Type 2 DM and Cardiovascular disorders: Focus on Recent Indian Evidence of Remogliflozin in Heart Failure patients

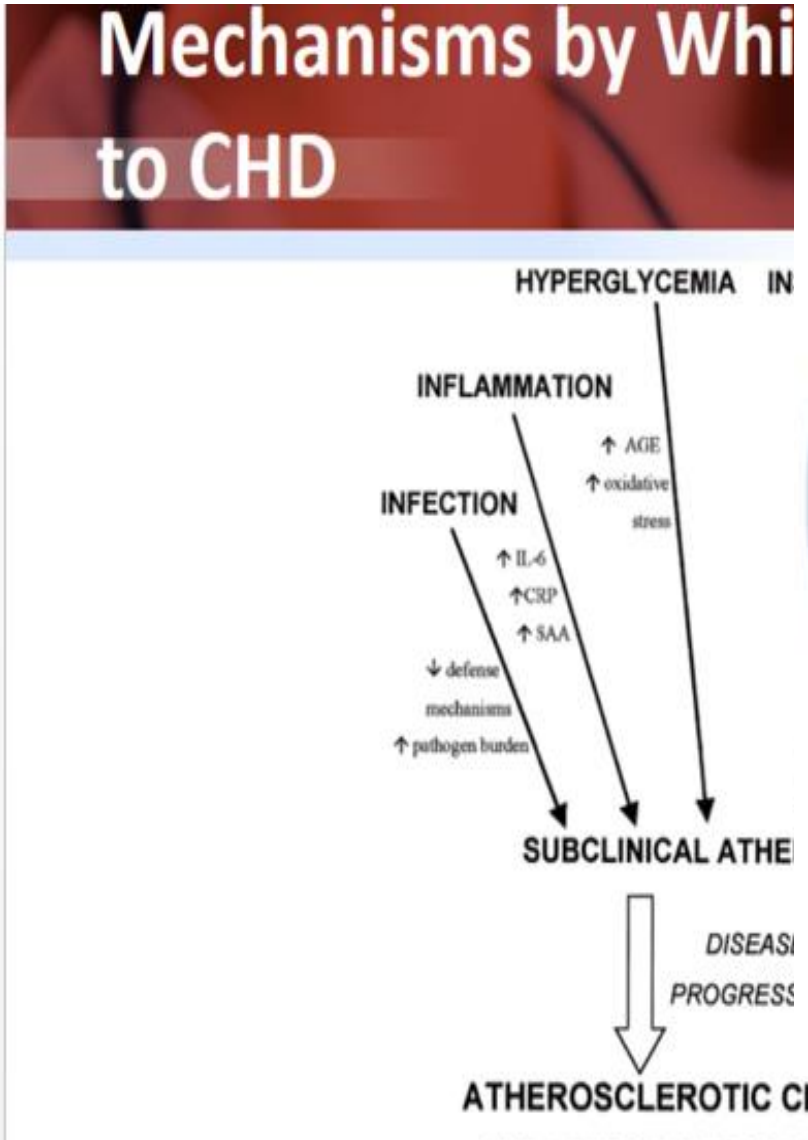
REMIT- HF STUDY

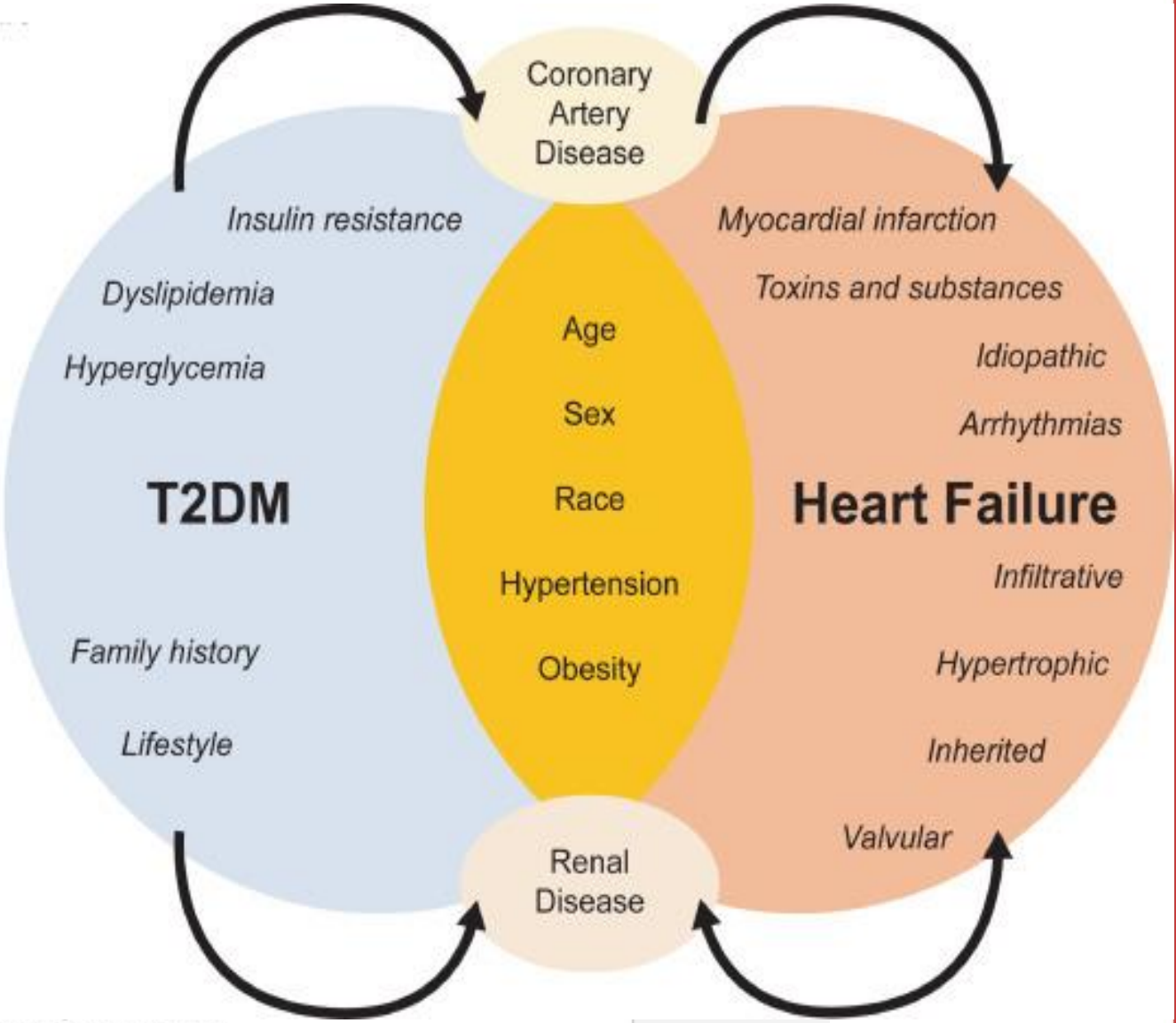
Background

- **Heart failure is one of the major causes of mortality in patients with type 2 diabetes mellitus (T2DM).**
- Patients with T2DM often experience cardiovascular (CV) complications with Heart failure (HF) being one of the most frequent.
- **T2DM occurs in almost 40% of patients hospitalized for HF and up to 30% of those with chronic Heart Failure.**
- SGLT2 inhibitors have shown to reduce the incidence of hospitalization for heart failure and also N-terminal pro-brain natriuretic peptide **(NT-proBNP)** levels in HF.
- The aim of the present study was to evaluate the effect of Remogliflozin in patients of T2DM with CHF in different age group and gender as compared to Empagliflozin using NT-proBNP as the index of the therapeutic effects in T2DM patients with CHF.

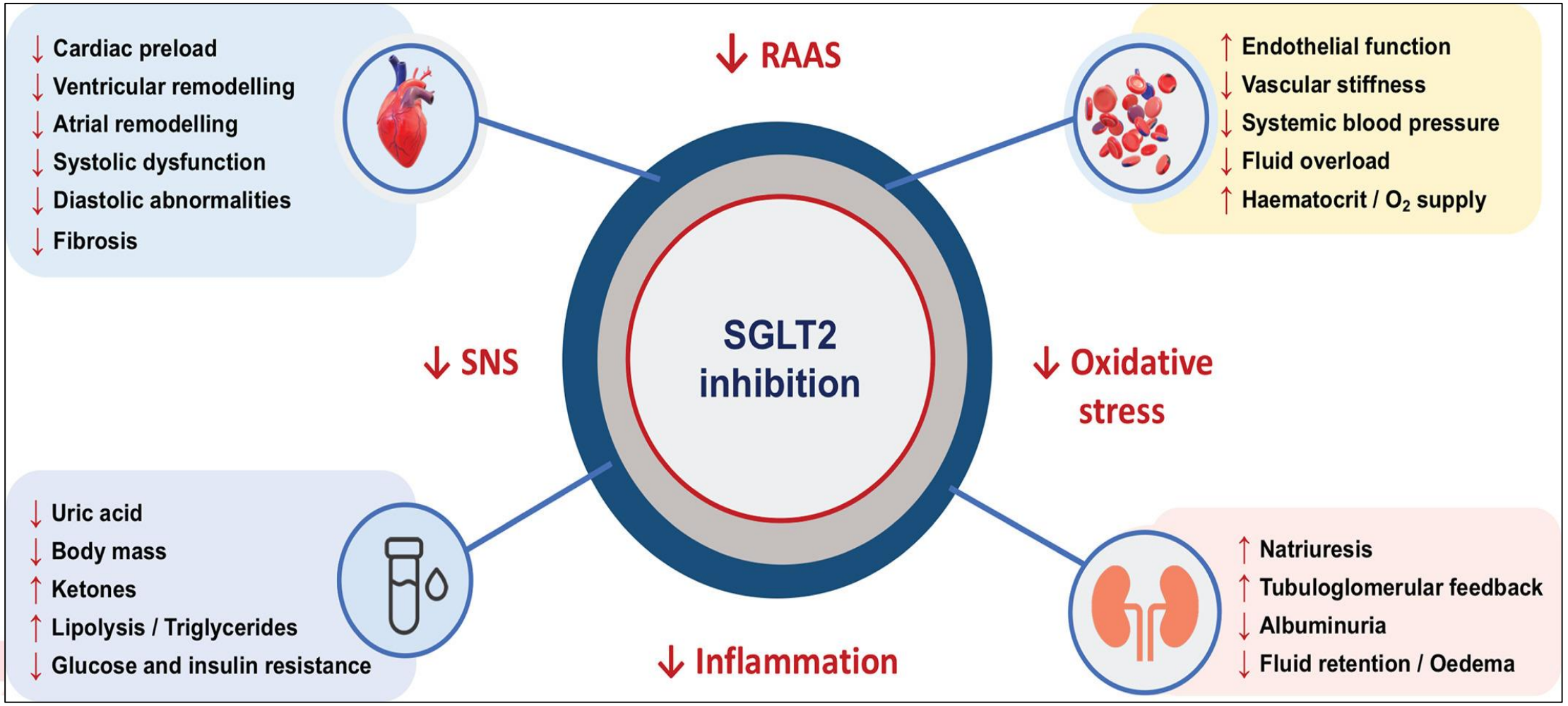
Sodium-Glucose Cotransporter-2 Inhibitors Improve Heart Failure with Reduced Ejection Fraction Outcomes by Reducing Edema and Congestion. Diagnostics (Basel). 2022 Apr 14;12(4):989.

Mechanism by which diabetes leads to CHD





Beneficial Role of SGLT-2 inhibitors in Cardiovascular diseases



Anker, S.D., Khan, M.S., Shahid, I., Filippatos, G., Coats, A.J.S. and Butler, J. (2021), Sodium–glucose co-transporter 2 inhibitors in heart failure with preserved ejection fraction: reasons for optimism. Eur J Heart Fail, 23: 1250-1255. https://doi.org/10.1002/ejhf.2279

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A Prospective Multicenter Randomized Open Label, Active Controlled Study To Assess Effect Of Remogliflozin On Biomarkers Of Heart Failure Compared To Empagliflozin In Indian Patients Of Type 2 Diabetes Mellitus With Chronic Heart Failure

REMIT HF

N=250, Sites -13 Effect of Remogliflozin on biomarkers of HF compared to Empagliflozin in patients of T2DM & CHF

ACC.23 TOGETHER WITH WCC

Accepted as moderated poster to the 72nd Annual Scientific Session of the American College of Cardiology

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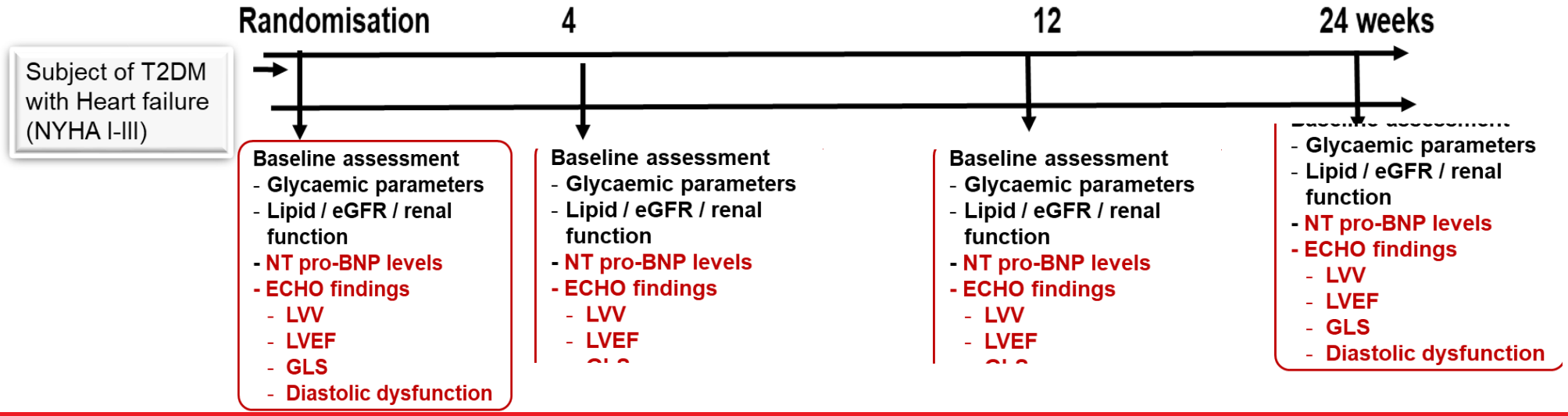
Study Design Overview

- A prospective multicenter randomized open label active controlled study
- To assess effect of Remogliflozin on biomarkers of heart failure compared to Empagliflozin in Indian patients of T2DM with chronic heart failure.
- **Study duration is 24 weeks.**
- **The study recruited 250 patients from 12 sites across INDIA.**

Site	Investigator	Site	City
01	Dr. Shantanu Sengupta	Sengupta Hospital	Nagpur
02	Dr. Jayagopal P B	Lakshmi Hospital	Palakkad
03	Dr. Soumitra Kumar	Fortis Hospital	Kolkata
04	Dr. JPS Sawhney/Dr. Ashwani Mehta	Sir Gangaram Hospital	Delhi
05	Dr. Satish Suryavanshi	SMC Heart Institute	Raipur
06	Dr. Hasmukh Gujar	Inamdar Hospital	Pune
07	Dr. Naveen Jamwal	RML	Lucknow
08	Dr. Dilip Kadam	Care Hospital	Pune
09	Dr. Ambanna Gowda	Citizen Hospital	Bangalore
10	Dr. Ramesh Dargad	Stress Test Clinic	Mumbai
11	Dr. Amit Suresh Bhate	Jeevan Rekha	Belagavi
12	Dr. Vinod Kr. Kapoor	New Leelamani	Kanpur



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Study Objectives

- **Primary Objective**:

Evaluate effect of Remogliflozin in patients of T2DM with CHF compared to Empagliflozin on Cardiac markers of HF.

- **Secondary Objective**:

Evaluate effect of Remogliflozin in patients of T2DM with CHF compared to Empagliflozin on Glycemic efficacy, Lipid profile, Body weight, Blood pressure, Renal function, Safety and tolerability.

Eligibility and Exclusion Criteria

Inclusion Criteria

1. Adults (≥ 18 years); HbA1c >7.0 & <8.5% no change in anti-diabetic treatment therapy since last 8 weeks
2. NYHA HF Class I to III , LVEF <40% within 6 months from the screening visit
3. Having elevated NT-proBNP levels >600 pg/mL (or >1200 pg/mL in patients with AF)
4. Patients who understand & willing to comply with study requirements & provide written informed consent.

Exclusion Criteria

1. Patients treated with SGLT2i in past 12 weeks
2. H/o of MI, CABG, Stroke or TIA in past 12 weeks prior & Cardiomyopathy, HOCM, Any severe valvular heart disease
3. Acute decompensated HF (exacerbation of chronic HF), Atrial fibrillation or atrial flutter with a resting heart rate >110 bpm documented by ECG at Visit 1(Screening)
4. SBP ≥ 180 mmHg at Visit 2. If SBP >150mmHg and <180mmHg at Visit 2, receiving at least 3 antihypertensive drugs & Symptomatic hypotension and/or a SBP < 100 mmHg at Visit 1 or Visit 2
5. Patients with eGFR <60 ml/min/1.73 m2 , CHF (NYHA functional classification IV) , Patients with low or high body weight (BMI <18.5 kg/m2 or >45 kg/m2)

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Initial Analysis Results on 71 Indian Patients with T2DM & CHF who have completed 3 months of follow up

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EFFECT OF REMOGLIFLOZIN ON BIOMARKERS COMPARED TO EMPAGLIFLOZIN INPATIENTS OF TYPE 2 DIABETES MELLITUS WITH CHRONIC HEART FAILURE OPEN ACCESS

Heart Failure And Cardiomyopathies

Shantanu Sengupta, Jayagopal Pathiyil Balagopalan, ashwani mehta, Satish Chainsingh Suryavanshi, Naveen Jamwal, Sumit Bhushan, Ambanna Gowda, Sachin Suryawanshi, Rujuta Gadkari, and Hanmant Barkate

J Am Coll Cardiol. 2023 Mar, 81 (8_Supplement) 316

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Background

SGLT2 inhibitors reduce heart failure hospitalisation and N-terminal pro-brain natriuretic peptide (NTproBNP) levels in HF. Aim of study was to evaluate effect of Remogliflozin in patients of T2DM with CHF as compared to Empagliflozin using NT-proBNP as index of therapeutic effects.

Information

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REMIT HF Study Abstract presented at ACC 2023

ACC.23 TOGETHER WITH WCC — MARCH 4 - 6, 2023 NEW ORLEANS

Session 1030 - Hot Topics in Heart Failure and Cardiomyopathies

Add to My Itinerary

1030-13 - EFFECT OF REMOGLIFLOZIN ON BIOMARKERS COMPARED TO EMPAGLIFLOZIN INPATIENTS OF TYPE 2 DIABETES MELLITUS WITH CHRONIC HEART FAILURE

March 4, 2023, 4:15 PM - 4:25 PM

Heart Failure and Cardiomyopathies Moderated Poster Theater 11_Hall F

Disclosure
https://disclosures.acc.org/Public/AnnualMeetingAppConsol?pid=12841

Authors
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Abstract

Background: SGLT2 inhibitors reduce heart failure hospitalisation and N-terminal pro-brain natriuretic peptide (NTproBNP) levels in HF. Aim of study was to evaluate effect of Remogliflozin in patients of T2DM with CHF as compared to Empagliflozin using NT-proBNP as index of therapeutic effects.
Methods: In this multicentric, prospective study, 71 patients of DM with CHF (EF<40%) with NTproBNP>600pg/ml were included. 38 patients were in Remogliflozin (R) group and 33 in Empagliflozin (E) group. Baseline demographic, glycaemic, cardiac and renal parameters were comparable between 2 groups (p>0.05).
Results: Mean NT-proBNP level improved from baseline to 3 months in both groups (R group: 2781±2695 to 1451±1183 pg/ml, p=0.0007); (E group: 2672±2181 to1602±1436 pg/ml, p=0.004) respectively, but no significant difference was seen between two groups (p= 0.64, Figure 1). Mean HbA1c was 7.87±1 at baseline and improved to 7.58±1.3 at 3 months in R-group; 7.78±0.1 at baseline and improved to 7.44±1.2 at 3 months in E-group. The mean eGFR was 75.6±27.4 at baseline and 81.7±28.4 at 3 months in R-group; 78.1±21.3 at baseline and 71.7±22.9 at 3 months in E-group. Systolic BP reduced from 127±21 mmHg at baseline to 123±14 mmHg at 3 months in R group (p<0.05). No adverse events occur in either group.
Conclusion: Remogliflozin improved glycaemic parameters and NTproBNP as an index of therapeutic effects in T2DM patients with CHF. Remogliflozin was well tolerated and non-inferior to Empagliflozin in T2DM patients with CHF.

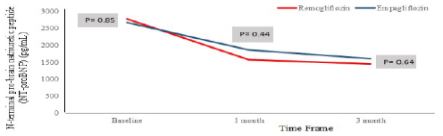

Fig. 1: Change in NT-proBNP levels of Remogliflozin and Empagliflozin

(https://files.abstractsonline.com//CTRL/ba/2/4ca/6a8/866/446/0a8/f5e/432/a8e/2aa/ca/g12841_1.jpg)

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Presenting

Interim Analysis on 106 Indian Patients with T2DM & CHF who have completed 6 months of follow up

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Summary of Subject Disposition & Demographics

- A total of 106 subjects were included in interim analysis who had completed their 24 weeks follow-up period

Parameters		n	Remogliflozin Mean ± SD	n	Empagliflozin Mean ± SD	P-Value
Age (years)		61	55.74 ± 12.24	45	56.24 ± 10.85	0.82248
Gender	Female	13	21.31%	8	17.78%	0.65187
	Male	48	78.69%	37	82.22%	
Weight (kg)		61	66.24 ± 10.38	45	66.05 ± 10.54	0.92686
Pulse rate (beats/min)		61	85.13 ± 13.56	45	85.96 ± 13.52	0.75729
Respiratory rate (breaths/ min)		61	21.28 ± 3.47	45	21.91 ± 3.38	0.34936
Body Temperature (Fahrenheit)		**61**	97.62 ± 1.05	45	97.60 ± 0.89	0.94278
Systolic blood pressure (mmHg)		61	124.51 ± 19.85	45	125.22 ± 10.69	0.81241
Diastolic blood pressure (mmHg)		61	74.84 ± 10.90	45	75.87 ± 10.56	0.62533

- All the baseline demographic parameters were comparable among both Remogliflozin and Empagliflozin groups

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Summary of Blood Pressure and Weight Improvement

Summary of Blood pressure

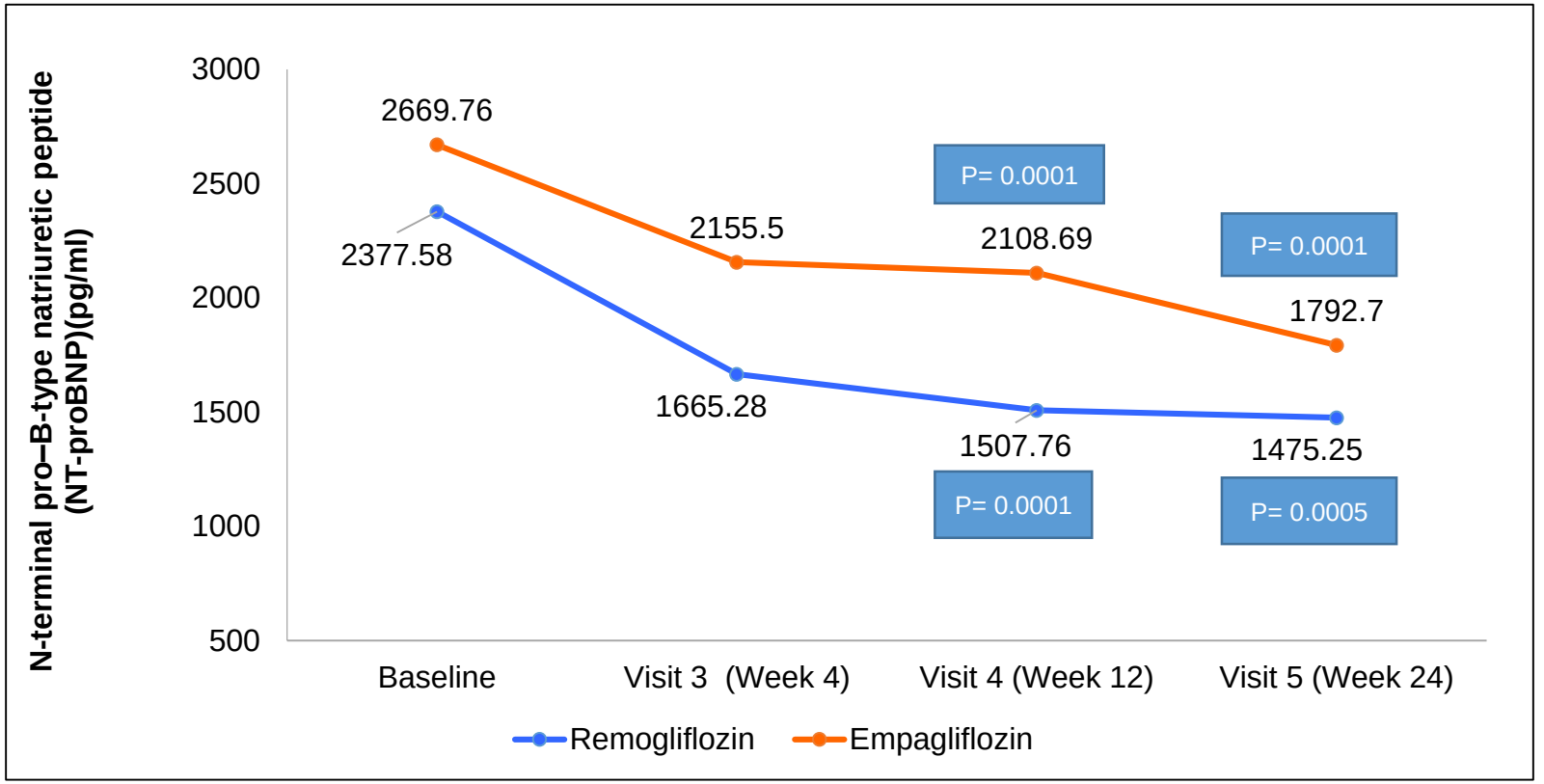
Lab Test	Visits	n	Remogliflozin Mean ± SD	P-Value	n	Empagliflozin Mean ± SD	P-Value
Systolic blood pressure (mmHg)	Baseline	61	124.51 ± 19.85	-	45	125.22 ± 10.69	-
	Visit 4 (Week 12)	59	122.73 ± 12.55	0.56174	45	124.18 ± 16.38	0.14059
	Visit 5 (Week 24)	54	121.78 ± 10.66 ↓2.73	0.99092	41	123.83 ± 16.91 ↓1.39	0.05525
Diastolic blood pressure (mmHg)	Baseline	61	74.84 ± 10.90	-	45	75.87 ± 10.56	-
	Visit 4 (Week 12)	59	73.08 ± 10.01	0.22997	45	73.89 ± 9.61	0.42582
	Visit 5 (Week 24)	54	72.50 ± 7.24 ↓2.34	0.12633	41	73.71 ± 6.42 ↓2.16	0.30679

Summary Statistics of Body Weight (kg) & Waist Circumference (cm)

Parameter	Visits	n	Remogliflozin Mean ± SD	P-Value	n	Empagliflozin Mean ± SD	P-Value
Weight (kg)	Baseline	61	66.24 ± 10.38	-	45	66.05 ± 10.54	-
	Visit 4 (Week 12)	59	65.21 ± 10.04	0.09943	44	65.24 ± 10.07	0.16667
	Visit 5 (Week 24)	54	64.03 ± 8.97 ↓2.21	0.00542	41	63.95 ± 11.01 ↓2.1	0.04905
Waist Circumference (cm)	Baseline	58	72.09 ± 29.84	-	43	76.88 ± 35.58	-
	Visit 4 (Week 12)	58	71.01 ± 28.78	0.00097	44	75.02 ± 32.17	0.8709
	Visit 5 (Week 24)	54	69.83 ± 29.26	0.00919	39	74.67 ± 32.83	0.50177

There was also similar improvement in Heart Rate, Blood pressure reduction (systolic/diastolic), weight reduction over 24 weeks of treatment in both the groups

Efficacy Results: NT proBNP comparison between Remogliflozin and Empagliflozin at 6 months from baseline



- NT proBNP levels in the Remogliflzoin reduced from 2377.58 ± 2349.67 to 1475.25 ± 1405.61 at 6 months while it reduced from 2669.76 ± 2142.04 to 1792.70 ± 2205.27 in the Empagliflzoin group
- The NT proBNP reduction from baseline to week 24 was significant across both the groups, while it was non-inferior between the groups at 5 weeks **(No significant difference seen between the groups)**

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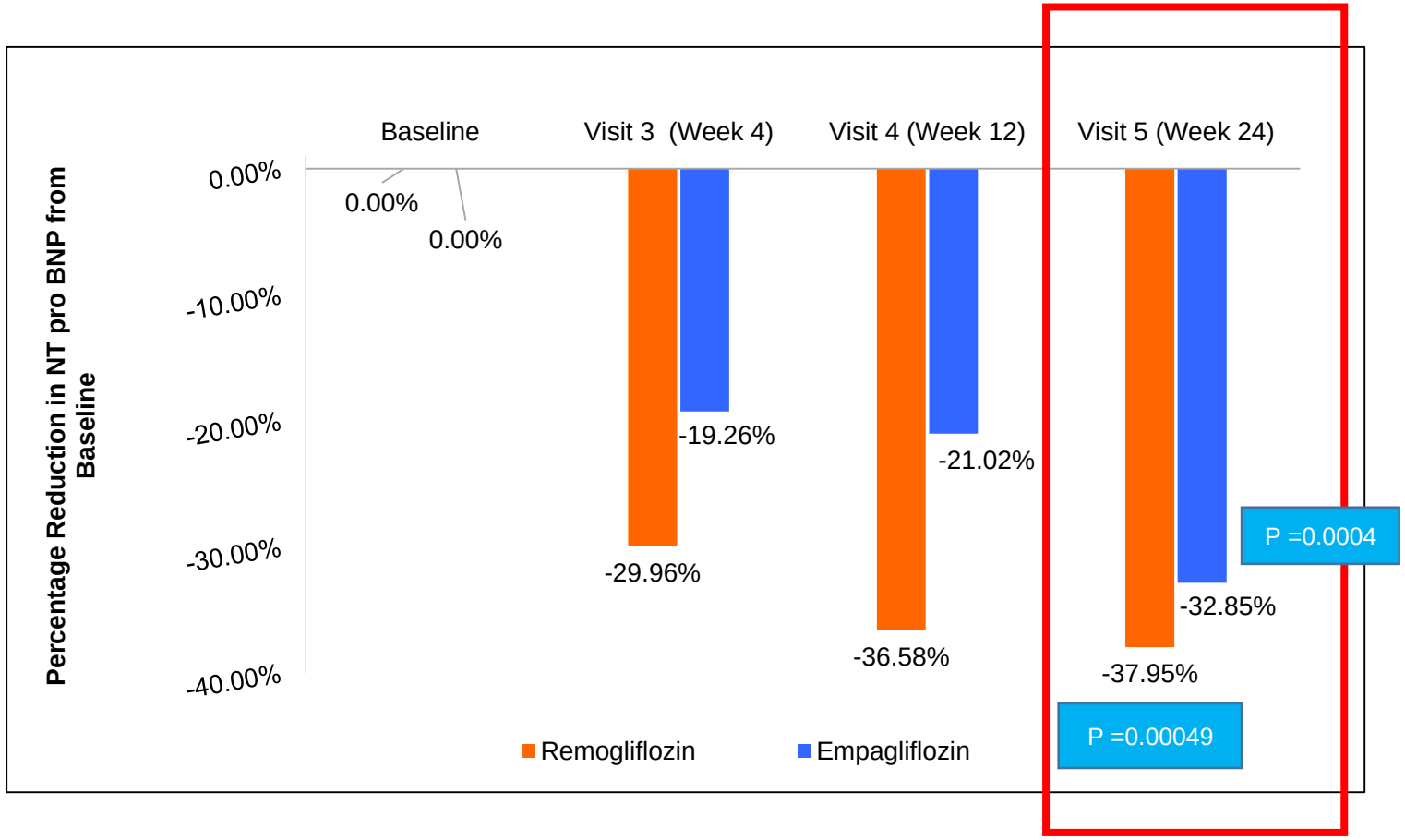
Efficacy Results: Percentage of NT proBNP between Remogliflozin and Empagliflozin at 6 months from baseline



- **Percentage NT proBNP level reduction in the Remogliflzoin group (37.95%) was numerically higher than that seen with Empagliflozin group (32.85%)**
- Percentage NT proBNP reduction from baseline to week 24 was significant across both the groups, while it was non-inferior between the groups at week 24. The reduction was significant across both Remogliflozin and Empagliflozin group (p<0.001)

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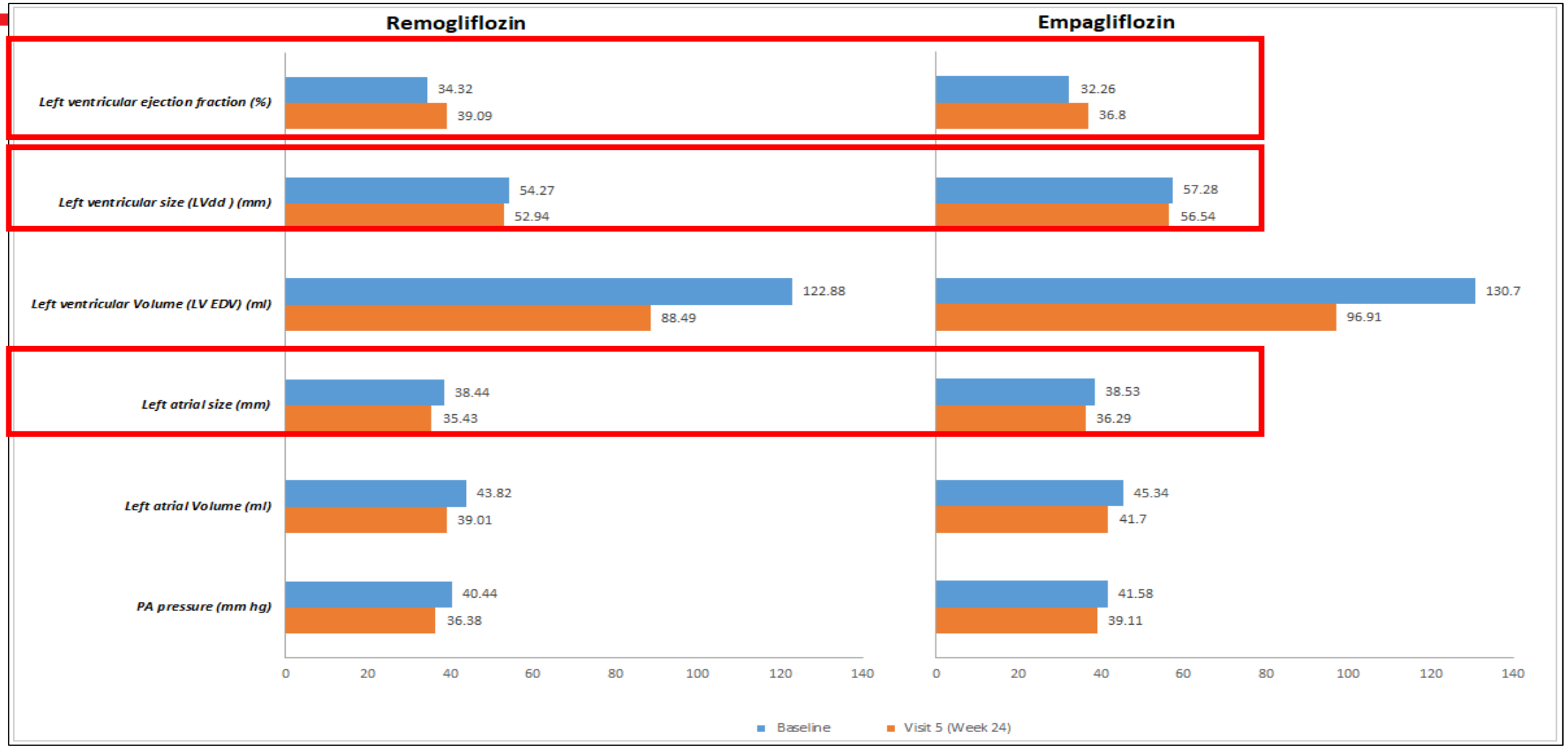
Efficacy Results: ECHO Parameters at Baseline and at 6 Month Visit



- All the ECHO parameters (LVEF, Left ventricular size, LVV, Left atrial size, left atrial volume and pulmonary artery pressure) were significantly improved in both the Remogliflozin and Empagliflzoin groups at 6 months as compared to baseline.

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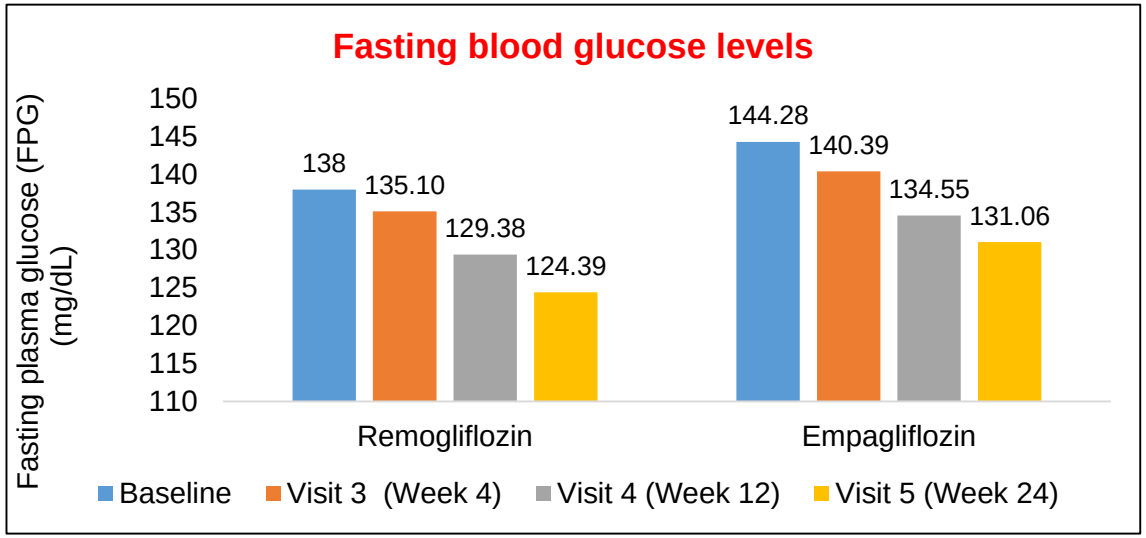
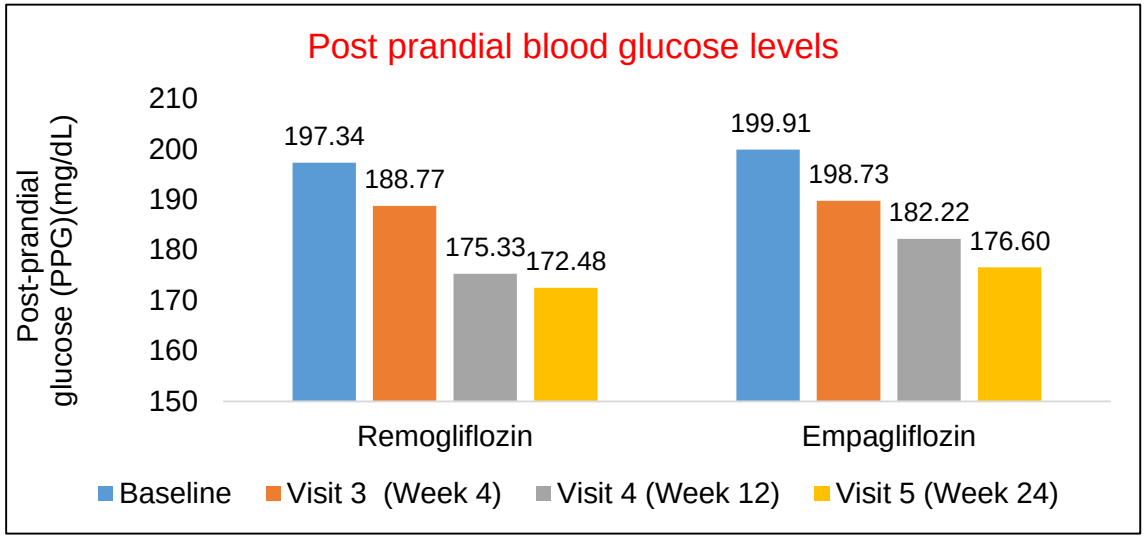
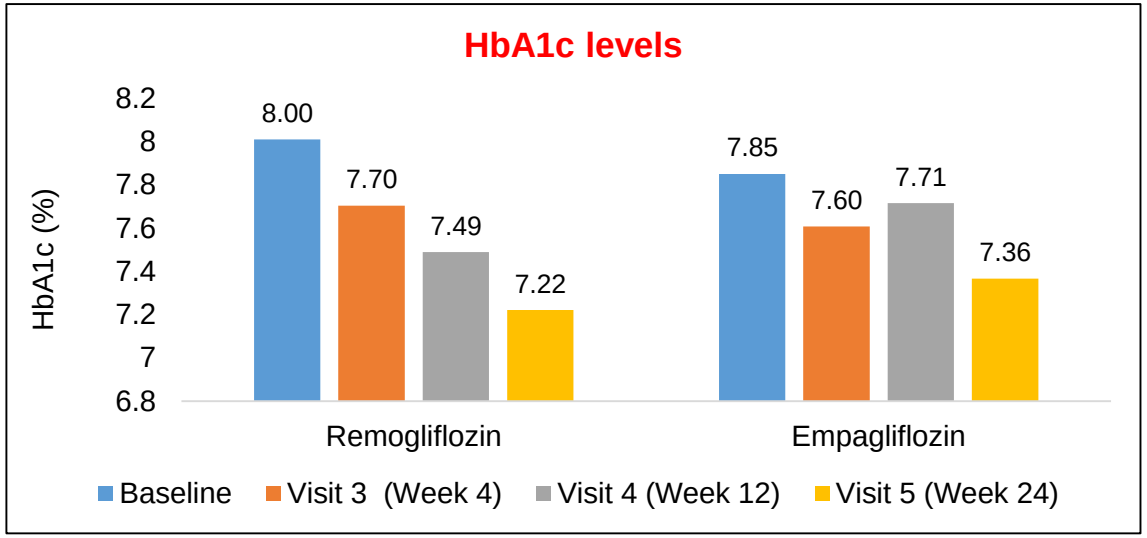
Efficacy Results: Glycemic Parameters (FBS, PPBS and HbA1C)





- All the **Glycemic parameters** (HbA1c, FPG and PPG) demonstrated a **significant reduction from baseline to week 24** in both the Remogliflozin and Empagliflozin group.



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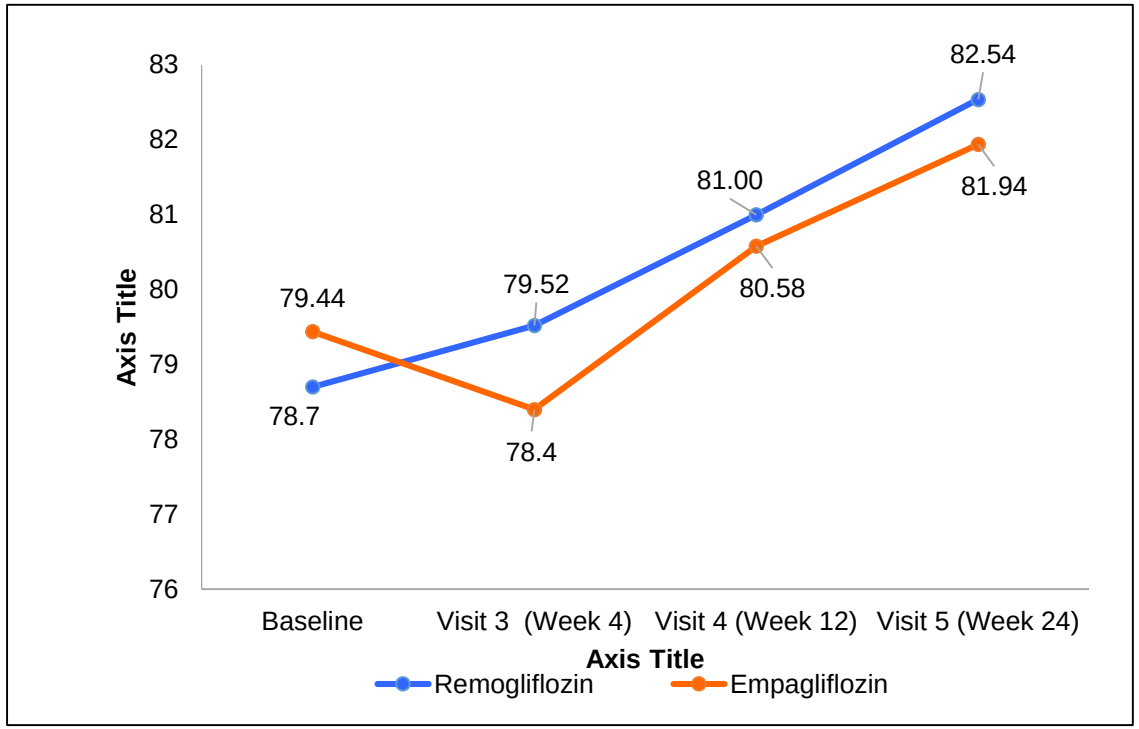
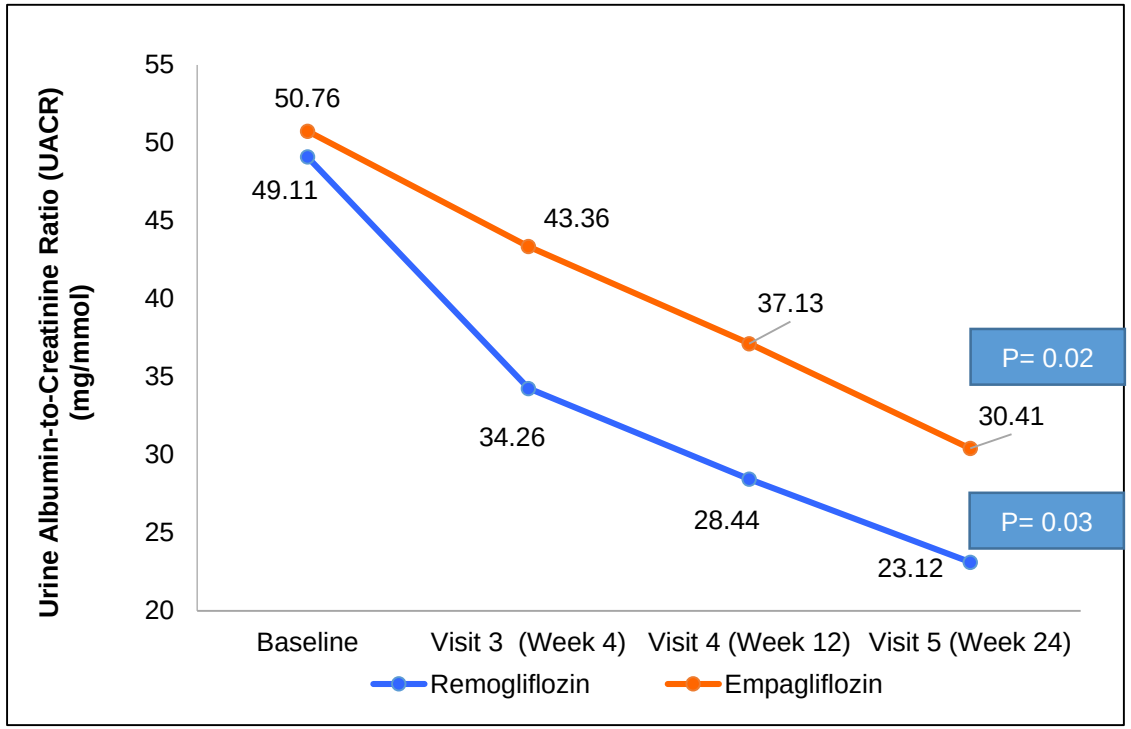
Efficacy Results: Renal Parameters at Baseline and at 6 Month Visit

eGFR



UACR



- The mean eGFR was 78.70 ± 22.07 at baseline and 82.54 ± 22.69 at 6 months in R-group and 79.44 ± 22.72 at baseline and 81.94 ± 21.50 at 6 months in E-group;
- Urine Albumin Creatinine Ratio (UACR) was 49.11 ± 71.68 at baseline and improved to 23.12 ± 17.22 at 6 months in R-group and 50.76 ± 100.51 at baseline and 30.41 ± 26.41 at 6 months in E-group.

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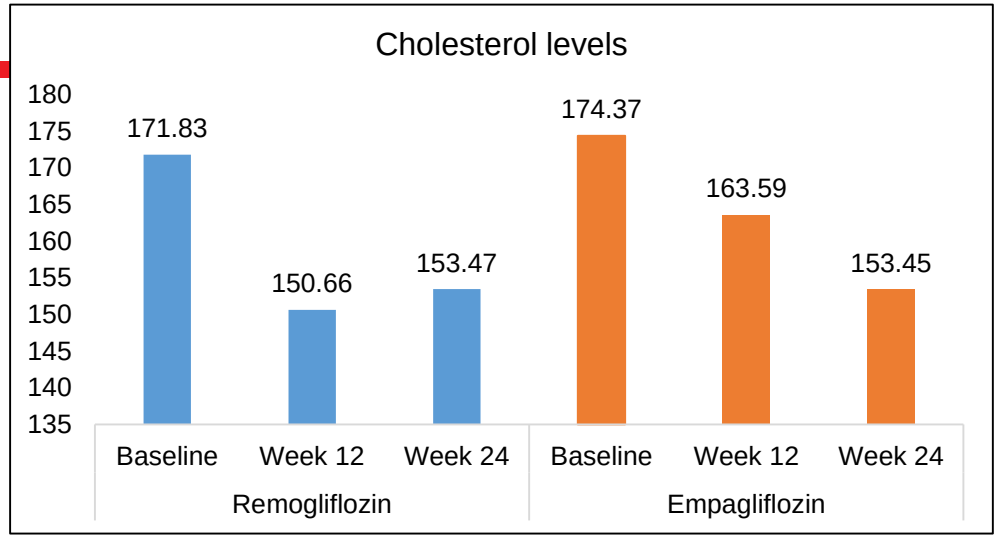
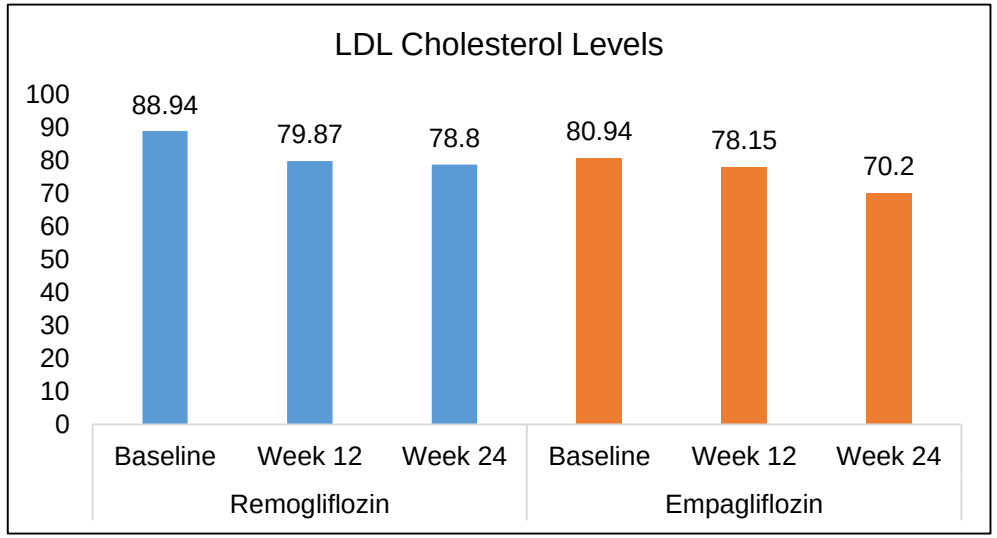
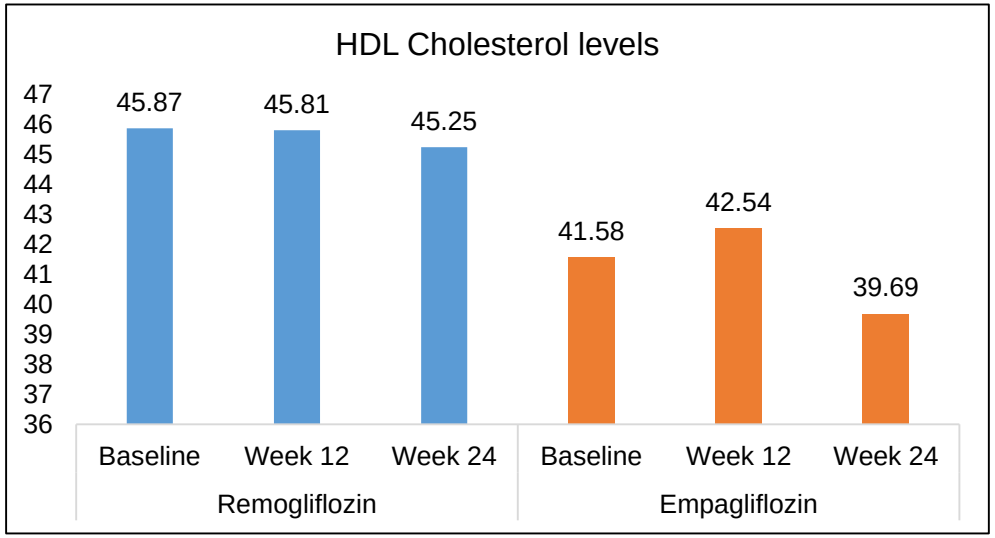
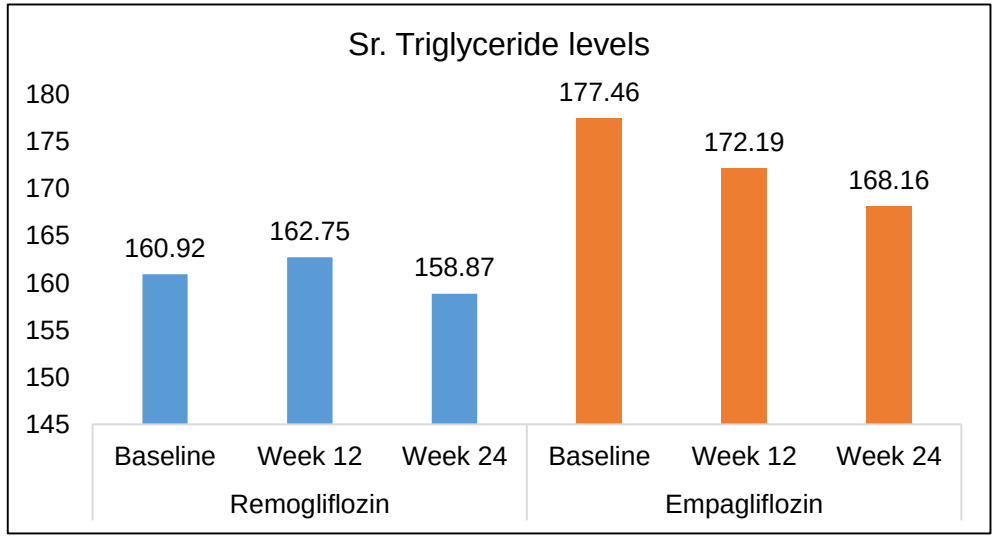
Efficacy Results: Lipid Profile at Baseline and at 6 Month Visit









- The reduction in the Lipid parameters (Cholesterol, LDL-C, HDL-C, VLDL-C and Sr. Triglycerides was comparable among both the Remogliflozin and Empagliflozin group

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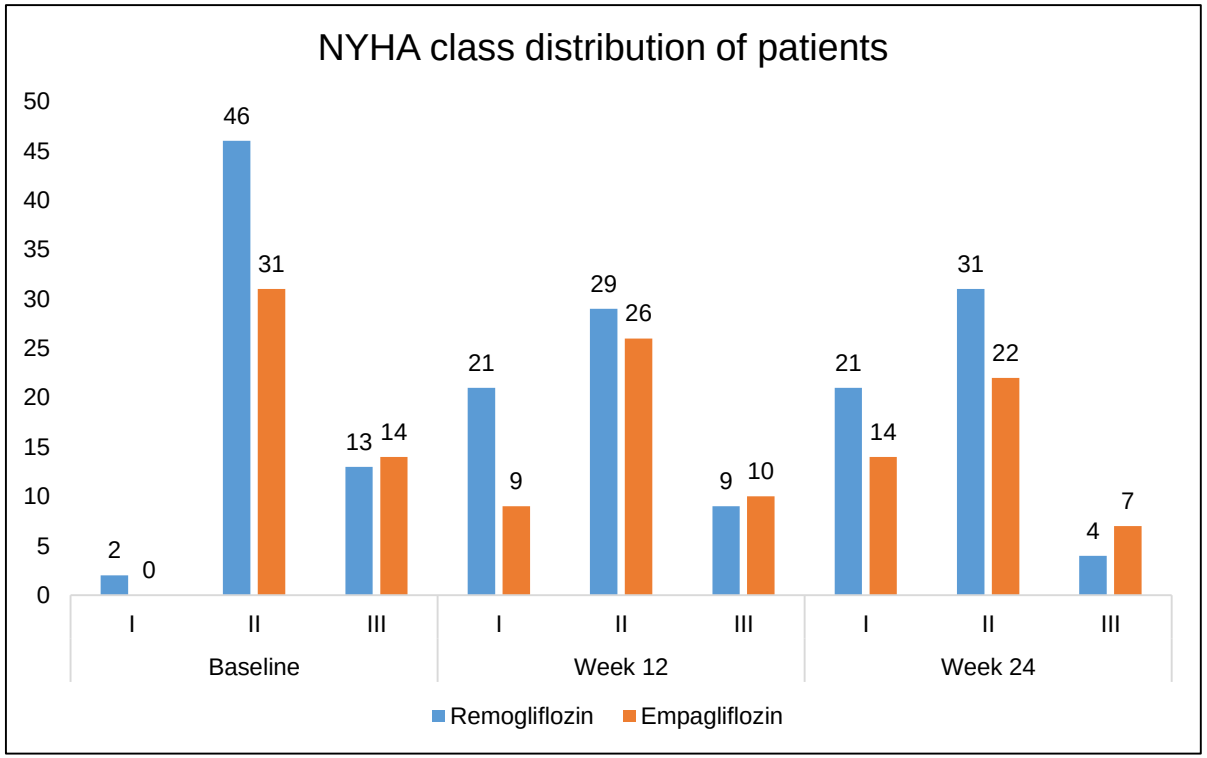
Efficacy Results: NYHA class distribution in patients at Baseline and at week 24

Lab Test	Visits	Class	n	Remogliflozin	n	Empagliflozin
				%		%
NYHA Class	Baseline	I	2	3.28%	-	-
		II	46	75.41%	31	68.89%
		III	13	21.31%	14	31.11%
	Week 24	I	21	34.43%	14	31.11%
		II	31	50.82%	22	48.89%
		III	4	6.56%	7	15.56%



- The NYHA grade has shown progressive improvement in both Remogliflozin and Empagliflozin group at week 12 and week 24.
- At week 24, only 6.56% of the patients on Remogliflozin are in NYHA grade III, while 15.56% of patients in the Empagliflozin group are in NYHA grade III at the end of study.

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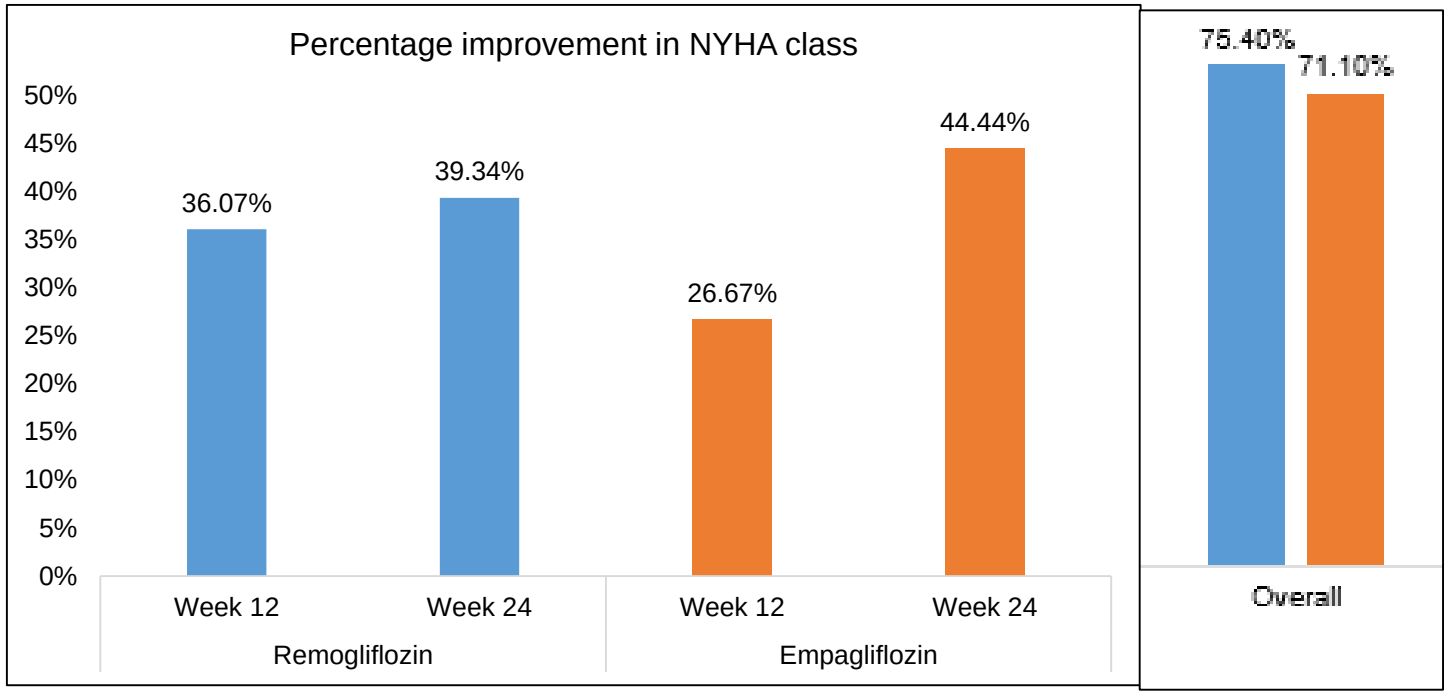
Efficacy Results: Improvement in NYHA class by atleast 1 grade over week 24 compared to Baseline



- NYHA grade improvement was seen across Both the Remogliflozin (75.40%) and Empagliflozin (71.10%) at 6 months as compared to the Baseline.
- Numerically higher improvement was seen with Remogliflozin as compared to Empagliflozin

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Safety Results

Summary of Adverse Events Terms

Parameters	Remogliflozin (N=61)	Empagliflozin (N=45)
	[AE's] n (%)	[AE's] n (%)
Overall	**[7] 5 (8.20%)**	**[4] 4 (8.89%)**
Chest Pain	[1] 1 (1.64%)	-
Cough	[1] 1 (1.64%)	-
High BP	[1] 1 (1.64%)	-
Hyperglycemia	-	[1] 1 (2.22%)
Hypoglycemia	[1] 1 (1.64%)	[1] 1 (2.22%)
Left Hand Pain	-	[1] 1 (2.22%)
Mild Headache	[1] 1 (1.64%)	-
Nausea	[1] 1 (1.64%)	-
Vomiting	[1] 1 (1.64%)	-
Weakness Doe	-	[1] 1 (2.22%)

No serious adverse events (SAEs) were reported during the study duration in either groups

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Conclusion:

- There was significant improvement in mean NT-proBNP level in both Remogliflozin and Empagliflozin group from baseline to 3 months; **however, no significant difference was seen between the two groups**.

- Remogliflozin significantly improved **glycaemic parameters** and **the N-terminal pro-brain natriuretic peptide (NT-proBNP)** as the index of the therapeutic effects in **Indian** T2DM patients with CHF.

- There was also similar improvement in Blood pressure reduction (systolic/diastolic), weight reduction over 24 weeks of treatment in both the groups

- No serious adverse events (SAEs) were reported during the study duration in either groups.

- **Remogliflozin was found to be well tolerated and non-inferior to Empagliflozin in Indian patients of T2DM with CHF.**

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