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Active topical nail solution versus placebo for the treatment of pedal onychomycosis

Submission date
18/07/2024

Recruitment status
No longer recruiting

Registration date
27/07/2024

Overall study status
Completed

Last Edited
27/05/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
This study focuses on onychomycosis (toenail fungus) and aims to compare therapeutic outcomes between an active topical solution that is applied to the affected toenail and a placebo (inactive) solution. Toenail fungus, also known as onychomycosis or tinea unguium, is a very common pathology that affects many people the world over, and it can be difficult to eradicate.

Who can participate?
Males and non-pregnant females 18 years of age or older who have been diagnosed with pedal onychomycosis involving at least one toenail

What does the study involve?
Participants will be randomly allocated to either the active or placebo (inactive) topical toenail solution group. At the first (baseline) study visit, the participant will answer a questionnaire that provides information about the influence that toenail fungus has on the individual, the study doctor will take a photograph of the most representative (index) toenail and make a measurement of the thickness of the nail, a specimen of the nail will be obtained for mycological assessment (a PAS stain to identify the microscopic presence or absence of fungus in the toenail), and basic information about the participants medical history and physical status will be obtained. At follow-up visits 3, 7 and 9 months later, the medical history and physical status information, questionnaire, a new photograph and measurement of the index toenail, and a specimen for the PAS stain test will be obtained. The outcomes will be compared between the active and placebo (inactive) treatment groups, with the aim of determining whether or not the active treatment group eliminated the presence of fungus in the toenail and improved the participants' outcomes.

What are the possible benefits and risks of participating?
Participants may potentially benefit by getting the active topical agent toenail solution and if a participant is randomly assigned to the placebo topical nail solution, they will be eligible to receive the active agent after completion of the study follow-up period. Potential risks of participating in the study are unlikely and include the possibility of developing skin irritation or sensitivity to the applied solution. It is also possible that toenail fungus could worsen in a

participant assigned to the placebo group. However, as noted, such participants will be eligible to receive the active solution.

Where is the study run from?
The office of D. Scot Malay, DPM, MSCE, Philadelphia (USA)

When is the study starting and how long is it expected to run for?
April 2019 to October 2024

Who is funding the study?
Marlinz Pharma (USA)

Who is the main contact?
D. Scot Malay, malaydsm@gmail.com

Contact information

Type(s)
Public, Scientific

Contact name
Dr Donald Scot Malay, DPM, MSCE

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Type(s)
Principal investigator

Contact name
Dr Peter Bregman, DPM

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Additional identifiers

Protocol serial number
AFMC 16

Study information

Scientific Title
A randomized, controlled trial to determine the efficacy of active topical nail solution versus placebo nail solution for the treatment of pedal onychomycosis

Acronym
RCTATNP

Study objectives
Participants undergoing topical application of the active topical nail solution for the treatment of toenail onychomycosis will display a higher incidence of nail plate improvement, both clinical and mycological, in comparison to participants undergoing application of the topical placebo agent.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 14/05/2021, WCG IRB (1019 39th Avenue, Suite 120, Puyallup, Washington, 98374, United States of America; +1 (0)855 818 2289; jkelly@cgirb.com), ref: 20211891

Primary study design
Interventional

Study design
Multicenter interventional double-blind randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Onychomycosis (tinea unguium) localized to toenails

Interventions
The main clinical disease under evaluation is toe onychomycosis. Participants will be males and non-pregnant females 18 years of age or older who have been diagnosed with distal subungual onychomycosis (DSO) involving at least one toenail. Diagnosis of this condition is to be made on the basis of history, physical examination, and a mycological inspection that includes a tissue examination for fungal hyphae (PAS stain). Evidence of fungal hyphae will be considered a positive confirmation of the diagnosis of toenail onychomycosis. All participants will be randomized to either the active topical nail solution group, antifungal solution treatment, or to the placebo nail solution group.

Randomization will be carried out by means of electronic random number generation under the authority of a co-investigator (HRK), who will prepare sealed, sequentially numbered envelopes for each study site (A to J), and mail the envelopes to the designated coordinator for each study site. In each sealed envelope will be a tube containing a topical solution, either the active topical nail solution or the placebo nail solution, consistent with the random number list, which will determine whether or not the placebo or active topical nail solution is contained in the tube. Each tube will be numbered in sequential numeric order from 1 to n, and recorded in the investigator's master list, which will serve to record the random allocation code, detailing whether or not the placebo nail solution or the active topical nail solution was dispensed in the designated tube dispensed to each volunteer participant enrolled. Each tube will be labelled with the alphanumeric designation that denotes the distinct study site (A to J), and the distinct participant (1, 2, 3,…n). The labeled tubes will be mailed to the study sites in blocks of 10, and replenished based on the prevalence of enrolment at each site. At each study site, the investigator will open, in sequential numeric order, a sealed envelope and dispense the labeled tube to the eligible participant in consecutive order. Neither the study doctors responsible for enrolling and assessing the participants, nor the participants themselves, will know which of the treatment groups the participant will be in. The nail solution with its labelled envelope will be stored in a secure location at each site investigator's office.

The topical antifungal medication under investigation is Tolcylen™. It will be provided by Marlinz Pharma, Houston, TX, the study funding Sponsor. The topical therapy will be applied in accordance with the existing FDA-approved method for the use of this cosmetic agent. Administration of the interventions, active and placebo, will continue for no longer than nine (9) months. Administration of the topical agent may stop sooner if clinical and mycological evidence of cures are identified prior to nine (9) months. Participants in the control group will apply a placebo topical solution to the involved toe nail/s. Preparation of the placebo solution, dimethicone 5%, was undertaken with the aim of making it as close as possible to the active topical nail solution in terms of color and texture, and other physical characteristics. The placebo nail solution, like the active topical nail solution, meets the FDA's safe ingredient criteria for an over-the-counter topical agent. The placebo, like the active topical nail solution, will be supplied in three (3) 7.5 ml tubes with a controlled-release applicator mechanism that allows a thin coat of the solution to be applied at a time, and the instructions for application specify that only a thin coat of solution to be applied daily to under the leading edge, borders of the toenail and the entire surface of the toenail.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Tolcylen™

Primary outcome(s)
Mycological presence or absence of fungal hyphae detected using Periodic Acid-Schiff (PAS) stain of toenail fragments at baseline, 3, 7 and 9 months

Key secondary outcome(s)
1. Quality of life measured using ONYCOE-t™ quality of life outcome score at baseline, 3, 7 and 9 months

2. Clinical appearance of an involved toenail assessed using the Visible Nail Plate Involvement Score at baseline, 3, 7 and 9 months

Completion date
01/10/2024

Eligibility

Key inclusion criteria
1. Male or female participants aged 18 years or older
2. If female is of childbearing potential, she must not be pregnant at the time of enrollment and she must be using an accepted form of birth control during the study treatment period (acceptable forms include: post-menopausal, surgical sterility, complete abstinence, sterilized sexual partner, tubal occlusion, copper-T intrauterine device, levonorgestrel-releasing intrauterine device, medroxyprogesterone injections, etonogestrel implants, combined pills, norelgestromin/ethinyl estradiol transdermal system, intravaginal device, or Cerazette pill; and for males the use of a condom with spermicide or surgical sterility)
3. Participant has a diagnosis of onychomycosis diagnosed by means of history, physical examination, and positive (evidence of fungal hyphae) mycological tissue examination by periodic acid-Schiff (PAS) staining
4. At least one toenail with distal subungual involvement, localized to any toe, with at least 10% involvement and including up to 100% involvement of the visible nail plate, any nail plate thickness, with the index nail being the most involved per inspection by the on-site investigator and agreed upon by the designated co-investigator study doctor (Hye Kim, DPM), who will inspect specific clinical photographs of the involved nail/s (the photographs will be obtained at each study site using a specified method, as demonstrated to site investigators, so that the clinical features are appropriately demonstrated)
5. Participant has an intact protective cutaneous sensation as measured with the Ipswich test for loss of protective sensation (10-gram monofilament)
6. Participant has an intact cutaneous barrier, with or without the presence of hyperkeratotic lesions, with or without concomitant tinea pedis or interdigital maceration, or with or without a history of previous skin ulceration, but without active or current pedal ulceration
7. Participant must be a satisfactory candidate for the proposed topical antifungal or placebo intervention
8. Participant must display the ability to understand and give informed consent to participation, on a voluntary basis, in the research study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Key exclusion criteria
1. Presence of dermatophytoma, defined as thick masses of fungal hyphae and necrotic keratin between the nail plate and nail bed
2. Use of any systemic antifungal therapeutic agents within 7 months before the baseline visit, or topical antifungal agent on the feet within 1 month preceding the baseline measurement visit
3. Candidate with moccasin tinea pedis involving greater than 50% of either plantar surface
4. Candidate requires the use of narcotic analgesic or non-steroidal anti-inflammatory drug/s for 48 hours prior to baseline visit or at any follow-up clinical evaluations
5. Candidate has an active drug/alcohol dependence or abuse history
6. Candidate has a loss of protective pedal sensation or open cutaneous compromise involving the ipsilateral foot
7. Candidate has trauma to the nail that resulting in permanent nail plate discoloration or shape
8. Candidate displays radiographic evidence of abnormal lytic or proliferative bone lesion in the toe/s of interest, including recent or healing of an acute fracture, if clinical inspection indicates the potential presence of subungual exostosis (radiographs will be obtained and paid for in the course of usual and customary care, outside of participation in this study)
9. Candidate has had previous nail matrix ablative surgery, either chemical or cold steel, on any of the involved digits
10. Candidate presents systemic or local contraindications to the proposed application of the topical antifungal nail solution or the placebo agent, such as an uncontrolled cardiac, neurological, hepatic, renal, metabolic, or hematological disease or impairment that has been identified
11. Candidate suffers from malignant, or bacterial or viral infectious cause/s of nail plate dystrophy
12. Candidate shows signs of substantial peripheral circulatory insufficiency
13. Candidate is currently participating in another surgical, device, or drug study or has participated in any research study involving an investigational device or drug, or surgical procedure, within the preceding 30 days
14. Candidate is allergic to any of the study products
15. Candidate is unwilling or unable to comply with the study procedures
16. Candidate is affiliated with the investigator or persons working at a study site, or patient who is an employee of the sponsor’s company
17. Candidate is institutionalized because of legal or regulatory order
18. Candidate is unable to provide informed consent to voluntarily participate in clinical research.

Date of first enrolment
25/08/2021

Date of final enrolment
31/07/2024

Locations

Countries of recruitment
United States of America

Study participating centre
Ankle and Foot Associates (Greg Kramer, DPM)
204 Westside Drive
Douglasville, Georgia
United States of America
31533

Study participating centre
St Cloud Foot and Ankle (Ashton Nelsen, DPM)
106 Doctors Park
St Cloud, Minnesota
United States of America
56303

Study participating centre
National Foot and Ankle (Franklin Polun, DPM)
12400 Park Potomac Avenue, Suite R2
Potomac, Maryland
United States of America
20854

Study participating centre
Family Foot Care (Nancy Quimby, DPM)
6 Maple Lane South
Valatie, New York
United States of America
12184

Study participating centre
Foot and Ankle Specialists of Nevada (Peter Bregman, DPM)
7150 West Sunset Road, Suite 110
Las Vegas, Nevada
United States of America
89135

Study participating centre
A Step Ahead Foot and Ankle (Kate Johnson, DPM)
2001 South Shields, Bldng. F

Fort Collins, Colorado
United States of America
80526

Study participating centre
Augusta Podiatry (Mickey Stapp, DPM)
1416 Wainbrook Drive
Augusta, Georgia
United States of America
30909

Study participating centre
Juan Gonzalez, DPM
5460 Paredes Line Road, Ste. 209
Brownsville, Texas
United States of America
78526

Sponsor information

Organisation
Marlinz Pharma

Funder(s)

Funder type
Industry

Funder Name
Marlinz Pharma

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Stored in non-publicly available repository, Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		25/05/2025	27/05/2025	Yes	No
Dataset	Excel file		22/01/2025	No	No
Other files	Case report forms, consent forms, other files		12/08/2024	No	No
Other files	OnyCOE form		22/01/2025	No	No
Other files	VNPIS form		22/01/2025	No	No
Protocol file		01/07/2019	12/08/2024	No	No
Statistical Analysis Plan			12/08/2024	No	No