Tuberculosis in 2017: Searching for new solutions in the face of new challenges

6th TB Symposium – Ministry of Health of the Republic of Belarus, Republican Scientific and Practical Center for Pulmonology and Tuberculosis, and Médecins Sans Frontières

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TB-Practecal - designing of TB trials to ensure pre-XDR and XDR needs are met

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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
• Key sub-studies
• Challenges and opportunities ahead
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:
One day of M/XDR treatment today

One day of TB-PRACTECAL (arm 1)
Trial Arms

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
Identify regimens containing bedaquiline and PA-824 for further evaluation based on safety and efficacy outcomes after 8 weeks.

Stage 1

Randomisation

8 weeks

ARM 1 – 24 weeks

ARM 2 – 24 weeks

If at 8 weeks, the % of discontinuation and death is >45% and/or the % of culture conversion is < 40%

ARM 3 – 24 weeks

SOC 36+ weeks

Stop the corresponding arm
Evaluate the safety and efficacy of the experimental regimens containing bedaquiline and PA-824 compared with the SOC at 72 weeks post-randomisation.
Progress update 02/03/17

- Recruited x pts so far
- Of 630 target sample size
- LPLV target: 31st March 2021

Nukus site:
- Site activation: 21st Dec 2016
- FPFV: 17th January 2017
- xx recruited
- 3 additional centres to open in 2017

Minsk site:
- Regulatory and Ethics approval Dec 2016
- Site activation target April 2017
- FPFV target: April 2017

Tashkent site
- Regulatory and Ethics approval February 2016
- Site activation target:
- FPFV target: July 2017

THINK site:
- Regulatory and Ethics: submission by 10th March
- Site activation target: June 2017
- FPFV target: July 2017
- Dorothy Goodwin site and one additional centres to open in 2017
Substudies

• Pharmacokinetic study
  – Regimen Population PK +/- intensive focused on Linezolid
  – GCLP-accredited bioanalytical facility
• Economic evaluation
• Tolerability: patient reported outcomes
Challenges/Opportunities

- Laboratory EQA
- Whole genome sequencing
- High precision and accurate mass spectrometry for PK measurements
- Staff training and retention
International collaboration

Sponsor sites

Statistics

Developers of pretomanid

External Monitor

Overall Trial Support

Data management

Laboratory monitors

Cardiac safety