Treating Patient, Not Disease: People-Centered Approach

7th TB Symposium – Ministry of Health of the Kyrgyz Republic and Médecins Sans Frontières

1-2 March, 2018, BISHKEK, KYRGYZSTAN

TB Practecal clinical trial

Bern Nyangwa
A RANDOMISED, CONTROLLED, OPEN-LABEL, PHASE II-III TRIAL TO EVALUATE THE SAFETY AND EFFICACY OF DRUG REGIMENS CONTAINING BEDAQUILINE AND PRETOMANID FOR THE TREATMENT OF ADULT PATIENTS WITH PULMONARY MULTIDRUG RESISTANT TUBERCULOSIS
OUTLINE

- Goals of TB-PRACTECAL
- Main Trial design
- Sites and progress update
- Sub-studies
- Challenges
Goals of PRACTECAL

- Identify a new regimen(s) for M/XDR-TB that is radically shorter, tolerable, effective and feasible to scale up through an ICH-GCP trial.

- Target the World Health Organization (WHO) new TB drugs policy task force for adoption of successful regimens into global guidance:

AIM: Patient Centred Treatment

- Oral medication / no injectable
- Usable for people living with HIV
- Easy to take small pill number
- 6 month regimen
- Minimal side effects

TB Practecal
Innovating MDR-TB Treatment
One day of M/XDR treatment today

One day of TB-PRACTECAL (arm 1)

PATIENT’S PERSPECTIVE

MEDECINS SANS FRONTIERES

TB Practecal
Innovating MDR-TB Treatment
**Investigational arms:**
1. Bedaquiline + PA-824 + linezolid
2. Bedaquiline + PA-824 + linezolid + moxifloxacin
3. Bedaquiline + PA-824 + linezolid + clofazimine

**Control arm:**
Locally accepted standard of care which is consistent with the WHO recommendations for the treatment of M/XDR-TB
Recruited 65 pts so far
Of 630 target sample size

Nukus site:
• Site activation: 21st Dec 2016
• FPFV: 17th January 2017
• 61 recruited

Minsk site:
• Site activation: 29th Dec 2017
• FPFV: 31st January 2018
• 3 recruited

Tashkent site
• Regulatory and Ethics approval
  February 2016
• Site activation target: Q2 2018
• FPFV target: Q2 2018

THINK site:
• Site activation: 17th Nov 2017
• FPFV: 23rd November 2017
• 1 recruited
• Don McKenzie subsite to open Q2 2018
• 240 pts
• Sparse population PK
• Sites that can export samples
Social science sub-studies

HEALTH ECONOMIC EVALUATION

DECISION PROBLEM
SHOULD THE NHS FUND NEW DRUG OR EXISTING DRUG?

STANDARD TREATMENT
COSTS (C)
HEALTH OUTCOMES (Q)

NOVEL TREATMENT
COSTS (C)
HEALTH OUTCOMES (Q)

INCREMENTAL COMPARISON

INCREMENTAL COST-EFFECTIVENESS RATIO
ICER = (Q2 - Q1) / (C2 - C1)

COMPARISON OF ICER AGAINST THRESHOLD λ
Reasons for non-inclusion in the clinical trial:

- Did not meet inclusion criteria
- Refused hospitalisation
- Deemed unsuitable by CT team
- Refused any treatment
- Geographical/distance
- Refused general
- Already on effective treatment
- Uncontactable
- Afraid of new drugs/side effects
- Wants to start treatment ASAP
- In prison
- Does not understand CT
- Disabled
Acceptance

Context:
- Low TB knowledge
- Low research literacy
- Mistrust of new treatment
- Authoritarian practitioner-patient relationship

Practitioner role (scepticism -> coercion)

Main drop-out point (60% of refusals)

TB story:
- Individual/family experience and knowledge of TB/ treatment
- Timing of trial proposal

MDR GeneXpert

Joint consultation MoH + MSF MDs

3 x counselling sessions

Screening

Randomisation

Inaccessibility of patient-to-patient information
- ‘Official’ information overload
- Lack of transparency, ‘air of secrecy’, rumours
International collaboration

Sponsor sites

Patient reported outcome

Statistics + Economic Evaluation

Developers of pretomanid

External Monitor

Medical monitoring

Data management

Laboratory monitoring

Cardiac safety