Ambition Trial Coordinating Centre
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AMBITION-*cm*
AMBIsome Therapy Induction OptimizatioN

Work Practice Document: 1
Patient Screening

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		
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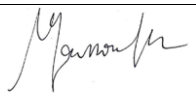
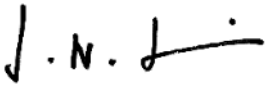
Reviewer(s)	Nabila Youssouf Trial Manager		20/07/2017
Approved by	Joseph Jarvis CI		20/07/2017

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

Working Practice Document 1: Patient screening

Purpose

This document describes the process of screening patients for the Ambition trial.

References

Ambition trial protocol

Scope

This WPD applies to the process of patient screening

Associated materials

WPDs: 'Informed Patient Consent', 'Patient Enrolment and Follow-up' and 'Patient exclusion following study enrolment', 'Electronic Data Capture Tool'

Screening and enrolment log

Screening CRF

All screened patients must be entered into the electronic data capture (EDC) system at the Screening page. In addition patients must be added to a paper Screening and Enrolment Log which must detail the patient's initials, date of birth and reason for non-inclusion, if applicable.

The Screening and Enrolment Log will be kept in the Investigator Site File (ISF) in a locked cupboard, only accessible to study personnel when not in use.

I. INITIAL IDENTIFICATION OF POTENTIAL STUDY PATIENTS

a) Referrals

- Patients with positive cerebrospinal fluid (CSF) India ink stain, and/or positive CSF cryptococcal antigen (CrAg), and/or positive serum CrAg will be identified directly from records kept by laboratory staff in the microbiology laboratory.

- Laboratory staff are encouraged to call study staff directly on their cell phones with any new positive India ink and/or CrAg results.

- Medical staff may also refer eligible patients directly to the study team.

- Trial staff may take responsibility for patients with CNS infections and therefore may conduct the screening LP and CrAg as part of routine care. They may also visit the wards to look for patients who may meet the eligibility criteria.

b) Tracing patients

For patients who are not referred directly by a medical team, patients will be traced according to their said location, as documented on the microbiology CSF request form.

II. INCLUSION/EXCLUSION CRITERA

a) Inclusion criteria

The inclusion criteria include

1. Consecutive patients ≥ 18 yrs with a first episode of cryptococcal meningitis (CSF India ink or CrAg test)
2. Known to be HIV positive or willing to undertake an HIV test
3. Willing to agree to participate in the study or, if obtunded, has a next of kin who agrees to the patient participating in the study

b) Exclusion criteria

Patients meeting the following criteria are to be excluded from enrolment into the study.

Exclusion criteria include:

1. Pregnancy (confirmed by urinary or serum pregnancy test) or lactation
2. Previous serious reaction to study drugs
3. Already taking antifungal treatment at cryptococcal meningitis treatment doses (amphotericin B ≥0.7mg/kg or fluconazole ≥800mg/day) for >48 hours
4. Concomitant medication that is contraindicated with study drugs (terfenadine, cisapride, pimozide, astemizole, quinidine and erythromycin in the case of fluconazole; cytarabine in the case of flucytosine)
5. HIV negative

Early withdrawal criteria include:

- a) ALT>5 times upper limit of normal (i.e. > 200 IU/ml) on baseline blood testing
- b) PMNs<500x10^6/L on baseline blood testing
- c) Platelets<50,000x10^6/L on baseline blood testing

See WPD 4: Early patient withdrawal

There is no specific exclusion or inclusion criteria for renal function. Clinicians are advised to use their best judgement whether to randomise a patient with impaired renal function. If they feel that treatment with intravenous fluids is warranted they may start fluconazole and wait to see if the renal function improves. If they feel the patient can have amphotericin then randomise and give at the stated dose with subsequent doses dictated by WPD 8: Toxicity management.

III. APPROACHING PATIENTS FOR INCLUSION INTO THE STUDY

Once study personnel are satisfied that the patient is eligible for recruitment into the study, the patient's informed consent must be sought.

Obtaining informed consent requires excellent communication. In practice, the study nurse will obtain written informed consent from most patients.

Please refer to the 'Informed Patient Consent' and 'Patient Enrolment and Follow-up' Working Practice Documents for further information regarding consenting and enrolling study patients.

In rare cases, a patient may be identified for screening who is found to be moribund, in multiorgan failure and unlikely to survive more than a few hours. In such cases it may be inappropriate to seek consent from relatives. This should be recorded on the screening log.

The Screening electronic Case Report Form (eCRF) and screening and enrolment log must be filled in for all screened patients, regardless of enrolment in the study.

Screened patients who are excluded are assigned a "dummy" PID. Screened patients who are enrolled are assigned a study PID.

Refer to eCRF WPD for details on completing the CRF and assigning dummy and screening PIDs.

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 training log located in the Investigator Site File (ISF).

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

Working Practice Document 1: Patient screening

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

Date	Name (Please print)	Signature