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

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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.

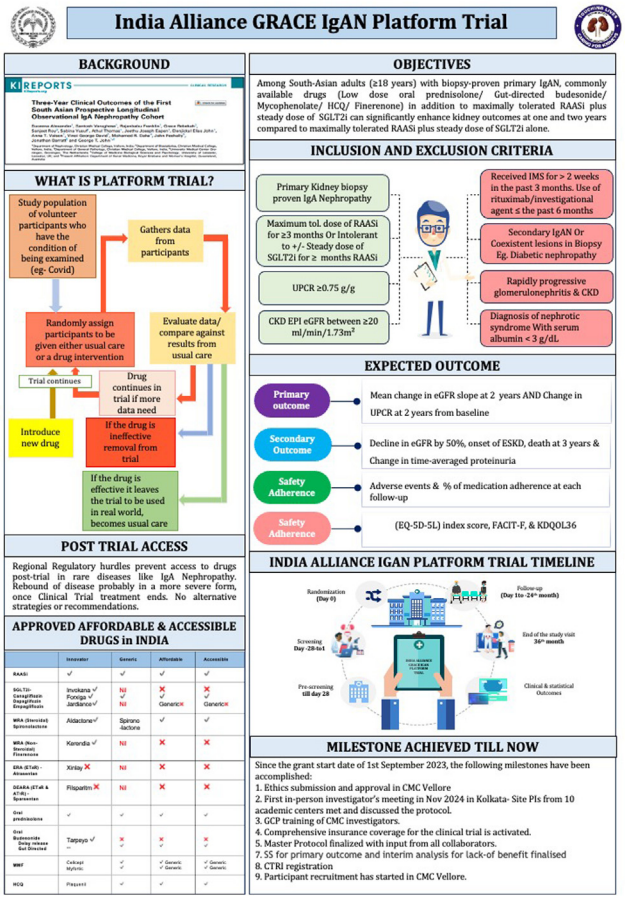
Methods: Hypothesis: The overarching study hypothesis is that commonly available and approved drugs (oral steroids, gut-directed budesonide hydroxychloroquine, mycophenolate mofetil, or naMRA) in addition to maximally tolerated RAASi and SGLT2i (SoC) can significantly improve the kidney outcomes at 2 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.

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

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

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