An open label, single dose study to assess safety and efficacy of a novel patch infusor device and novel SUBCUTaneous furosemide formulation combination in patients with Heart Failure: a phase I clinical trial

Protocol

ACRONYM: SUBCUT-HF I

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This study will be performed according to the Research Governance Framework for Health and Community Care (Second edition, 2006) and The Medicines for Human Use (Clinical Trials) Regulations, 2004 SI 2004:1031 (as amended) and World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects 1964 (as amended).

Study Synopsis:

Title of Study	**An open label, single dose study to assess safety and efficacy of a novel patch infusor device and novel SUBCUTaneous furosemide formulation combination in patients with Heart Failure: a phase I clinical trial**
Study Centre	1 site in Queen Elizabeth University Hospital in Glasgow
Investigational Product and Medical Device	The drug and device combination is called SQIN-01. SQIN-01 is a combination of SQIN-Infusor and SQIN-Furosemide Investigational pump (SQIN-Infusor, medical device) intended for subcutaneous infusion of investigational product, SQIN-Furosemide. SQIN-Furosemide is investigational subcutaneous furosemide formulation at 30mg/mL at pH 7.4 (range 7.0 to 7.8) intended for slow subcutaneous infusion using a biphasic delivery profile. 80mg of SQIN-Furosemide will be administered using SQIN-Infusor by subcutaneous infusion over 5 hours using biphasic delivery profile of 30mg in the first hour and 50mg over the remaining 4 hours.
Study Phase	I
Primary Objective	To investigate the safety, tolerability, efficacy and on-body performance of a novel patch infusor device and novel furosemide formulation combination (SQIN-01).
Secondary Objective	To investigate the efficacy of SQIN-01 To investigate skin reactions and patient acceptability.
Primary Outcomes	• Safety as determined by treatment emergent adverse events (TEAEs), (including serious adverse events [SAEs]) and adverse drug events (ADEs)(including serious adverse drug events [SADEs]) • Infusion site pain measured using a Numerical Pain Rating Scale(1) (Appendix 3) • Any device failures (e.g. adhesive failure and drug delivery failure) • Serum furosemide concentration at 0, 60 and 240 minutes after start of SQIN-Furosemide infusion
Secondary outcomes	• Urine volume and sodium concentration in urine collected 8 hours after start of SQIN-Furosemide infusion • Presence of local skin reactions, recorded with photography and assessed using standardised erythema/edema assessment tool (2) (Appendix 4) • Patient acceptability using System Usability Scale(3) (Appendix 5)
Rationale	A new formulation of (neutral pH) furosemide (SQIN-Furosemide) that can be delivered subcutaneously by a pump placed on a patient abdomen has been developed. This trial will test the on-body performance of new subcutaneous pump device (SQIN-Infusor) and clinical efficacy of SQIN-Furosemide in patients with heart failure (HF).

Study design	Prospective, open-label, single dose study in 20 patients previously diagnosed with HF being treated with intravenous furosemide therapy at a dose of ≥40 mg/day mg/day as in-patients.
Sample Size	20
Screening	Coronary care unit and cardiology wards.
Main Inclusion Criteria	• Written informed consent • Male or female ≥18 years of age • Meet ESC criteria for diagnosis of HF(4) • Inpatient with a primary diagnosis of HF requiring treatment with intravenous furosemide at dose ≥40 mg/day per day
Main Exclusion Criteria	• Unable to consent to inclusion in study due to lack of capacity • Requiring treatment with intravenous furosemide at dose >200 mg per day as determined by the usual care team • Current inotropes, vasopressors or intra-aortic balloon pump therapy • Concomitant use of diuretics in 12 hours preceding administration of study drug with SQIN-Infusor • Systolic blood pressure (SBP) <90 mmHg • Pregnancy or breastfeeding • Left sided valve disease with planned surgery or percutaneous intervention • Type 1 myocardial infarction during index hospitalisation (type 2 myocardial infarctions are allowed)(5) • Any surgical or medical condition which prevents patient from ambulation during the infusion • Renal impairment, defined as eGFR < 30 mL/min/1.73 m^2 at screening. • Patient on active cardiac transplant waiting list • Potassium <3.0 mmol/L • Potassium >6.0 mmol/*L* • Sodium <125 mmol/L • Any contraindications for furosemide administration as per furosemide SmPC • Any surgical or medical conditions, which in the opinion of the investigator may pose an undue risk to the subject, interfere with participation in the study or which may affect the integrity of the data
Randomisation	None
Duration of Treatment	5 hours
Statistical Analysis	Determination of sample size was based on a pragmatic assessment to characterise PK/PD. A statistical plan will include all subjects who were placed SQIN-Infusor and which was activated in accordance with the instructions (Intent to treat). Additional analyses include participants who received 1 dose (80mg) of study drug (SQIN-Furosemide) administered with the investigational pump (SQIN-Infusor).

	All primary and secondary safety outcomes will be listed by the subject. TEAEs and SAEs will be summarised for each event by system organ class, preferred term, severity, and relationship to study device and drug. Any observed values and changes from baseline for clinical and laboratory data, physical examination results and vital signs will be summarised using appropriate descriptive statistics. Furosemide concentrations at pre-specified times (0, 60 and 240 minutes from start of the infusion) will be summarised using descriptive statistics (including N, mean, standard deviation, coefficient of variation, median, minimum and maximum). Urinary volume and sodium concentration measure at 8 hours will be summarised using descriptive statistics (including N, mean, standard deviation, coefficient of variation, median, minimum and maximum).