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Expanded access protocol for the use of tecovirimat for the treatment of monkeypox infection

Submission date
04/06/2021

Recruitment status
No longer recruiting

Registration date
09/08/2021

Overall study status
Completed

Last Edited
10/05/2024

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Mpox (monkeypox) is a serious disease that causes fever and chills, fatigue, aching of the head, muscles, and back. It also causes lymph nodes to swell, and the skin to be scattered with lesions or scabs. This may last for 2–4 weeks. In some cases, mpox can cause long-lasting effects, even after recovery, and in a minority of cases may even be fatal. At the moment there is no treatment available that can cure mpox, but the drug tecovirimat might help patients recover more quickly and get better sooner. As there are no alternative treatments, the main aim of this study is to provide patients with access to this drug, but the researchers also hope to collect some additional information about how it works that will help them understand whether tecovirimat could help more patients in the future.

Who can participate?
Patients admitted to Hôpital de District de Mbaïki with laboratory-confirmed mpox infection

What does the study involve?
If patients agree to participate, on admission they will be asked about their health and other medicines that they might be taking. All patients will be offered an HIV test and all females of child-bearing potential will be offered a pregnancy test. These tests are voluntary.
Patients will stay at the hospital and take tecovirimat twice a day for 14 days. Tecovirimat is a tablet that must be taken with food. Patients will then have follow-up visits with a doctor 15 days and 28 days after they first started taking tecovirimat.
Five blood samples will be taken in total. One sample will be taken before patients start taking tecovirimat and further samples will be taken on days 4, 8, 14 and 28. These blood samples will be used to look at how the body reacts to tecovirimat.
The researchers will also collect some information about patients while they are taking tecovirimat to help them to decide whether they can use this medicine for other people in the future. This information will be collected on admission, throughout treatment and at the two follow-up visits patients will attend after they have finished taking tecovirimat. The researchers would also like to take some photos of the rashes or blisters that have been caused by mpox.

What are the possible benefits and risks of participating?
It is hoped that tecovirimat will help patients get better, but the researchers don't know that it definitely will. It is hoped that the information collected will help other people in the future. However, because tecovirimat is not normally used to treat mpox, there may be risks that are not known at this time. The side effects the researchers know about are headache, stomach ache, nausea and/or vomiting. There may be other side effects that are not known yet and the researchers don't know what effect tecovirimat has in pregnancy. Patients may also feel a small scratch when blood samples are taken.

Where is the study run from?
1. Institut Pasteur de Bangui (Central African Republic)
2. Oxford University (UK)

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

Who is funding the study?
1. African Coalition for Epidemic Research Response
2. UK Foreign, Commonwealth and Development Office and Wellcome Trust (UK) (ref: 215091/Z/18/Z)
3. Bill & Melinda Gates Foundation (USA) (ref: OPP1209135)

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Additional identifiers

Protocol serial number
1-20

Study information

Scientific Title
Expanded access protocol for the use of tecovirimat for the treatment of monkeypox infection

Study objectives
This is an Expanded Access Protocol that aims to provide access to tecovirimat (TPOXX) to patients with monkeypox. There is currently no satisfactory alternative treatment for patients with monkeypox and enrolment to clinical trials is not possible at this time. As well as providing access to TPOXX, the protocol also aims to generate information about its safety and effectiveness that could help inform future use and clinical development.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 02/12/2019, Oxford Tropical Research Ethics Committee (OxTREC) (, , , United Kingdom; ;), ref: (University of Oxford Research Services, University Offices, Wellington Square, Oxford, OX1 2JD, United Kingdom; +44 (0)1865 (2)82585; oxtrec@admin.ox.ac.uk), ref: 1-20

2. Approved 20/05/2020, Université de Bangui Faculté des Sciences de la Santé Comité d'Ethique et Scientifique [University of Bangui Faculty of Health Sciences Ethics and Scientific Committee] (Université de Bangui, Bangui, None available, Central African Republic; None available; not@available.com), ref: None available

Primary study design
Interventional

Study design
Single-centre expanded access protocol

Study type(s)

Treatment

Health condition(s) or problem(s) studied
Mpox (monkeypox)

Interventions
All patients who receive a laboratory-confirmed diagnosis of monkeypox will be eligible to access treatment with tecovirimat.

If patients agree to participate, on admission they will be asked about their health and other medicines that they might be taking. All patients will be offered an HIV test and all females of child-bearing potential will be offered a pregnancy test. These tests are voluntary.

Patients will stay at the hospital and take tecovirimat twice a day for 14 days. Tecovirimat is a tablet that must be taken with food.

Tecovirimat dosage is based on age and weight:
Adults: 600 mg (three 200 mg capsules) twice daily for 14 days
Paediatric patients weighing 13 kg or more:
13 kg to less than 25 kg: 200 mg (one capsule) of tecovirimat twice daily for 14 days
25 kg to less than 40 kg: 400 mg (two capsules) of tecovirimat twice daily for 14 days
40 kg or more: 600 mg (three capsules) of tecovirimat twice daily for 14 days

Patients will then have follow-up visits with a doctor 15 days and 28 days after they first started taking TPOXX. Five blood samples will be taken in total. One sample will be taken before patients start taking tecovirimat and further samples will be taken on days 4, 8, 14 and 28. These blood samples will be used to look at how the body reacts to tecovirimat.

The researchers will also collect some information about patients while they are taking tecovirimat to help them to decide whether they can use this medicine for other people in the future. This information will be collected on admission, throughout treatment and at the two follow-up visits patients will attend after they have finished taking tecovirimat. The researchers would also like to take some photos of the rashes or blisters that have been caused by monkeypox.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Tecovirimat

Primary outcome(s)
Expanded Access Programs (EAPs) do not use or assess outcome measures in their analysis. This is because EAPs are primarily conducted to provide patients with access to drugs that would not normally be available and this is done outside of a clinical trial setting. EAPs cannot measure outcomes for a variety of reasons: a) only limited research data on safety and efficacy is collected, b) sample sizes are too small and there’s too much heterogeneity for any inferences to be made, c) unlike a clinical trial, the data collected as part of an EAP wouldn’t normally support

the regulatory process. So while research data is collected as part of an EAP, outcome measures aren't evaluated as they would not yield any meaningful analyses. The data collected to monitor efficacy has been described under 'Secondary outcome measures'.

Key secondary outcome(s)
1. Total number, type and location of lesions measured clinically/visually at days 1 – 14 and 28
2. Temperature measured using a thermometer at days 1 to 14
3. Degree of incapacity measured assessed clinically at days 1 to 15 and 28
4. Complications: (1) gastrointestinal (diarrhoea or vomiting), (2) upper respiratory (includes runny nose and sore throat), (3) lower respiratory (includes wheeze, cough, and respiratory distress), (4) systemic (includes lymphadenopathy, muscle ache, back pain, headache); (5) ocular (keratitis, corneal ulceration); (6) neurological (confusion, seizures) assessed clinically at days 1 – 15 and 28
5. Whether the subject has survived with or without sequelae or succumbed to disease, assessed clinically at day 15 (after completion of treatment) and day 28
6. Viral load and serology: total exposure to the virus in the bloodstream over the course of treatment (area under the curve), maximum viral load, time to clearance of viral DNA from the blood, and antibody responses, measured using blood (5 ml) collected prior to the first dose and then on days 4, 8, 14 and 28

Completion date
18/01/2024

Eligibility

Key inclusion criteria
1. Male and female patients weighing ≥13 kg
2. Present with monkeypox disease as determined by clinical signs and symptoms that include a characteristic rash preceded by fever. Blood and lesion swab will be taken for confirmation by qPCR positivity for monkeypox virus DNA.
3. Close contacts of patients with confirmed monkeypox who develop fever may be tested by qPCR (prior to or after rash development) and if positive would be eligible for treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
All

Sex
All

Key exclusion criteria
Subjects taking repaglinide

Date of first enrolment
01/08/2021

Date of final enrolment
22/12/2023

Locations

Countries of recruitment
Central African Republic

Study participating centre
Hôpital de District de Mbaïki
Mbaïki
Central African Republic
-

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Research organisation

Funder Name
African Coalition for Epidemic Research Response

Funder Name
Foreign, Commonwealth and Development Office

Alternative Name(s)
Foreign, Commonwealth & Development Office, Foreign, Commonwealth & Development Office, UK Government, FCDO

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Bill and Melinda Gates Foundation

Alternative Name(s)
Bill & Melinda Gates Foundation, Gates Foundation, Gates Learning Foundation, William H. Gates Foundation, BMGF, B&MGF, GF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the results publication

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		09/05/2024	10/05/2024	Yes	No