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Study to evaluate the safety, tolerability and efficacy of a medicinal product called KM-001 for the treatment of the skin diseases type I punctate palmoplantar keratoderma or pachyonychia congenita

Submission date	Recruitment status	[X] Prospectively registered
20/09/2022	No longer recruiting	[_] Protocol
Registration date	Overall study status	[_] Statistical analysis plan
02/11/2022	Completed	[_] Results
Last Edited	Condition category	[_] Individual participant data
11/03/2024	Skin and Connective Tissue Diseases	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
The planned trial intends to evaluate whether a newly developed drug is safe, tolerable, and efficacious for the treatment of type I punctate palmoplantar keratoderma (PPPK1) or pachyonychia congenita (PC). Both conditions are rare diseases for which standard therapies are available, which can alleviate the symptoms but cannot cure the disease. The sponsor of the trial - Kamari Pharma Ltd. - is developing a new therapy to cure these diseases. The test product is KM-001 cream 1%., which has not yet been approved for treatment. In this trial, it is tested for the duration of 84 days. All participants are treated with the same test product.

Who can participate?
Patients diagnosed for PPPK1 and PC may participate in the trial which is conducted at the clinical research facility of the Royal London Hospital, Whitechapel, London.

What does the study involve?
Overall, the trial will take up to 17 weeks with 8 on-site visits and 4 phone calls. Except for 2 visits the visits will take approximately 90 min with several examinations and assessments including but not limited to blood sampling, blood pressure and heart rate measurement, questionnaires for itch and pain assessment. At two visits, blood samples will be taken at different timepoints after application of the test drug to examine drug levels. These stays will take approximately 6.5 hours.
Certain medications are not permitted prior to the start and during the trial, i.e., participants may need to discontinue any medications they are taking. Concomitant medications during the trial are allowed after consultation with the investigator if they do not affect the trial results or participants' safety.

Based on the research results so far, the sponsor and investigator hope that the treatment with KM-001 cream reduces symptoms, e.g., pain, itch, and the disease severity in treated lesions. However, this is to be proven in the trial.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
The test product has been characterised in pre-clinical (animal) studies in which the test product did not result in irritation or test product-related side effects.
The test product is being investigated in 2 currently ongoing clinical (human) studies. Up to the date of this application, 6 participants were exposed to 0.3% or 1% KM-001 or matching vehicle for a period of 2 to 4 weeks and no side effects related to the test product have been observed so far.
Currently, there is no information concerning the effect of KM-001 cream on pregnancy nor about excretion of KM-001 into breast milk. Therefore, women must not participate in this clinical trial if they are pregnant, breast feeding or planning a pregnancy in the period from when screening starts until 4 weeks after the last dose of the test product. Exposure to the test product may involve unknown risks to a pregnant woman, an embryo, or a foetus (unborn baby). Women who can become pregnant must use an adequate and reliable type of contraception. Men having sexual relations with women who can become pregnant must agree to inform their partner to use an adequate and reliable type of contraception (details of contraception are given in the participant information).
In addition, the assessments carried out within the scope of this clinical trial may be associated with risks or lead to complaints. The non-invasive procedures (clinical assessments, measurement of vital signs and ECG) do not pose a risk or stress for the participants. Any experience of discomfort should be reported to the investigator or trial personnel.
Blood samples are taken using a single-use cannula (or permanent venous cannula) usually from a blood vessel in the arm. This may occasionally cause mild pain, inflammation, swelling, hardening of the blood vessel, formation of blood clots, and bleeding into the surrounding tissue ("bruising") at the puncture site. In rare cases, inflammation and occlusion of the blood vessels or possibly permanent damage to adjacent nerves may occur.
In sensitive individuals, blood collection may in some cases cause pallor, nausea, sweating, slow pulse and/or drop in blood pressure with dizziness or fainting.
In the scope of the scheduled blood examinations, it is possible that incidental findings will be made that could possibly have negative consequences for the participants (e.g., a need for treatment with risks of therapy and side effects or an effect on taking out insurance). In that case the investigator will explain the findings to the participant and encourage them to seek further advice, if appropriate.
Furthermore, it is possible in this trial that skin irritation may occur due to the application of the test product. This effect may resolve after the treatment has ended.
Allergic reactions or non-allergic intolerance reactions to the components of the test product, may occur. An allergic or intolerance reaction may manifest itself as itching, reddening of the skin, or with palpable bumps or fluid-filled blisters in the treated area. In exceptional cases skin reactions may occur over the entire body. These reactions subside after discontinuation of the treatment. Effects on the body are not expected due to the small total amount of the cream applied.
Due to the repeated applications in this trial, there is a possibility, that participants may develop an allergy to the components of the test product. The development of an allergy may be permanent, meaning that whenever the trial participant having developed an allergy to the components come into contact with the allergy-causing substance, allergic reactions may occur.
To minimise the risk and potential burden of the participants they are instructed as well as

encouraged to notify the trial site staff of any medical conditions, illnesses, or injuries that occur during the course of the clinical trial. If these are serious, notification should be performed immediately by telephone, if appropriate.
Participants are instructed to record any discomfort in a diary on a daily basis. These recordings will be checked by experienced site personnel at every visit at the clinical site. In addition, occurrence of discomfort will be asked about during phone calls. Thus, occurrence of discomfort will be assessed weekly during the treatment phase of the trial. Participants attend to the clinical trial site on a regular basis every 1-2 weeks, so that any untoward medical condition can be detected by experienced site personnel and appropriate measures to treat the condition can be started immediately.

Where is the study run from?
Kamari Pharma Ltd. (Israel)

When is the study starting and how long is it expected to run for?
January 2023 to November 2024

Who is funding the study?
Kamari Pharma Ltd. (Israel)

Who is the main contact?
Dr Ephraim Brener, ephraim@kamaripharma.com

Study website
https://kamaripharma.com/patients/

Contact information

Type(s)
Scientific

Contact name
Dr Ephraim Brener

Contact details
3 Pinhas Sapir St.
Nes Ziona Science Park
Nes Ziona
Israel
7403630
+972-54-3161579
ephraim@kamaripharma.com

Type(s)
Principal Investigator

Contact name
Prof Edel O'Toole

Contact details

Whitechapel Road
London
United Kingdom
E1 1FR
+44 20 78827161
e.otoole@nhs.net

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1006297

ClinicalTrials.gov number
NCT05956314

Secondary identifying numbers
KM001-B1B, IRAS 1006297, CPMS 53602

Study information

Scientific Title
Phase Ib, open label study to evaluate the safety, tolerability, and efficacy of a 1% topical formulation of KM-001 for the treatment of type I punctate palmoplantar keratoderma or pachyonychia congenita

Study objectives
Primary objective:
To assess the safety and tolerability of KM-001 1% topical formulation applied twice daily for 12 weeks for the treatment of patients with PPPK1 and PC

Secondary objective:
To assess the efficacy of KM-001 1% topical formulation applied twice daily for 12 weeks in clearing lesions resulted from PPPK1 and PC

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/11/2022, Health and Care Research Wales (Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 (0)2920 785738; Wales.REC1@wales.nh), ref: 22/WA/0272

Study design
Interventional non-randomized study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Home, Hospital, Other

Study type(s)
Treatment, Safety, Efficacy

Participant information sheet

Health condition(s) or problem(s) studied
Type I Punctate Palmoplantar Keratoderma (PPPK1) or Pachyonychia Congenita (PC)

Interventions
Single treatment arm in an open-label study: Twice daily topical applications of 2gr KM-001 1% cream on the plantar surfaces for 84 consecutive days with a 7 +/- 3 days screening and a 28 – 3 days follow-up period.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic

Phase
Phase I

Drug/device/biological/vaccine name(s)
KM-001 cream 1%

Primary outcome measure
1. Incidence rate of TEAEs and SAEs grouped by body system up to the patient´s end of trial (Day 112 [Visit 12]) or early termination [ET] visit]).
2. Mean changes from baseline (Day 1) in clinical laboratory parameters to Day 84 (end of treatment [EoT]) and from Day 84 (EoT) to Day 112.
3. Mean changes from baseline (Day 1) in vital signs (body temperature, pulse, blood pressure) to Day 84 (EoT) and from Day 84 (EoT) to Day 112.
4. Mean changes from baseline (Day 1) in ECG parameters to Day 84 (EoT) and from Day 84 (EoT) to Day 112.

Secondary outcome measures
1. Percent responders in CGI-S scale (0= “none” to 4= “very severe”) on Day 84 [Visit 10, EoT] compared to baseline (Day 1); a responder is defined to have an improvement of at least 2 points in disease severity on Day 84 [Visit 10, EoT] compared to baseline (Day 1).
2. Mean change from baseline (Day 1 [Visit 2] to Day 84 [Visit 10, EoT]) in PGI-S.
3. Mean change from baseline (Day 1 [Visit 2] to Day 84 [Visit 10, EoT]) in PGI-C.

Overall study start date
22/08/2022

Completion date
01/11/2024

Eligibility

Key inclusion criteria
1. Read, understood, and signed an informed consent form (ICF) before any investigational procedure(s) are performed.
2. Male and female and aged 18 – 65 years (inclusive) at the time of screening.
3. Clinical diagnosis of:
• Punctate palmoplantar keratoderma type I disease with confirmed heterozygous mutation in AAGAB gene.
OR
• PC with confirmed heterozygous mutation in either KRT16, KRT17, KRT6A, KRT6B or KRT6C mutations.
4. The target treatment region is 0.5% to 4% BSA including target lesion.
5. CGI-S score (as assessed by the CI at the screening visit) of ≥2.
6. Female patients of childbearing potential1 must use a highly effective birth control method2 (failure rate 1% per year when used consistently and correctly) (28) throughout the trial and for at least 4 weeks after last application of IMP.
In addition to the hormonal contraception, female patients must agree to use a supplemental barrier method during intercourse with a male partner (i.e., male condom) throughout the trial and for at least 4 weeks after last application of IMP.
Female patients must be having regular menstrual periods (interval of 21 to 35 days, duration of 2 to 7 days for several months) at the baseline visit (as reported by the patient); exception: patients using hormonal contraceptives that preclude regular menstrual periods, menopausal or hysterectomised patients.
A male patient with a pregnant or non-pregnant female partner of childbearing potential1 must use adequate contraceptive methods (adequate contraceptive measures as required by local regulation or practice; as a minimum, the male patient must agree to use condom during treatment and until the end of relevant systemic exposure in the male patient (7 days post-treatment).
7. Female patients must refrain from donating eggs throughout the trial and for 4 weeks after the last IMP administration.
Male patients must refrain from sperm donation throughout the trial and for 7 days after the last IMP administration.
8. Female patients of non-childbearing potential must meet 1 of the following criteria:
8.1. Absence of menstrual bleeding for 1 year prior to screening without any other medical reason.
8.2. Documented hysterectomy or bilateral oophorectomy at least 3 months before the trial.
9. Patient is willing and able to comply with all the time commitments and procedural requirements of the protocol.

Participant type(s)
Patient

Age group
Adult

Lower age limit

18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
16

Key exclusion criteria
1. History of drug or alcohol abuse in the past 2 years.
2. Regular alcohol consumption in males >21 units per week and females >14 units per week (1 unit = ½ pint beer, 25 mL of 40% spirit or a 125 mL glass of wine).
3. Positive hepatitis B surface antigen [HbsAg], hepatitis B core antibody [HbcAb], hepatitis C antibody, or human immunodeficiency virus (HIV) antibody serology results at the screening visit.
4. Known hypersensitivity or any suspected cross-allergy to the API and/or excipients.
5. Any medical or active psychological condition or any clinically relevant laboratory abnormalities, such as, but not limited, to elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST) (>3 × upper limit of normal [ULN]) in combination with elevated bilirubin (>2 × ULN), at the screening/baseline visit.
6. Planned or expected major surgical procedure during the clinical trial.
7. Patient is unwilling to refrain from using prohibited medications during the clinical trial.
8. Currently participating or participated in any other clinical trial of an IMP or device, within the past 4 months before the screening visit.
9. Cutaneous infection or another underlying condition of the skin which may impact the assessments or trial participation.
10. Cutaneous infection of the area to be treated with IMP within 2 weeks before the screening visit or any infection of treatment area requiring treatment with oral, parenteral antibiotics, antivirals, antiparasitics or antifungals or any topical within 2 weeks before the screening visit.
11. Pregnant or breastfeeding patient.
12. Failure to satisfy the investigator of fitness to participate for any other reason.
13. Having received any of the prohibited treatments within the specified timeframe before the baseline visit.

Date of first enrolment
17/01/2023

Date of final enrolment
30/10/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
The Royal London Hospital
Clinical Research Facility
Whitechapel
London
United Kingdom
E1 1BB

Sponsor information

Organisation
Kamari Pharma Ltd.

Sponsor details
3 Pinhas Sapir St.
Nes Ziona Science Park
Nes Ziona
Israel
7403630
+972-54-3161579
ephraim@kamaripharma.com

Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Kamari Pharma Ltd.

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Conference presentation
Publication on website
Submission to regulatory authorities

Intention to publish date
01/03/2025

Individual participant data (IPD) sharing plan
Plan Description: Since this is an early phase trial with only a small number of participants data will not automatically be shared, Anonymized data obtained through this study may be provided to qualified researchers with academic interest in keratoderma. Approval of the request and execution of all applicable agreements (i.e. a material/data transfer agreement) are prerequisites to the sharing of data with the requesting party.
Time Frame: Data requests can be submitted starting 9 months after article publication and the data will be made accessible for up to 24 months. Extensions will be considered on a case-by-case basis.
Access Criteria: Access to trial IPD can be requested by qualified researchers engaging in independent scientific research, and may be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). For more information or to submit a request, please contact Dr. Ephraim Brener ephraim@kamaripharma.com

IPD sharing plan summary
Available on request

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