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

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Activity Reports

We publish an International Activity Report each year which recaps our field work during the preceding 12 months.
As of October 2016, MSF, in partnership with national ministries of health, has initiated more than 1,000 DR-TB patients with bedaquiline and/or delamanid in 12 countries.

Globally, there is still an unacceptable gap between those who would benefit from the new drugs and those who have been able to access them. To date, through programmatic or compassionate use - only 5,718 DR-TB patients have been able to access bedaquiline and just 405 have been able to access delamanid.
Principles for designing future regimens for multidrug-resistant tuberculosis
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- At least one new class
- At least 3 and max 5 effective drugs
- Effective against MDR and XDR strains
- 6 -9 months
- Oral
- Simple dosing schedule
- Good side effect profile, limited monitoring
- Minimal interaction with antiretrovirals
Goals

- 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 WHO policy change
Investigational arms:
1. Bedaquiline + PA-824 + linezolid + moxifloxacin
2. Bedaquiline + PA-824 + linezolid + clofazimine
3. Bedaquiline + PA-824 + linezolid

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 pretomanid 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

ARM 3 – 24 weeks

SOC 36+ weeks

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

= Stop the corresponding arm
Evaluate the safety and efficacy of the experimental regimens containing bedaquiline and pretomanid compared with the SOC at 72 weeks post-randomisation.
Progress update

- **FPFV:** 17th January 2017
- **LPLV target:** 31st March 2021

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

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

**Tashkent site**
- Regulatory and Ethics approval February 2016
- Site activation target: December 2017
- **FPFV target:** January 2018

**THINK site:**
- Regulatory and Ethics: submission by 10th March
- Site activation target: July 2017
- **FPFV target:** August 2017
- Dorothy Goodwin and Don McKenzie hospitals
Sub-studies

- Pharmacokinetic studies (Liverpool Uni)
- Economic evaluation (LSTM)
- Tolerability: patient reported outcomes
collaborators

Sponsor + clinical ops sites

Statistics

Developers of pretomanid

External Monitor

Overall Trial Support

Data management

Laboratory monitors

Cardiac safety