TB Practecal

Innovating MDR-TB Treatment

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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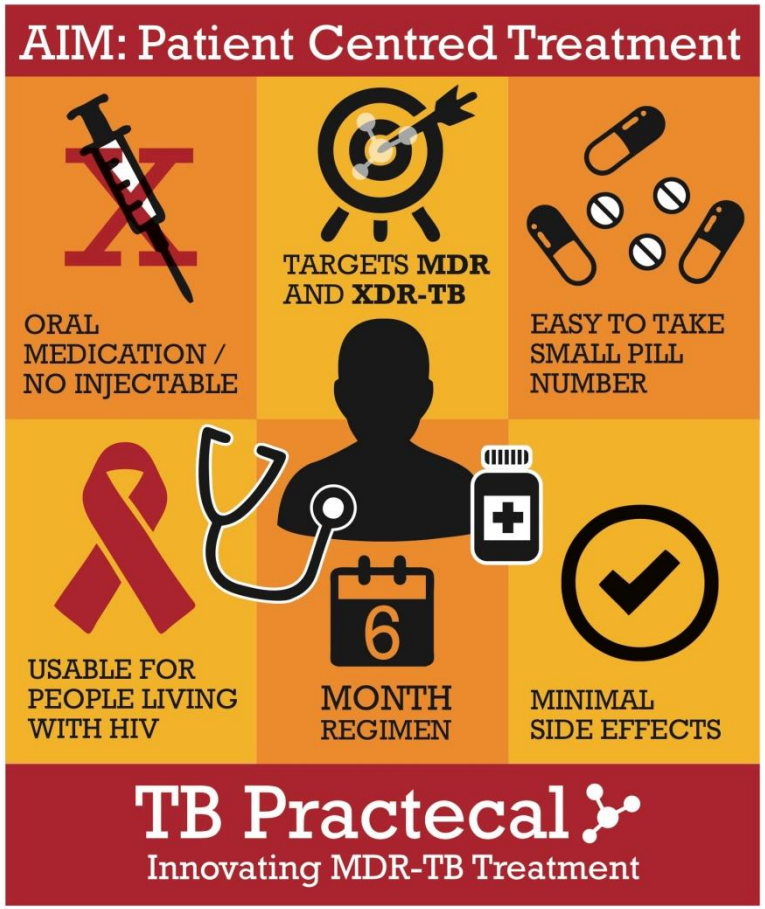
Goals of PRACTECAL

- Identify a new regimen(s) for M/XDR-TB that is radically shorter, tolerable, effective and feasible to scale up through a clinical trial compliant with international standards for Good Clinical Practice (ICH-GCP);

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



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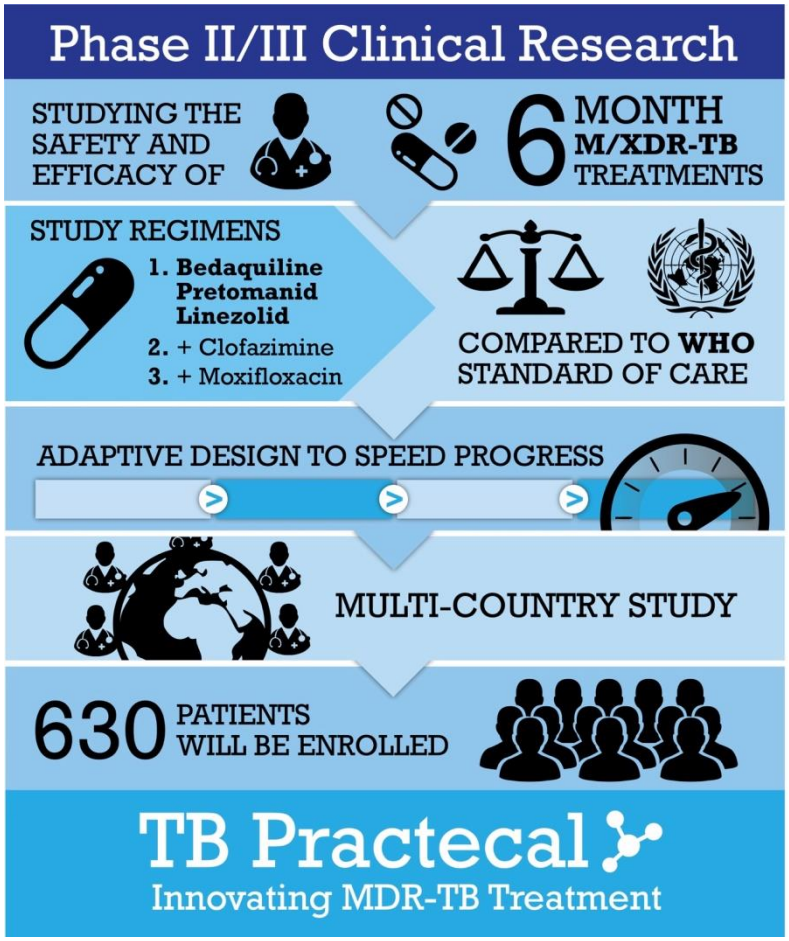
Trial Arms



Intervention 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

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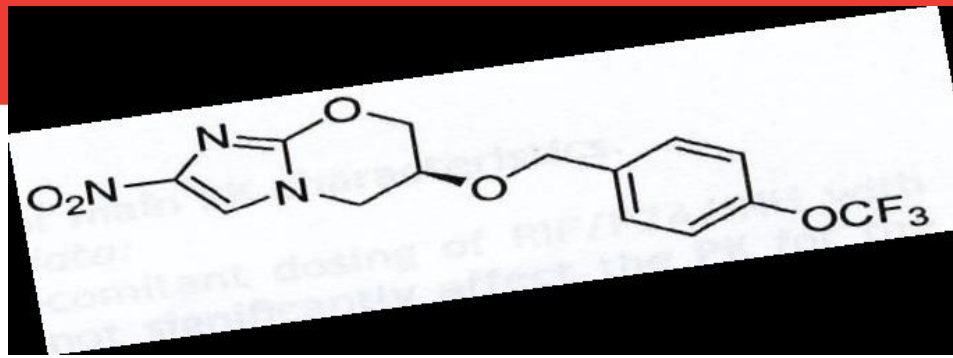
Pretomanid



- PA-824
- Nitroimidazole
- Inhibits synthesis of bacterial cell wall
- 200mg tab
- 200mg o.d. x 24 wks
- Phase 3

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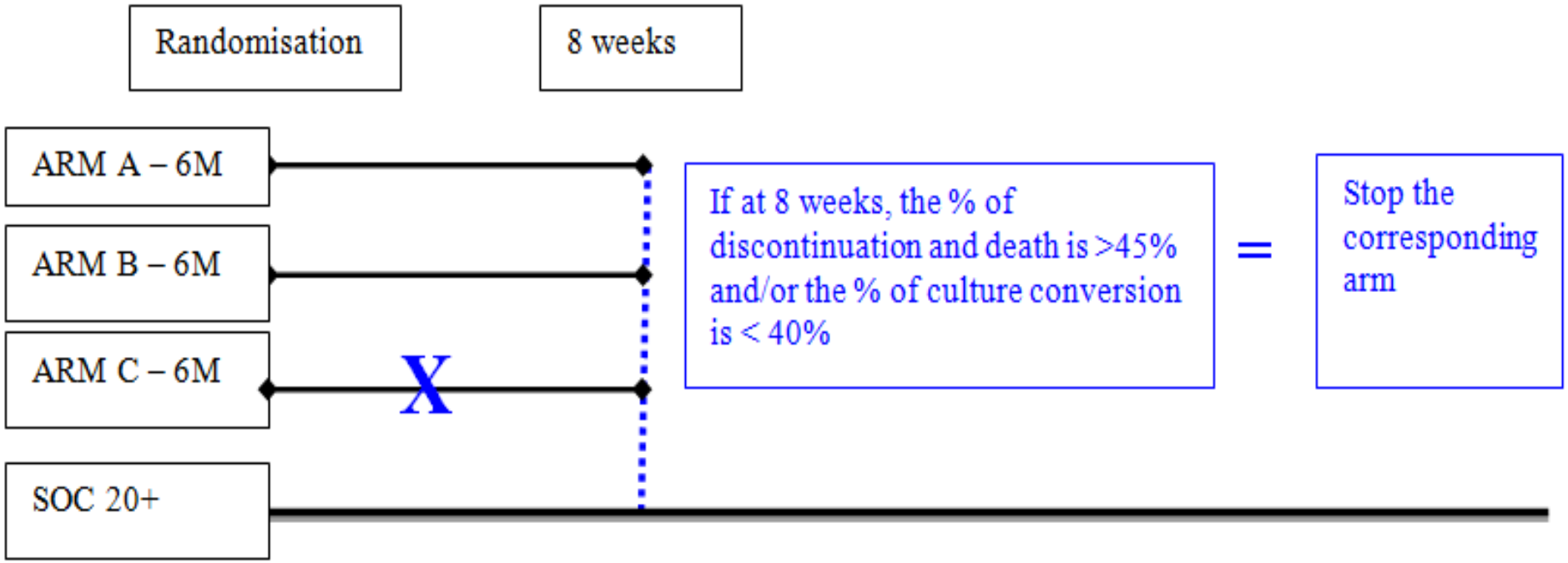
Stage 1: objective & design

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



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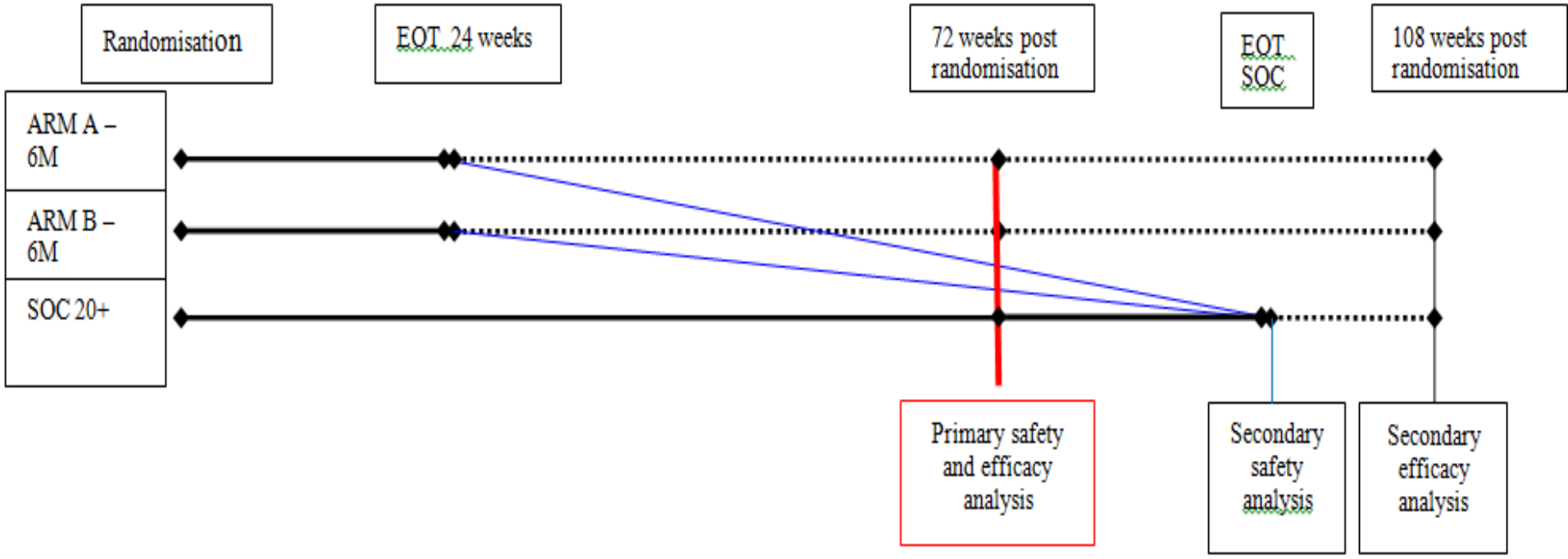
Stage 2: objective & design

Evaluate the safety and efficacy of the experimental regimens containing bedaquiline and PA-824 compared with the SOC at 72 weeks post-randomisation.



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PRACTECAL 2016 timeline

2015 – Q1 2016
Set up, approval

- Institutional Ethics approval (MSF, LSHTM)
- Uzbekistan Ethics and regulatory approval
- Upgrade Uzbekistan

Q2 2016
recruitment

- FPFV Site 1 (KKP Uzbekistan)
- Upgrade Site 2 (Tashkent)
- Submission Site 3

Q3-4 2016
recruitment

- Submission site 4
- Upgrade sites 3 & 4
- ? Recruitment site 2 & 3

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Lessons learnt thus far…

- Regulatory frameworks challenging
- Early involvement of local trial experts key
- Upgrading new trial sites requires varied and dedicated expertise
- Community engagement key from outset: adapted to context
- Lab EQC & strain identification challenging

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International Collaboration

MEDECINS SANS FRONTIERES DOCTORS WITHOUT BORDERS	Sponsor
	Country Lead
	Trial Site Lead
LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE	Statistics
TB ALLIANCE GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT	Developers of pretomanid
Swiss TPH Swiss Tropical and Public Health Institute Schweizerisches Tropen- und Public Health-Institut	Interim Trial Management
TDR For research on diseases of poverty UNICEF • UNDP • World Bank • WHO	Overall Trial Support
DNDi Drugs for Neglected Diseases initiative	Data management
UCL	Reference mycobacteriology lab
ERT	Cardiac safety

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