WTP?!? – What the Predict: How the NIAID tested and stretched the limitations of DataFax

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Content

• 2016: TB Epidemic / Multi-drug resistant TB
• PredictTB protocol objectives / overview
• PET/CT randomization & PET/CT scan replication process
• PET/CT automated data consensus checking between Image reviewers
• Participant randomizations
• PET/CT image header data extraction (DICOM) and automatic importation into DataFax
• Drug Adherence (the MERM) & Drug Adherence data flow
• DataFax automated email notification for clinical study management
• DataFax Demo
2016: Status of the TB epidemic and MDR-TB

- 10.4 Million new cases
- 1.4 million deaths
- 0.4 million TB+HIV deaths
- Treatment too long:
  - Drug susceptible TB tx takes 6 months
- Under treatment fuels concerns about resistant TB strains:
  - MDR treatment > 12 months
  - 580,000 new cases of MDR TB
- 45% of the MDR TB cases are in India, China, and the Russian Federation

Source - WHO Global Tuberculosis Report 2016

Pathology mini tutorials
https://www.youtube.com/channel/UCeSFXM6UGR8ryO68vOPcOw
PredictTB: Research Objective
Shortening treatment duration/Lower TB drug resistance

- ~620 participants
- 5 sites in South Africa, 4 sites in China

- Most patients don’t require extensive treatment duration, identifying those cured before 6 months has proven challenging
- PredictTB uses tools (e.g. PET/CT images) to identify participants with lower disease burden who has strong early response to treatment
- Study tests whether TB treatment can be shortened to 16 weeks (4 months) in this lower risk cohort
PredictTB: Global footprint

Project Overview
~620 Participants
9 Sites
Hybrid CRF (Paper & eDC)
CRF, Imaging, Adherence and Randomization data in CDMS

USA
2 PET/CT Image reviewers

China
4 Sites enrolling patients
2 PET/CT scan institutions
1 PET/CT upload hub
1 PET/CT Image reviewer

South Africa
5 Sites enrolling patients
2 PET/CT scan institution
1 PET/CT upload team
2 PET/CT Image reviewers
PET/CT Randomization & Sync process
PET/CT Randomization & Sync process

Image Randomization Assignments

2x CRF Trigger

2x Reviewer Assignment File
PET/CT Automated consensus checking

Image Reviewer 1

Baseline & Week 4

PET/CT Scan Image review

DataFax Clinical Data Management System Entry

PET/CT Scan Image Consensus Checks (DataFax)

Protocol Criteria Arm Assignment (DataFax)

Image Reviewer 2

PET/CT Scan Image review

DataFax Clinical Data Management System Entry

PET/CT Scan Image Consensus Checks (DataFax)

DataFax Comparison with Image Reviewer 1

Image Reviewer 3

PET/CT Scan Image review

DataFax Clinical Data Management System Entry

PET/CT Scan Image Consensus Checks (DataFax)

DataFax Comparison with Image Reviewer 2

Image Reviewers cannot see other Image Reviewers' Entry in DataFax DFopen_patient_blinder()
PET/CT Automated consensus checking

PET/CT Image Review 1 → DataFax eDC Entry

Image review consistency checks

PET/CT Image Review 2 → DataFax eDC Entry

3rd Image Reviewer Assignment → CRF Auto completion

CRF Auto completion
PET/CT DICOM data extraction / importation

- **Patient Enrollment Visit**
  - PET/CT Scan upload to NIAID Aspera Server using Aspera Drive
  - Clinical Data Management System Entry

- **PET/CT Scan (Day 0)**
  - Patient Study Visits
  - PET/CT Scan upload to NIAID Aspera Server using Aspera Drive

- **PET/CT Scan (W4, W16, W24)**
  - End of Study

- NIAID Aspera Server
  - Extracted PET/CT metadata
  - Deflected file containing PET/CT scan protocol settings
  - Daily import into Clinical Data Management System

- Clinical Data Management System
  - Study team
  - Automated emailing of protocol deviations to study teams
The MERM (Medication Event Reminder Monitor)

• The MERM device is used to (i) store medication, (ii) medication reminder, (iii) record dosing history, and (iv) refill medication reminder (next visit date)

• Types of Alerts:
  o Daily Medication Reminder: Green LED & Buzzer
  o Medication Refill Reminder: Yellow LED
  o Low Battery Alert: Red LED

MERM data automatically transferred to Clinical Data Management System
The MERM – Participant usage

1. At pre-programmed time, Green LED lights up and Buzzer activated to alert participant of dosing time

2. Participant opens MERM container by opening the box to access the stored medication

3. Participants follows the medication taking instructions

4. Upon completion of medication taking, participant closes the box and stores the MERM to be used again the next day
The MERM – Participant Dosing Reminders

Medication Reminding Period lasts for a total 30 minutes as follows – 3 cycles (10 minutes each) of the following:

i. For first 5 minutes: the Green LED will flash + the Buzzer will sound

ii. For next 5 minutes: all alerts will stay OFF (no flash or sound)

iii. After a total of 30 minutes the Medication Reminding Period will end and no further alerts will occur until the next day
Drug adherence data flow

1. **Patient Enrollment Visit**
2. **Medical Event Reminder Monitor (MERM) Setup**
3. **Clinical Data Management System Entry**
4. **Patient Study Visits**
5. **Patient Drug Adherence Interview**
6. **End of Study**

Flow continues through:
- Medical Event Reminder Monitor (MERM) Follow-up

Process continues via:
- Daily Imports
  - Transfer to Aspera Server
  - Data Import into Clinical Data Management System
MERM – Visual Data Analytics

MERM User Interface

- Very basic user interface to setup and test the alarm reminders
- Also “links” the Participant ID to the MERM data

Drug Adherence Visual Graph

- Graph will show all days where pill box (MERM) was opened
- Different color graph if there are “gaps” in drug adherence compliance
- Enhances the drug adherence interview with participant to determine final compliance
DataFax Automated Email notifications

- ~20 Automated emails – assist with clinical study management
- Enrollment, Randomization, Image assignment, Reminders, SAE Alerts, etc.

**PredictTB: PET/CT Random Assignment**
Sent: Friday 15 September 2017 at 16:49
To: michael.duvenhage@nih.gov emerald_liang@hotmail.com

Predict TB: This is a HIGH PRIORITY PET/CT Image Review Assignment for Lili Liang. The following PET/CT scan has been assigned to you: Participant - 12005. Visit - Day 0. Please note this HIGH PRIORITY PET/CT scan needs be be assessed by 21/SEP/2017. The other Image reviewer assigned to this PET/CT scan is: Ray Chen

**PredictTB: PET/CT Read Reminder**
Sent: Saturday 23 September 2017 at 8:00
To: michael.duvenhage@nih.gov doddy@niaid.nih.gov rchen@niaid.nih.gov friedrich.thiemenmann@uct.ac.za caiy2@niaid.nih.gov

Predict TB: Dear Friedrich Thiemenmann, The following PET/CT scan has been assigned to you: Participant - 13005. Visit - Day 0. REMINDER: Please note this HIGH PRIORITY PET/CT scan must be assessed by - 24/SEP/2017.

**PredictTB: Week 12 Randomization Notification**
Sent: Thursday 14 September 2017 at 9:54
To: rchen@niaid.nih.gov doddy@niaid.nih.gov caiy2@niaid.nih.gov michael.duvenhage@nih.gov arorakriti@niaid.nih.gov jwinter@catalysisfoundation.org

You replied to this message on 2017/09/14, 14:53.

PredictTB: Please note that Participant - 13001 was randomized at Week 12 (on 14/SEP/2017) to Arm A - Image at week 24.
DataFax Automated Email notifications

- PET and DT DICOM Imported data – PET/CT scan settings warnings/alerts

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**PredictTB: CT Scan Problem Notification**

**Sent:** Monday 25 September 2017 at 16:57

**To:** michael.duvenhage@nih.gov, rchen@nlaide.nih.gov

PredictTB: CT Scan for Participant: 12001 at visit: W0 for series: lungs has the following error notification(s): ECD20. Please review this CT Scan.

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Problem 1: ECD20 - 1f11008 (mm axial FOV) value error
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**Patient ID:** 101067270
**Age:** 34
**Weight:** 61.000000
**Scan Rel Path:** PD_12001_W0/DICOM/S206210/S30
**Acquisition Date:** 28/JUL/2017
**Interval Between Scans:** 0
**Institution Name:** Western Cape PET/CT
**Series Description:** lungs
**KVP:** 120
**XRay Tube Current:** 200
**Exposure:** 342
1f11008 (mm axial FOV): 432
1f11026 (Pitch): 0.438000
1f11027 (Rotation time): 0.750000
1f11046 (Collimation): 0.750000
1f1104b (Thickness): 16x0.75
**CTD Ivol:** 19.800000
DataFax Demo
Acknowledgements

NIAID TB Research Section
Dr. Clifton Barry III
Dr. Ray Chen
Dr. Laura Via
Chrissie Cai
Kriti Arora
Hong Zhu
Jingcai Gao

Wisepill
James Deck

NIAID Office of Cyber-infrastructure and Computational Biology
Michael Tartakovsky, CIO
Amy Gentzel
Chris Whalen
Brian Moyer
Kanwaldeep Bajwa
Francis Appiah
Michael Holdsworth
Michael Hurst
David Ireland
Sergey Grinkrug
Vadim Provotorov

University of Cape Town (Cliff Barry Lab)
Taeksun Song

NIAID Biostatistics Research Branch
Dr. Lori Dodd
Jing Wang
Keith Lumbard

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