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A randomized trial of disulfiram and zinc administered together to treat diarrhea caused by Entamoeba histolytica

Submission date
22/09/2025

Recruitment status
Not yet recruiting

Registration date
24/09/2025

Overall study status
Ongoing

Last Edited
24/09/2025

Condition category
Infections and Infestations

[X] 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
Amebiasis, caused by Entamoeba histolytica, is a significant global health concern and one of the leading causes of severe diarrhea and death from parasitic infections worldwide. Despite its prevalence, treatment options are limited to a single class of drugs, posing a public health risk in the event of drug resistance or intolerable side effects. This study will evaluate the safety and effectiveness of oral disulfiram combined with a nutritional zinc supplement as a novel treatment for symptomatic E. histolytica diarrhea.

Who can participate?
Ambulatory patients aged 18 years and older with symptomatic diarrhea due to E. histolytica.

What does the study involve?
Participants who meet all eligibility criteria and consent to participation will be randomly allocated to receive either low dose disulfiram (250 mg) daily plus 50 mg zinc gluconate thrice daily x 10 days; high dose disulfiram (500 mg) daily plus 50 mg zinc gluconate thrice daily x 10 days or the active control metronidazole (500 mg) thrice daily x 10 days). Participants will be followed for safety and effectiveness outcomes.

What are the possible benefits and risks of participating?
Participants will benefit from close monitoring throughout the study. Similar patients with amebic colitis may benefit in the future from alternative therapies if resistance to metronidazole develops or there is an intolerance to metronidazole.
Participants may experience side effects from the study treatment, including nausea, liver toxicity, or allergic reactions from the study drug. Severe reactions can occur if alcohol is consumed during treatment. Blood draws may cause temporary pain, bruising, or lightheadedness. There is also a small risk of a breach of confidentiality, though strict data protection measures will be in place to minimize this.

Where is the study run from?
The study is an international study that will be conducted in Manila, Philippines.

When is the study starting and how long is it expected to run for?
August 2025 to August 2029

Who is funding the study?
National Institutes of Health (USA), grant R34AI165304

Who is the main contact?
Debbie-Ann Shirley, dshirley1@ufl.edu

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRB202501125

Study information

Scientific Title
Disulfiram for Entamoeba histolytica Enteric Diarrhea (DEED) trial

Acronym
DEED

Study objectives
Amebiasis, caused by Entamoeba histolytica, is a leading cause of severe diarrhea and death from parasitic infection worldwide. Globalization, immigration, travel to and from endemic areas, and sexual practices are contributing to re-emergence in developed countries. There is

only one drug class available for treatment, which is a major public health concern as there is no option if resistance or intolerable side effects were to develop. Treatment options for parasitic infections remain limited, hence identification of new anti-parasitic drugs is priority.

We found that zinc ditiocarb, a metabolite of the inexpensive, globally available, oral FDA-approved drug disulfiram, was 1000-fold more potent than metronidazole and was an effective anti- amebic agent in pre-clinical animal studies of amebic colitis. Zinc ditiocarb is safely given as disulfiram plus nutritional zinc supplement. We propose to test the hypothesis that oral disulfiram plus zinc supplement effectively treats Entamoeba histolytica diarrhea. If our hypothesis holds true, the proposed trial could result in an innovative repurposed indication for the first new drug treatment for amebiasis in over 60 years.

The primary safety objective is:
1.1. To evaluate the safety and clinical acceptability of a 10-day course of oral disulfiram once daily plus zinc three times daily in participants with diarrhea due to E. histolytica.

The primary efficacy objective is:
1.2. To examine the efficacy of a 10-day course of disulfiram once daily plus zinc three times daily in treating participants with diarrhea due to E. histolytica. The endpoint will be proportion with resolution of diarrhea (no loose stools for 24 hours) after a 10-day course.

The secondary efficacy objective is:
2. To determine the efficacy of disulfiram in eradicating infection in participants with diarrhea due to E. histolytica.

Ethics approval required
Ethics approval required

Ethics approval(s)
notYetSubmitted, University of Florida Institutional Review Board (Address not provided, Gainesville, 32610, United States of America; Telephone number not provided; Email not provided), ref: Reference number not provided

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Symptomatic diarrhea due to E. histolytica

Interventions
Participants who meet all eligibility criteria and consent to participation will be randomized to receive either low dose disulfiram (250 mg) daily plus 50 mg zinc gluconate thrice daily x 10 days; high dose disulfiram (500 mg) daily plus 50 mg zinc gluconate thrice daily x 10 days or the active control metronidazole (500 mg) thrice daily x 10 days). Participants will be followed for safety and efficacy outcomes.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Disulfiram plus 50 mg zinc gluconate

Primary outcome(s)
Primary safety endpoint:
The proportion of participants experiencing a grade 3 or greater adverse event during a 10-day course of study treatment

Primary efficacy endpoint:
The proportion of participants with resolution of diarrhea (no loose stools for 24 hours i.e. Bristol type 6-7) at end of therapy after a 10-day course of study treatment course

Key secondary outcome(s))
Secondary efficacy endpoint:
The proportion of participants with negative stool microscopy at end of therapy after a 10-day course of study treatment course

Completion date
09/08/2029

Eligibility

Key inclusion criteria
1. Age 18–65 years inclusive at enrollment in good health, with diarrhea and microbiologically confirmed E. histolytica infection
2. Willing/ able to give informed consent to be enrolled in and comply with trial procedures follow-up
3. Willing to abstain from alcohol ingestion while on therapy through 28 days
4. For females of reproductive potential, agreement to use highly effective contraception through 28 days

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit

65 years

Sex
All

Key exclusion criteria
1. Hypotension or shock
2. Intestinal obstruction, including megacolon and moderate to serve ileus
3. Acute abdomen
4. Admitted to hospital or intensive care unit atenrolmentt
5. Inability to tolerate oral medication
6. Other suspected etiology for diarrhea e.g. other enteric pathogen, other intestinal disease
7. Pregnant and/ or breastfeeding women
8. Consumption of alcohol within 48 hours of enrollment
9. History of alcohol or substance use disorder
10. History of psychosis
11. Severe myocardial dysfunction
12. History of chronic liver disease
13. History of end stage renal disease
14. Prolonged prothrombin time
15. Concomitant treatment with theophylline or warfarin
16. Concomitant use of phenytoin
17. Concomitant use of isoniazid
18. Concomitant use of bictegravir, cabotegravir, dolutegravir, or raltegravir
19. Concomitant treatment with prednisone 40 mg or more daily [or equivalent corticosteroid]
20. Exposure to ethylene dibromide
21. History of known sensitivity or allergic reaction to disulfiram
22. History of known sensitivity or allergic reaction to metronidazole or nitroimidazole derivates
23. History of rubber contact dermatitis
24. Concurrent participation in another investigational trial within the previous 30 days
25. Has any condition that would, in the opinion of the site investigator, place the participant at an unacceptable risk of injury or render the participant unable to meet the requirements of the protocol

Date of first enrolment
09/08/2026

Date of final enrolment
09/08/2028

Locations

Countries of recruitment
Philippines

Study participating centre
Philippine General Hospital
Taft Avenue, Ermita
Manila

Philippines
Metro Manila 1000

Sponsor information

Organisation
University of Florida

Funder(s)

Funder type
Government

Funder Name
National Institutes of Health

Alternative Name(s)
US National Institutes of Health, Institutos Nacionales de la Salud, NIH, USNIH

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United States of America

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
Data sharing statement to be made available at a later date