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Antibiotic prophylaxis to prevent infections in human immunodeficiency virus (HIV)-infected post-natal women

Submission date	Recruitment status	[_] Prospectively registered
06/04/2009	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
22/04/2009	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
31/10/2019	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
N/A

Study information

Scientific Title
Randomised, double-blind, placebo-controlled clinical trial of trimethoprim-sulfamethoxazole as prophylaxis for opportunistic infections in human immunodeficiency virus (HIV)-infected post-natal Zambian women

Acronym
TOPAZ

Study objectives
Bacterial infections cause high morbidity and mortality rates in human immunodeficiency virus (HIV)-infected post-natal women in southern Africa. The case for antibacterial prophylaxis in HIV-infected post-natal women needed evaluating through a placebo-controlled, randomised trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. University of Zambia research ethics committee approved on the 16th May 2000 (ref: TOPAZ co-trimox 2)
2. The joint UCL/UCLH committees on the ethics of human research, University College London approved on the 19th July 2000 (ref: TOPAZ co-trimox 2)

Study design
Prospective double-blind placebo-controlled randomised clinical 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 provided in the Interventions field to request a patient information sheet

Health condition(s) or problem(s) studied
HIV/bacterial infections

Interventions
Sample size:
In the present study it was planned to randomise 400 women and follow them for an average of 18 months on the assumption that there would be a loss of about 20% of women years, i.e., 480

evaluable woman years. This would provide at least 90% power to detect, at the 5% level, a 45% reduction in the first occurrence of the primary endpoint if the incidence was 35 per 100 woman years in the placebo group, a 40% reduction for an incidence of 45 per 100 or a 35% reduction if the incidence was 60 per 100. In any event, losses to follow-up were disappointingly high and the intake was extended to a total of 600 women.

Randomisation:
The randomisation schedule was determined using computer generated balanced randomised blocks, prepared by the MRC Clinical Trials Unit, London, UK. Names of eligible women were entered on the next available line of the study registers at site to determine their study number and the pre-labelled drug assigned to them. The number was used on all documents relating to the trial. None of the staff working on the trial in Zambia were aware of the allocated treatment, and at no stage was it necessary to unblind them. We issued participants with a container of study drug bearing their trial number, gave them instructions about taking the trial tablets and what to do in the event of possible adverse reactions, and gave them an appointment date four weeks later. We provided a study identity card bearing the name of the study and the participants study number. We encouraged participants to attend whenever they were unwell and asked them to inform the clinic if they were moving either within or out of Lusaka.

Interventions:
Each participant received a supply of pre-labelled trial drug, two tablets to be taken daily. Tablets contained: 400/80 mg co-trimoxazole (total daily prophylactic dose of 800 mg sulfamethoxazole/160 mg trimethoprim) or matching placebo. The randomisation was in the ratio of 1:1.

The minimum total follow-up time for participants was 12 months or up to loss to follow-up.

Participants were seen every 4 weeks to 16 weeks then every 8 weeks thereafter by a study clinical officer or physician. A brief questionnaire concerning patient well-being and clinical status was filled in. Details of visits to local clinics and general practitioners and treatment accorded were obtained. Appropriate referral or admission to hospital was arranged for those who develop illnesses during the study. All hospital admissions and outpatient assessments for serious illness or significant drug toxicity were recorded. At each visit we recorded information on visits to clinics or traditional healers or unscheduled visits to the study clinic for illness since the previous routine study attendance. We recorded details of possible adverse drug effects. When necessary, participants were admitted to hospital for investigation. When participants failed to attend an outpatient appointment their names were carried forward to the next week of the diary; if they still failed to attend the home visitor team visited the home address. If they were absent from home or had moved to another address we made efforts to find them, by interviewing relatives and neighbours and visiting alternative addresses listed in the locator form.

Adherence to therapy:
At each clinic visit, patients were asked how many study drug doses they missed and a pill count made of tablets. Urine was tested according to a random schedule provided by MRC CTU to test for sulfonamide. No patients were excluded from the study on basis of non-adherence. At the time of a home visit the home visitor counted the number of pills remaining in the container(s).

Toxicity and adverse events:
Adverse reactions to the intervention regimens were monitored. Guidelines for management and study discontinuation to be followed in the event of side effects were made available to study investigators. The adverse events of co-trimoxazole are well documented and include

nausea and rashes amongst a long list. We monitored carefully any adverse effects of the trial drug by setting up a clinic to which women were encouraged to come whenever they were unwell whether as a consequence of HIV-infection or because of possible drug related effects. Participants were instructed to stop the trial drug in the event of any new symptoms which might be drug-related. Women wishing to become pregnant during the course of the study were excluded from randomisation. Those who become pregnant during any period after enrollment were told to stop the trial drug for the duration of the pregnancy. Very low doses of co-trimoxazole does pass to the baby via the breast milk. We monitored any possible adverse effects that may occur together with any evidence of a concomitant benefits in the babies whose mothers were allocated to receive co-trimoxazole.

Contact details for patient information material:
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Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Trimethoprim-sulfamethoxazole

Primary outcome measure
1. Mortality from any cause or hospital admission, measured at end of trial; all deaths will be recorded as they occur
2. Safety (serious adverse events)

Secondary outcome measures
Adherence and completion rates, recorded throughout the trial.

Overall study start date
01/08/2000

Completion date
01/01/2004

Eligibility

Key inclusion criteria
1. Women who have recently given birth
2. Aged 16 years or more
3. HIV-seropositive at stage 2 or 3 of the World Health Organization (WHO) staging system for HIV infection
4. Evidence of residence at a permanent address in Lusaka

5. Willing to attend at two-monthly intervals for follow-up
6. Informed written or verbal consent

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
400 post-natal women followed up for 18 months

Total final enrolment
600

Key exclusion criteria
1. Current opportunistic infection or currently receiving co-trimoxazole
2. History of sulphonamide allergy
3. Breast feeding women with premature babies
4. Advanced HIV-disease or serious non-HIV disease (i.e. unlikely to survive more than 2 weeks)

Date of first enrolment
01/08/2000

Date of final enrolment
01/01/2004

Locations

Countries of recruitment
England

United Kingdom

Zambia

Study participating centre
Department of Infection
London
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Sponsor information

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Sponsor type
University/education

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ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Research organisation

Funder Name
Department for International Development (DFID) (UK) - Health and Population Division

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	01/04/2011	31/10/2019	Yes	No