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 CHFrEF 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) ≤ 40% on imaging study within last 12 months prior to enrolment Patient on stable GDMT of heart failure for ≥4 weeks Both diabetic and non-diabetic patients 2) EXCLUSION CRITERIA Type-1 diabetics or patients having any history of DKA Patients having eGFR ≤ 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

Phone
+92 300 8546013

Email address
saimarafiqu34@gmail.com

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) ≤ 40% on imaging study within last 12 months prior to enrolment Patient on stable GDMT of heart failure for ≥4 weeks Both diabetic and non-diabetic patients

Exclusion criteria:

Type-1 diabetics or patients having any history of DKA Patients having eGFR ≤ 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, fournier’s gangrene, DKA and any amputation before and after intervention. MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE) including heart failure hopsitalisations, 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

Street address
Army Medical College, Abid Majeed Road, Rawalpindi, Wah Cantt

City
Rawalpindi

Postal code
46000

Phone
+92 300 8546013

Email
saimarafiqu34@gmail.com

Sponsors / Funding sources

1

Sponsor

Name of organization / entity
National University of Medical Sciences

Full name of responsible person
Dr. Dilshad Khan

Street address
Army Medical College, Abid Majeed Road, Rawalpindi Cantt

City
Rawalpindi

Postal code
46000

Phone
+92 300 8546013

Email
saimarafiqu34@gmail.com

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

Street address
Army Medical College, Abid Majeed Road, Rawalpindi Cantt

City
Rawalpindi

Province
Punjab

Postal code
46000

Phone
+92 51 5516755

Email
saimarafiqu34@gmail.com

Person responsible for scientific inquiries

Contact

Name of organization / entity
Army Medical College, National University of Medical Sciences, Pakistan

Full name of responsible person
Saima Rafique

Position
Assistant Professor

Latest degree
Master

Other areas of specialty/work
Cardiology

Street address
Army Medical College, Abid Majeed Road, Rawalpindi Cantt

City
Rawalpindi

Province
Punjab

Postal code
74600

Phone
+92 51 5516755

Email
saimarafiqu34@gmail.com

Person responsible for updating data

Contact

Name of organization / entity
Army Medical College, National University of Medical Sciences

Full name of responsible person
Saima Rafique

Position
Assistant Professor

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Other areas of specialty/work
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Street address
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Province
Punjab

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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