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Safety of discontinuing co-trimoxazole prophylaxis among Ugandan adults on antiretroviral therapy (ART)

Submission date	Recruitment status	[X] Prospectively registered
28/06/2010	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
27/08/2010	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
17/02/2021	Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Version 4.0 March 2010; G0902150

Study information

Scientific Title
Safety of discontinuing co-trimoxaxole prophylaxis among human immunodeficiency virus (HIV) infected adults in Uganda: a randomised controlled trial

Acronym
COSTOP

Study objectives
Stopping concurrent prophylactic treatment with co-trimoxazole in adult Ugandan patients on antiretroviral therapy, will not lead to an excess of clinical events (predefined co-trimoxazole preventable clinical events) or death, but will lead to a significant reduction in the incidence of grade 3 or 4 haematological adverse events of antiretroviral therapy (ART).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Uganda Virus Research Institute Science and Ethics Committee approved on the 17th June 2010 (ref: GC/127/10/07)

Study design
Randomised double-blind placebo-controlled non-inferiority trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

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
Chronic human immunodeficiency virus (HIV) infection

Interventions
Patients who fulfil the inclusion criteria and who do not meet exclusion criteria will be recruited sequentially and will be randomised 1:1 to the experimental or control group:

1. Experimental group: Patients with CD4 count 250 or more cells/mm3 discontinue prophylaxis with co-trimoxazole (CTX), receive CTX placebo and continue taking antiretroviral therapy.
2. Standard/control group: Patients with CD4 count 250 or more cells/mm3 continue prophylaxis with co-trimoxazole (CTX), receive active CTX and continue taking antiretroviral therapy.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Co-trimoxazole

Primary outcome measure
1. Efficacy: time to the occurrence of the first clinical event (pre-defined CTX-preventable opportunistic clinical event or death)
2. Safety: time to the occurrence of the first grade 3 or 4 haematological adverse event

Recorded at first occurrence during the trial and assessed at the end of the trial.

Secondary outcome measures
1. Incidence of all CTX preventable events, recorded at time of occurrence
2. All cause mortality, recorded at time of occurrence
3. Incidence of all clinical events and related events requiring hospitalisation, recorded at time of occurrence
4. Incidence of all confirmed malaria episodes* asymptomatic and symptomatic, recorded at time of occurrence
5. Severity and outcome of all confirmed malaria episodes* asymptomatic and symptomatic, recorded at time of occurrence
6. Incidence of grade 3 or grade 4 adverse events, recorded at time of occurrence
7. Mean change in CD4 count after 12 months on the trial
8. Mean change in haematologic indices after 12 months on the trial
9. Serious adverse events (SAEs)-according to International Conference on Harmonisation (ICH) /Good Clinical Practice (GCP) definitions, recorded at time of occurrence
10. Adherence to use of ART, trial drug and insecticide-treated mosquito nets, evaluated at end of trial

* confirmed by positive parasitaemia on a blood slide

Overall study start date
01/09/2010

Completion date
30/03/2014

Eligibility

Key inclusion criteria

1. Human immunodeficiency virus (HIV) infected patient taking co-trimoxazole for at least 6 months
2. Aged 18 - 59 years, either sex
3. Documented intake of ART for at least 6 months
4. Clinically asymptomatic
5. Two CD4 counts (not more than 6 months apart) greater than or equal to 250 cells/mm3, the most recent no more than 4 weeks prior to enrolment
6. Able to attend 3-monthly study clinics for appointments and in event of intercurrent illness

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
59 Years

Sex
Both

Target number of participants
2000

Key exclusion criteria
1. Acute illness (opportunistic infection or other co- morbidity). Patients will be considered for inclusion into the trial after resolution of the illness.
2. First trimester pregnancy. Pregnant women who reach their second trimester of pregnancy could then be re-evaluated for inclusion into the trial.
3. Known hypersensitivity to co-trimoxazole

Date of first enrolment
01/09/2010

Date of final enrolment
30/03/2014

Locations

Countries of recruitment
Uganda

Study participating centre
MCR/UVRI Uganda Research Unit on AIDS
Entebbe

Uganda
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Sponsor information

Organisation
MRC/UVRI Uganda Research Unit on AIDS (Uganda)

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Sponsor type
Research organisation

Website
http://www.mrcuganda.org/

ROR
https://ror.org/04509n826

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) (UK) (ref: G0902150)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

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	Incidence of malari results	20/02/2016		Yes	No
Results article	Longitudinal effect results	15/07/2016		Yes	No
Results article	Effect of antiretroviral therapy results	20/02/2017		Yes	No
Results article	immunology substudy results	06/07/2020	17/02/2021	Yes	No