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Comparative Efficacy and Safety of Remogliflozin 100 mg Versus Dapagliflozin 10 mg in Patients with T2DM and CKD: A Randomized, Open-Label Study

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ABSTRACT

Background: In diabetic patients, managing glycaemic control while preserving renal function is a challenge, necessitating the use of sodium-glucose cotransporter-2 inhibitors, which have demonstrated reno-protective and cardiovascular benefits. Remogliflozin, a novel sodium-glucose co transporter-2 inhibitors, has shown efficacy in glycemic control, but its renal effects in chronic kidney disease patients remain unexplored.

Aim: To assess the non-inferiority of remogliflozin compared to dapagliflozin in terms of renal and glycaemic parameters in patients with Type 2 diabetes mellitus and chronic kidney disease.

Methods: A prospective, multicentre, randomized, open-label, active-controlled, non-inferiority study was conducted in patients diagnosed with Type 2 diabetes mellitus and chronic kidney disease. Participants were assigned to receive either remogliflozin or dapagliflozin over a treatment period of 24 weeks. Primary endpoints included changes in renal parameters such as estimated glomerular filtration rate, urinary albumin-to-creatinine ratio, serum creatinine, blood urea nitrogen, and uric acid. Secondary endpoints included measures of glycemic control, body weight, and safety outcomes

Results: Both treatment groups showed significant improvement in renal parameters from baseline to weeks 12 and 24 ($p<0.001$), with no significant difference between groups. Glycaemic parameters also improved significantly in both groups, with similar mean % reductions in HbA1c [Remogliflozin: 8.46% to 7.40%; Dapagliflozin: 8.11%to 7.49%]. The incidence of a ≥50% sustained decline in eGFR was comparable (Remogliflozin: 9.46%; Dapagliflozin: 6.67%; $p>0.05$). End-stage renal disease was observed in 4.05% and 2.67% of patients in the remogliflozin and dapagliflozin groups, respectively. No cases of cardiovascular or renal death were reported. Both groups demonstrated reductions in body weight and body mass index. Adverse events were mild and comparable between groups, with no serious safety concerns.

Conclusion: Remogliflozin demonstrated non-inferiority to dapagliflozin in renal and glycaemic outcomes, with a comparable safety profile. These findings suggest that remogliflozin is a viable treatment option for patients with Type 2 diabetes mellitus and chronic kidney disease. Further long-term studies are warranted to validate these findings.

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Introduction

Diabetes is a major global health concern with the rise of early onset type 2 diabetes mellitus (T2DM) in adolescents and young adults. The Global Burden of Disease Study 2019 estimates 783 million adults to suffer with T2DM by 2045 [1]. In 2023, the prevalence of T2DM in India was estimated to be 101 million according to the Indian Council of Medical Research (ICMR) – India Diabetes (ICMR-INDIAB) 2023 study, re-positioning India as the diabetic capital of the world [2]. As many as 40% of individuals with diabetes are expected to develop chronic kidney disease (CKD) during their lifetime, a condition that significantly elevates the risk of mortality. This leads to cardiovascular complications as well, increasing hospitalization, and a decline in the quality of life [3,4]. Diabetic nephropathy is primarily driven by chronic hyperglycaemia, which damages renal microvasculature and disrupts filtration. This condition exacerbates hyperglycaemia and insulin resistance, creating a detrimental feedback loop that accelerates both CKD and diabetes progression, making the management of diabetes more complex and also increasing the likelihood of adverse events [4].

Hence, achieving a balance between glycaemic control and preserving renal function is imperative. CKD (Stage 2 and above,

estimated glomerular filtration rate (eGFR) ≤ 60mL/min/1.73 m²) complicates the use of common antidiabetic medications, as impaired renal function often necessitates dosage adjustments or contraindications due to reduced drug clearance, limiting treatment options [4].

Both International and National guidelines such as American Diabetes Association (ADA), Kidney Disease: Improving Global Outcomes (KDIGO), and the Research Society for the Study of Diabetes in India (RSSDI) emphasize the need of "reno-protection" in patients with T2DM and CKD [5,6]. Sodium-glucose cotransporter-2 inhibitor (SGLT2i) are particularly beneficial, as they lower the risk of both CKD progression and cardiovascular disease [7].

SGLT2i exert reno-protective effects by reducing glomerular hyperfiltration through tubuloglomerular feedback, which decreases intraglomerular pressure. They also improve outcomes in CKD by mitigating kidney damage and offering cardiovascular benefits, such as reduced heart failure and cardiovascular mortality, particularly in patients with T2DM [8].

The complex and mutually impactful relationship between diabetes mellitus and CKD remains a key area of focus in current healthcare landscape. The advent of SGLT2i has reformed treatment strategies by not only ensuring effective glycaemic control but also providing renal protection [9].

The 2024 ADA guidelines recommend the use of SGLT2i for individuals with CKD which is aimed at reducing the progression of CKD and the risk of cardiovascular events in patients with an eGFR of ≥20 mL/min/1.73 m² and urinary albumin levels of ≥200 mg/g creatinine [10]. The RSSDI recommends adding SGLT2i as part of dual therapy when glucose targets are not achieved with metformin alone [6].

Remogliflozin etabonate was approved by Drugs Controller General of India (DCGI) on 26 April 2019 [11]. This is an oral prodrug of remogliflozin, is another potent and selective SGLT2i. SGLT2i as a class exhibit a consistent effect on glucose lowering. While significant urinary glucose excretion is observed with single doses of remogliflozin etabonate, twice-daily dosing ensures continuous 24-hour glucose-lowering effects, offering improved control over glycaemic variability [12]. The REMIT-GV study found that remogliflozin's twice-daily regimen provides comparable glycaemic control to once-daily dapagliflozin, with better post-prandial and 24-hour management [13]. Similarly, the REMIT-HF study showed remogliflozin is as effective as empagliflozin in managing cardiovascular and glycaemic outcomes in T2DM patients with heart failure with reduced ejection fraction (HFrEF), suggesting it may offer better overall management than once-daily SGLT2i [14].

Dapagliflozin has established itself as a widely utilized SGLT2i, recognized for its benefits in glycaemic management, renal protection, and cardio protection. However, there is no evidence currently on Remogliflozin when used in patients of T2DM with CKD with GFR ranging from 25 to 60 ml/min/1.73m². Therefore, this investigator-initiated study was planned to address this critical gap by evaluating the effects of remogliflozin on renal parameters in patients with T2DM and CKD, assessing its non-inferiority compared to dapagliflozin. By delivering robust clinical insights, this research seeks to enhance the management of T2DM in patients with renal complications and ultimately improve patient outcomes.

Methodology

Study Design

This was a prospective, multicentre, randomized, open-label, active-controlled, non-inferiority trial conducted between May 2023 and January 2024. The study evaluated the efficacy and safety of oral Remogliflozin 100 mg twice daily versus Dapagliflozin 10 mg once daily, both administered alongside standard care, in patients with T2DM and comorbid CKD, defined by an eGFR between ≥25 and ≤60 ml/min/1.73m² at the time of treatment initiation.

The study was conducted in accordance with the protocol, the New Drugs and Clinical Trials Rules (2019, India), the ethical principles outlined in the Declaration of Helsinki, and the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, along with all applicable local regulatory requirements.

Prior to initiation, the study protocol was reviewed and approved by the Institutional Review Boards (IRBs) and Ethics Committees (IECs) of all participating centres. Written informed consent was obtained from all participants in accordance with ICH-GCP standards. The trial was registered with the Clinical Trials Registry - India (CTRI/2023/03/050384) [Registered on: 06/03/2023].

Study Population

The study population included adult patients aged 18 years or older diagnosed with T2DM for at least six months and uncontrolled glycemia (HbA1c >7.0% &<9.0%), on stable therapy (>6weeks prior to screening) with metformin or dual therapy with metformin and another oral hypoglycemic agents (OHA) [15]. Participants were included if they had a confirmed diagnosis of CKD with eGFR ≥ 25 ml/min/1.73m2 to ≤ 60 ml/min/1.73m2 at the time of initiation of treatment, with evidence of increased albuminuria for a minimum of 3 months or more. Along with this, their urinary albumin-to-creatinine ratio (UACR) was ≥200 and ≤5000 mg/g.

Exclusion criteria included pregnant or breastfeeding females, individuals with liver or kidney dysfunction (eGFR < 25 ml/min/1.73m²), patients with autosomal dominant or recessive polycystic kidney disease, lupus nephritis, or ANCA-associated vasculitis, those receiving cytotoxic, immunosuppressive, or other renal-related therapies within six months, individuals with a history of organ transplantation, patients treated with an SGLT2i within eight weeks or with prior intolerance to SGLT2i, those classified as NYHA class IV congestive heart failure at the time of enrolment. Episode of MI, unstable angina, stroke or transient ischemic attack within 12 weeks prior to enrolment.

Interventions

Participants were randomized in a 1:1 ratio to receive either remogliflozin 100 mg twice daily or dapagliflozin 10 mg once daily according to a pre-established randomization plan. In addition to the assigned treatments, all participants continued with their standard care for CKD and T2DM, which remained stable for the duration of the study.

Study Procedures and Assessments

At the time of screening demographic and clinical data, including age, gender, duration of T2DM, CKD status, and background treatment were collected. Physical examinations and laboratory investigations were conducted per the assessment schedule. During the Day 1 visit, eligibility criteria were confirmed, and eligible patients were randomized to receive either Remogliflozin 100 mg or Dapagliflozin 10 mg. A detailed medical history and any changes in medications were recorded. Participants maintained stable

background treatment for at least 6 months before randomization.

Follow-up visits occurred at 12 weeks and 24 weeks, where Body Mass Index (BMI), body weight, waist circumference, vitals, and concomitant medications were assessed. Laboratory tests, including hemogram, renal function, and glycaemic parameters, were performed at all physical visits. (Figure 1)

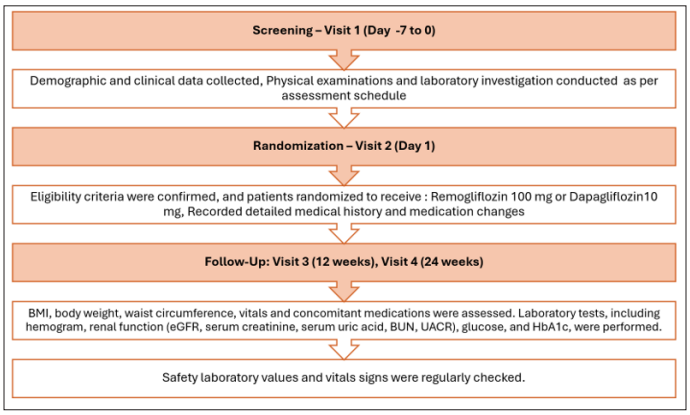

Figure 1: Overall Study Plan

Endpoints

The primary endpoint of the study was to assess the non-inferiority of remogliflozin compared to dapagliflozin, focusing on changes in renal parameters (eGFR, UACR, serum creatinine, Blood Urea Nitrogen (BUN), uric acid) at 12 weeks and 24 weeks relative to baseline. Secondary endpoints included changes in Fasting Plasma Glucose (FPG), Postprandial Glucose (PPG), and HbA1c levels at 12 weeks and 24 weeks, with particular attention to the number of patients achieving an HbA1c level of <7% at 24 weeks. The study aimed to determine if Remogliflozin is non-inferior to Dapagliflozin in reducing the incidence of composite endpoint of the incidence of a composite endpoint comprising a ≥50% sustained decline in eGFR; progression to ESRD defined as a sustained eGFR <15 mL/min/1.73 m², and the occurrence of cardiovascular or renal death in T2DM patients with eGFR ≥25 and ≤60mL/min/1.73m2 at 24 weeks. Additionally, changes in body weight at 24 weeks compared to baseline and the incidence of Treatment-Emergent Adverse Events (TEAEs) were monitored.

Statistical Analysis

The baseline and safety characteristics comprised frequencies and proportions for categorical variables and mean and standard deviations for continuous variables. The p-value is calculated using the Chi-Square test for categorical variables and the unpaired t-test for continuous variables. For within-group comparisons at different time intervals, the p-value is calculated using the Mann-Whitney U test. For differences between two groups, the p-value is calculated using the unpaired t-test.

The primary and secondary endpoints were analysed in both the per-protocol (PP) and intention-to-treat (ITT) populations. The PP population comprised all patients without major protocol deviations, with data available for baseline, 12 weeks, and 24 weeks for the primary and secondary parameters. The ITT population included all patients who received at least one treatment dose during the study and had at least one post-baseline value, provided they had no serious protocol violations. Non-inferiority criteria considered was < 10% [16].

No formal sample size calculation was performed for this study. A convenient sample size of 128 completed patients, with 64 patients per arm, was deemed adequate for analysis. To account for an anticipated drop-out rate of approximately 15%, a total of 150 patients were enrolled to ensure sufficient statistical power and completeness of data across both study arms.

Results

A total of 150 subjects were enrolled in the study, with 75 assigned to the Remogliflozin group and 75 to the Dapagliflozin group (Figure2). One subject from the Remogliflozin group was lost to follow up, while all participants in the Dapagliflozin group completed the study. A summary of the demographic and baseline characteristics has been shown in Table 1.

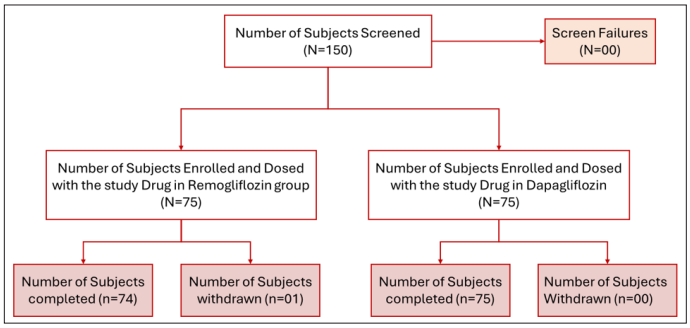

Figure 2: Overall Patient Disposition During Study

Table 1: Baseline Characteristics of Study Groups

Parameters	Remogliflozin 100mg (N=75)	Dapagliflozin 10mg (N=75)	P value
Age (years) - mean ± SD	48.27 ± 8.67	49.16 ± 9.12	0.597
Gender - [n (%)] **Female** **Male**	 37 (49.33%) 38 (50.67%)	 37 (49.33%) 38 (50.67%)	
Body weight (Kg) - mean ± SD	67.75 ± 6.11	68.47 ± 6.38	0.509
Body mass index (kg/m²) - mean ± SD	25.05 ± 2.27	26.33 ± 1.85	<0.001
Waist circumference (cm) - mean ± SD	97.71 ± 4.91	97.74 ± 5.02	0.084
CKD Stages [n(%)]			
CKD stage 3a	32 (42.67%)	23 (30.67%)	
CKD stage 3b	38 (50.67%)	42 (56%)	
CKD stage 4	5 (6.67%)	10 (13.33%)	

Concomitant Medications (n)			
Anti-diabetic			
• Sulfonylurea monotherapy	56	51	
• Biguanide monotherapy	69	72	
• DPP4i monotherapy	13	18	
• Biguanide + DPP4i		1	
Anti-hypertensive			
• Alpha Blockers	3		
• ACEI monotherapy	34	36	
• Combination of ACEI + Thiazide diuretic		1	
• ARB monotherapy	12	6	
• Combination of ARB + diuretic	59	58	
• Calcium Channel Blockers	13	13	
• Diuretics	40	47	
• Mineralocorticoid Receptor Antagonist	5	3	
• Potassium-Sparing Diuretics		1	
Others			
• Antilipidemic Agents	19	28	
• Anti-infectives	2	4	
• Anticonvulsants		2	
• Bronchodilators		1	
• Anticholinergic + Benzodiazepine	1		
• Antihistamine + Leukotriene Antagonist	1		

In the remogliflozin group, 32 (42.67%) of subjects were in CKD stage 3a, 38 (50.67%) in stage 3b, and 5 (6.67%) in stage 4. In the Dapagliflozin group, 23 (30.67%) were in CKD stage 3a, 42 (56%) in stage 3b, and 10 (13.33%) in stage 4.

Efficacy Results

Renal Parameters

Both treatment groups demonstrated significant improvements in renal parameters (eGFR, serum creatinine, BUN, serum uric acid, and UACR) from baseline to week 12 and week 24. (Figure 3) However, no significant difference was observed between the two treatment groups. ($P > 0.05$)

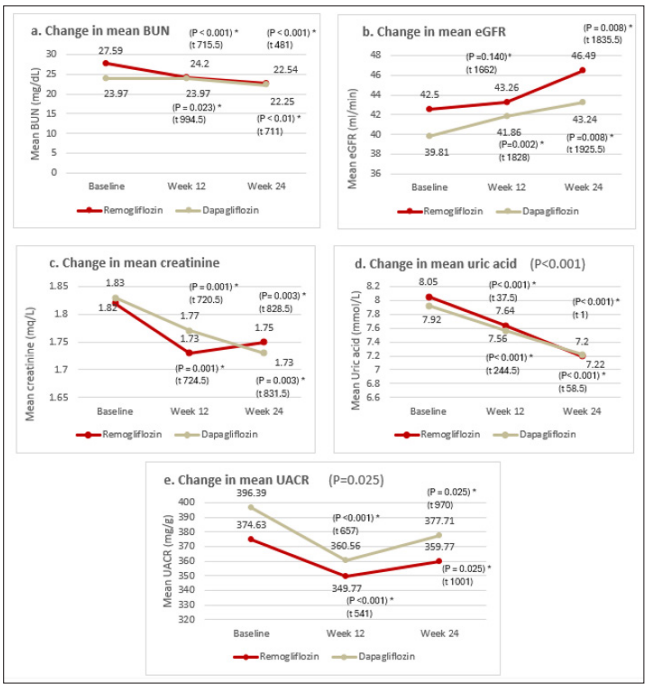

Figure 3: Change in Renal Parameters (eGFR, Serum Creatinine, BUN, Serum Uric Acid, and UACR) Between Study Groups from Baseline to 24 Weeks

BUN, Blood Urea Nitrogen; eGFR, Estimated Glomerular Filtration Rate; UACR, urine albumin-to-creatinine ratio; p, p-value; t; t-test*results are significant #results are not significant; T test: a,715.5; b,481; c, 994.1; d, 711; e, 1662; f, 1835.5; g;1828; h,1925.5; i,724.5; j,831.5; k,720.5; l,828.5; m,37.5; n,1;o,244.5;p,58.5; q,657;r, 970; s;541;t,1001

Figure 3: Change in renal parameters between study groups from Baseline to 24 weeks (a) Change in Mean BUN (b) Change in Mean eGFR (c) Change in Mean Creatinine (d) Change in Mean Uric Acid (e) Change in Mean UAC

Both groups exhibited significant reductions in glycaemic parameters such as HbA1c, FPG and PPG from baseline to week 12 and week 24 (P<0.001 for each group). Overall, the changes in glycaemic control did not differ significantly between the two groups. Both Remogliflozin and Dapagliflozin improved glycaemic parameters over 24 weeks. In the Remogliflozin group, mean HbA1c decreased from 8.46% to 7.40%, while in the Dapagliflozin group, it decreased from 8.11% to 7.49%. FPG levels improved from 174.51 mg/dl to 142.05 mg/dl with Remogliflozin and from 171.42 mg/dl to 145.91 mg/dl with Dapagliflozin. Similarly, PPG levels reduced from 236.76 mg/dl to 188.00 mg/dl in the Remogliflozin group and from 230.70 mg/dl to 192.62 mg/dl in the Dapagliflozin group. At Week 24, 31 (41.89%) of patients in the Remogliflozin group achieved HbA1c ≤7%, compared to 28 (37.33%) in the Dapagliflozin group. (Figure 4)

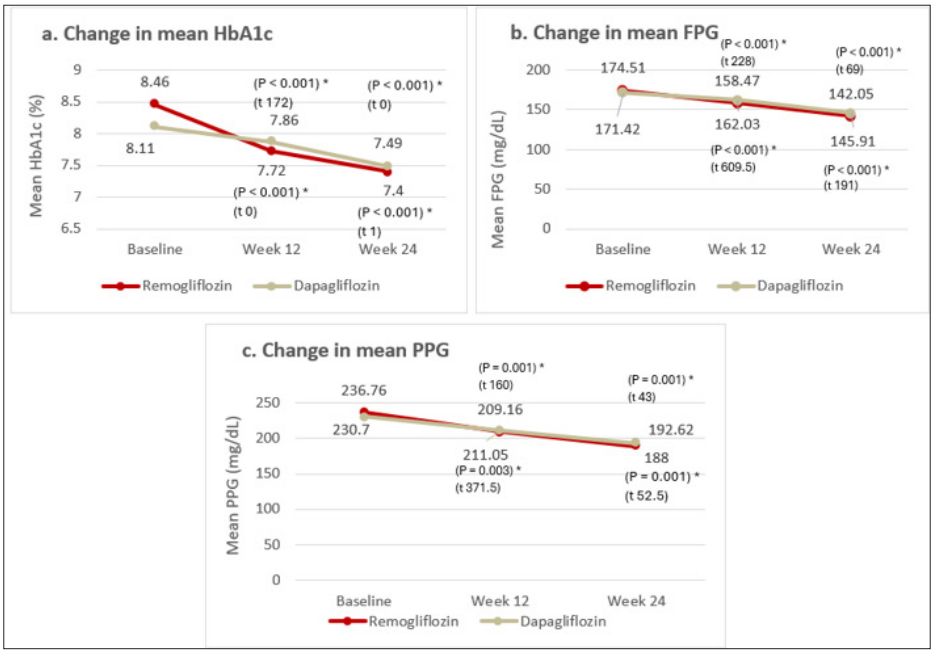

Figure 4: Change in Glycaemic Parameters (HbA1c, FPG and PPG) Between Study Groups from Baseline to 24 Weeks

HbA1c, Glycosylated haemoglobin; FPG, fasting plasma glucose; PPG, postprandial glucose. p, p-value; t, t-test

*Results are significant; T test: a,172; b,0; c,0; d,1; e;609.5; f,228; g,69; h;191; i;371.5; j, 160; k, 43; l,52.5

Figure 4: Change in glycemic parameters between study groups from Baseline to 24 weeks (a) Change in Mean HbA1c (b) Change in Mean FPG (c) Change in Mean PP

At 24 weeks, the incidence of a ≥50% sustained decline in eGFR was comparable between the remogliflozin group (7 patients;9.46%) and the dapagliflozin group (5patients;6.67%), with a difference of less than 10%, which was not statistically significant. Additionally, end-stage renal disease (ESRD) was reported in 3 (4.05%) patients receiving remogliflozin and 2 (2.67%) of those receiving dapagliflozin, further supporting the non-inferiority of remogliflozin. Notably, no cases of cardiovascular or renal death occurred in either treatment group [Table 2].

Table 2: Summary of Non-Inferiority Parameters of Remogliflozin to Dapagliflozin

Parameter	Remogliflozin (N=74)	Dapagliflozin (N=75)
50% sustained decline in eGFR at 24 weeks; n (%)	7 (9.46%)	5 (6.67%)
Reaching ESRD, n (%) (Sustained* eGFR <15mL/min/1.73m2	3 (4.05%)	2 (2.67%)
Cases with CV or renal death n (%)	None	None

eGFR, estimated glomerular filtration rate; CV, cardio-vascular ESRD, end-stage renal disease

Both groups demonstrated consistent reduction in body weight, BMI and waist circumference by week 24. Remogliflozin resulted in a slightly greater reduction in body weight and BMI compared to Dapagliflozin. At Week 24, the mean body weight in the Remogliflozin group decreased from 67.75 ± 6.11 kg to 65.62 ± 5.83 kg, while in the Dapagliflozin group, it decreased from 68.47 ± 6.38 kg to 66.89 ± 6.49 kg. Similarly, BMI decreased from 25.05 ± 2.27 kg/m² to 24.26 ± 2.01 kg/m² in the Remogliflozin group and from 26.33 ± 1.85 kg/m² to 24.46 ± 1.55 kg/m² in the Dapagliflozin group. Mean change in body weight, BMI and waist circumference at week 12 and week 24 was similar between both the study groups (P >0.05 for all) [Table 3].

Table 3: Change in Body Weight, BMI, Waist Circumference, Metabolic and Renal Outcomes at 12 and 24 Weeks as Compared to Baseline

Parameter	Visits	Remogliflozin (N=75)			Dapagliflozin (N=75)			P value *
		n	Mean ±SD	P value#	n	Mean ±SD	P value#	
Body Weight (kg)	Baseline	75	67.75 ± 6.11	-	75	68.47 ±6.38	-	0.509
	Week 12	74	66.25 ± 7.89	<0.001	75	68.03 ±7.39	<0.001	0.281
	Week 24	74	65.62 ± 5.83	<0.001	75	66.89 ±6.49	<0.001	0.214
BMI (kg/m²)	Baseline	75	25.05 ± 2.27	-	75	26.33 ±1.85	-	<0.001
	Week 12	74	24.49 ± 2.85	<0.001	75	24.89 ±2.07	<0.001	0.675
	Week 24	74	24.26 ± 2.01	<0.001	75	24.46 ±1.55	<0.001	0.356
Waist Circumference (cm)	Baseline	75	97.71 ± 4.91	-	75	97.74 ±5.02	-	0.084
	Week 12	74	96.41 ± 4.36	<0.001	75	95.40 ±9.24	<0.001	0.087
	Week 24	74	95.54 ± 4.01	<0.001	75	95.22 ±4.28	<0.001	0.397
BUN (mg/dL)	Baseline	75	27.59 ± 3.91	-	75	26.38 ± 5.01	-	0.225
	Week 12	74	24.20 ± 4.91	<0.001	75	23.97 ± 4.68	0.023	0.697
	Week 24	74	22.54 ± 5.42	<0.001	75	22.25 ± 5.68	<0.001	0.602
eGFR (ml/min)	Baseline	75	42.50 ± 7.71	-	75	39.81 ± 8.10	-	0.049
	Week 12	74	43.26 ± 10.28	0.140	75	41.86 ± 10.29	0.002	0.329
	Week 24	74	46.49 ± 14.65	0.008	75	43.24 ± 15.38	0.008	0.201
Serum creatinine (mq/L)	Baseline	75	1.82 ± 0.24	-	75	1.83 ± 0.21	-	0.982
	Week 12	74	1.73 ± 0.32	0.001	75	1.77 ± 0.33	0.001	0.323
	Week 24	74	1.75 ± 0.64	0.003	75	1.73 ± 0.52	0.003	0.669
Uric acid (mmol/L)	Baseline	75	8.05 ± 1.37	-	75	7.92 ± 1.44	-	0.623
	Week 12	74	7.64 ± 1.33	<0.001	75	7.56 ± 1.46	<0.001	0.843
	Week 24	74	7.20 ± 1.42	<0.001	75	7.22 ± 1.39	<0.001	0.945
UACR (mg/g)	Baseline	75	374.63 ± 119.06	-	75	396.39±121.02	-	0.202
	Week 12	74	349.77 ± 103.19	<0.001	75	360.56±111.45	<0.001	0.355
	Week 24	74	359.77 ± 120.79	0.025	75	377.71±138.53	0.025	0.443
HbA1c (%)	Baseline	75	8.46 ± 0.50	-	75	8.11 ± 0.48	-	<0.001
	Week 12	74	7.72 ± 0.54	<0.001	75	7.86 ± 0.53	<0.001	0.122
	Week 24	74	7.40 ± 0.62	<0.001	75	7.49 ± 0.68	<0.001	0.279
FPG (mg/dL)	Baseline	75	174.51 ± 20.77	-	75	171.42 ± 18.06	-	0.286
	Week 12	74	158.47 ± 19.15	<0.001	75	162.03 ± 17.67	<0.001	0.179
	Week 24	74	142.05 ± 19.03	<0.001	75	145.91 ± 20.52	<0.001	0.197
PPG (mg/dL)	Baseline	75	236.76 ± 30.82	-	75	230.70 ± 28.24	-	0.239
	Week 12	74	209.16 ± 24.92	<0.001	75	211.05 ± 26.52	<0.001	0.410
	Week 24	74	188.00 ± 22.76	<0.001	75	192.62 ± 25.51	<0.001	0.084

Note: # p-value is calculated by Mann-Whitney U Test; * p-value is calculated by Unpaired t-Test; P value#: within group comparison; P value*: between-group comparison; There is a drop in "n" at week 12 and week 24 for Remogliflozin group, as 1 patient was lost to follow-up.

Safety

A total of 50 adverse events were reported in 38 subjects (25.33%) during the study period [Table 4]. In the remogliflozin group, 27 events were observed in 20 subjects (26.67%), while 23 events occurred in 18 subjects (24.00%) in the dapagliflozin group.

All reported adverse events were mild, with 9 events in 7 subjects (9.33%) in the Remogliflozin group and 2 events in 2 subjects (2.67%) in the Dapagliflozin group were considered probably related to Remogliflozin or Dapagliflozin. All adverse events were resolved, and no deaths, serious, or other significant adverse events were reported during the study.

Table 4: Summary of Overall Adverse Events in Study Groups

Event	Remogliflozin (N=75)	Dapagliflozin (N=75)
	AE n (%)	AE n(%)
Cold	4 (5.33%)	1 (1.33%)
Cough	3 (4.00%)	4 (5.33%)
Diarrhoea	4 (5.33%)	1 (1.33%)
Fever	5 (6.67%)	5 (6.67%)
Headache	8 (10.67%)	6 (8.00%)
Increased urination	1 (1.33%)	1 (1.33%)
Nausea		1 (1.33%)
Sore throat	1 (1.33%)	-
Urinary Tract infection	1 (1.33%)	2 (2.67%)
Vomiting		2 (2.67%)
Overall	27 (26.67%)	23 (24%)

AE: Adverse events Note: N-Number of Subjects in Group; n- Number of subjects with AE's; percentage of AE's is calculated based on Number of Subjects with Adverse Events.

Discussion

The present study demonstrated that Remogliflozin 100 mg twice daily was non-inferior to Dapagliflozin 10 mg once daily with respect to efficacy and safety outcomes in patients with Type 2 diabetes mellitus and chronic kidney disease. Both treatment groups showed significant improvement in renal and glycaemic parameters. No serious adverse events were reported, thus demonstrating the overall safety of both remogliflozin and dapagliflozin.

The Dapagliflozin and Prevention of Adverse Outcomes in CKD Trial demonstrated that dapagliflozin, compared to placebo, was associated with a lower risk of causing any major adverse kidney and cardiovascular events. It also prolonged overall survival in a broad group of individuals with proteinuric CKD [17]. This phase III trial of Remogliflozin etabonate has demonstrated non-inferiority of Remogliflozin etabonate 100mg as compared to Dapagliflozin 10mg in the efficacy outcomes of renal and glycaemic parameters and in the safety, outcomes relating to adverse effects and overall tolerability. The study has also shown Remogliflozin etabonate to reduce not only the glycaemic parameters like HbA1c and plasma glucose levels but also the blood pressure, weight and serum uric acid levels like other SGLT2i. However, there is no evidence currently on Remogliflozin when used in patients of T2DM with Chronic kidney disease (CKD) [18].

The current study results showed that there was significant improvement in mean renal parameters (eGFR, Sr Creatinine, BUN, Sr Uric acid and UACR) from baseline to week 12 and week 24 in both Remogliflozin and Dapagliflozin group. However, no significant difference was seen between the two groups.

Our findings are consistent with those from the DAPA-CKD study, which demonstrated the efficacy of dapagliflozin in improving renal function, specifically eGFR and UACR [19]. Similar results were found in another observational study by P. S. Jhund et al., highlighted the renal protective role of dapagliflozin in patients with severe CKD [20].

Our study also included patients with stage 4 CKD, with an eGFR ≥25 mL/min/1.73 m², demonstrating improvements and maintenance of renal function in both treatment arms. In our study, a sustained decline in eGFR of 50% or more was observed in a small fraction of patients and remained comparable between the two groups, with only a few cases progressing to ESRD. These findings show comparable renal protection between the two drugs. Similar results were observed in H. J. L. Heerspink et al., where a 50% eGFR decline occurred in 5.2% of dapagliflozin patients, confirming the reno-protective effects of both SGLT2i [17].

Also, the study results showed that there was a significant reduction in glycaemic parameters (HbA1c, FPG and PPG) with similar improvement in Heart Rate, Blood pressure, BMI and weight over 6 months of treatment in both the groups. The incidence of adverse events was similar in both the groups and no serious adverse events were reported in either group.

The ADA and KDIGO guidelines recommend using "SGLT2i with proven renal and cardiovascular benefits in patients with T2DM, CKD, and an eGFR ≥20 ml/min/1.73 m². Once initiated, SGLT2i therapy can be continued at lower levels of eGFR." This recommendation is based on strong evidence demonstrating that SGLT2i reduce the risk of CKD progression to ESRD, heart

failure, and atherosclerotic cardiovascular disease (ASCVD) in these patients. These benefits are independent of glycaemic control, making SGLT2i essential even when glycaemic targets have already been met.

Based on our study findings, remogliflozin demonstrates comparable renal and glycaemic protection to dapagliflozin in patients with T2DM and CKD. Healthcare providers should consider remogliflozin as a viable alternative, especially for patients who may have contraindications to metformin or other SGLT2i.

Conclusion

Remogliflozin was found to be non-inferior to dapagliflozin in terms of renal and glycaemic outcomes, with a comparable safety profile. These findings support its potential role in the management of patients with T2DM and CKD. Further long-term studies and real-world evidence are warranted to confirm its sustained efficacy, safety, and clinical utility. Subgroup analyses may help identify patient populations who benefit most, thereby guiding more personalized treatment.

Declaration

Conflict of Interest: Rahee Borulkar, Sumit Bhushan, Rujuta Gadkari, Mayur Jadhav, Sanjay Choudhari, Saiprasad Patil and Hanmant Barkate are employees of Glenmark. All other investigators/authors have no conflicts of interest that are directly relevant to the content of this article.

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Authors' Contributions: C.S contributed to conceptualization and validation, A.P performed methodology and investigation, R.B drafted the original manuscript, S.B carried out formal analysis and project administration, M.J and S.C were involved in writing – review and editing, and S.P and H.B provided supervision. All authors read and approved the final manuscript.

Ethical Standards: The work presented in this study was in accordance with the study protocol, the New Drugs and Clinical Trials Rules 2019 issued by the Government of India, the ethical principles that have their origin in the Declaration of Helsinki, International Council for Harmonisation (ICH) Good Clinical Practice (GCP), and all applicable local regulatory requirements. Informed consent was obtained from all the study subjects who took part in the trial. Ethic committee approval was obtained from all respective sites, and study was registered in CTRI (CTRI/2023/03/050384).

Consent to Publish: Yes

References

1. Xie J, Wang M, Long Z, Ning H, Li J, et al. (2022) Global burden of type 2 diabetes in adolescents and young adults, 1990-2019: systematic analysis of the Global Burden of Disease Study 2019. BMJ. British Medical Journal Publishing Group 379: e072385.
2. Anjana RM, Unnikrishnan R, Deepa M, Pradeepa R, Tandon N, et al. (2023) Metabolic non-communicable disease health report of India: the ICMR-INDIAB national cross-sectional study (ICMR-INDIAB-17). Lancet Diabetes Endocrinol. Elsevier 11: 474-489.
3. Afkarian M, Zelnick LR, Hall YN, Heagerty PJ, Tuttle K, et al. (2016) Clinical Manifestations of Kidney Disease Among US Adults with Diabetes, 1988-2014. JAMA 316: 602-610.
4. Kumar M, Dev S, Khalid MU, Siddenthi SM, Noman M, et al. (2023) The Bidirectional Link Between Diabetes and Kidney Disease: Mechanisms and Management. Cureus 15: e45615.
5. de Boer IH, Khunti K, Sadusky T, Tuttle KR, Neumiller JJ, et al. (2022) Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and kidney disease: Improving Global Outcomes (KDIGO). Diabetes Care 45: 3075-3090.
6. RSSDI Clinical Practice Recommendations for the Management of Type 2 Diabetes Mellitus 2022. Int J Diabetes Dev Ctries 2022;42: 1-143. https://doi.org/10.1007/s13410-022-01129-5.
7. Hahr AJ, Molitch ME (2022) Management of Diabetes Mellitus in Patients With CKD: Core Curriculum 2022. Am J Kidney Dis. Elsevier 79: 728-736.
8. Di Costanzo A, Esposito G, Indolfi C, Spaccarotella CAM (2023) SGLT2 Inhibitors: A New Therapeutical Strategy to Improve Clinical Outcomes in Patients with Chronic Kidney Diseases. Int J Mol Sci 24: 8732.
9. Krishnan A, Shankar M, Lerma EV, Wiegley N (2023) Sodium Glucose Cotransporter 2 (SGLT2) Inhibitors and CKD: Are You a #Flozinator? Kidney Med. Elsevier 5: 100608.
10. American Diabetes Association Professional Practice Committee (2024) 11. Chronic Kidney Disease and Risk Management: Standards of Care in Diabetes-2024. Diabetes Care 47: S219-S230.
11. Central Drugs Standard Control Organization (CDSCO). List of new drugs approved in the year; 2019. [Internet]. [cited 2025 Oct 15]. https://cdsco.gov.in/opencms/resources/UploadCDSCOWeb/2018/UploadApprovalNewDrugs/ndapprovejuly19.pdf.
12. Dharmalingam M, Aravind SR, Thacker H, Paramesh S, Mohan B, et al. (2020) Efficacy and Safety of Remogliflozin Etabonate, a New Sodium Glucose Co-Transporter-2 Inhibitor, in Patients with Type 2 Diabetes Mellitus: A 24-Week, Randomized, Double-Blind, Active-Controlled Trial. Drugs 80: 587-600.
13. Sethi B, Modi KD, Srikanth K, Erande S, Khaladkar K, et al. (2022) A Prospective Multicenter Open-label Study to Assess Effect of Remogliflozin on Glycemic Variability Compared to Dapagliflozin Using Continuous Glucose Monitoring (REMIT - GV study). J Diabetes Treat. Gavin Publishers.
14. Sengupta S, Pathiyilbalagopalan J, Mehta A, Sawhney JPS, Suryavanshi S, et al. (2024) Are Two Gliflozins Different: A Prospective Multicenter Randomized Study to Assess Effect of Remogliflozin Compared with Empagliflozin on Biomarkers of Heart Failure in Indian Patients with Type 2 Diabetes Mellitus with Chronic Heart Failure (REMIT-HF Study). J Card Fail 31: 158-162.
15. American Diabetes Association Professional Practice Committee (2024) 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes—2024. Diabetes Care 47: S111-S125.
16. Research C for DE and. Non-Inferiority Clinical Trials [Internet]. FDA; 2020. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/non-inferiority-

clinical-trials.

17. Heerspink HJL, Stefánsson BV, Correa-Rotter R, Chertow GM, Greene T, et al. (2020) Dapagliflozin in Patients with Chronic Kidney Disease. N Engl J Med 383: 1436-1446.
18. Dharmalingam M, Kumar Sharma S, Prakash V, Maiti A, Kumar R, et al. (2024) Evaluating the Efficacy, Safety, and Tolerability of Combination Therapy of Dapagliflozin and Linagliptin Over Dapagliflozin and Vildagliptin in Patients with Type 2 Diabetes Mellitus Inadequately Controlled with Metformin. Cureus 16: e58115.
19. Wheeler DC, Toto RD, Stefánsson BV, Jongs N, Chertow GM, et al. (2021) A pre-specified analysis of the DAPA-CKD trial demonstrates the effects of dapagliflozin on major adverse kidney events in patients with IgA nephropathy. Kidney Int 100: 215-224.
20. Jhund PS, Solomon SD, Docherty KF, Heerspink HJL, Anand IS, et al. (2021) Efficacy of Dapagliflozin on Renal Function and Outcomes in Patients with Heart Failure with Reduced Ejection Fraction: Results of DAPA-HF. Circulation 143: 298-309.