# Effectiveness of generic split adult tablets and paediatric fixed dose combination (FDC) of d4T /3TC/NVP in the treatment of HIV infected Malawian children

Submission date	Recruitment status	Prospectively registered
12/05/2010	No longer recruiting	[_] Protocol
Registration date	Overall study status	[] Statistical analysis plan
20/05/2010	Completed	[_] Results
Last Edited	Condition category	Individual participant data
17/03/2011	Infections and Infestations	[_] Record updated in last year

### Plain English summary of protocol

Not provided at time of registration

### **Contact information**

#### **Type(s)** Scientific

**Contact name** Dr Ralf Weigel

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## Additional identifiers

EudraCT/CTIS number

**IRAS number** 

ClinicalTrials.gov number

## Study information

#### Scientific Title

Effectiveness of generic split adult tablets and paediatric fixed dose combination (FDC) of d4T /3TC/NVP in the treatment of HIV infected Malawian children: A part open-label randomised controlled trial and part cohort study

#### Acronym

TrioPed

#### **Study objectives**

We examine the effectiveness of standard paediatric 1st line ART regimens in Malawi in HIV infected children eligible for ART according to national guidelines.

The aim of the study is examine the effectiveness of Triomune baby in children <10kg and compare effectiveness of split adult FDC of d4T/3TC/NVP (recommended 1st line paediatric regimen) with Triomune baby for children 10kg and above.

Please note that as of 23/06/10 details of the extended ethics approval have been added to this record. More details can be found in the relevant field with the above update date.

#### Ethics approval required

Old ethics approval format

#### Ethics approval(s)

1. National Health Sciences Research Committee (NHSRC), Lilongwe, Malawi, approved on the 7th of April 2008 (Protocol no: 394; approval valid until 16/3/2010) 2. Baylor College of Medicine, Houston, USA, approved on the 15th of May 2009 (Protocol no: H-23674; approval valid until 4/5/2011)

#### Added 23/06/10:

3. National Health Sciences Research Committee (NHSRC), Lilongwe, Malawi extended their approval on the 17th of March 2010 (Protocol no: 394; approval valid until 16/03/11)

#### Added 17/03/2011:

Approvals extended:

1. Baylor College of Medicine approval valid from 18/02/2011 to 25/01/2012 2. National Health Sciences Research Committee (NHSRC) of Malawi valid from 15/03/2011 to 14 /3/2012

#### Study design

Children with body weight 10kg and above: Open label, randomized controlled trial Children less than 10 kg body weight: Cohort study

#### 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 contact details below to request a patient information sheet

#### Health condition(s) or problem(s) studied

Human Immunodeficiency Virus (HIV)

#### Interventions

Two different formulations of generic fixed dose combination of d4T/3TC/NVP tablets are compared in children 10kg and above: split adult tablets and a specific paediatric formulation (Triomune babyTM). Children less than 10kg bodyweight will be only started on Triomune baby.

#### Intervention Type

Drug

#### Phase

Not Specified

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

d4T/3TC/NVP (didehydrodeoxythymidine [d4T] / dideoxythiacytidine [3TC] / nevirapine [NVP]) - generic and Triomune®

#### Primary outcome measure

Proportion of children with viral load of <400 copies/ml at 12 months follow-up

#### Secondary outcome measures

- 1. Monitoring patients' clinical response during routine visits
- 1.1. Change in body weight and height (z-scores)
- 1.2. Proportion of patients dying and lost to follow up
- 1.3. Time from enrolment to death and lost to follow up
- 1.4. Proportion of patients presenting with new symptoms and signs from enrolment
- 1.5. Proportion of patients requiring hospital admission

2. Monitoring patients' immunological response (CD4 count adjusted for age at entry, 3, 6, and 12 months)

- 2.1. Proportion of patients with immunological failure
- 2.2. Time until immunological failure occurs from enrolment
- 2.3. Change of Median CD4 percentage
- 3. Monitoring patients' virological response (HIV RNA at Entry, 3, 6, and 12 months)
- 3.1. Proportion of children with HIV RNA <400 copies/ml
- 3.2. Mean plasma viral load log10 change adjusted to baseline value
- 3.3. Proportion of patients with virological failure:
- 3.3.1. HIV RNA not suppressed to undetectable levels (<400 copies/ml) at 6 months or
- 3.3.2. Less then 10fold (1 log10) decrease from baseline viral load after 6 months of ART or

3.3.3. Repeated detection of HIV RNA in children who had <400 copies/ml

3.3.4. A reproducible increase in viral load of children who had an substantial virological response but still have low levels of detectable HIV RNA who then had an greater than 3fold (>0. 5 log10) increase in copy number (children ≥ 2 years)

3.4. Time until virological failure occurs from enrolment

4. Monitoring Adverse Reactions

4.1. Signs and symptoms likely to be related to ART according to routine clinic checklist

4.2. Laboratory:

4.2.1. Complete Blood Count (CBC)

4.2.2. Aspartate Aminotransferase (AST)

4.2.3. Alanine Aminotransferase (ALT)

4.2.4. Lipase

4.2.5. Creatinine

4.3. Proportion of patients requiring modification of dosing regimen (e.g. prolonged lead in phase, intermittent stop)

4.4. Proportion of patients permanently stop/withdrawn from initial regimen and/or started on alternative 1st line regimen

5. Proportion of patients with >95% adherence by reported or observed pill count during clinic visits

6. Proportion of patients with >95% adherence with medication intake (ART) according to pill counts during unannounced home visits

7. Proportion of patients presenting in the clinic upon agreed appointment

8. Proportion of patients with detectable and undetectable NVP drug- plasma concentration in samples taken during pharmcokinetics (PK) study

9. Proportion of patients with NVP levels above the threshold at steady state

10. Proportion of patients having HIV drug resistance at baseline, 6 and 12 month, or when study treatment needs to be discontinued

#### Overall study start date

01/05/2008

#### **Completion date**

01/08/2011

# Eligibility

#### Key inclusion criteria

1. Confirmed HIV infection (either HIV antibody test or, if <18 months, by HIV DNA test)

- 2. Caregiver and child, if applicable, counselled about HIV infection
- 3. Age <15 years
- 4. Body weight ≥3kg and <25kg

5. Informed consent given by caregiver and child if applicable

6. Eligible to start Anti-Retroviral Therapy (ART) according to Malawi National ART guidelines (3rd edition 2008)

7. Likely to comply with the study protocol (e.g. a main caregiver, responsible for administrating medication has been identified, caregiver and child have undergone an ART education session using the national paediatric ART education flipchart to understand the implications of ART, patient lives within the Lilongwe district)

Participant type(s)

Patient

#### **Age group** Child

**Upper age limit** 15 Years

**Sex** Both

Target number of participants

RCT: 204; Cohort Study: 206

#### Key exclusion criteria

- 1. Previous exposure to ART except Prevention of Mother-To-Child Transmission (PMTCT)
- 2. Patient requires hospital admission according to assessment of study clinician
- 3. Obvious liver disease on clinical examination (e.g. jaundice)
- 4. Obvious renal disease on clinical examination (e.g. lid oedema, hypertension)

Date of first enrolment 01/05/2008

Date of final enrolment 01/08/2011

### Locations

**Countries of recruitment** Malawi

**Study participating centre Lighthouse at Kamuzu Central Hospital** Lilongwe Malawi PO Box 106

### Sponsor information

**Organisation** Ministry of Health (Malawi) - HIV department

**Sponsor details** Community Health Sciences Unit, Private Bag 65 Lilongwe Malawi Private Bag 65 +265 (0)1 759 614 fchimbwandira@yahoo.com

Sponsor type Government

**Website** http://www.hivunitmohmw.org/Main/HomePage

ROR https://ror.org/0357r2107

### Funder(s)

**Funder type** Government

Funder Name Ministry of Health (Malawi) - HIV department

**Funder Name** Clinton Foundation (USA) - Malawi Country Office

**Funder Name** German Agency for Technical Cooperation (Deutsche Gesellschaft für Technische Zusammenarbeit [GTZ]) (Germany) - Malawi Country Office

**Funder Name** Private donor

### **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