Efficacy & safety of Remogliflozin in T2DM patients: Results from 24-week double blind double dummy phase III study

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Background & Objective

Remogliflozin etabonate, a novel SGLT2 inhibitor, developed for use in Type 2 Diabetes Mellitus (T2DM), has been recently approved in India. This Phase III study was conducted with objective to evaluate efficacy & safety of remogliflozin etabonate (100mg & 250mg) as compared to dapagliflozin (10mg) on various glycemic & non-glycemic parameters

Study Design

Selection Criteria

- T2D, either gender, ≥18 to ≤ 65 years
- Stable monotherapy of metformin > 1500 mg/day for at least 8 weeks (> 1000 mg/day for subjects not tolerating)
- Inadequate glycemic control (HbA1c of >7% to ≤10%)
- FPG <240mg/dL before randomization
- Provides written informed consent
- Willing to exercise effective contraception
- BMI ≤45 kg/m^2; eGFR ≥ 60mL/min; Normal lipid profile
- No symptomatic UTI / Mycotic GTI

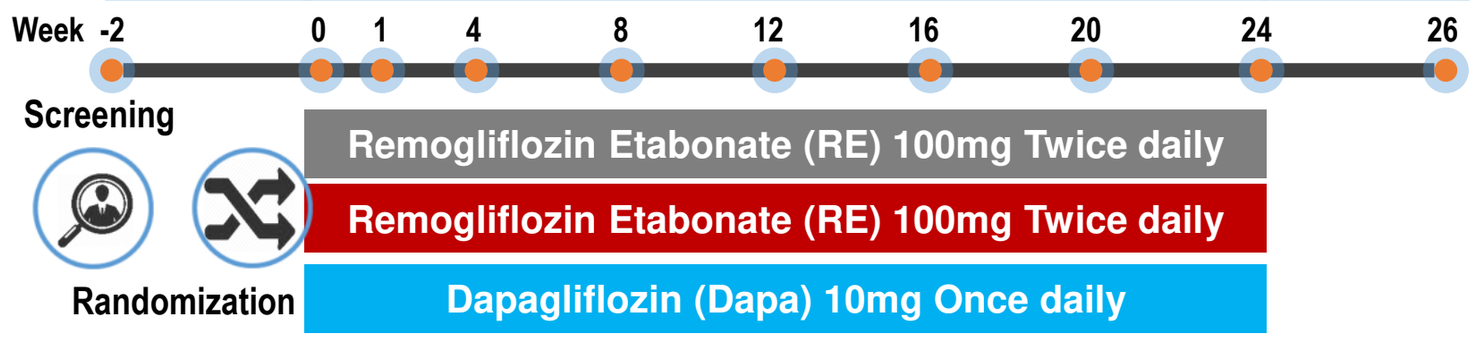
Treatment allocation
Randomized, stratified by HbA1c

Blinding
Double blind, Double dummy

Study Arms

Number of Sites
58 sites across India

Duration of therapy
24 weeks



Primary Endpoint: Change from baseline in HbA1c at 24 weeks

Secondary Endpoints: Change from baseline in FPG & PPG; Body Weight, Lipid profiles at 24 weeks

Safety Endpoints: Treatment-emergent AEs, Blood pressure, Safety lab values & clinical signs

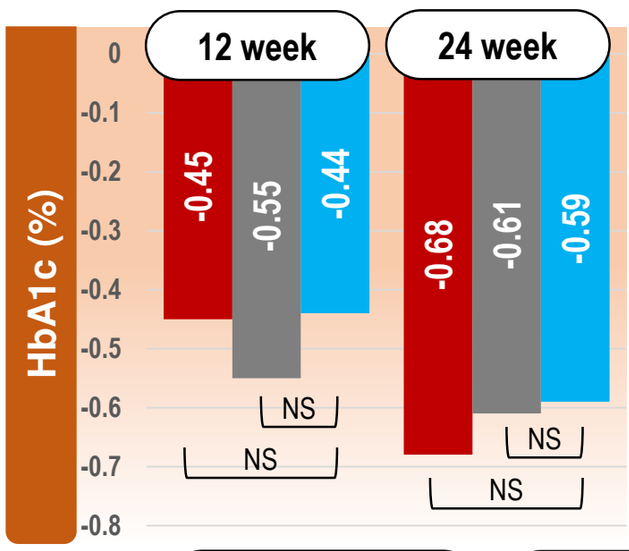
Study Results

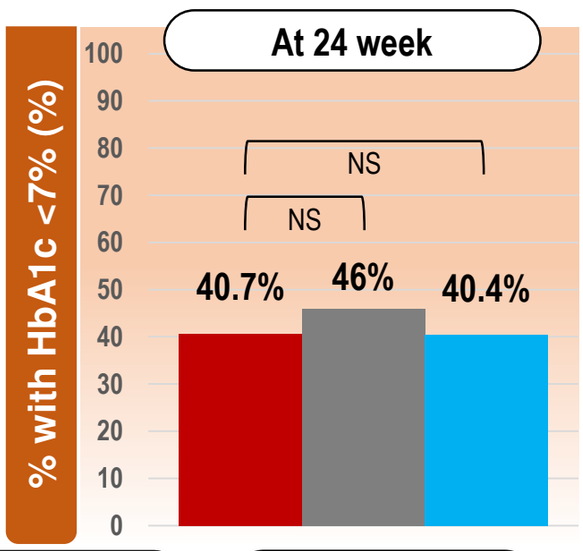
Total Screened = 1865 → Randomised = 906

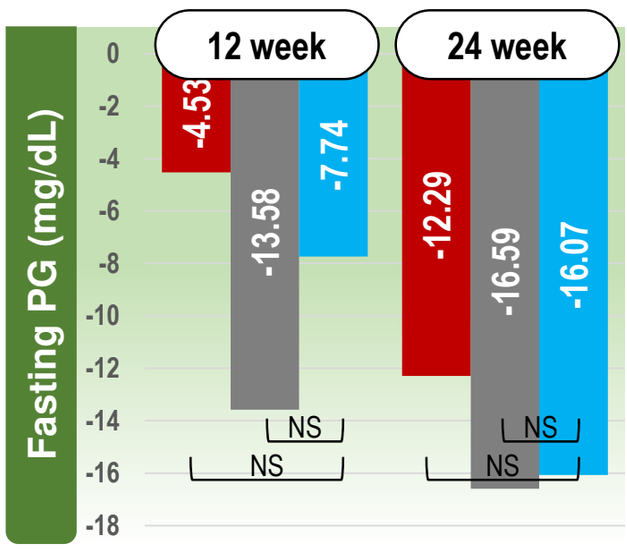
Analysis Sets	RE 100mg	RE 250mg	Dapa 10mg
Randomized	**N=347**	**N=362**	**N=197**
Withdrawn (%)	**78 (22.8)**	**102 (28.2)**	**53 (26.9)**
PP Population (%)	263 (75.8)	250 (69.1)	141 (71.6)
mITT population (%)	333 (96.0)	350 (96.7)	182 (92.4)
Safety population (%)	346 (99.7)	362 (100)	197 (100)

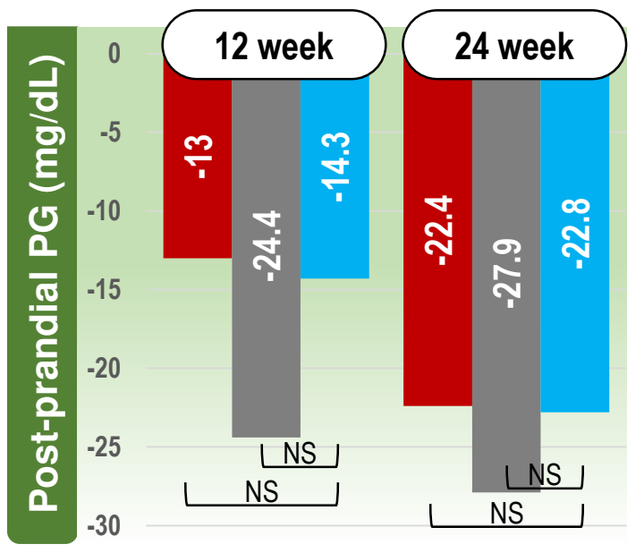
Baseline Demographics & Characteristics

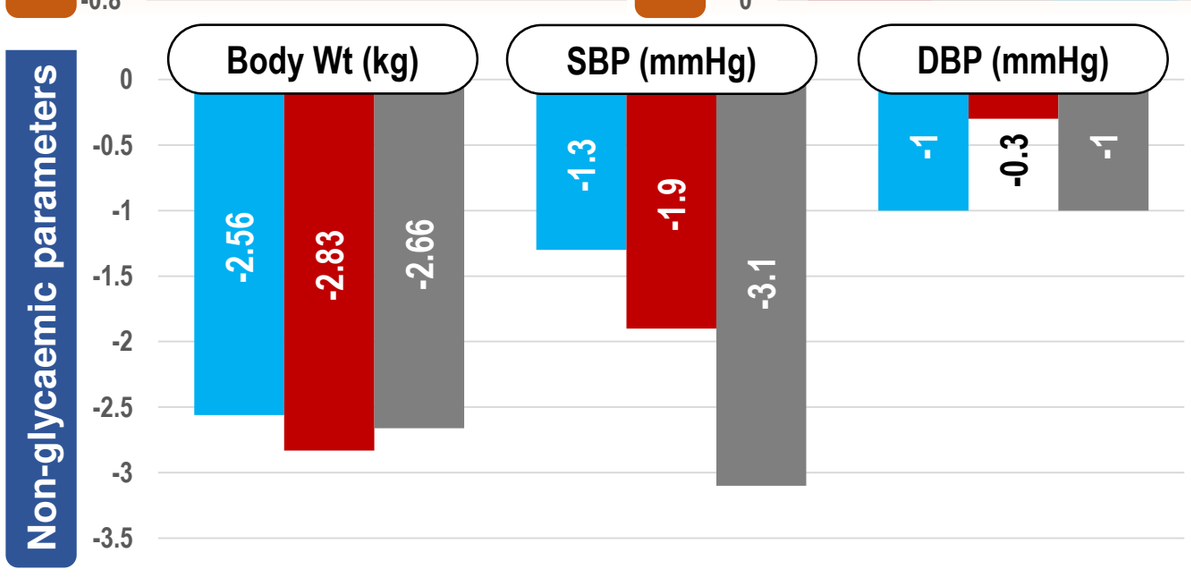
Parameter		RE100 mg	RE 250 mg	Dapa 10 mg
Age (year)		50.49 ± 8.888	51.03 ± 8.468	50.23 ± 9.563
Gender, %	Male	55.8	53.6	55.8
	Female	44.2	46.4	44.2
Body Weight (kg)		71.47 ± 12.307	69.83 ± 12.341	72.52 ± 13.020
BMI (kg/m2)		28.19 ± 4.615	27.82 ± 4.767	28.00 ± 4.956
Baseline HbA1c (%)		8.28 ± 0.835	8.22 ± 0.796	8.29 ± 0.796











Lipid profile

Lipid Parameter	RE100	RE250	Dapa10
TC, mg/dL	1.1	4.8	-1.4
LDL-C, mg/dL	4.5	6.1	1.3
HDL-C, mg/dL	1.6	2.2	1.2
TGs, mg/dL	-7.4	-6.3	-8.1
TC/HDL ratio	-0.11	-0.03	-0.1
HDL/LDL ratio	-0.02	-0.00	0.00

Adverse Events

Parameter	RE 100mg	RE 250mg	Dapa 10mg
TEAEs (%)	29.5	28.7	27.4
Study related AEs	8.1	11.6	6.6
Hypoglycemia	**0.9**	**0.6**	**1**
UTIs	**3.2**	**5.5**	**1.5**
Mycotic GTIs	**1.7**	**1.1**	**2.5**
Increased Creatinine	**10.7**	**8.8**	**8.1**

Observations & Conclusions

In this Phase III study, it was observed that remogliflozin etabonate (100mg and 250mg) reduced HbA1c levels at 24 weeks & when compared with dapagliflozin 10mg demonstrated non-inferiority with statistical significance. Both 100 mg and 250 mg doses of remogliflozin etabonate were found to be effective, safe and well tolerated with safety profile comparable to dapagliflozin 10mg.

Acronyms: BID= Twice daily; eGFR= estimated glomerular filtration rate; FPG= fasting plasma glucose; GTI= Genital tract infections; HbA1c= Glycosylated Hemoglobin; N= number of patients; PPG=Post-prandial plasma glucose; QD= Once daily; T2DM= Type-2 diabetes Mellitus; UTI= Urinary Tract infection. All values are Mean ± Standard deviation unless otherwise specified; NS= Not significant