure 2). Only one third reported having access to clinical geneticists, genetic associates or genetic counsellors. However, half of units had a genetics multi-disciplinary team.

The estimated proportion of people with a confirmed clinical diagnosis of ADPKD offered genomic testing varied widely (5%-100%). Half of units offer testing to fewer than one-third of patients, while nine units reported near-universal adoption (≥80%) leading to a bimodal pattern of genomic testing uptake for index cases (defined as the first individual within a family to be identified).

40.5% (17/42) of units use the PROPKD score in clinical practice for prognostication and as an indication for tolvaptan. There was strong support for KDIGO statements on screening for intracranial aneurysms (95.1%) and lipid-lowering therapy (78.0%) as well as moderate support for the blood pressure targets given for younger adults (52.4%) and older adults (46.3%) (Figure 3).

60.4% (26/43) of units reported offering genomic screening to some or all first-degree relatives of people with ADPKD. When a pathogenic variant is not identified in the index

case, 41.9% (18/43) of respondents indicated they would not proceed with screening by any method.

Discussion and Conclusions:
The combination of substantial variation in the provision of genomic services for ADPKD and its utilisation in clinical practice between UK kidney units may result in unequal patient access to genomic testing. Consequently, some patients may miss the opportunity this gives for earlier diagnosis and access to individualised treatment. At-risk relatives are not consistently offered any form of screening. Limited availability of genetics expertise and structured genomic services across units may restrict the consistent implementation of KDIGO recommendations, despite strong overall support. This study is, to our knowledge, the first in the UK to systematically document such variation, highlighting an important source of inequity in patient access to genomic testing and its clinical benefits.

WK3

Pegcetacoplan for 52 weeks results in sustained proteinuria reduction to remission (≤0.5 g/g) and normalisation (≤0.2 g/g): Phase 3 VALIANT trial

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Introduction: Natural history studies report improved outcomes in C3 glomerulopathy (C3G) and primary immune complex-membranoproliferative glomerulonephritis (IC-MPGN) with proteinuria <0.88 or 1 g/g or proteinuria reduction ≥50%.
Pegcetacoplan, a targeted C3/C3b inhibitor, may prevent deposition of C3 breakdown products, reducing glomerular inflammation and kidney damage in C3G and primary IC-MPGN.
VALIANT (phase 3; NCT05067127) investigated the efficacy and safety of pegcetacoplan for adolescents (≥12 years) and adults with native or post-transplant C3G or primary IC-MPGN. The primary endpoint was met, with 68.1% (95% CI –76.2, –57.3) geometric mean reduction of UPCR in pegcetacoplan vs. placebo arms at week 26 ($p<0.0001$). Results were consistent across all subgroups (disease type, age, transplant status, and baseline immunosuppression use).

Methods: During VALIANT's 26-week randomised controlled period (RCP), patients received subcutaneous pegcetacoplan 1080 mg (or weight-based doses for adolescents weighing <50 kg) (n = 63) or placebo (n=61) twice weekly. The RCP was followed by a 26-week open-label period (OLP) in which all patients received pegcetacoplan. 59 of 63 patients who remained on pegcetacoplan for the whole study period (pegcetacoplan-to-pegcetacoplan) and 55 of 61 patients who switched from placebo to pegcetacoplan after 26 weeks (placebo-to-pegcetacoplan) completed 52 weeks of treatment. This post-hoc analysis assessed proteinuria change from baseline at week 26 and week 52 in both groups.

Results: At week 26, 20 (31.8%) pegcetacoplan-to-pegcetacoplan patients achieved proteinuria remission (≤0.5 g/g); 11 (17.5%) achieved proteinuria normalisation (≤0.2 g/g) (Figure). Results were maintained at week 52, with 23 (36.5%) and 11 (17.5%) achieving proteinuria remission and proteinuria normalisation, respectively. Similar results were seen at week 52 in placebo-to-pegcetacoplan patients with 20 (32.8%) achieving remission and 7 (11.5%) achieving normalisation (following switch to pegcetacoplan from placebo at week 26).
In the pegcetacoplan-to-pegcetacoplan group, 38 (60.3%) achieved ≥50% proteinuria reduction at week 26 with 34 (54.0%) achieving ≥50% reduction at week 52. In the placebo-

to-pegcetacoplan group, only 3 patients (4.9%) had achieved ≥50% proteinuria reduction at week 26 whilst on placebo; this number increased to 25 (41.0%) at week 52 having switched to pegcetacoplan at week 26.

Discussion: Proteinuria reductions to normalisation/remission achieved at 26 weeks in the RCP were maintained by patients who received pegcetacoplan for 52 weeks, confirming pegcetacoplan's sustained efficacy. Consistent results were achieved in placebo-to-pegcetacoplan patients in the OLP. Furthermore, a considerable proportion of patients achieved ≥50% proteinuria reduction at the timepoints studied- an important finding considering the significance this has on long-term kidney outcomes as observed in natural history studies.

FIGURE: Proteinuria* shifts during VALIANT
*Baseline UPCR value was calculated as the average of the UPCR measurements from at least 6 of the 9 FMU samples collected between the start of screening and day 1, inclusive. Week 26 and 52 UPCR values were calculated using triplicate FMU collections. FMU, first-morning urine; UPCR, urine protein-to-creatinine ratio.

WK4

Ravulizumab in atypical haemolytic uraemic syndrome: analysis of quality of life outcomes in adult and paediatric phase 3 trials

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Introduction: Atypical haemolytic uraemic syndrome (aHUS) is a rare thrombotic microangiopathy (TMA) caused by complement dysregulation. Patients with aHUS often present with acute renal failure and have an impaired quality of life (QoL) from the symptoms they experience, and challenges associated with medical care. Ravulizumab is a complement C5 inhibitor approved for the treatment of aHUS and has demonstrated immediate, complete, and sustained terminal complement inhibition in clinical trials. The aim of this analysis was to assess the effect of ravulizumab on QoL in patients with aHUS.

Methods: This analysis reports data from complement C5 inhibitor-naive patients with aHUS in two completed phase 3, single-arm clinical trials in adult (NCT02949128) and paediatric populations (NCT03131219). Intravenous ravulizumab was administered every 4–8 weeks. The two main QoL assessments were the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue scale; for adult and paediatric patients) and the 5-dimension 3-level EuroQol questionnaire (EQ-5D-3L; for adult patients). The FACIT-Fatigue score ranges from 0 to 52 and the mean score in the general population is 44; a ≥ 3-point improvement from baseline is considered clinically meaningful (FACIT-Fatigue version 4 [patients ≥ 18 years]; paediatric FACIT-Fatigue [patients < 18 years]). The EQ-5D-3L is a participant-reported questionnaire that scores: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, and index scores generally range from 0 to 1. Normal EQ-5D-3L population values range from 0.8 to 1.0. QoL measures were summarized at baseline and each post-baseline time point using descriptive statistics for continuous variables for the observed value as well as the change from baseline; an increase in either score indicates an improvement in QoL. Data were collected through the extension period of each trial, which was up to 4.5 years or at product approval/registration (whichever occurred first).

Results: Overall, 56 adult and 20 paediatric patients were included in the full analysis set. At baseline, the mean adult FACIT-Fatigue score was 24 (n=51) and the paediatric score was 31 (n=9). Across Days 8–71, mean FACIT-Fatigue scores generally improved; at Day 71 scores were 42 (adults; n=50) and 48 (paediatric; n=9). Scores were generally stable over the extension period (Figure 1). Among adult patients, by Day 8, 63.3% (31/49) of patients had a ≥ 3-point improvement in FACIT-Fatigue score, which increased to 77.1% (n =37/48) at Day 29, and 79.4% (n = 27/34) at Day 743. Among paediatric patients, by Day 8, 33.3% (n=3/9) of patients had a ≥ 3-point improvement in FACIT-Fatigue score, which increased to 100%

(n=9/9) at Day 71 and then remained constant through Day 911 (7–8 patients reporting on Days 575, 743, and 911). At baseline, adult patients with available data (n=53) had a mean EQ-5D-3L score of 0.56. From Day 29 through the extension period, mean EQ-5D-3L scores ranged between 0.8 and 0.9 (Figure 2).

Conclusion: This analysis demonstrated that ravulizumab treatment was associated with rapid clinically meaningful improvement in QoL measures. Scores improved following ravulizumab treatment and were sustained at or near normal ranges throughout the extension period.

WK5

The Efficacy of SGLT2 Inhibitors in Slowing Cyst Growth in Autosomal Dominant Polycystic Kidney Disease (ADPKD): A Real-World Evidence Study

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Background
Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most common inherited kidney disorder, characterized by the progressive growth of renal cysts that leads to kidney failure. In Egypt, as globally, this condition represents a significant burden on patients and healthcare systems. Current treatment options are limited. Sodium-glucose cotransporter-2 (SGLT2) inhibitors, known for their cardiorenal protective effects, have mechanisms that could be beneficial in ADPKD. They induce osmotic diuresis and reduce cellular energy stress, potentially inhibiting pathways involved in cyst proliferation. However, clinical evidence in the ADPKD population, particularly from the North African region, is lacking. This study aimed to evaluate the real-world impact of SGLT2 inhibitor use on the rate of total kidney volume (TKV) increase and eGFR decline in Egyptian patients with ADPKD.
Methods
We conducted a retrospective, multi-center cohort study using patient medical records from the nephrology departments of three major university hospitals in Cairo and zagazig in Egypt. Data was collected for the period between January 2018 and December 2024. We identified adult patients with a confirmed diagnosis of ADPKD and at least two abdominal MRI or CT scans separated by a minimum of 24 months. The study group consisted of patients prescribed an SGLT2 inhibitor for any indication (n=78), and they were matched 1:2 on age, sex, baseline eGFR, and Mayo Clinic Imaging Classification (MCIC) with a control group of patients not receiving SGLT2 inhibitors (n=156). The primary outcomes were the annualized rate of TKV increase (%) and the annualized slope of eGFR decline (mL/min/1.73m²). Statistical analysis was performed using mixed-effects models.
Results
Baseline characteristics were well-matched between the two groups. Over a median follow-up of 3.6 years, the SGLT2 inhibitor group demonstrated a significantly slower annualized rate of TKV increase compared to the control group (3.3% vs. 6.1%, $p<0.001$). Furthermore, the annualized eGFR decline was significantly attenuated in patients treated with SGLT2 inhibitors compared to controls (-2.1 mL/min/1.73m² per year vs. -3.8 mL/min/1.73m² per year, $p=0.003$). The beneficial effects were observed across all Mayo classes but were most pronounced in patients with MCIC 1C and 1D. Adverse events were consistent with the known safety profile of SGLT2 inhibitors and did not lead to a high rate of treatment discontinuation.
Conclusion
In this real-world study of an Egyptian cohort, the use of SGLT2 inhibitors was associated with a significant reduction in the rate of both cyst growth and renal function decline in patients with ADPKD. These findings provide novel evidence suggesting a potential disease-modifying role for SGLT2 inhibitors in this population. This warrants further investigation

through prospective, randomized controlled trials to confirm these promising results and establish SGLT2 inhibitors as a potential new therapeutic strategy for slowing ADPKD progression in Egypt and beyond.

WK6

Small molecule drug treatments for inherited kidney disease: Nephronophthisis

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Renal ciliopathies are a heterogeneous class of disorders caused by dysfunctions of the primary cilia. They are often multisystem disorders characterized by extensive genetic heterogeneity and clinical variability with high levels of lethality and there is marked phenotypic overlap among distinct ciliopathy syndromes. Nephronophthisis (NPHP) is a typical renal ciliopathy phenotype that causes kidney failure often within early childhood, for which there are no curative treatments beyond dialysis and transplantation.

To identify novel therapeutics for NPHP, we designed a high-throughput ciliary phenotype-driven screening strategy to interrogate the TOCRIS library of 1120 biologically active compounds, making use of the Operetta high-content imaging system with Harmony/Columbus software. Initially, 33 compounds were identified that restored ciliary phenotype in renal epithelial cells derived from Cep290 mutant mice. These compounds were subjected to a secondary screen using NPHP patient fibroblasts (P-BB), carrying compound heterozygous CEP290 mutations, including an allele that we had previously shown to be amenable to Anti-sense Oligonucleotide (ASO) mediated exon skipping. In this screen, 12 compounds either restored ciliogenesis or corrected cilia length defects.

A tertiary phenotypic screen of the 12 TOCRIS compounds was then carried out in human urine-derived renal epithelial cells (hURECs) from a NPHP patient (P-HB) carrying CEP290 mutation (p. (Thr832Asnfs*12) and p.(Gly1890*)) along with control hURECs from an unaffected sibling. The initial hUREC phenotypic screen of P-HB cells displayed a ciliogenesis defect with elongated cilia typically found in CEP290 patients, compared to the unaffected sibling who had normal cilia. Two of the TOCRIS chemical compounds rescued the ciliary phenotype in patient (P-HB). We will employ RNAseq to identify the underlying molecular pathways using the TOCRIS compounds which may reveal novel insights into the mechanisms underlying NPHP secondary to CEP290 mutations and explore this in additional genetic causes.

WK7

Target-Release Budesonide in IgA Nephropathy: Rapid Proteinuria Reduction with Notable Steroid-Related Toxicity in Real-World Practice

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WEDNESDAY - Moderated Poster Session, HALL Q, March 11, 2026, 13:45 - 14:45

Background:
IgA nephropathy (IgAN) is the most common primary glomerulonephritis and a significant contributor to kidney failure. Target-release formulation (TRF) budesonide (Kinpeygo®) acts on Peyer's patches to reduce mucosal immune activation, offering a gut-targeted approach with limited systemic exposure. While phase III trials have demonstrated efficacy, real-world experience remains scarce.

Methods:
We conducted a single-centre observational study of adults with biopsy-proven IgAN treated with TRF-budesonide for 9 months (tapered at completion), in addition to renin–angiotensin system blockade (± SGLT2 inhibitors). Patients were reviewed every 3 months with urine protein:creatinine ratio (PCR), estimated glomerular filtration rate (eGFR), and safety monitoring blood tests. Primary outcomes were proteinuria reduction (PCR <90 mg/mmol) and kidney function preservation (no ≥30% eGFR decline).

Results:
Ten patients were initially considered; one declined treatment after dispensing, and two discontinued early due to adverse effects (one with Cushingoid features, and one with new-onset diabetes mellitus). Seven patients initiated TRF-budesonide (median age 45 years, 57% female). At time of analysis, three patients had completed 9 months of therapy. Median baseline PCR was 300 mg/mmol, falling to 58 mg/mmol at 9 months (median reduction ~81%). Of the three patients with evaluable 9-month data, two achieved PCR <90 mg/mmol, and one achieved PCR <50 mg/mmol. Most proteinuria reduction occurred by 3–6 months, with continued improvement through to month 9.. Median eGFR increased from 60 to 72 mL/min/1.73m². No patients experienced a ≥30% eGFR decline during treatment, fulfilling the kidney preservation endpoint.

Conclusions:
In this real-world cohort, TRF-budesonide produced a rapid and sustained fall in proteinuria with stable or improved kidney function. However, 20% of patients discontinued due to steroid-related toxicity, including metabolic complications. These findings highlight the importance of careful patient selection and close monitoring, even with gut-targeted steroid therapy.

WK8

Clinical experience of Obinutuzumab in the management of refractory ANCA associated vasculitis

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Background:
Antineutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) comprises a group of autoimmune conditions that cause necrotising inflammation in blood vessels. While rituximab or cyclophosphamide, combined with steroids and / or avacopan, as standard therapy for inducing remission has a high success rate, some patients experience severe, non-remitting disease. Obinutuzumab, a type II anti-CD20 monoclonal antibody, is suggested to be more potent at inducing B-cell cytotoxicity, with some suggestion of potent effect on the tissue B-cells niches and hence may be effective in these refractory cases. However, clinical data on its use in AAV are limited. We have previously reported our preliminary experience with Obinutuzumab in AAV (UKKW 2024). Here we report long term follow up of our clinical experience of using Obinutuzumab in patients with severe refractory AAV.
Methods:
We conducted a retrospective case series at a tertiary centre, reviewing the use of Obinutuzumab in AAV patients over the last five years. The series describes six patients who received Obinutuzumab for severe, non-remitting disease that was refractory to conventional therapy.
Results:
All six patients were diagnosed with granulomatosis with polyangiitis and had severe disease that was unresponsive to rituximab. Two had also failed to respond to cyclophosphamide. In the rest of the patients Obinutuzumab was used due to prior cyclophosphamide use with high cumulative dosage, or fertility concerns.
All patients presented with severe, non-remitting ENT or head and neck disease. In most cases, patients had demonstrable ongoing active disease despite complete peripheral B cell depletion and in some cases negative ANCA titres. Following induction and maintenance therapy with Obinutuzumab, patients demonstrated significant clinical improvement, with 5 out of 6 patients achieving sustained remission with reduced or negative ANCA titres. Obinutuzumab was well tolerated with no serious adverse events.
Conclusion:
In this case series, Obinutuzumab was an effective and well-tolerated treatment for inducing remission and improving clinical symptoms in patients with severe AAV refractory to conventional therapy. These findings support the need for further research, such as randomised controlled trials, to directly compare the efficacy of Obinutuzumab to Rituximab in the management of AAV. Indeed, the first such phase 2, experimental clinical trial, ObiVas, is currently underway with results eagerly awaited.

WK9

Treatment and Outcomes in Anti-Glomerular Basement Membrane Disease

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WEDNESDAY - Moderated Poster Session, HALL Q, March 11, 2026, 13:45 - 14:45

Background/Aims:
KDIGO 2021 Glomerular Diseases Guidelines recommend treatment for anti-Glomerular Basement Membrane (GBM) disease except in patients dialysis-dependent at presentation, with 100% crescents or >50% global glomerulosclerosis on biopsy, and no pulmonary haemorrhage.

Methods:
Case series of all patients diagnosed with anti-GBM disease between January 2017 and July 2025 in 2 UK tertiary centres. Clinical and laboratory data were obtained from electronic records.

Results:
Of 72 patients with anti-GBM disease, 49% (n=35) were female, median age 64 years and 32% (n=23) were ANCA-positive; 18% (n=13) PR3, 14% (n=10) MPO-ANCA. Median creatinine at presentation was 700µmol/litre (range 35-3494µmol/litre). Pulmonary haemorrhage occurred in 26% (n=19). Patients received a median of 7 plasma exchange (PLEX) sessions (range 0–51) and 3 doses of intravenous cyclophosphamide (range 0-8).

Twenty-eight patients (38.9%) were dialysis independent at presentation; 3/27(11.1%) progressed to end stage kidney disease by 12 months. Of the 44 (61.1%) patients requiring dialysis at presentation, 5/42 (11.9%) recovered renal function; these 5 had a median creatinine at presentation of 777 µmol/litre and 14 PLEX sessions (range 7–38).

Renal biopsy was performed in 54.2% (n=39); 3/39 had 100% crescents and four >50% global sclerosis. One with 100% crescents, and 2/4 with >50% global sclerosis did not require dialysis at presentation and remained dialysis independent at 12 months. Of those requiring dialysis at presentation who underwent a biopsy, 13/39 (33.3%) had <10% normal glomeruli (2/13(15.4%) recovered renal function); 7 patients had ≥10% normal glomeruli and 2/7(28.6%) recovered. Anti-GBM antibody titres were >600 in 41.6% (n=30); 73% were dialysis dependent at presentation (n=22). Only 1 was dialysis independent at 12 months.

Conclusions:
Patients dialysis-independent at presentation largely maintained renal survival at 12 months, regardless of biopsy findings. Even with adverse histology or high creatinine, renal recovery was possible, supporting treatment in most patients with anti-GBM disease.

WK10

Infusion-related reactions (IRRs) and haematological events associated with obinutuzumab in lupus nephritis: a secondary analysis of a phase III trial

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Background: The REGENCY (NCT04221477) trial demonstrated superior efficacy of obinutuzumab and standard therapy (OBI+ST) over placebo and ST (PBO+ST) in patients with active lupus nephritis (LN). Insights related to IRRs and haematological effects of obinutuzumab would help guide future management of LN. This study characterised the IRR profile and occurrence of neutropenia in the REGENCY trial.

Methods: Incidence, severity and attribution of IRRs and haematological abnormalities, including drug-related neutropenia, were determined based on investigator and NCI CTCAE v5.0 adverse event grading.

Results: The proportion of patients who experienced at least one IRR was higher in the OBI+ST vs the PBO+ST arm (21 [15.4%] vs 15 [11.4%]). In the OBI+ST arm, the majority (19 [14.0%]) experienced IRRs of Grade 1-2, which resolved. In the OBI+ST arm, 2 patients (1.5%) experienced Grade 3-4 IRRs; both events resolved. No Grade 5 IRRs were observed. The most frequently reported symptoms of IRRs in the obinutuzumab vs placebo arms respectively were nausea (4 [2.9%] vs 4 [3.0%]), headache (4 [2.9%] vs 3 [2.3%]) and vomiting (4 [2.9%] vs 2 [1.5%]). IRR incidence and severity was highest at first infusion, with Grade 3-4 observed only then (Table 1).

The shifts observed from Grade 1-2 at baseline to Grade 3-4 post-baseline were notably different between the treatment arms for neutrophils and lymphocytes. As lymphopenia is an expected pharmacological effect of anti-CD20 therapies, this analysis focused on drug-related neutropenia. The proportion of patients who experienced at least one drug-related neutropenia was higher in the OBI+ST arm vs the PBO+ST arm (17 [12.5%] vs 5 [3.8%]). Most cases of neutropenia were incidentally detected during routine haematology labs at scheduled study visits. Median time for resolution was 16 days (min-max: 4-378 days) and 50.5 days (min-max: 21-371 days) in the OBI+ST and PBO+ST arm, respectively. Seven patients (4.1%) had Grade 3-4 drug-related neutropenia (including 1 febrile neutropenia), while none occurred in the PBO+ST arm. All drug-related neutropenia resolved with treatment except for one placebo patient where it was resolving at clinical cutoff. No Grade

5 neutropenia was observed. Five patients received G-CSF treatment for drug-related neutropenia (4 in the OBI+ST arm vs 1 in the PBO+ST arm).

Conclusion: The incidence of IRRs and drug-related neutropenia was higher in patients receiving OBI+ST but risks remained low overall; many were Grade 1-2, self-limited, easily manageable and without consequence. These data provide insights into adverse events related to obinutuzumab.

WK11

Evaluation of side effects and evidence of systemic absorption in patients with IgA Nephropathy treated with targeted-release budesonide (Kinpeygo)

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WEDNESDAY - Moderated Poster Session, HALL Q, March 11, 2026, 13:45 - 14:45

Targeted-release formulation budesonide (TRf-budesonide) uses TARGIT® technology to deliver budesonide to the distal ileum/ proximal colon where it acts on Peyer's patches to reduce the production of Gd-IgA1. In clinical trials, a 9-month course of TRf-budesonide 16mg daily resulted in a sustained reduction of proteinuria and improved preservation of eGFR. Budesonide is a highly potent steroid; 16mg is equivalent to oral prednisolone 213mg1. After extensive first pass metabolism (via CYP3A4), systemic bioavailability of budesonide is 10%. This equates to a daily dose of prednisolone 20mg. Concern remains over the side effects of systemic absorption of TRf-budesonide. We aimed to evaluate this in our patient cohort.

In this retrospective study at a single glomerulonephritis clinic with an ethnically diverse population, we evaluated adverse effects and metabolic parameters in patients treated with TRf-budesonide.

29 patients started treatment (Table 1: Demographics). To date, 13 patients have completed a >9-month course of treatment (full dose: n=9; reduced dose: n=4), 4 patients discontinued treatment early at a duration of 16.2 weeks (range: 10.3 - 26). Reasons for discontinuation were steroid-induced central serous retinopathy (n=1), Cushingoid features (n=1), death following admission with pneumonia (n=1), lymphoma treatment (n=1). 12 patients remain on treatment between 2.6 to 32 weeks (full dose: n=11; reduced dose: n=1). 5 patients required a dose reduction, 4 were due to weight gain, acne, and mood changes; 1 patient's reason was not documented. Among the 13 patients who completed 9 months of treatment, the urine protein creatinine ratio showed a mean reduction of 19.9%.

Side effects are shown in Table 2. These were most commonly weight gain, acne and Cushingoid facies. 14/29 patients experienced weight gain of a median of 3.8 kg (1.5 – 8.6) on treatment. 8/29 patients developed acne, 7/29 Cushingoid facies and 2/29 developed striae. 6/29 patients had infections requiring antibiotics, 2 patients required admission to hospital for treatment. One patient died secondary to pneumonia. Serum cortisol was measured in 14 patients whilst on treatment, levels were undetectable in 6/14 (43%), reduced in 5/14 (36%) and normal in 3/14 (21%). 12/29 (41.3%) patients required a dose

increase or new antihypertensive medication during the treatment period. All patients with pre-diabetes (n=3) and T2D (n=1) at the start of treatment had a mean increase in HbA1c of 4.75 mmol/mol during treatment period. A further two patients developed pre-diabetes.

There was a reduction in proteinuria consistent with that seen in clinical trials, however adverse effects appeared to be high in our cohort. Most patients had sufficient systemic absorption to suppress endogenous cortisol production. Weight gain, acne, facial changes and mood changes were frequent, as was an increased need for antihypertensive medication and an observed deterioration in glycaemia. Patients should be counselled and appropriately monitored for side effects before starting, and for the duration of treatment. Future work to evaluate the longer-term effects of TRf-budesonide in different ethnic populations, including effects on the hypothalamic-pituitary-adrenal axis and adverse effects is required.

References:

1: Equivalent dosage of commonly used steroids (Journal of Allergy and Clinical Immunology): https://www.jacionline.org/cms/10.1016/j.jaci.2015.07.046/attachment/9e6d93c6-b64b-4468-8cf5-38a0e9b551e9/mmc2.pdf