Observation plan - Synopsis

A multicentre, prospective registry to evaluate the safety and efficacy of minimally invasive ultrafiltration treatment and its effect on symptoms and rehospitalisation in patients with advanced volume overload

"GENTLE-UF REGISTRY"

Global rEgistry on decongestioN Therapy using Less invasivE UltraFiltration

Study code:	UF-HF-01-INT
NCT No:	NCT02769351
Investigational device:	Chiara, peripheral ultrafiltration device
Protocol status:	English version V3.0
Date of current version:	22.12.2015
Sponsor responsible for study:	Fresenius Medical Care Deutschland GmbH Else-Kröner-Straße 1 61352 Bad Homburg Germany

Observational Plan - Synopsis

Title:	**GENTLE-UF REGISTRY:** Global rEgistry on decongestioN Therapy using Less invasivE UltraFiltration
Study code:	UF-HF-01-INT
Investigational device:	Chiara, peripheral ultrafiltration device
Aim:	In this prospective registry of the performance and safety of minimally invasive ultrafiltration, in some cases in combination with a post-hospitalisation disease management programme (in a subgroup of patients), treatment data will be collected using an electronic data recording system. The eCRF, which represents the clinical database, will be run on a server located in Germany and complies with current data protection regulations. It is intended to recruit about 300-500 patients with advanced volume overload at a minimum of 10 sites. The treatment data for each patient will be recorded over a period of 12 months. An interim analysis will be performed after 150 patients have been observed for 6 months. The aim of the registry is to expand the knowledge about ultrafiltration therapy in volume overload and to support the development of an evidence-based recommendation for routine clinical practice.

Endpoints:

Clinical endpoints

- Symptom status on discharge (NYHA class) after the first hospitalisation
- Weight change (time of 1st treatment until discharge from first hospitalisation); weight change metrically and weight loss categorially (yes/no)
- Rehospitalisation (yes/no) due to exacerbation of heart failure/volume overload of other origin within 12 months
- Unscheduled outpatient medical treatment for exacerbation of heart failure/volume overload of other origin (medical practice, outpatient department, emergency admission) within 12 months

Safety endpoints

- Significant deterioration of kidney function (on the basis of kidney retention parameters and eGFR)
- Significant electrolyte shift (serial measurement of electrolytes according to clinical requirements: sodium, potassium)

- Periprocedural (= emerging during the ultrafiltration treatment) symptomatic hypotension (yes/no)
- Periprocedural inotropic support required
- Events: related to venous access, apparatus-related, anticoagulation-related, UF procedure-related, unrelated
- Tolerability of treatment from the patient's perspective (subjective assessment on a 5-point scale)

Feasibility endpoints

- Successful treatments (duration of treatment defined at the discretion of the treating doctor and improved urinary output, no premature discontinuation)
- Successful peripheral accesses
- Need to change to another peripheral access (yes/no)
- Need to change to a central venous access (yes/no)

Performance endpoints

- Duration of UF therapy (in hours)
- UF flow rate in mL/h
- Total ultrafiltrate in mL/treatment
- Total ultrafiltrate in mL/hospitalisation

Other parameters

- Incidence of diuretic-resistant study participants
- Symptom status (NYHA) (during routine medical care, usually after 6 and 12 months)
- Changes in echocardiographic parameters (LVEF, LVEDD, LVESD, sPAD) (first hospitalisation, in the course of routine medical care (usually after 6 and 12 months), unscheduled hospitalisation)
- 6-minute walking test (on initial hospitalisation and in the course of routine medical care (usually after 6 and 12 months)
- Feasibility of home monitoring in a subgroup of patients at high risk of rehospitalisation (at the investigator's discretion)
- Home monitoring parameters (body weight, blood pressure, pulse, drug intake)
- Body water analysis by in-body device (body water composition [total body water, intracellular water, extracellular water], if device is available)
- Serial NTproBNP or BNP analysis (for recruitment, discharge after first hospitalisation, follow-up observation times in the course of routine medical care (usually 6 and 12 months), unscheduled hospitalisation)
- Anticoagulation regimen
- Oedema status (for times see Table 2)
- Diuretic dosage regimen (inpatient and outpatient)
- Regimen of guideline-adherent heart failure drugs (inpatient and outpatient)

Selection criteria:

- Age ≥ 18 years
- Inpatient-treated patients with acute volume overload, preferably in association with cardiac decompensation with signs of incipient diuretic resistance (lack of increase in urine output despite significant escalation of diuretic therapy; e.g. ≥ 80 mg furosemide / 24 h or <1375 mL urine output/40 mg furosemide per 24 h or equivalent dose of other loop diuretics [established clinically or from the medical history]).
- New York Association Functional Class (NYHA) III-IV at inclusion
- Systolic or diastolic cardiac dysfunction (HF-REF or HF-PEF)
- Adequate venous access (preferably peripheral arm vein) allowing a flow rate ≥ 60 mL / min
- Written consent to the use of data in the registry (where necessary, by a legal guardian).

Exclusion criteria:

- Contraindication to anticoagulation (e.g. known heparin-induced thrombocytopenia, severe bleeding)
- Terminal renal failure (stage V, GFR < 15 mL)
- Cardiogenic shock, e.g. in association with acute coronary syndrome (ACS)
- Other diseases or factors that, in the study doctor's opinion, constitute a potential contraindication to ultrafiltration
- Pregnant women, women in labour, breast-feeding women or women of childbearing potential, who are without adequate contraception or are planning a family. NB: a pregnancy test is performed systematically in women of childbearing age and the patient is not included in the event of pregnancy (positive test). It is absolutely essential that women, who have a negative test and who are included in the study, have an effective contraception.

Statistical analysis:

The aim of the GENTLE-UF Registry is to evaluate the safety and performance of a novel, minimally invasive ultrafiltration treatment.

The recorded data will be analysed using descriptive statistical methods. For metric variables (e.g. age), the following statistical parameters will be determined: number of valid data, mean, standard deviation and selected quantiles (minimum, 25% (lower quartile), 50% (median), 75% (upper quartile), maximum). With categorial variables (e.g. sex), absolute and relative frequency distributions will be calculated.

The effect of possible prognostic variables (e.g. age, sex) on the study parameters can be evaluated by means of subgroup analyses or statistical models.