P1108

Training
RECRUITMENT OF STUDY PARTICIPANTS

CM013 - Standard Operating Procedure (SOP)

Presented by Dr Jana Winckler, Sub-Investigator
Background

- Obtaining eligible study participants is vital
  - Adequate numbers
  - Study success
- Appropriate recruitment facilities need to be identified
  - TB referral hospitals
  - Tertiary referral hospitals
  - TB clinics
- Effective recruitment strategies should be in place
  - Adult contact tracing
  - Build relationships with TB local TB programmes
- All these processes need to be within the framework of Good Clinical Practice Guidelines.
- Aim: Describes procedures to be followed when recruiting potential participants at local hospitals and clinics.
Recruitment: DTTC site

- All sites well integrated into existing research infrastructure including our pharmacokinetic research unit at BCH.

1) Hospital-based
   - Routinely hospitalized in MDR treatment inpatient wards
   - 3 main recruitment hospitals:
     • Tygerberg hospital (TBH)
     • Brooklyn Chest Hospital (BCH)
     • Brewelskloof hospital (BKH) located in Worcester. Evaluated at our pediatric TB/HIV clinics at Tygerberg Hospital

2) Pediatric TB outpatient clinics evaluated at our pediatric TB/HIV clinics at Tygerberg Hospital.
Recruitment strategy: Pre-screening

• Provide information to the parents in their language of preference
• Assess willingness
  – Formal informative session at BCH (end point: consent)
  – Sharing contact information (address, phone numbers)
• Important principles when approaching participant and caregivers
  – Confidentiality
  – Home language
  – Respect cultural norms and values
  – No financial incentives except travel reimbursement
Discussion: Recruitment strategies

Sites given the opportunity to discuss different site specific recruitment strategies and potential challenges
DOTS (DIRECTLY OBSERVED TB THERAPY) FOR P1108

CM013 - Study Specific Standard Operating Procedure
Directly observed tuberculosis treatment strategy (DOT or DOTS)

- Directly observed tuberculosis treatment strategy (DOT or DOTS)
  - Recommended by the World Health Organization (WHO)
  - Requirements:
    - DOT supporter watches a patient swallowing medication
    - All or majority of doses over the course of TB treatment
    - In/out patient basis
- Goal: ensures that a TB patient takes medication correctly
  - TB drugs
  - Dose
- DOTS SUPPORTER
  - Formal health worker
  - Trained lay community health worker trained by the research site.
THE DOTS STRATEGY

• The DOTS STRATEGY:
  – Standard of care in most TB programmes internationally.
  – Implemented on a national level in South Africa’s fight against TB

• The current DOTS options for routine TB care in South Africa under the National TB Programme (NTP) are as follows:
  – TB Clinic based DOT
  – Hospital-based DOT
  – Work or school-based DOT
  – Community based DOT (a community DOT supporter/DOT-trained family member/friend supervises treatment, typically at home)
DOTS in the context of clinical research

• When required by the protocol, as in P1108 study specific DOTS supporters will be used:
  – Employed and trained by the study team (CRS)
  – Support adherence, specifically for research participants
  – Direct accountability to the study team
  – Not employed by the routine South African TB programme (SANTP)
  – Discussion with patients and families:
    – Acceptability of DOT support plan to ensure most appropriate model of support
    – Confidentiality
DOTS OBJECTIVES

• Support adherence to bedaquiline and routine MDR-TB treatment (OBR)
  – Ensure correct dosing process
  – Monitor
  – Support and encourage

• Support adherence to ARVs

• Clinical monitoring for any potential AR
Study Specific DOTS requirements

• Specific DOT supporter allocated per participant

• DOTS card will be used as an adherence tool
  – Study-specific TB treatment card
  – Separate card for initial daily dosing phase and 22 weeks’ continuation phase

• All aspects should be well documented

• OBR and ARVs adherence completed during IMP (bedaquiline) dosing phase of the study (24 weeks)
Study Specific DOTS requirements continued

A) Initial daily bedaquiline dosing period: 2 weeks
   - At least 5 of the 7 doses observed (excluding PH)
   - Other 2 days (weekends) may be supervised by the parent/caregiver.

B) Subsequent 22 weeks of bedaquiline dosing
   - All 3 of the intermittent doses of IMP observed (excluding PH)
   - Parents or caregivers may administer bedaquiline treatment on PH

C) Following completion of 24 weeks of bedaquiline
   - DOT for OBR (ARVs) by study team not required
   - Adherence support according to local standard of care
   - Routine TB treatment card, typically used to support adherence
Dispensing of medication

• Study drug
  – Dispensed by the study pharmacist
  – Adherence check by study pharmacist
    • Pill counts of dispensed and returned bedaquiline

• Routine OBR and ARV’s
  – NOT routinely dispensed by study pharmacist
  – Provided in public sector
  – Study staff may complete pill counts to support adherence, at their discretion.
DOTS PROCEDURE: Hospitalization

• Bedaquiline provided by:
  – Trained study nurses
  – Trained and delegated routine nursing staff
  – Trained research DOTS supporter

• Observation of Dosing
  – Preferably by the study team (study nurse or DOTS supporter
  – First 2 weeks: 5/7 doses
  – Subsequent 22 weeks: all 3 doses
  – If routine hospital personnel dispense and observe
  – Certified copy of hospital dispensing chart should be filed as record
DOTS PROCEDURE: Hospitalization continued

• Upon discharge from hospital remember....

1) Issue the TB treatment
2) Provide relevant discharge information
   – Site/Investigator contact details
   – DOTS supporter’s name and contact details
   – Dates of study visits
   – Information about using the IMP
   – Remind re use of contraception, if applicable.
   – NB Remind about disallowed medications
DOTS: Outpatients

• Participants and caregivers
  – Trained regarding use of bedaquiline, OBR and ARVs
    • Preparation
    • Timing
    • Dosing
  – DOTs training to support adherence
    • Weekends and PH
    • Documentation of IMP administration
DOTS: Outpatients continued

• **Study pharmacist**
  – Pill counts to monitor adherence
  – Drug accountability
    • All used and unused IMP dispensed should be returned
  – IMP must be sent home with a participant and their caregiver (not with the DOT supporter)
  – OBR and ARVs dispensed by local TB and HIV clinics

• **Study staff**
  – Support DOTS
  – Correct use of TB treatment card
    • Reviewed and returned at every visit
    • New TB treatment card issued
DOTS: Outpatients continued

- **DOTS supporters**
  - Home visits
  - Verify that OBR taken
  - Complete DOTS card daily
  - Routine TB treatment (OBR DOT) cards may be completed by the local clinics (certified copy)
  - Establish contact with local community-based TB and HIV clinics where patients receive routine MDR-TB care OBR treatment as appropriate
  - Collect relevant OBR treatment documentation during 24 week bedaquiline dosing period, from local TB clinics or other treatment centers
DOTS Supporters: Training and responsibilities

- NB: Close supervision early on: demonstrate effective and consistent DOTS
- Ongoing training and support
- Attend follow up visits with participants (feedback, training)

Specific training:
- Dosing of IMP/OBR and ARVs according to visit schedule
  - Timing of bedaquiline in relation to meals
  - How it must be taken (crushing and given with water as needed)
  - Storage of IMP
  - The danger of an IMP being given to anyone other than the patient
  - Instruct the participant or parent on the correct administration of IMP and on appropriate storage of IMP
DOTS Supporters: Training and responsibilities continued

- Documentation of DOTS treatment card
- Importance adherence
- TB infection control
- Return to the study site all completed study related documentation such as DOT cards.
- Contact details of relevant site staff members
  - PI, sub-investigators and DOTS coordinator.
DOTS Supporters: Training and responsibilities continue

• Awareness of clinical well-being of participant
  • Recognition of side effects
  • Identify and report telephonically any information regarding change in health status
  • Assisting in identifying potential AEs and SAE’s
  • Messenger between the participant and the research team
  • The study team to contact the participant, obtain detailed information and decide if on site evaluation is needed
DOTS responsibilities of Study Coordinator

• Primary contact person for DOTS supporters
  – Remain in constant communication as needed
• Complete DOTS before participant is enrolled or early during study participation
• Identify and assign a DOTS supporter per participant
  – Able to travel to the participant’s home
• Arrange a meeting with the DOTS supporter, participant and/or parent
  – Before or at the time the participant is dispensed first bedaquiline during outpatient treatment.
• Visit schedule
• Documentation completed
ADHERENCE BOOKLETS P1108

• Exercise: Please read the instructions provided with your booklet and complete the correct dosing card provided
## IMPAACT P1108 DOTS Booklet 1

<table>
<thead>
<tr>
<th>Date:</th>
<th>[27/JAN/2015]</th>
<th>Day of the week (circle)</th>
<th>Mo</th>
<th>Tu</th>
<th>We</th>
<th>Th</th>
<th>Fr</th>
<th>Sa</th>
<th>Su</th>
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### MORNING

1. Time study medication (BDQ) was taken

   

2. Was BDQ given with a meal? (BDQ should be given after breakfast)  
   *This would mean breakfast was taken no longer than 30 minutes before dosage*
   **If no, please specify reason below**

   Yes | No

3. Was the study medication (BDQ) prepared according to instructions?  
   **Please refer to instructions at the back of this booklet**
   **If no, please specify below**

   Yes | No

4. Did you do a hand and mouth check to see if the medication (BDQ) was swallowed?

   Yes | No

First give the study medication (BDQ). Give routine TB (OBR) and ARV medications (if HIV-infected) directly after the study medication has been given.

### EVENING

1. Time routine TB medication (OBR) was taken

   

2. Time ARV medication was taken (if HIV+)

   

3. Did any problems occur? IF "YES" complete comments section (4)  
   (Problems could be vomiting, dosing at the incorrect time, spillage of medicine etc.)

   Yes | No

4. 

   

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**Person observing treatment:**

<table>
<thead>
<tr>
<th>Date</th>
<th>initials and surname</th>
<th>signature</th>
</tr>
</thead>
</table>

**Person observing treatment:**

<table>
<thead>
<tr>
<th>Date</th>
<th>initials and surname</th>
<th>signature</th>
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<tbody>
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<td>EVENING</td>
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<tr>
<td><strong>MORNING</strong></td>
<td><strong>EVENING</strong></td>
<td></td>
</tr>
<tr>
<td>1. Time study medication (BDQ) was taken.</td>
<td>N/A <strong>Should only be given on Mondays, Wednesdays and Fridays.</strong></td>
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<tr>
<td><strong>If no, please specify reason below</strong></td>
<td><strong>If no, please specify reason below</strong></td>
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<td></td>
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<tr>
<td><strong>If no, please specify reason below</strong></td>
<td><strong>If no, please specify reason below</strong></td>
<td></td>
</tr>
<tr>
<td>3. Did you do a hand and mouth check to see if the medication (BDQ)</td>
<td><strong>Please note that the study medication bedaquiline is not given at night.</strong></td>
<td></td>
</tr>
<tr>
<td>4. Was the study medication (BDQ) prepared according to instructions?</td>
<td><strong>Please refer to instructions at the back of this booklet</strong></td>
<td></td>
</tr>
<tr>
<td><strong>If no, please specify below</strong></td>
<td><strong>If no, please specify below</strong></td>
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</table>

First give the study medication (BDQ). Give routine TB (OBR) and ARV medication (if HIV-infected) directly after the study medication has been given.

| PERSON OBSERVING TREATMENT DATE (MM/ DD/YYYY) (INITIALS AND SURNAME) (SIGNATURE) | PERSON OBSERVING TREATMENT DATE (MM/ DD/YYYY) (INITIALS AND SURNAME) (SIGNATURE) |
### IMPAACT P1108 TB TREATMENT CARD (DOTS) Booklet 3
For routine MDR-TB (OBR) treatment after BDQ has been discontinued

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#### MORNING

1. Time routine TB medication (OBR) was taken

   ![Image of pills](image1)

   Time: _____ : _____

2. Time ARV medication was taken (if HIV+)

   ![Image of ARV](image2)

   N/A Time: _____ : _____

3. Complete this comment section if any problems occurred

   (Problems could be vomiting, spillage of medicine etc.)

   ________________________________________________________________

#### EVENING

1. None. TB medicines are usually only given in the morning

   ![Image of pills](image3)

   Time: N/A _____ : _____

2. Time ARV medication was taken (if HIV+)

   ![Image of ARV](image4)

   N/A Time: _____ : _____

3. Complete this comment section if any problems occurred

   (Problems could be vomiting, spillage of medicine etc.)

   ________________________________________________________________

<table>
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<tr>
<th>Person observing treatment</th>
<th>__/<strong><strong>/</strong></strong> (date)</th>
<th>________________ (initials and surname)</th>
<th>________________ (signature)</th>
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<tr>
<th>Person observing treatment</th>
<th>__/<strong><strong>/</strong></strong> (date)</th>
<th>________________ (initials and surname)</th>
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</table>
Dots feedback from sites

- Current DOTS practises
- Opportunity to share lessons learnt
DOTS: CASE STUDY

• You are a DOTS worker and doing a home visit for a participant who is receiving 3x weekly Bedaquiline, today is Friday (morning). The patient is also receiving, TB OBR in the mornings and ARV’s once daily in the evening. On arrival there the mom is cooking eggs for the child’s breakfasts. Child takes the tablet well at around 08h00 that morning, but when given the OBR at 08h15 vomits. The mom also wants to know what time you will be there the next morning to do DOTS. Please complete the dosing card and comment on the management of this child.