

Clinical Trial Protocol

Iranian Registry of Clinical Trials

10 Jun 2026

CLINICAL EFFICACY OF DAPAGLIFLOZIN IN ASSOCIATION WITH GENETIC POLYMORPHISM AND ITS PLASMA LEVELS IN CHRONIC HEART FAILURE PATIENTS

Protocol summary

Study aim

To evaluate clinical efficacy of Dapagliflozin in association with genetic polymorphism and its plasma levels in patients with CHF_rEF in Pakistani population

Design

Randomized Controlled Trial

Settings and conduct

Department of Pharmacology & Therapeutics, Army Medical College, National University of Medical Sciences (NUMS), Rawalpindi

Participants/Inclusion and exclusion criteria

1) INCLUSION CRITERIA Pakistani patients of 18 years and above, males and females Diagnosed symptomatic heart failure (NYHA class 1-IV) Ejection fraction (EF) \leq 40% on imaging study within last 12 months prior to enrolment Patient on stable GDMT of heart failure for \geq 4 weeks Both diabetic and non-diabetic patients 2) EXCLUSION CRITERIA Type-1 diabetics or patients having any history of DKA Patients having eGFR \leq 25 ml/ min/ 1.73 m² as per (CKD-EPI formula), systolic blood pressure (SBP) < 95 mmHg Patients having MI, unstable angina, stroke, acute heart failure (HF) or any hospitalization due to acute HF <4 weeks preceding enrolment Patients undergoing PCI /CABG or valvular replacement, any previous transplantation of heart or infixing of ventricular assistance device (VAD), implantation of Cardiac resynchronization therapy (CRT) within 3 months preceding enrolment or any plan to undergo after randomization

Intervention groups

Include Dapagliflozin in addition to GDMT.

Main outcome variables

BIOCHEMICAL TESTS: Serum uric acid and creatinine, Urine R/E and P/C ratio, HbA1c at day 0 and after intervention at 12th week. Echocardiography & eGFR will be calculated at day 0 and 12th week. Plasma levels of Dapagliflozin will be determined by High

Performance Liquid Chromatography (HPLC) Improvement in symptoms and QoL will be ascertained by KCCQ questionnaire & NYHA classification.

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20230331057788N1**

Registration date: **2023-04-04, 1402/01/15**

Registration timing: **prospective**

Last update: **2023-04-04, 1402/01/15**

Update count: **0**

Registration date

2023-04-04, 1402/01/15

Registrant information

Name

Saima Rafique

Name of organization / entity

National University of Medical Sciences

Country

Pakistan

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+92 300 8546013

Email address

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2023-04-10, 1402/01/21

Expected recruitment end date

2024-04-10, 1403/01/22

Actual recruitment start date

empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title
CLINICAL EFFICACY OF DAPAGLIFLOZIN IN ASSOCIATION WITH GENETIC POLYMORPHISM AND ITS PLASMA LEVELS IN CHRONIC HEART FAILURE PATIENTS

Public title
Dapagliflozin in Chronic Heart failure patient

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Pakistani patients of 18 years and above, males and females Diagnosed symptomatic heart failure (NYHA class 1-IV) Ejection fraction (EF) \leq 40% on imaging study within last 12 months prior to enrolment Patient on stable GDMT of heart failure for \geq 4 weeks Both diabetic and non-diabetic patients

Exclusion criteria:
Type-1 diabetics or patients having any history of DKA Patients having eGFR \leq 25 ml/ min/ 1.73 m² as per (CKD-EPI formula), systolic blood pressure (SBP) < 95 mmHg Patients having MI, unstable angina, stroke, acute heart failure (HF) or any hospitalization due to acute HF <4 weeks preceding enrolment Patients undergoing PCI /CABG or valvular replacement, any previous transplantation of heart or infixing of ventricular assistance device (VAD), implantation of Cardiac resynchronization therapy (CRT) within 3 months preceding enrolment or any plan to undergo after randomization Patients having active myocarditis, uncorrected primary valvular disease, restrictive or hypertrophic (obstructive) cardiomyopathy; bradycardia, 2nd or 3rd degree heart block without having any pacemaker Patients received any SGLT2i within 12 weeks preceding screening visit or hypersensitivity to Dapagliflozin Pregnant ladies and nursing mothers, severe COPD leading to dyspnea, any malignancy or hepatic impairment

Age
No age limit

Gender
Both

Phase
4

Groups that have been masked
No information

Sample size
Target sample size: **170**

Randomization (investigator's opinion)
Randomized

Randomization description
Patients will be randomized on basis of computer-generated random numbers. Each patient will be given a particular code number.

Blinding (investigator's opinion)
Not blinded

Blinding description
Placebo
Not used

Assignment
Parallel

Other design features

Secondary Ids
empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethical Review Committee

Street address

Army Medical College, Abid Majeed Road, Rawalpindi Cantt

City

Rawalpindi

Postal code

46000

Approval date

2023-01-06, 1401/10/16

Ethics committee reference number

ERC/ID/254

Health conditions studied

1

Description of health condition studied

Chronic Heart Failure

ICD-10 code

I50.42

ICD-10 code description

Chronic combined systolic (congestive) and diastolic (congestive) heart failure

Primary outcomes

1

Description

Primary outcome will include exploration of clinical efficacy of Dapagliflozin in CHF patients

Timepoint

At day 0 and after 12 weeks

Method of measurement

By biochemical parameters including (BNP/ NT-pro BNP, serum uric acid, creatinine, HbA1c, urine R/E, spot urine P/C ratio, echocardiography), improvement in quality of life by KCCQ questionnaire, NYHA functional class. SAFETY ANALYSIS OF DAPAGLIFLOZIN will be analyzed by observing number of events of major hypoglycemia, hypotension urogenital infection, fourrier's gangrene, DKA and any amputation before and after intervention. MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE) including heart failure hospitalisations, urgent heart

failure visits, stroke, arrhythmia, MI, acute kidney injury and cardiogenic death will be observed for a number of episodes before and after intervention with Dapagliflozin.

Secondary outcomes

1

Description

1)To determine the prevalence of Dapagliflozin transporter genes SLC5A2 for its single nucleotide polymorphism (SNPs) of SLC5A2 (rs3813008 G>A ,rs9934336 G > A and rs3116150 G>A) encoding SGLT2 transporter in Pakistani CHF population. 2)To estimate steady state plasma drug levels of Dapagliflozin and evaluate association of (SNPs) of Dapagliflozin transporter genes on steady state concentration in Pakistani CHF patients.3)To evaluate association of SNPs and plasma levels of Dapagliflozin with clinical efficacy in Pakistani CHF patients.

Timepoint

After intervention of 12 weeks with Dapagliflozin

Method of measurement

Polymerase Chain Reaction (PCR) will be performed for genetic analysis of SNPs of SLC5A2 (rs3813008 G>A and rs3116150 G>A) followed by Restriction Fragment Length Polymorphism (RFLP). Allele Specific- Polymerase Chain Reaction (AS-PCR) will be performed for genotyping of variant allele (rs9934336 G>A) of SLC5A2. Drug levels will be estimated by HPLC.

Intervention groups

1

Description

Experimental Group: (n=85), This group will receive intervention of drug Dapagliflozin (10mg) daily orally in addition to guideline directed medical therapy (GDMT) in Chronic heart failure patients

Category

Treatment - Drugs

2

Description

Control group: This group will receive only guideline directed medical therapy GDMT in chronic heart failure patients

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Army Medical College, Pak Emirates Military Hospital

Full name of responsible person

Dr. Saima Rafique

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

National University of Medical Sciences

Full name of responsible person

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Grant name

PhD grant

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source

National University of Medical Sciences

Proportion provided by this source

10

Public or private sector

Public

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin

Type of organization providing the funding

Academic

Person responsible for general inquiries

Contact

Name of organization / entity

Army Medical College, National University of Medical Sciences

Full name of responsible person

Dr. Saima Rafique

Position

Assistant Professor

Latest degree

Master

Other areas of specialty/work

Cardiology

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Sharing plan

Deidentified Individual Participant Data Set (IPD)

No - There is not a plan to make this available

Justification/reason for indecision/not sharing IPD

Data of Army Personnel can not be shared due to
security reasons.

Study Protocol

No - There is not a plan to make this available

Statistical Analysis Plan

No - There is not a plan to make this available

Informed Consent Form

No - There is not a plan to make this available

Clinical Study Report

No - There is not a plan to make this available

Analytic Code

No - There is not a plan to make this available

Data Dictionary

No - There is not a plan to make this available