MDR-TB Current status

Stellah Mpagama

Background

Tanzania stated MDR-TB case management in Nov 2009

KNTH

Capacity building UCSF

Scaling up to

Regional referral hospital

2015 at least 6

Regional Hospitals

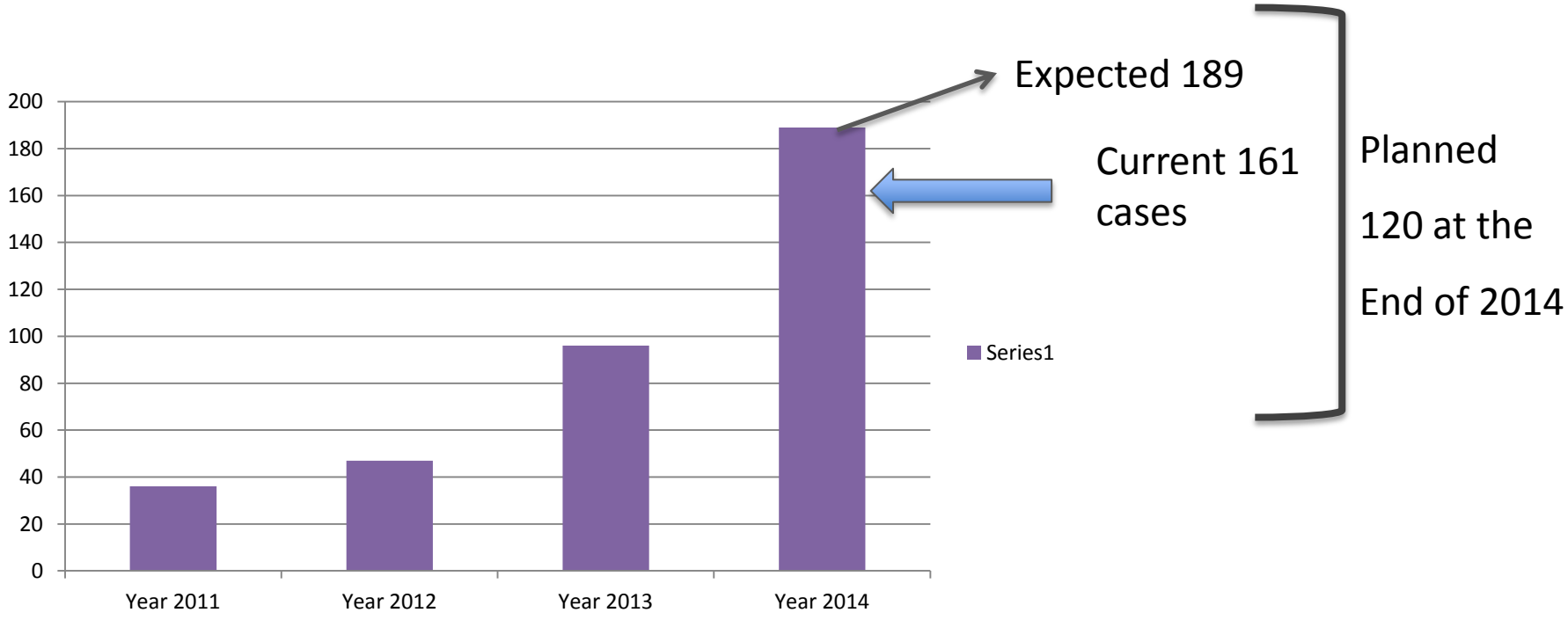
HSSP III 2009 - 2015

Background

From Nov 2009 until yesterday

– admitted 339 MDR-TB patients

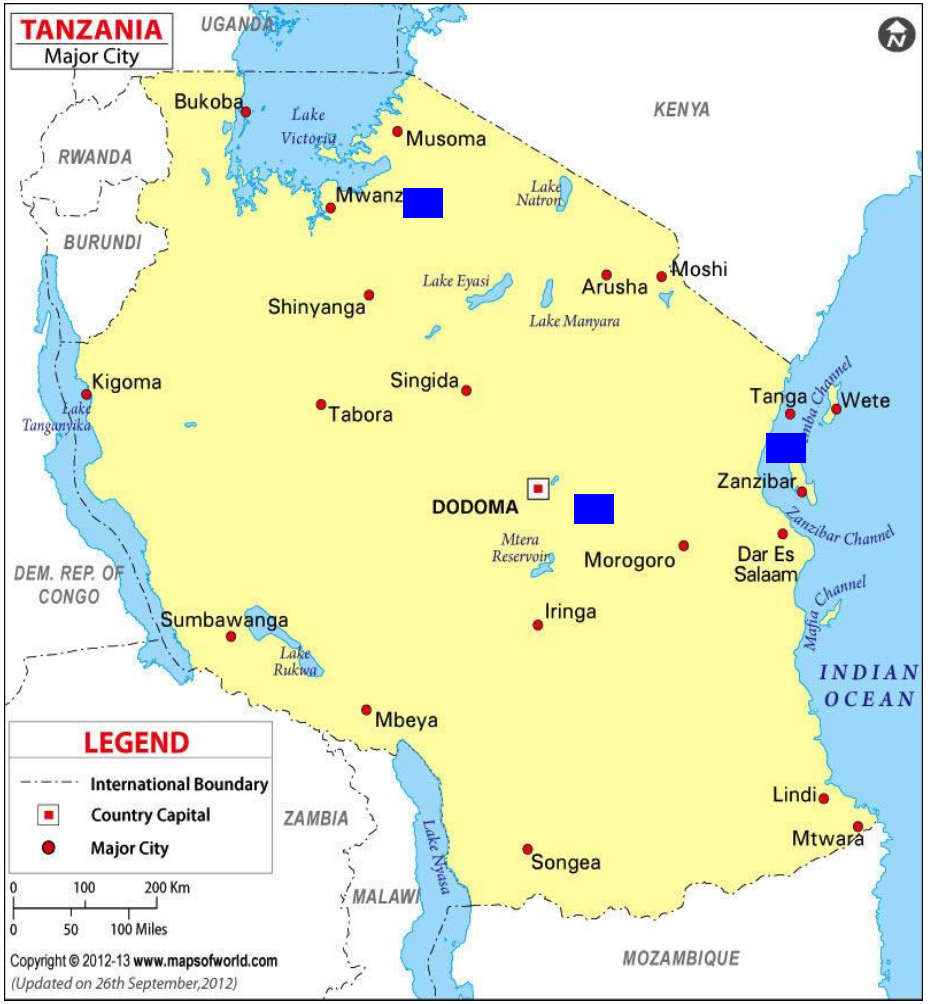
MDR-TB cases reported for treatment at Kibong'oto hospital



Scaling of MDR-TB Centers

HSSP 2009 – 2015

Scale MDR-TB to the regional referral hospitals



Scale depends

On the # of cases

diagnosed

Background

MDR-TB case management

Group 1	**First line oral anti-tuberculosis medicines:** Isoniazid, rifampicin, **pyrazinamide**, ethambutol
Group 2	**Flouroquinolones:** ofloxacin, levofloxacin, moxifloxacin
Group 3	**Injectable anti-tuberculosis medicines:** streptomycin, kanamycin, amikacin, capreomycin
Group 4	**Less effective second-line anti-tuberculosis medicines:** Ethionamide/prothionamide, cycloserine/terizidone, P-aminosalicylic acid (acid/salt)
Group 5	**Less effective medicines or medicines for which clinical data are sparse:** clofazimine, amoxicillin with clavulanate, linezolid, imipenem, clarithromycin, high dose isoniazid, thiacetazone

Intensive phase = 8months

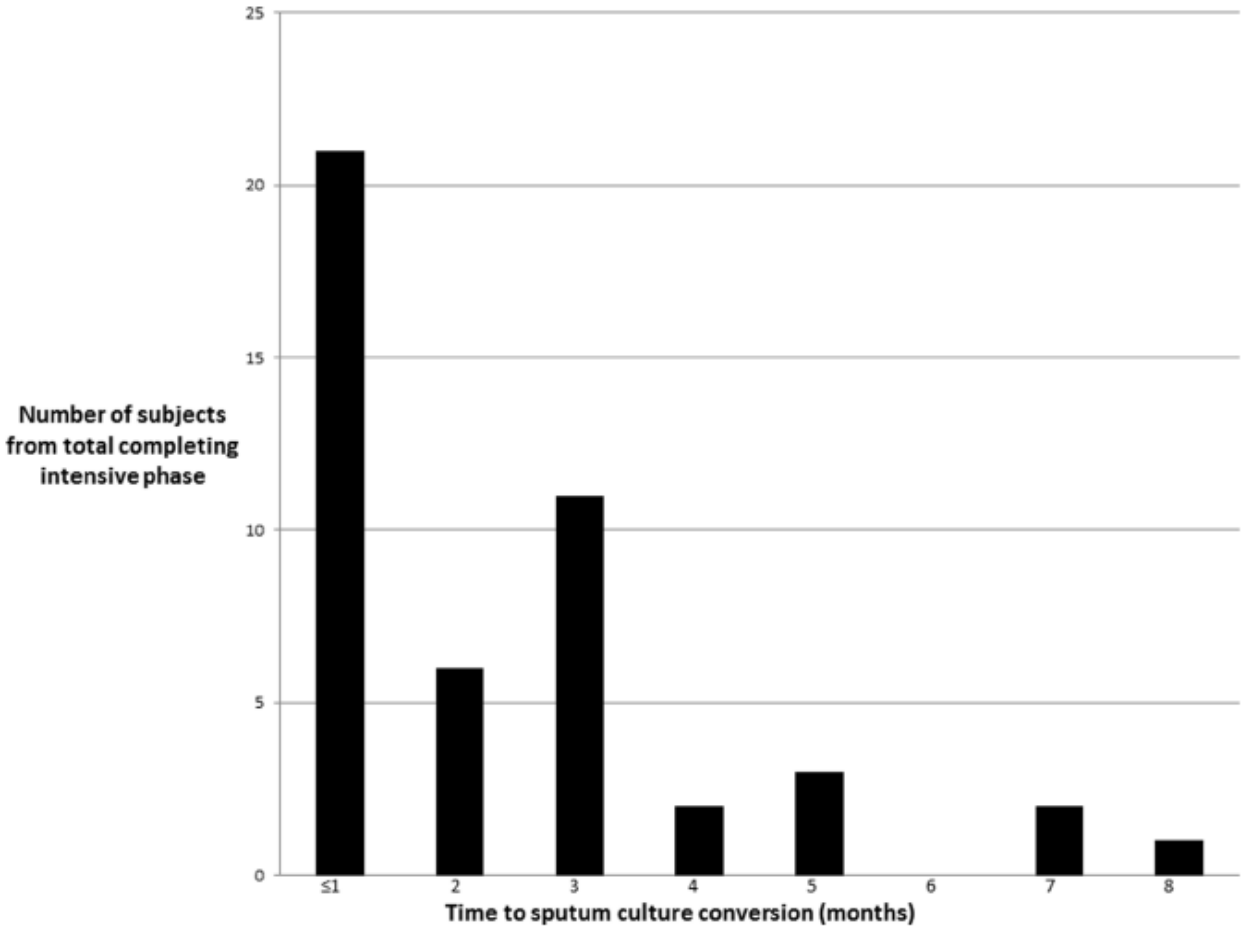
Continuation phase = 12-18

Microbiological monitoring
Monthly culture/smear

Adverse events monitoring
Daily

Background

Distribution of culture conversion in MDR-TB Patients



Mpagama et al, PLoS ONE. 2013

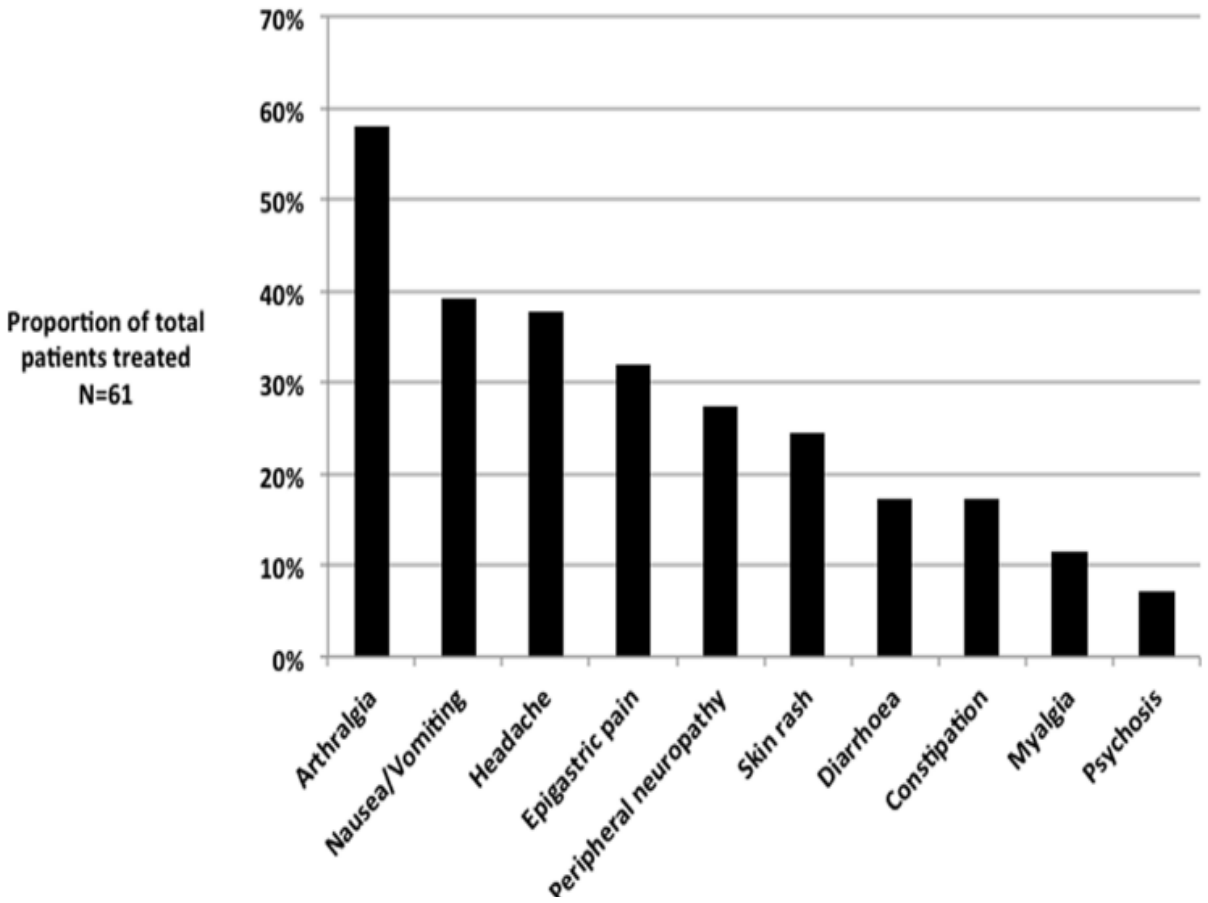
Drug Susceptibility Testing of MTB from MDR-TB Patients

Characteristics	Sub-category	Number
Secondline(DST) resistant MTB	XDR-TB	2 (13%)
	Ethionamide	6 (40%)
	PAS	5 (23%)
	Moxifloxacin	1 (5%)
	Amikacin/Kanamycin	2(10%)

Mpagama et al, BMC Infect Dis 2013

Treatment monitoring

Distribution of adverse events (reported top 10 events



Ototoxicity = 3 (1%)

Nephrotoxicity = (2%)

Both nephrotoxicity Ototoxicity = (1)

Mpagama et al, PLoS ONE. 2013

Challenges in diagnosis

Estimate of MDR-TB Burden in 2012 (WHO Report 2013)

TB case notification 2012	Prevalence of MDR-TB	# Tested	MDR-TB diagnosed
New (61,126)	1.1%	639 (3%)	12
Retreatment (2, 766)	5.9%	108 (4%)	12

Challenges in MDR-TB treatment

Treatment Regimen

- Lengthy
- Complex
- Poor tolerated

Bulletin of the World Health Organization

Principles for designing future regimens for multidrug-resistant tuberculosis

Bridgden et al , 2013

- Regimen contain at least 1 new class of drug
- Treat both MDR or XDR TB
- Contain 3 -4 effective drugs from a different drug class
- Exclusive oral delivery

Bulletin of the World Health Organization

Principles for designing future regimens for multidrug-resistant tuberculosis

- Simple dosing schedule
- Good side effect profile that allow limited monitoring
- Minimal interaction with ART drugs
- Maximal duration of 6 months

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Am J Respir Crit Care Med. 2010 Sep 1;182(5):684-92. doi: 10.1164/rccm.201001-0077OC. Epub 2010 May 4.

Short, highly effective, and inexpensive standardized treatment of multidrug-resistant tuberculosis.

Van Deun A[1], Maug AK, Salim MA, Das PK, Sarker MR, Daru P, Rieder HL.

Author information

Abstract

RATIONALE: Based on expert opinion, the global guidelines for management of multidrug-resistant tuberculosis impose lengthy and often poorly tolerated treatments.

OBJECTIVES: This observational study evaluates the effectiveness of standardized regimens for patients with proven multidrug-resistant tuberculosis previously untreated with second-line drugs in low-income countries.

METHODS: Consenting patients were sequentially assigned to one of six standardized treatment regimens. Subsequent cohorts were treated with regimens adapted according to results in prior cohorts. The study was designed to minimize failure and default while reducing total treatment duration without increasing relapse frequency.

MEASUREMENTS AND MAIN RESULTS: We report the treatment outcome of all patients with laboratory-confirmed, multidrug-resistant tuberculosis enrolled from May 1997 to December 2007. The most effective treatment regimen required a minimum of 9 months of treatment with gatifloxacin, clofazimine, ethambutol, and pyrazinamide throughout the treatment period supplemented by prothionamide, kanamycin, and high dose isoniazid

1997 - 2007

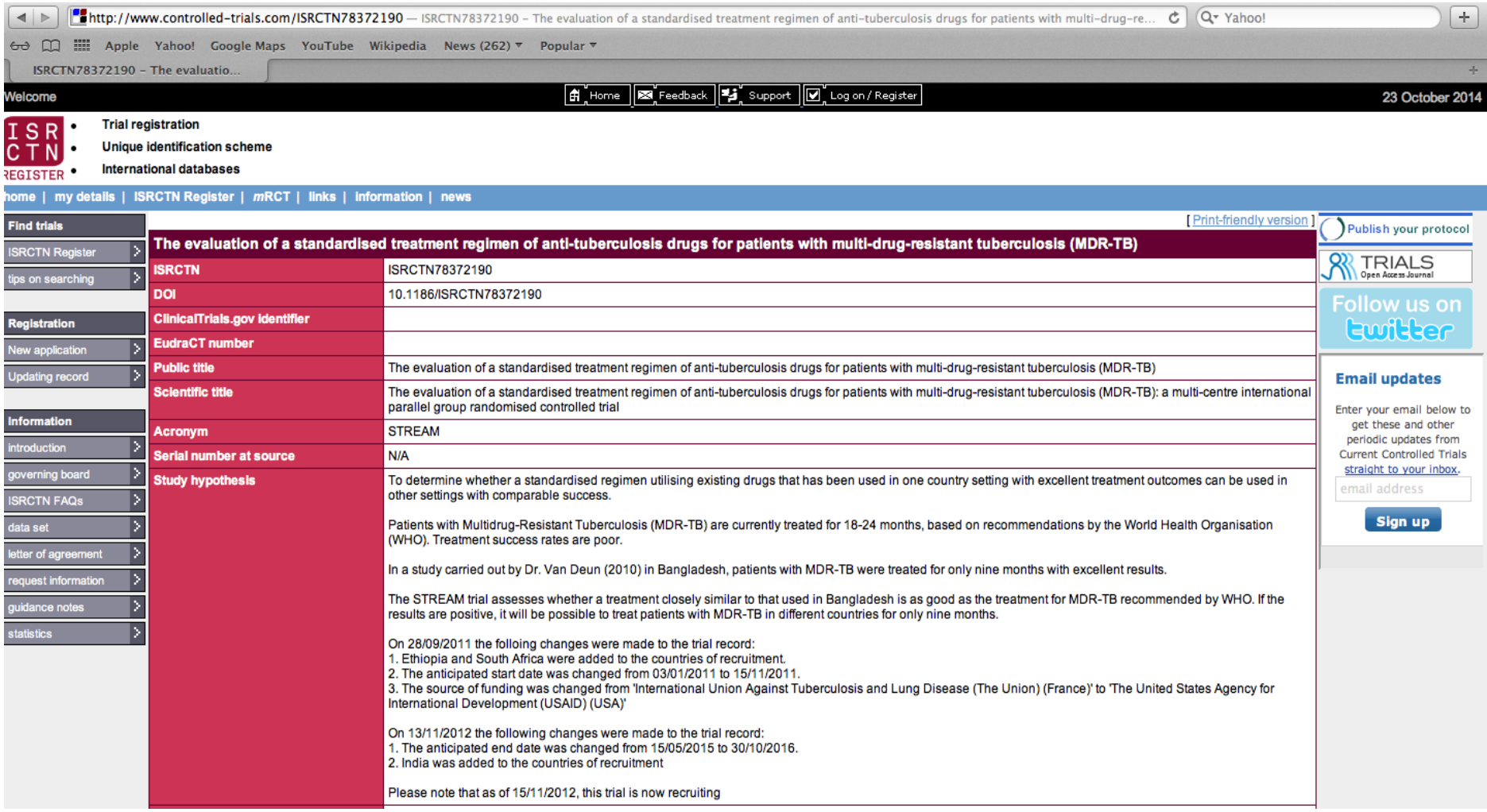
Treated 207

Short regimen 9 month

Containing Gatifloxacin, Clofazimine, Ethambuto, Pyrazinamide throughout

Supplemented by Kanamycin, High dose Isoniazid and Prothionamide for a minimum of 4/12

Relapse free 87.9%



-Ethiopia
-South Africa

Not yet recruiting	**A Phase 2 Open Label Partially Randomized Trial to Evaluate the Efficacy, Safety and Tolerability of Combinations of Bedaquiline, Moxifloxacin, PA-824 and Pyrazinamide in Adult Subjects With Drug-Sensitive or Multi Drug-Resistant Pulmonary Tuberculosis.** **Condition:** Tuberculosis **Interventions:** Drug: Pa-824; Drug: bedaquiline; Drug: moxifloxacin; Drug: pyraziminide; Drug: isoniazid, rifampicin, pyrazinamide and ethambutol combination tablet


Thank you for your attention