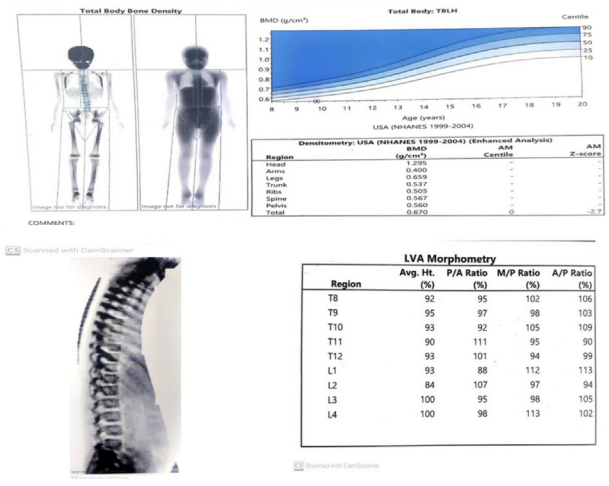
steroid arm- fourteen were girl children and fifteen were in the pre-pubertal stage. All children met the daily recommended calcium intake. 18 children were on steroids for nephrotic syndrome, 4 for lupus nephritis and 1 each for Takayasu arteritis,atypical HUS and C3GN. Out of the 25, only 9 children had a height less than 3rd centile. Serum Vitamin D was low (<30 IU) in 14 children.Bone density assessed by AP spine Z score was low in 84% (21 out of 25 ) children in the steroid arm compared to 12% (3 out of 25) in non-steroid arm . The Z Score of Total Body Less Head was low in 15 of 19 children in the steroid arm compared to 1 of 21 children in the non steroid arm. The lowest TBLH Z Score was- 2.6

| | Steroid arm(n=25) | Non-steroid arm (n=25) |
|---|---|---|
| Age group<br>5-9 years<br>10-14 years<br>15-18 years | <br>7<br>11<br>6 | <br>6<br>14<br>5 |
| Gender<br>Male<br>Female | <br>9<br>14 | <br>14<br>11 |
| Height for age<br><3rd centile<br>3rd- 95th centile<br>>95th centile | <br>9<br>14<br>2 | <br>2<br>19<br>4 |
| BMI centiles<br><5 Undernourished<br>5-85 Normal<br>85-95 Overweight<br>>95 Obese | <br>0<br>17<br>6<br>2 | <br>0<br>16<br>8<br>1 |
| Sexual Maturity Rating (Tanner)<br>Stage 1<br>Stage 2<br>Stage 3<br>Stage 4<br>Stage 5 | <br>3<br>8<br>4<br>5<br>5 | <br>2<br>9<br>5<br>4<br>5 |
| AP spine Z score<br><-1<br>-1 to 0<br>0 to +1<br>>+1 | <br>9<br>12<br>3<br>1 | <br>0<br>1<br>12<br>12 |
| TBLH Z Score (Children older than 7 years)<-1<br>-1 to 0<br>0 to +1<br>>+1 | N-19<br><br>4<br>11<br>3<br>1 | N-21<br><br>0<br>1<br>11<br>9 |







**Conclusions:** Linear growth retardation is a late marker of steroid toxicity. Pediatric BMD evaluation, when done in indicated cases, aids in early detection of bone changes. This could alert the clinician to adopt a steroid minimizing protocol where possible and address correctable factors such as Vit D insufficiency. The challenge of Pediatric BMD is the lack of reference data from the same population. The study suggests the usefulness of inculcating BMD DEXA as a supplementary tool to growth assessment by anthropometry to help minimise long term steroid toxicity on bone growth. The study is limited by the small sample size and paucity of normative BMD data in paediatric population from India. However, BMD study can serve as an ancillary investigation to evaluate early bone changes in children on steroids.

I have no potential conflict of interest to disclose.

I did not use generative AI and AI-assisted technologies in the writing process.

## WCN25-3676

### RESULTS FROM THE REGENCY TRIAL ASSESSING EFFICACY AND SAFETY OF OBINUTUZUMAB IN ACTIVE LUPUS NEPHRITIS

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**Introduction:** Obinutuzumab, a humanized type II anti-CD20 monoclonal antibody, is approved for B-cell malignancies. In the Phase II NOBILITY trial of patients with active lupus nephritis (LN;NCT02550652), study participants receiving obinutuzumab in addition to standard therapy were significantly more likely to achieve complete renal response than those receiving placebo in addition to standard therapy. The results of the Phase III REGENCY trial (NCT04221477), performed to verify NOBILITY, are presented here.

**Methods:** REGENCY, a Phase III, double-blind placebo-controlled trial, randomized adults with biopsy-proven active proliferative LN 1:1 to placebo or one of two intravenous obinutuzumab dosing schedules (1000 mg: Day 1, Weeks 2, 24, 26, ±50 and 52) in addition to standard therapy. The primary endpoint was complete renal response (CRR, defined as urine protein-to-creatinine ratio [UPCR] <0.5 g/g, estimated glomerular filtration rate [eGFR] ≥85% of baseline and no intercurrent events of rescue therapy, treatment failure, death or early study withdrawal) at Week 76 and assessed in the intention-to-treat population. Key secondary endpoints included CRR at Week 76 with successful prednisone taper to ≤7.5 mg/day between Weeks 64 and 76, and UPCR <0.8 g/g at Week 76 with no intercurrent events, change in eGFR from baseline to Week 76 and renal-related events or death through Week 76. Incidence and severity of adverse events through Week 76 were compiled.

**Results:** Of 271 patients randomized, 135 were randomized to obinutuzumab and 136 to placebo. At Week 76, 46.4% of patients in the obinutuzumab group and 33.1% in the placebo group achieved CRR (adjusted difference, 13.4%; 95% CI, 2.0% to 24.8%; $P$=0.0232) (Table). More patients in the obinutuzumab group achieved CRR at Week 76 with successful prednisone taper (42.7% vs 30.9%, adjusted difference, 11.9%; 95% CI, 0.6% to 23.2%; $P$=0.0421) and a proteinuric response (UPCR <0.8 g/g) with no intercurrent events at Week 76 (55.5% vs 41.9%; adjusted difference, 13.7%; 95% CI, 2.0% to 25.4%; $P$=0.0227). Numerical changes in eGFR from baseline to Week 76 favored obinutuzumab compared with placebo, and fewer patients in the obinutuzumab group experienced the composite outcome of death or renal-related events through Week 76. Pre-specified subgroup analyses demonstrated numerically greater CRR rates with obinutuzumab in patients with potentially more active disease at enrollment, such as those with class IV LN, concomitant class V disease, baseline UPCR ≥3 g/g or greater baseline serologic activity. No new safety signals were observed based on the established safety profile of obinutuzumab in oncology indications. More coronavirus disease 2019 (COVID-19) events were observed in the obinutuzumab group, which primarily occurred during the acute phase of the COVID-19 pandemic. There were 3 deaths in the obinutuzumab group and 1 in the placebo group, which were mainly complications of COVID-19.

**Conclusions:** Obinutuzumab plus standard therapy was more effective than placebo plus standard therapy for achieving CRR, a clinically meaningful surrogate of kidney function, in patients with LN, while exhibiting an acceptable safety profile.

I have potential conflict of interest to disclose.

This wasfundedbyHoffman-La Rocheand Genetech Dr. Rovin is on the advisory board of Hoffman-La Roche and Genetech

I did not use generative AI and AI-assisted technologies in the writing process.

## WCN25-3803

### DESIGN OF RANDOMIZED EMBEDDED ADAPTIVE PLATFORM CLINICAL TRIAL IN SOUTH ASIAN KIDNEY BIOPSY-PROVEN PRIMARY GLOMERULAR DISEASES: MULTI-CENTER, MULTI-ARM AND MULTI-STAGE

Suceena Alexander*[1], Selvin Sundar Raj Raj[2], Santosh Varughese[2], Vinoi George David[2], Nisha Jose[2], Reka K[2], Babak Choodari-Oskooei[3], Jonathan Barratt[4], George T. John[5]; IA GRACE IGA PLATFORM TRIAL INVESTIGATORS[6]

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**Introduction:** Global Burden of Diseases ranks CKD as the 12th leading cause of death. India is the most populous country in the South Asian region which has one-fourth of the global population. Glomerular diseases are the most common cause of CKD after diabetes and hypertension and IgAN is the most common primary glomerular disease in adults. Our group has shown that South Asian ethnicity is associated with much severe phenotype, rapid progression in the first prospective longitudinal IgAN (GRACE-IgANI) cohort. The KDIGO guidelines does not specifically address IgAN patients who are on SOC but remain high risk on maximally tolerated RAASi with residual proteinuria and/ or renal function impairment and advocate enrolling patients prospectively in 'Clinical Trials'. Moreover, there is a dearth offundedacademic pragmatic clinical trials looking at commonly available and approved generic drugs that can be effective long term strategies for better clinical outcomes in the South Asian region.

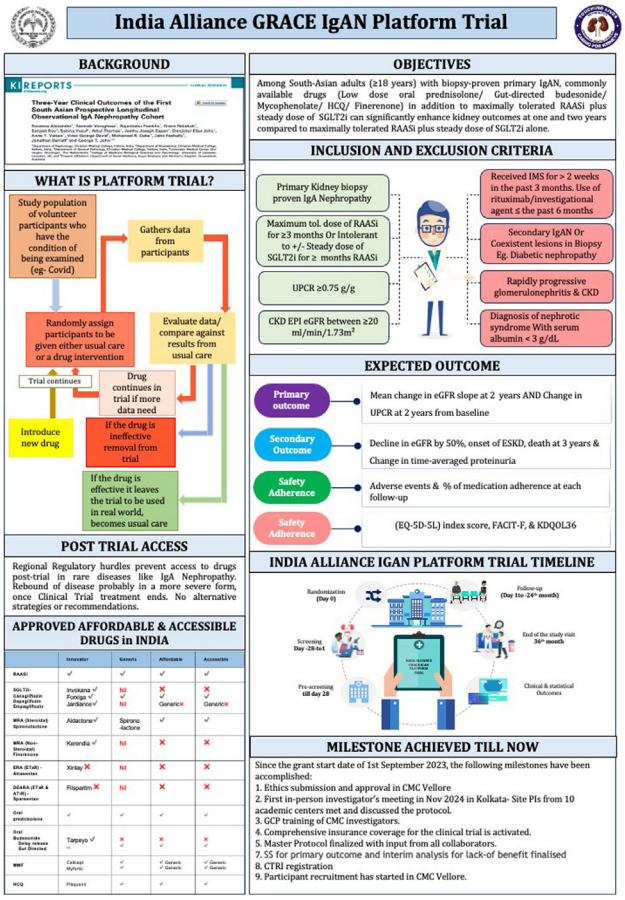
**Methods:** Hypothesis: The overarching study hypothesis is that commonly available and approved drugs (oral steroids, gut-directed budesonide hydroxychloroquine, mycophenolate mofetil, or naMRA) in addition to maximally tolerated RAASi and SGLT2i (SoC) can significantly improve the kidney outcomes at 2 years when compared to SoC alone in South-Asian kidney biopsy proven adult (≥18 years) primary IgAN who are on SOC and on follow-up remain at high risk of progression defined as UPCR ≥0.75g/g and baseline eGFR ≥20ml/min/1.73m2 despite good BP control. The investigators are allowed to use IS regime of their choice and there will be a six month wash out period between end of IS and inclusion in the trial.

Phase IV Randomized Embedded Adaptive MAMS Platform Trial with Concurrent Comparator arm and four Interventional arms in two stages inclusion and exclusion criteria. Inclusion criteria: 1. Adults between 18-75 years of age 2. Males or Females 3. eGFR between ≥25 ml/min/1.73m2 4. UPCR ≥1 g/g 5. Renal biopsy proven primary IgA nephropathy 6. Patient on maximum tolerated dose of RAASi and SGLT2i (SoC) for at least 3 months with a goal BP of <140/90 mmHg. Exclusion criteria: 1. Patients who received immunosuppressive treatment in the preceding 6 months 2. Secondary IgAN 3. Female patients planning pregnancy 4. Concomitant co-morbidities like systemic autoimmune disorders, chronic infections, chronic liver disease etc. 5. Evidence of rapidly progressive glomerulonephritis 6. Concomitant chronic renal disease in addition to IgAN in kidney biopsy 7. Uncontrolled diabetes. Sample size: We plan to recruit a total of 585 patients (allocation 1:1 in control arm; ~117 in each of the interventional arms) over approximately two years. Sample size calculations were based on change in eGFR slope at 2 years in the intervention compared to control group with 90% power and a one-sided type I error of 2.5% for each pair-wise comparison.

This trial isfundedbyDBTWellcomeUKIndia AllianceSenior Fellowshipgrantedto thePI[SA].

**Results:** The trial is a pragmatic Platform Trial. Milestones achieved:

1. Ethics submission and approval in CMC Vellore 2. First in-person investigator's meeting in Nov 2023 in Kolkata- Site Pis from 10 academic centers met and discussed the protocol. 3. GCP training of CMC investigators. 4. Comprehensive insurance coverage for the clinical trial is activated. 5. Pre-screening activities for participant recruitment have started in CMC Vellore. 6. Master Protocol is finalised with input from all collaborators. 7. SS for primary outcome and interim analysis for lack-of benefit revisited and finalised. 8. CTRI registration completed. 9. Participant recruitment started in the main site.




**Conclusions:** We will be able to generate primary evidence of clinical efficacy and toxicity of anti-proteinuric and immunomodulatory therapies in primary glomerular diseases in South Asian population. Platform MAMS trial design is being used for the first time in proteinuric kidney diseases and it will help establish 'GRACE- Clinical Trial Network' for similar studies in glomerular diseases.

I have no potential conflict of interest to disclose.

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## WCN25-4625

### MAXIMISATION OF RENIN-ANGIOTENSIN-ALDOSTERONE INHIBITORS IN HEART FAILURE PATIENTS WITH CKD USING POTASSIUM BINDER; PRELIMINARY ANALYSIS OF A RANDOMISED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

Debasish Banerjee*[1], Irina Chis Ster[2], Mahrukh Ali[1], Lisa Anderson[3], Ella Tumelty[1], Simran Parmar[1], Souradip Mookherjee[1], Daniel Murphy[1], Tony Lopez[1], Hilary Warrens[1]

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