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A clinical trial with Sodium Thiosulfate for the treatment of Calciphylaxis

Submission date
22/07/2014

Recruitment status
No longer recruiting

Registration date
02/09/2014

Overall study status
Completed

Last Edited
28/05/2020

Condition category
Circulatory System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Calciphylaxis is a serious, but rare, condition in which calcium and phosphate accumulate in the blood vessels and soft tissues in the body. Most people suffering from calciphylaxis have advanced (end stage) kidney failure or have just had a kidney transplant. It has a high mortality rate (proportion of people dying from the condition) of up to 80% due to cardiovascular (for example, heart) disease and sepsis caused by infected skin ulcers. There is some data that suggests that sodium thiosulfate (STS) may be useful in treating calciphylaxis. It can bind to calcium, which may help prevent the mineral from accumulating inside the body and it can also dissolve calcium deposits that already exist. Here, we will look at how STS may help treat calciphylaxis.

Who can participate?
Adults (aged at least 18 years) diagnosed with calciphylaxis.

What does the study involve?
Patients are treated with STS for at least 24 weeks and up to 48 weeks. The starting dose is 25g per day, 3 times a week but this may be reduced if the patient cannot tolerate such a high dose. The dose may also be reduced after 24 weeks if the patients skin ulcers have disappeared (gone into remission). The results are analysed after 48 weeks.

What are the possible benefits and risks of participating?
Benefits of taking part in the trial may include a decrease in ulcer wound area of between 20-50% within 24 weeks and a reduced mortality rate (35%). Side effects include feeling sick, vomiting, headaches, low blood pressure, blood clots and being more sensitive to smells. Side effects may be alleviated by reducing the dose of STS given.

Where is the study run from?
The University Hospital of Bern, Department of Nephrology and Hypertension (Switzerland)

When is the study starting and how long is it expected to run for?
October 2014 to May 2018

Who is funding the study?
Dr. F. Köhler Chemie GmbH (Germany)

Who is the main contact?
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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2014-002128-28

Protocol serial number
STS-CSM-1/13

Study information

Scientific Title
A prospective Multicenter Phase 2/3 Clinical Trial with Sodium Thiosulfate for the Treatment of Calciphylaxis

Study objectives
Up to now, no prospective clinical trial with STS has been performed. Reasons are that calciphylaxis is a rare condition and treatment is not focused on certain centres. The previous case reports on successful treatments of calciphylaxis patients with STS support the intention to demonstrate the efficacy and safety of STS in this patient population under the conditions of a prospectively planned clinical trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Austria: Ethikkommission der Medizinischen Universität Graz, 06/02/2015, EK ref: 27-103 ex 14 /15
Germany: Ethikkommission der Landesärztekammer Baden- Württemberg, 10/02/2015, EK ref: AM-2014-045-ff-RS
Switzerland: Kantonale Ethikkommission Bern (KEK), approval pending

Study design
Prospective open uncontrolled multicenter Phase II/III clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Calciphylaxis

Interventions
The study will involve 40 female and male patients. At start of the run-in phase (VR) of 2 to 4 weeks, patients will be treated with conventional medications and measures. If the investigators

assess the patients as eligible for the treatment with STS and for participating in the clinical trial, a biopsy will be taken during the run-in phase to confirm the diagnosis of calciphylaxis by excluding other causes of necroses and ulcerations. At the end of the run-in phase, i.e. the day defined as baseline (V0), patients will be treated with STS for at least 24 weeks. The starting dose will be 25 g per day given 3x per week 30 min before end of HD over an infusion period of 60 min. In case of continued low tolerability of the STS high dose, it may be reduced to 18.75 g or if appropriate, further lowered to 12.5 g. As soon as a better tolerability of STS has been achieved, the dose should be increased again to 25 mg to avoid flares and recurrence of symptoms. In case of complete remission of the wound lesion after at least 24 weeks of STS treatment, the dose may be reduced for the remainder of the study to 18.75 g or if appropriate, further lowered to 12.5 g. However, before week 24 (V4) the dose may only be reduced for safety reasons. Time points of and reasons for any dose reduction or cessation of STS treatment will be assessed. The duration of participation for each patient will be up to 48 weeks plus 2 to 4 weeks run-in phase. The overall duration of the trial is expected to be approximately 4 years.

Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
Sodium Thiosulfate

Primary outcome(s)
Percent reduction of the total wound area after 24 weeks (V4) compared to baseline (V0) as assessed by 2 independent, blinded dermatologists using a serial photo documentation. The mean value of both assessments will be taken.

Key secondary outcome(s))
Status of skin lesions:
1. Total wound area at 8, 16, 36, 48 weeks compared to baseline (V0).
2. Complete remission of wound area.
3. Qualitative improvement of skin lesions at 8, 16, 24, 36, 48 weeks as assessed by the revised Photographic Wound Assessment Tool (revPWAT) score and evaluation of a serial photo documentation through 2 independent, blinded dermatologists.
4. Use of wound debridement
Pain:
5. Reduction of pain in the areas of calciphylaxis after 4, 8, 16, 24, 36 and 48 weeks after start of STS treatment will be compared to baseline (V0) and assessed by a visual analogue scale (VAS) for pain (0-10). This will be done directly before changing the wound dressing.
6. Consumption of pain medication (normalized to morphine equivalent with an appropriate conversion table) will be assessed at V0 and 4, 8, 16, 24, 36 and 48 weeks after start of STS treatment and compared to baseline (V0).
Clinical global impression:
7. Change in clinical global impression as assessed by the Clinical Global Impressions Improvement (CGI-I) score at each follow-up visit (after 4, 8, 16, 24, 36 and 48 weeks) compared to baseline (V0) and the Clinical Global Impression-Severity scale (CGI-S) through the investigators. The Clinical Global Impression-Severity scale (CGI-S) will be assessed at each visit from visit V0 to V6 (i.e. after 4, 8, 16, 24, 36 and 48 weeks).
Improvement leading to eligibility of the patient for kidney transplantation:

8. Eligibility for kidney transplantation is given when the patient is being actively listed on a transplant waiting list.
Occurrence of new lesions:
9. Time point of occurrence and if applicable healing as well as location of each lesion to be documented at each visit (V0 to V6)
Bone mineral density (BMD):
10. Bone scans by Dual Energy X-ray absorptiometry (DEXA) technique at baseline and after 48 weeks (V6)
Survival:
11. Median overall survival after start of STS treatment
12. One-year survival rate

Completion date
30/05/2018

Eligibility

Key inclusion criteria
1. All patients ≥ 18 years
2. Male or female hemodialysis (HD) patients with a diagnosis of calciphylaxis. (Patients on peritoneal dialysis or patients with the requirement for renal replacement therapy, who are diagnosed with calciphylaxis, may be switched to HD and included in the study after switching).
3. Able to understand character and individual consequences of the clinical trial and to provide written informed consent to participate in the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
5

Key exclusion criteria
Current exclusion criteria as of 09/07/2018:
1. Pregnant or lactating patients. As pregnancy is an extremely rare event in HD patients, a pregnancy test will only be performed in ambiguous cases.
2. Patients who have participated in any other investigational studies within 30 days previous to enrolment
3. History of alcohol abuse, illicit drug use, significant mental illness, physical dependence to any

opioid, or any history of drug abuse or addiction within 12 months of study enrolment
4. Good response to conventional treatment
5. Life expectancy less than 4 months in the judgment of the investigator

Previous exclusion criteria:
1. Sodium metabisulfite hypersensitivity, among others the history of bronchial asthma due to known sodium metabisulfite hypersensitivity
2. Pregnant or lactating patients. As pregnancy is an extremely rare event in HD patients, a pregnancy test will only be performed in ambiguous cases.
3. Patients who have participated in any other investigational studies within 30 days previous to enrolment
4. History of alcohol abuse, illicit drug use, significant mental illness, physical dependence to any opioid, or any history of drug abuse or addiction within 12 months of study enrolment
5. Good response to conventional treatment
6. Life expectancy less than 4 months in the judgment of the investigator

Date of first enrolment
01/04/2016

Date of final enrolment
30/05/2018

Locations

Countries of recruitment
Austria

Germany

Switzerland

Study participating centre
Inselspital Bern
Universitätsklinik für Nephrologie und Hypertonie
Freiburgstrasse 4
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3010

Study participating centre
Bürgerspital Solothurn
Schöngrünstrasse 38
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Switzerland
4500

Study participating centre
Nephrologisches Zentrum Villingen-Schwenningen
Albert-Schweitzer-Strasse 6
Villingen-Schwenningen
Germany
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Study participating centre
Landeskrankenhaus Feldkirch
Abteilung für Nephrologie und Dialyse
Carinagasse 47
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6807

Study participating centre
Allgemeines Krankenhaus Wien
Klin. Abteilung für Nephrologie und Dialyse
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Study participating centre
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Sponsor information

Organisation
Dr. F. Köhler Chemie GmbH (Germany)

ROR
https://ror.org/036ezxy46

Funder(s)

Funder type
Industry

Funder Name
Dr. F. Koehler-Chemie GmbH

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			28/05/2020	No	No