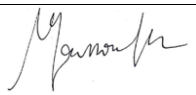
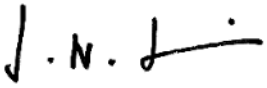
Ambition Trial Coordinating Centre
Private Bag 320, Princess Marina Hospital
Gaborone, Botswana

AMBITION-*cm*
AMBIsome Therapy Induction OptimizatioN

Work Practice Document: 15
Timing of clinical evaluations and tests

Title of study	High Dose AMBISOME© on a Fluconazole Backbone for Cryptococcal Meningitis Induction Therapy in sub-Saharan Africa: A Phase III Randomized Controlled Non-inferiority Trial		
Acronym	Ambition-cm – AMBIsome Therapy Induction OptimizatioN		
ISRCTN No.:	ISRCTN72509687		
WPD Current version	Version 1.0, 20/07/2017		
Author(s)	David Lawrence Lead Clinician		20/07/2017
	Timothée Boyer Chammard Clinical Advisor		20/07/2017
Reviewer(s)	Nabila Youssouf Trial Manager		20/07/2017
Approved by	Joseph Jarvis CI		20/07/2017

Revision History:		
Version Number	**Effective Date**	**Reason for Change**
1.0		First version

Working Practice Document 15: Timing of clinical evaluations and tests

Purpose
This document describes the processes to be followed over the treatment and follow-up period.

Scope
This WPD applies to the clinical evaluations and tests that are required on specific study days over the 16-week treatment and follow-up period.

Associated materials

Electronic data capture tool

Study Day 0/1

1. Patient is screened according to the procedures as set out in WPD 1 'Patient screening'.

2. If patient is eligible to be included in the study informed consent is taken according to the procedures as set out in WPD 2 'Informed patient consent'.

3. Patients are randomized to one of the two treatment arms using the stored electronic list. The 'Patient screening and randomization' eCRF is completed. Patient details are recorded on the 'Patient contact details' log and 'Screening and enrollment' log.

Study Day 1

1. Patient is weighed and started on treatment.

2. The 'Patient Medical History' eCRF is completed after the history and clinical examination.

3. Chest X-ray is performed if clinically indicated.

4. HIV test performed if status unknown, and with appropriate counselling

5. **Blood**: Full blood count, ALT, creatinine, urea and electrolytes tested. CD4 if not taken within last three months or clinically indicated due to significant patient deterioration. VL if ART exposed.

6. **CSF: NB** these tests may be recorded based on the routine sample taken on Day 0/1 or on a follow-up sample taken on Day 1.

Opening pressure is measured, cell count and differential, protein and glucose, India Ink exam or CrAg test, quantitative fungal culture, routine culture.

7. **Sample storage**: as determined by Lab Processing Chart

Treatment phase

1. Table 1 below outlines the tests to be taken on each study day throughout the treatment phase.

2. eCRFs should be completed in real time on the day each CRF is completed.

Follow-up

1. Patients may become outpatients from Day 7. If that is the case they will have a daily telephone consultation and will come for bloods as per the treatment phase

2. All patients will be followed up on weeks 2, 4, 6, 8 and 10

3. All patients will receive a telephone call on week 16

Working Practice Document 15: Timing of clinical evaluations and tests

Event Schedule	Screening	Week 1							Week 2							Wk 4	Wk 6	Wk 8	Wk 10	Wk 16
Study Day	≤D0	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14					
Consent forms																				
PIS and signed consent	X	X																		
Follow up																				
Screening and randomisation	X	X																		
Clinical review		X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Outpatient follow-up																X	X	X	X	
Week 16 telephone																				X
Clinical labs																				
HIV testing (if status unknown)*		X																		
Pregnancy Test (Urine/Serum) (2)		X																		
Full Blood Count		X						X							X	X				
CD4 count & Viral load (if needed)*		X																		
ALT		X						X							X	X				
Urea, creatinine and electrolytes		X		X		X		X			X		X		X	X				
Blood for drug levels (4)		X							X											
Clinical evaluation																				
Chest X-ray (1)		X																		
CSF																				
Opening pressure		X						X							X					
Cell count and differential*		X																		
Protein, glucose*		X																		
Routine culture *		X																		
India ink examination* (3)		X																		
Cryptococcal antigen* (3)		X																		
Quantitative fungal culture		X						X							X					
CSF Drug levels (4)		X						X							X					
Immune parameters (4)		X						X							X					

*Part of routine care. 1. If clinically indicated. 2. For women of childbearing age. 3. India ink or cryptococcal antigen required for inclusion. 4. As part of sub-studies at limited sites.

Training

Each staff member receives or has direct access to applicable Working Practice Documents (WPDs).

Each staff member reviews the applicable WPDs once a year.

All WPD training is documented and tracked in the WPD training logbook located in the Project Coordinator's office.

New staff is trained on applicable WPDs within 30 days of employment and all WPDs within 90 days of employment.

Staff members whose duties fall within this WPD scope are retrained within 14 days of the approval of each WPD revision.

References

1. Declaration of Helsinki, 2013: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ accessed 12th June 2017
2. International Conference on Harmonisation (ICH) Guideline For Good Clinical Practice E6(R1), 1996
3. Integrated Addendum To ICH E6(R1): Guideline For Good Clinical Practice E6(R2), 2016
4. Ambition Trial Protocol

Staff signatures: (signing below indicate that you have read this SOP and understand the material contained in it)

Date	Name (Please print)	Signature