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Death to Onchocerciasis and Lymphatic Filariasis: Comparison of Ivermectin alone with Albendazole (ALB) plus Ivermectin (IVM) in their efficacy against Onchocerciasis

Submission date
09/10/2012

Recruitment status
No longer recruiting

Registration date
18/10/2012

Overall study status
Completed

Last Edited
17/12/2020

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Onchocerciasis is an infection that is caused by the worm Onchocerca volvulus. This worm is transmitted by blackflies. Adult worms live in nodules under the skin and produce worm larvae (microfilariae).
This study is planned to learn whether taking the drugs albendazole (ALB) and ivermectin (IVM) will increase the effectiveness of treatment against onchocerciasis infection. IVM is the drug that one normally takes in the scope of the annual mass drug administration. The addition of ALB to IVM may shorten the period for which people would be treated for onchocerciasis. Administering the drugs twice per year may also increase the effectiveness of treatment. The study is performed with the aim to try to sterilize or kill adult worms.

Who can participate?
About two hundred and seventy-two (272) adult men and women in the Central and Ashanti Region of Ghana will take part in this study for a total period of 3 years. You are eligible if you are 18-60 years old, have at least one nodule and any microfilariae in the skin. To detect the microfilariae we will take two pieces of skin (2 skin snips) from your hip or buttock area (right or left iliac crest).

What does the study involve?
If you are eligible to be in this study you will be assigned to one of four treatment groups. Each of the four groups will have about 68 people in it. Your group may receive more pills than the other groups. This study is to find out if these additional pills will help get rid of the worms in your body. Even if you get the fewer pills we know that these pills help kill the worms in your body. You may also be in a group that does not receive drug pills at 6 or 18 months. Instead we will give you vitamin pills. These vitamin pills are good for you and may strengthen your body. They are unlikely, however, to have any effect on killing the worms in your body. Group 1 will receive the standard treatment for onchocerciasis [IVM 200 µg/kg body weight given at 0, 12 and 24 months]. You will receive a vitamin pill at 6 and 18 months.

Group 2 will receive IVM 200 µg/kg kg body weight plus ALB 800 mg (regardless of weight) given at 0, 6, 12, 18, and 24 months. Group 3 will receive IVM 200 µg/kg kg body weight plus ALB 800 mg (regardless of weight) given at 0, 12, 24 months plus vitamin pills at 6 and 18 months. Group 4 will receive IVM 200 µg/kg kg body weight given 0, 6, 12, 18, and 24 months. After 3 years any accessible nodules you may have will be removed (nodulectomy). The operation will be performed by a surgeon in the theatre of a nearby hospital under local anaesthesia. After the operation you will stay overnight in the hospital. When back in your village, a doctor will monitor your wound every other day to ensure optimal care is given to the wound until it is healed.

What are the possible benefits and risks of participating?
There may be a direct benefit to you to have nodules removed. You will also receive treatment that may speed up the sterility or death of worms. The addition of the drug ALB will help eliminate intestinal worms. If the addition of the drugs ALB to IVM proves successful for onchocerciasis, this double therapy may be widely adopted in areas where the infection occurs. This study may also help the government to develop and carry out policies and programs to better treat onchocerciasis.
Risk of venipuncture: The risk of drawing blood from your arm is small although some individuals become lightheaded after giving blood. You may experience momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or lightheadedness are also possible after drawing blood from your hand or arm, but these events are unlikely.
Risk by taking the study drugs: The following are some possible side effects of the two drugs you will be given, although these side effects are small with a single dose of the drug:
(ALB): You might experience headache, nausea, stomach pain and vomiting that are usually associated with heavy intestinal helminth (worms in the belly) infections. There is a very small chance that you might develop rash, hives, itching, difficulty breathing, tightness in the chest, swelling of the mouth, face, lips, or tongue, dark urine.
(IVM): You might experience diarrhea, dizziness and nausea. There is a very small chance that you might develop rash; hives; itching; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue; eye pain, swelling, or redness; fainting; and fast heartbeat.
Risk of skin biopsy: There might be some bleeding for only a short time. The small wounds should heal and leave you no scars.
Risk of nodulectomy: The operation to remove the nodules can give you some discomfort. This discomfort can be caused by the needle used for anesthesia and the wound made at the site of the operation. You will be injected with a drug to produce local anesthesia that can, in rare cases, cause you to have slight dizziness or circulatory problems. In some cases bleeding or wound infection with fever can happen after surgery.
If you experience any of these events listed under risks of the study, you will be watched and, if needed, treated for them until resolution by the medical doctor and the research team.

Where is the study run from?
This is a research study conducted jointly by the Kwame Nkrumah University of Science and Technology (KNUST), Case Western Reserve University in Cleveland, Ohio (USA), and the University of Bonn (Germany).

When is the study starting and how long is it expected to run for?
The study will start in October 2012 and the recruitment period will presumably take until end of November 2012.

Who is funding the study?
The study is funded by Case Western Reserve University, USA

Who is the main contact?
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Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
11-11-36

Study information

Scientific Title
Comparison of Ivermectin alone with Albendazole (ALB) plus Ivermectin (IVM) in their efficacy against Onchocerciasis: a randomised open label trial

Acronym
DOLF Oncho

Study objectives
This study will determine if repeated doses of ivermectin (IVM) combined with albendazole (ALB) given annually or semiannually is better than IVM alone given annually or semiannually for treatment of patients with filarial infections (Onchocerca volvulus) as measured by higher sterility of adult female worms and reduction in skin microfilariae (Mf). Such a drug regimen could reduce the frequency of Mass Drug Administration (MDA) rounds necessary to control onchocerciasis in endemic areas.

Ethics approval required

Old ethics approval format

Ethics approval(s)
1. Committee on Human Research Publication and Ethics, Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana: Protocol approved on 02/03/2012, 1st protocol amendment approved on 28/06/2012, 2nd protocol amendment approved on 18/04/2013
2. Institutional Review Board For Human Investigation, University Hospitals, Case Medical Center, Cleveland, Ohio, USA: Protocol approved on 20/01/2012, 1st protocol amendment approved on 07/08/2012, 2nd protocol amendment approved on 16/04/2013
3. Ethical Committee, University Hospital Bonn, Bonn, Germany: Protocol approved on 26/03 /2012, 1st protocol amendment approved on 05/09/2012, 2nd protocol amendment approved on 23/04/2013

Study design
Randomised open label trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Onchocerciasis (Onchocerca volvulus)

Interventions
Treatment regimen 1: The comparator (standard treatment): Ivermectin 200 µg/kg body weight given at 0, 12 and 24 months (annually) plus vitamin pills at 6 and 18 months. (n = 68)

Treatment regimen 2: Ivermectin 200 µg/kg body weight plus Albendazole 800 mg (regardless of weight) given at 0, 6, 12, 18, 24 months (bi-annually). (n = 68)

Treatment regimen 3: Ivermectin 200 µg/kg body weight plus Albendazole 800 mg (regardless of weight) given at 0, 12, 24 months (annually) plus vitamin pills at 6 and 18 months. (n = 68)

Treatment regimen 4: Ivermectin 200 µg/kg body weight given 0, 6, 12, 18, and 24 months (bi-annually). (n = 68)

Volunteers for this study are recruited based on the inclusion and exclusion criteria and treated directly in their villages. The study drugs will be distributed personally by the research staff.

To assess the skin microfilarial load, skin biopsies are taken pre-treatment, as well as at 6, 18 and 36 months after treatment.

Nodulectomies to assess worm vitality and embryogenesis will be performed 36 months after the start of drug administration. Onchocercomata will be removed under local anaesthesia in the hospital. Patients will be kept in hospital for the day of operation or one day longer (depending on the severity of operation) for observation before being discharged. Wound dressing will continue in the villages until all the wounds are healed.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Albendazole, Ivermectin

Primary outcome measure
Percent fertile female adult worms in accessible nodules at 36 months following initiation of therapy

Secondary outcome measures
1. Percent reduction in skin Mf/mg at 0, 6, 18, and 36 months after initiation of therapy.
2. Percent reduction in total number of live versus dead female worms in nodules at 36 months following initiation of therapy.
3. The number of nodules with intact microfilariae (Mf) at 36 months following initiation of therapy.
4. Assessment of the different treatment regimens on Soil Transmitted Helminth (STH) infections based on presence and intensity of ova in stools.

Overall study start date
10/10/2012

Completion date
30/04/2016

Eligibility

Key inclusion criteria
Current inclusion criteria as of 11/11/2013, as stated in the 2nd protocol amendment:
1. Men and women 18-60 years residing in Ashanti and Central Regions of Ghana
2. ≥1 accessible nodules
3. Any Mf based on skin snips

Previous inclusion criteria:
1. Men and women 18-60 years residing in Central Region of Ghana
2. ≥1 accessible nodules
3. ≥5 Mf/mg based on skin snips

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
Both

Target number of participants
272

Total final enrolment
272

Key exclusion criteria
Current exclusion criteria as of 11/11/2013, as stated in the 2nd protocol amendment:
1. Last IVM treatment <7 months
2. Pregnant (do pregnancy test) or breastfeeding
3. Permanent disability, serious medical illnesses such as a stroke, advanced heart disease, uncontrolled diabetes, emphysema, etc. that prevents or impedes study participation and/or comprehension
4. Weight of <40kg suggesting malnourishment
5. AST/ALT, gamma-glutamyltranspeptidase (γ-GT) > 1.5 upper limit of normal
6. Significant glycosuria or proteinuria (2+ or 3+ protein or glucose)

Previous exclusion criteria:
1. Last IVM treatment <1 year
2. Pregnant (do pregnancy test) or breastfeeding
3. Permanent disability, serious medical illnesses such as a stroke, advanced heart disease, uncontrolled diabetes, emphysema, etc. that prevents or impedes study participation and/or comprehension
4. Weight of <40kg suggesting malnourishment
5. AST/ALT, gamma-glutamyltranspeptidase (γ-GT) > 1.5 upper limit of normal
6. Significant glycosuria or proteinuria (2+ or 3+ protein or glucose)

Date of first enrolment
10/10/2012

Date of final enrolment
30/11/2012

Locations

Countries of recruitment

Germany

Ghana

Study participating centre
University Hospital Bonn
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Sponsor type
University/education

ROR
https://ror.org/051fd9666

Funder(s)

Funder type
University/education

Funder Name
Case Western Reserve University (USA) (grant number: WU-10-205)

Alternative Name(s)
Western Reserve College, Western Reserve University, Case School of Applied Science, Case Institute of Technology, CWRU

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United States of America

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
Results article	results	14/08/2020	17/12/2020	Yes	No