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

Bern-Thomas Nyang'wa
Chief Investigator, TB-PRACTECAL

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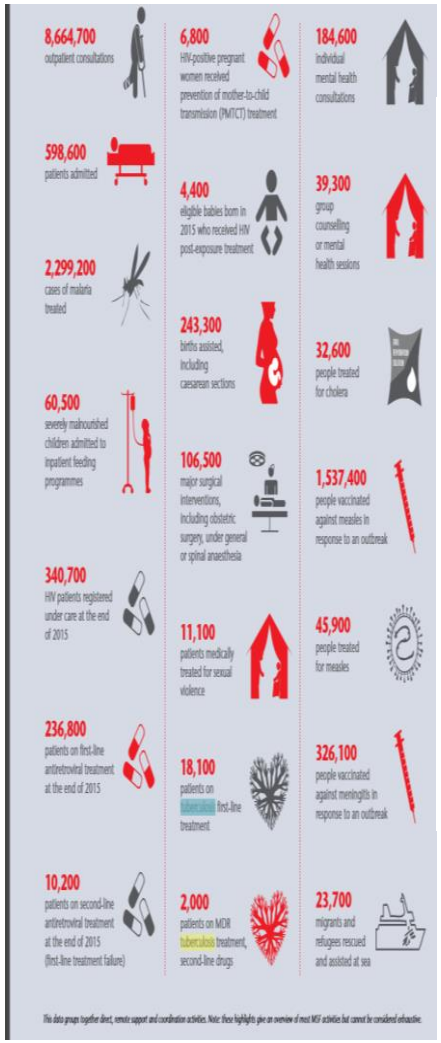
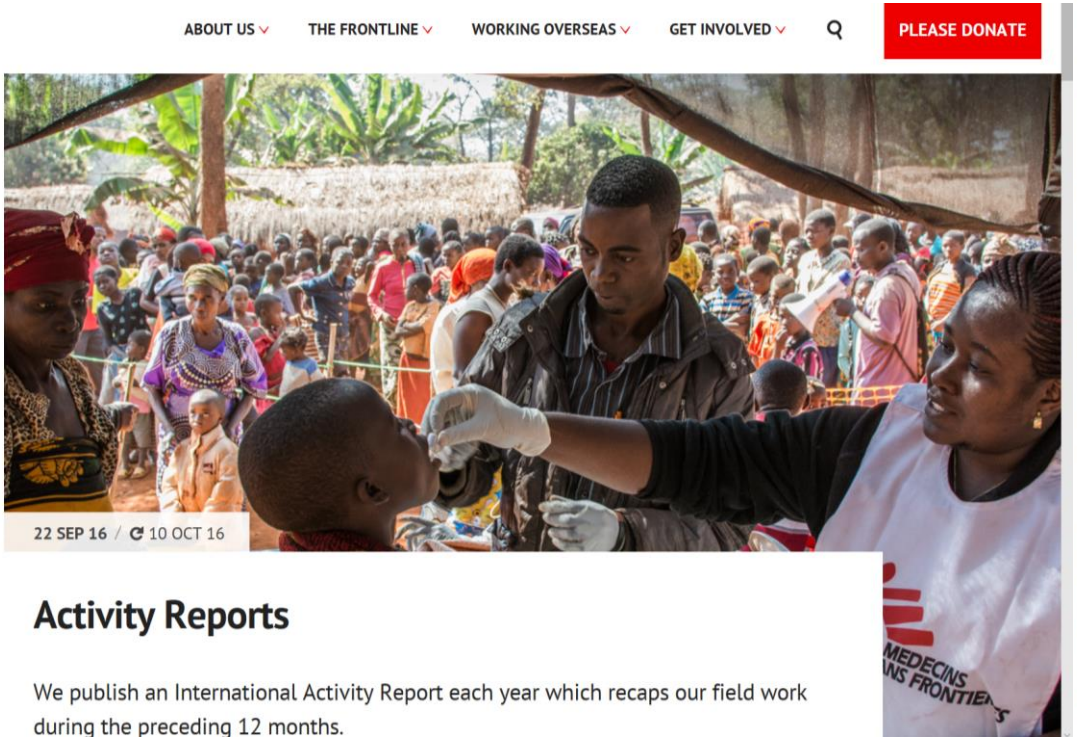
TB ALLIANCE
GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

MSF


8,664,700
outpatient consultations
598,600
patients admitted
2,299,200
cases of malaria treated
60,500
severely malnourished children admitted to inpatient feeding programmes
340,700
HIV patients registered under care at the end of 2015
236,800
patients on first-line antiretroviral treatment at the end of 2015
10,200
patients on second-line antiretroviral treatment at the end of 2015 (first-line treatment failure)
6,800
HIV-positive pregnant women received prevention of mother-to-child transmission (PMTCT) treatment
4,400
eligible babies born in 2015 who received HIV post-exposure treatment
243,300
births assisted, including caesarean sections
106,500
major surgical interventions, including obstetric surgery, under general or spinal anaesthesia
11,100
patients medically treated for sexual violence
18,100
patients on tuberculosis first-line treatment
2,000
patients on MDR tuberculosis treatment, second-line drugs
184,600
individual mental health consultations
39,300
group counselling or mental health sessions
32,600
people treated for cholera
1,537,400
people vaccinated against measles in response to an outbreak
45,900
people treated for measles
326,100
people vaccinated against meningitis in response to an outbreak
23,700
migrants and refugees rescued and assisted at sea
This data groups together direct, remote support and coordination activities. Note: these highlights give an overview of most MSF activities but cannot be considered exhaustive.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Activity Reports
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24 Activities by country

MSF

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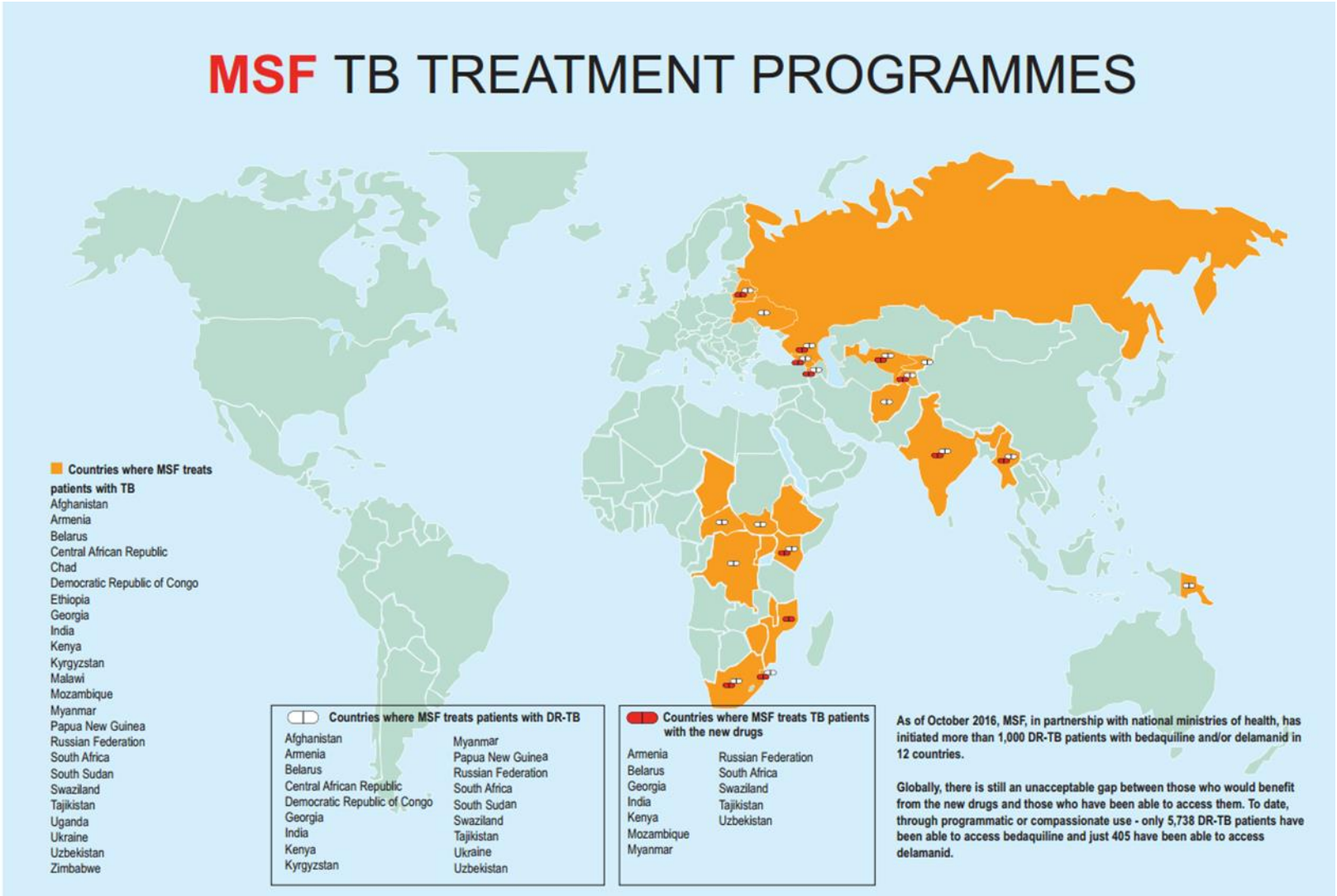

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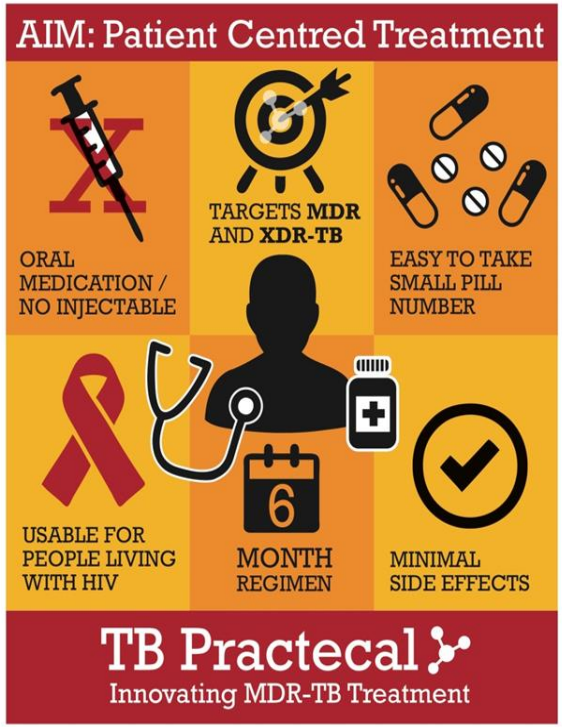
Principles for designing future regimens for multidrug-resistant tuberculosis

Grania Brigden,[a] Bern-Thomas Nyang'wa,[b] Philipp du Cros,[b] Francis Varaine,[c] Jennifer Hughes,[d] Michael Rich,[e] C Robert Horsburgh Jr,[f] Carole D Mitnick,[g] Eric Nuermberger,[h] Helen McIlleron,[i] Patrick PJ Phillips[j] & Manica Balasegaram[a]

- 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

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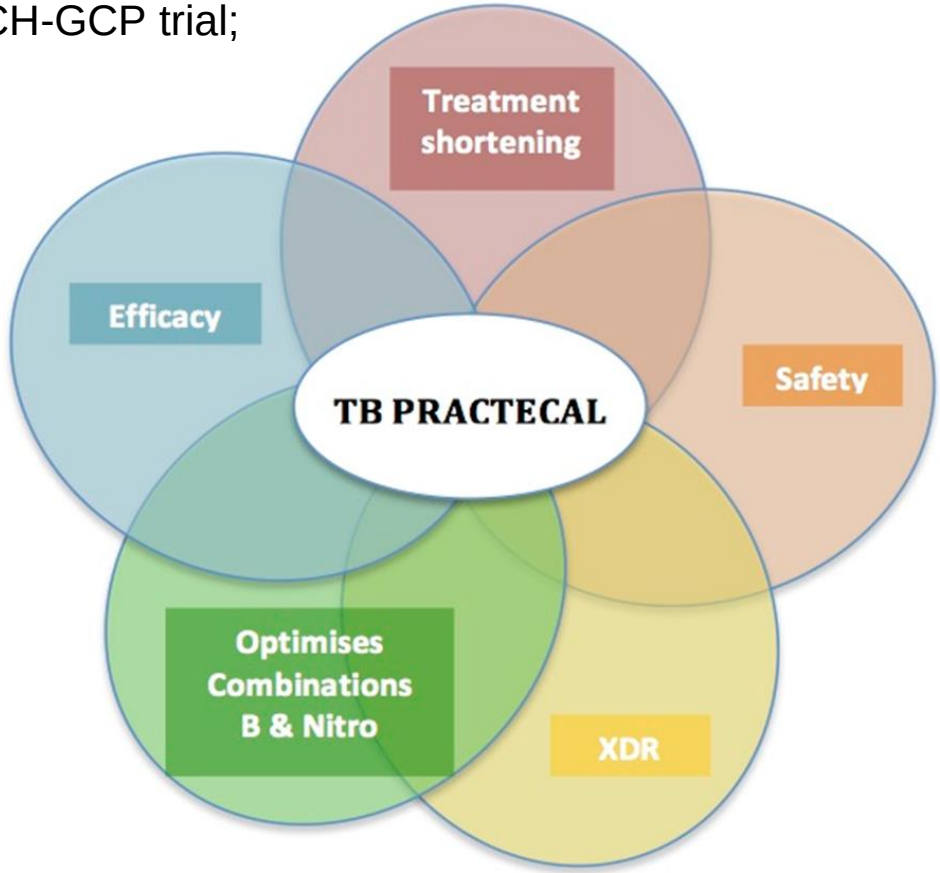
- Identify a new regimen(s) for M/XDR-TB that is radically shorter, tolerable, effective and feasible to scale up through an ICH-GCP trial;
- Target WHO policy change



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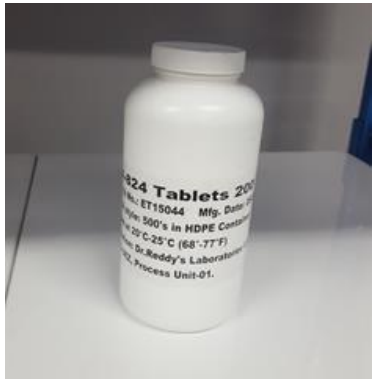
Investigational arms:

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

Stage 1

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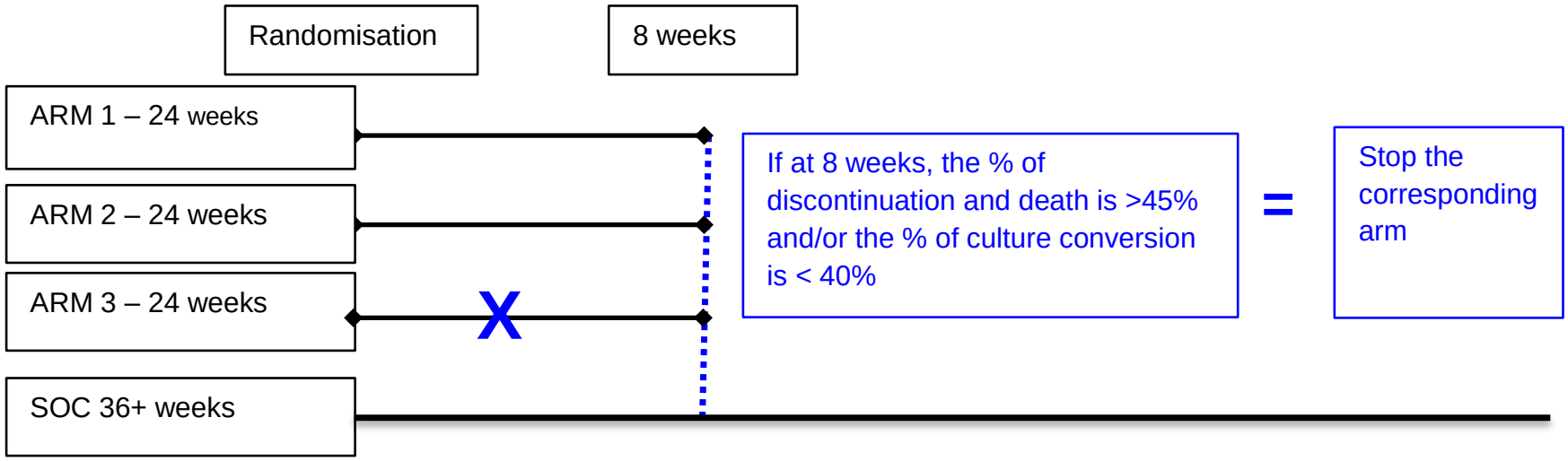
Identify regimens containing bedaquiline and pretomanid for further evaluation based on safety and efficacy outcomes after 8 weeks

Stage 1



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Stage 2

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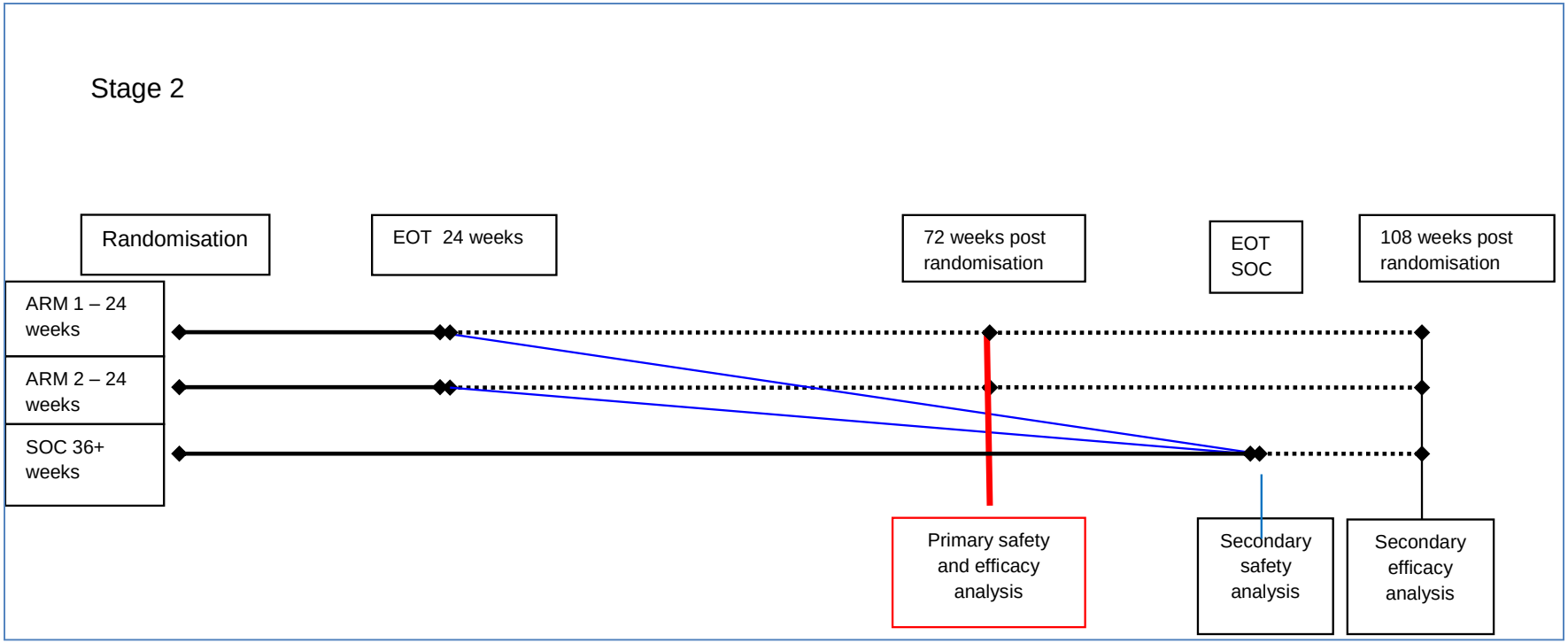
Evaluate the safety and efficacy of the experimental regimens containing bedaquiline and pretomanid compared with the SOC at 72 weeks post-randomisation.



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Progress update

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- 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

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Sub-studies

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

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collaborators

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DOCTORS WITHOUT BORDERS

Sponsor + clinical ops

THINK

sites

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Statistics

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Developers of pretomanid

Swiss TPH
Swiss Tropical and Public Health Institute
Schweizerisches Tropen- und Public Health-Institut

External Monitor

TDR For research on diseases of poverty
UNICEF • UNDP • World Bank • WHO

Overall Trial Support

DNDi
Drugs for Neglected Diseases initiative

Data management

UCL

Laboratory monitors

ERT

Cardiac safety