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People suffering from Chronic Kidney Disease-associated Pruritus (CKD aP) are treated with a new cream, MC2 25 Cream, or placebo (same Cream without active ingredient) for 12 weeks to reduce their burden and to prove the new cream is safe when used

Submission date
08/02/2022

Recruitment status
No longer recruiting

Registration date
18/05/2022

Overall study status
Completed

Last Edited
20/01/2025

Condition category
Skin and Connective Tissue Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Patients with chronic kidney disease are often suffering from pruritus (severe itching of the skin). This is mostly caused by the lack of correct kidney function and dialysis. The pruritus often presents with fluctuating intensity, often worse during night-time than daytime, resulting in sleep disturbances. Most patients report itching over large, alternating, non-dermatomal regions of skin. The significant impact of itch on these patients' quality of life is generally accepted. In 23,264 haemodialysis patients from 21 countries, the proportion of CKD patients on dialysis who are at least moderately bothered by self-reported pruritus is 37%, and 7% are extremely bothered. It has also been found that this itch was associated with higher risk for hospitalizations and death, higher rates of withdrawal from dialysis and missing scheduled dialysis treatments, and lower rates of employment.
The sponsor of this study has developed a new cream formulation which is deemed to reduce this the itch and therewith the associated complaints and disadvantages in dialysis patients.

Who can participate?
Adults over 18 years, with chronic kidney disease

What does the study involve?
Patients will either receive MC2-25-Cream or vehicle (placebo).

What are the possible benefits and risks of participating?
Benefits:
It is anticipated that the disease burden is reduced in participating patients.
Risks:

Study Drug:
This is the first clinical trial with MC2-25 cream so no clinical data are available. According to an SmPC from an IV product containing similar active ingredient, there are no known undesirable effects when administered correctly. In the present trial a maximum of 50 g MC2-25 cream 3% (w /w) will be used per day, which corresponds to ~0.02 g of the active ingredient/kg/day (1.5 g per day in a 70-kg adult) and a resulting safety margin of 25 compared to the IV administration assuming that all topically applied ingredient is absorbed into the systemic circulation.
As for every unknown drug, there may occur adverse effects not yet known for patients receiving MC2-25 cream or even vehicle group, if a patient is allergic to one of the ingredients. This should be minimised by Exclusion Criterion # 9. Furthermore, no application site reactions were observed after dermal application of MC2-25 cream and MC2-25 vehicle to minipigs (twice daily).
Study procedures:
It is not expected that patients will have a risk when filling study specific Questionnaires. Also, no risk is expected during physical examination, vital sign measurement or ECG. Skin biopsies are scientifically approved for examination of the skin. Patients may recognise the biopsy as unpleasant or painful. Pain induced by skin biopsies is usually not long lasting and disappears within a short time period. Blood samples will be taken from participants at several timepoints to assess the biochemistry and haematology. In some cases nausea could be observed when blood is taken. Furthermore, it might come to discomfort or pain and haematoma at the injection site with local infections. In very rare cases, skin nerves at the injection site can be damaged. Participants receiving MC2-creme could experience an improvement in their disease, which could also occur when patients receive the vehicle. For further information please refer to Table 1, "Summary of Risks and Mitigation Strategies" of the clinical trial protocol.

Where is the study run from?
SRE GmbH (Germany)

When is the study starting and how long is it expected to run for?
February 2022 to January 2024

Who is funding the study?
MC2 Therapeutics Ltd (UK)

Who is the main contact?
Dr Kieran McCafferty, kieran.mccafferty4@nhs.net
Jon Bondebjerg, jbo@mc2therapeutics.com

Study website
https://ckd-itch.com/

Contact information

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Additional identifiers

EudraCT/CTIS number
2021-006971-40

IRAS number
1004785

ClinicalTrials.gov number

Secondary identifying numbers
MC-25-C1, IRAS 1004785

Study information

Scientific Title
A parallel-group (2-arm), randomized, double-blind, 12 week trial to evaluate the efficacy and safety of MC2 25 cream and MC2-25 vehicle in subjects with chronic kidney disease-associated pruritus (CKD aP)

Acronym
ITCHINESS

Study objectives
1. Exploration of the clinical efficacy of MC2-25 cream compared to MC2-25 vehicle in adults with chronic kidney disease-associated pruritus (CKD-aP)
2. Exploration of the safety of MC2-25 cream compared to MC2-25 vehicle in adults with CKD-aP and other objectives are to explore the subclinical effects of MC2-25 cream in adults with CKD aP

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 22/03/2022, London City and East REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8144; cityandeast.rec@hra.nhs.uk), ref: 22/SW/0020

Study design
Interventional double blind randomized parallel group placebo controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Patients who are on dialysis and experience itch due to this.

Interventions
Patients will either receive MC2-25-Cream or vehicle (placebo).
Randomization is done via an electronic online system.
There will be a treatment period of 12 weeks for all arms plus a two week follow-up period (only in case of ongoing AEs).

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
MC2 25 cream

Primary outcome measure
Weekly mean WI-NRS recorded in the subject’s diary once daily from Baseline to Week 12. Calculated as the average of minimum 4 WI-NRS values recorded in the subject’s diary from 7 days prior to and including the visit days

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
03/02/2022

Completion date
02/02/2024

Eligibility

Key inclusion criteria
1. Adult males or non-pregnant females of any race or ethnicity who are ≥18 years of age at the time of screening
2. Able to understand the trial and willing to comply with trial requirements
3. Has provided written informed consent
4. Chronic (>3 months) kidney disease (CKD) stages G3-G5 (i.e., estimated glomerular filtration rate [eGFR] by CKD-EPI creatinine 2021 equation <60 mL/min/1.73 m^2)
5. Specifically for CKD subjects on haemodialysis (HD) or haemodiafiltration (HDF):
5.1. Subjects must be established on HD or HDF 3 times per week continuously for at least 3 months prior to the start of screening and must not have plans to change from HD to HDF or vice versa during the trial.
5.2. Subjects who require an occasional additional HD or HDF treatment to manage fluid overload may be enrolled as long as it is anticipated that no more than 4 such treatments will be required in any given month.
6. At least moderate CKD-aP defined as WI-NRS ≥4
7. Female subjects must be of either:
7.1. Non-childbearing potential, i.e., postmenopausal for a least 1 year or have a confirmed clinical history of sterility (e.g., hysterectomy or tubal ligation) or,
7.2. Childbearing potential with a negative urine pregnancy test at the Baseline visit or (in the case of anuria) a negative serum pregnancy test at the Baseline visit that is no more than 3 days old.
8. Female subjects of childbearing potential must agree to use a highly effective method of contraception (i.e., a method with a failure rate of less than 1% per year when used consistently and correctly) while receiving double-blind treatment. Highly effective contraception is defined as follows:
8.1. Combined (estrogen and progestogen-containing) hormonal contraception associated with inhibition of ovulation: oral, intravaginal, transdermal
8.2. Progestogen-only hormonal contraception associated with inhibition of ovulation: oral, injectable, implantable
8.3. Intrauterine device (IUD)
8.4. Intrauterine hormone-releasing system (IUS)
8.5. Bilateral tubal occlusion
8.6. Vasectomised partner (provided that is the sole sexual partner of the subject and that the vasectomised partner has received medical assessment of the surgical success)
8.7. Sexual abstinence if in line with the preferred and usual lifestyle of the subject and defined as refraining from heterosexual intercourse during the entire period of the trial. Periodic methods of abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) are not accepted methods of contraception.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
108

Key exclusion criteria
1. In the opinion of the investigator, the subject is unlikely to comply with the clinical trial protocol.
2. Has a functioning kidney transplant or is scheduled to receive a kidney transplant during the trial
3. Subjects who receive peritoneal dialysis
4. In the opinion of the investigator has pruritus attributed to a cause other than CKD or its complications, including but not limited to dermatological disease (e.g., atopic dermatitis, psoriasis) or liver disease (cholestatic pruritus)
5. Has localized itch restricted to the palms of the hands
6. Only has pruritus during haemodialysis sessions
7. Has concurrent skin conditions that may limit or prevent application of MC2-25 cream or MC2-25 vehicle or that may interfere with evaluation of the effects of MC2-25 cream or MC2-25 vehicle on the skin at the Screening or Baseline visits
8. Subjects who will have skin biopsies performed must not have any known hypersensitivity to the local anaesthetic or diagnosed bleeding disorders. Note: subjects with suspected uremic platelet dysfunction, without other bleeding diatheses, can be enrolled if the investigator agrees.
9. Known history of allergic reaction to any ingredients in MC2-25 cream or MC2-25 vehicle
10. Has a concurrent or recent medical condition that, in the opinion of the investigator, could pose undue risk to the subject, impede completion of the trial procedures, or would compromise the validity of the trial measurements, including, but not limited to:
10.1. known or suspected abuser of alcohol, drugs, or narcotic substances
10.2. severe physical, mental or cognitive disorder other than CKD
10.3. malignancy
10.4. failure to comply with local COVID-19 regulations on vaccination or testing (due to risk of transmitting the disease to other trial participants
or trial staff).
11. Has a known current generalized infection
12. Is pregnant, breast feeding, or planning a pregnancy
13. Start of a new or change to existing systemic treatment for CKD-aP, including but not limited to antihistamines, corticosteroids, opioids, GABA analogues, or kappa opioid receptor agonists within 21 days prior to the Baseline visit
14. Use of emollients on CKD-aP areas within 10 days prior to the Baseline visit
15. Use of any topical treatment on CKD-aP areas, including but not limited to antihistamines, or corticosteroids within 21 days prior to the Baseline visit
16. Use of any light therapy for CKD-aP, including but not limited to UV-B within 35 days prior to the Baseline visit
17. Use of non-biologic systemic immunosuppressive treatment, including but not limited to

corticosteroids, cyclosporin, and tacrolimus within 5 weeks prior to the Baseline visit
18. Use of biologic systemic treatment, including but not limited to etanercept, adalimumab, alefacept, infliximab, and ustekinumab within 3 months or 5 half-lives (whichever is longer) prior to the Baseline visit
19. Subjects who consent to having skin biopsies performed who are using anticoagulation treatment and are judged by the investigator to have an unacceptable risk of excessive bleeding in association with the skin biopsy
20. Subjects not currently on dialysis but who are likely to initiate routine dialysis during participation in the trial
21. Received another investigational drug within 30 days or 5 half-lives (whichever is longer) prior to screening or is planning to participate in another clinical trial while enrolled in this trial
22. Previously randomized in this trial

Date of first enrolment
19/04/2022

Date of final enrolment
09/11/2023

Locations

Countries of recruitment
Germany

Hungary

Poland

United Kingdom

Study participating centre
The Royal London Hospital
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Whitechapel Road
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Study participating centre
Leicester General Hospital
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LE5 4PW

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
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Mindelsohn Way
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Study participating centre
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IP33 2QZ

Study participating centre
University Hospitals Sussex NHS Foundation Trust
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BN11 2DH

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
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NE7 7DN

Study participating centre
Oxford University Hospitals
John Radcliffe Hospital
Headley Way
Headington
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United Kingdom
OX3 9DU

Study participating centre
York and Scarborough Teaching Hospitals NHS Foundation Trust
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YO31 8HE

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Hull University Teaching Hospitals NHS Trust
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HU3 2JZ

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Ipswich Hospital NHS Trust
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IP4 5PD

Study participating centre
South Tyneside and Sunderland NHS Foundation Trust
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Central Manchester University Hospitals NHS Foundation Trust
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Sponsor information

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
MC2 Therapeutics Ltd

Results and Publications

Publication and dissemination plan
Current publication and dissemination plan as of 20/01/2025:
No results publications are expected.

Current publication and dissemination plan as of 06/04/2023:
Trial results will be posted on ClinicalTrials.gov in accordance with applicable timelines for posting of results, i.e. no later than 1 year after the primary completion date corresponding to the above-stated overall trial end date

Previous publication and dissemination plan:
Other publication
Submission to regulatory authorities
Results of Study Data will be shared in the Clinical Study Report (CSR) after the completion of the trial.

Intention to publish date

Individual participant data (IPD) sharing plan
Due to uncertainty about the protection of participants' privacy, the sponsor does not plan to share the dataset(s).

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No