

Culture conversion and treatment outcomes of a short standardized regimen for multidrug resistant tuberculosis patients in Mozambique

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Background



- Mozambique is a country with a high prevalence of both HIV and TB (WHO 2016):
 - HIV prevalence among adults: 12.3% [10.6% - 13.9%]
 - TB incidence: 551/100000 (356-787)
 - Estimated % of TB cases with MDR/RR-TB
 - 3.7% (2.4 – 5.0) among new cases
 - 20% (2.1–37) among previously treated
-  Regions where MSF has projects
 Cities, towns or villages where MSF works

Short standardized course (DR-SSC) for the treatment of MDR-TB

- Based on observational cohorts in Bangladesh, and Western Africa, WHO made a recommendation to use short standardized regimen as a treatment option for patients resistant to R and H but still sensitive to all other drugs of the regimen, also mentioning that role of the SSR in treatment of HIV-positive patients is unclear
- Recent results of the Stage 1 STREAM trial shows very comparable success rates between shortened regimen and individualised 24 months regimen, although failed to demonstrate formally non-inferiority
- A SSC MDR-TB treatment regimen was prescribed under routine program conditions in this context of high TB prevalence and high HIV co-infection rates, and consisted of:
 - Intensive phase:** Pyrazinamide + Ethambutol + Isoniazid + Moxifloxacin + Kanamycin + Prothionamide + Clofazimine for at least 4 months and until one negative culture documented with a maximum of 6 months duration
 - Continuation phase:** Pyrazinamide + Ethambutol + Moxifloxacin + Prothionamide + Clofazimine for 5 months

Methods

Design and population

- Design**
 - A prospective interventional non-controlled cohort study in Maputo
- Population**
 - Patients with active pulmonary tuberculosis or case of PTB and EPTB disease diagnosed as rifampicin resistant by Xpert MTB/RIF and phenotypical DST, or children suspected of MDR-TB without bacteriological confirmation but documented as a close contact of a patient with confirmed MDR-TB
- Exclusion criteria**
 - History of prior anti-TB treatment with second line drugs for one month or more
 - Patients with probable or proven involvement of meninges or bones
 - Baseline contraindications to any medications
 - Patient in an advanced stage of a concomitant disease not suitable for anti-TB treatment
 - Pregnancy or breastfeeding
- Secondary exclusion**
 - Phenotypic DST doesn't confirm the initial rifampicin resistance result
 - Patient harbour strains resistant to injectable agents and fluoroquinolones (XDR-TB)
 - Patients resistant to fluoroquinolones and patients who harbour strains resistant to both injectable agents (Km and Cm) will continue the DR-SSC regimen if, once the DST results are available, their clinical condition has improved compared to baseline, otherwise withdrawn

Analysis

- Culture conversion (two consecutive negative cultures) at 6 months of treatment stratified by HIV-status and baseline resistance profile
- Treatment outcomes of the first patients enrolled in the study stratified by HIV-status and baseline resistance profile

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Results

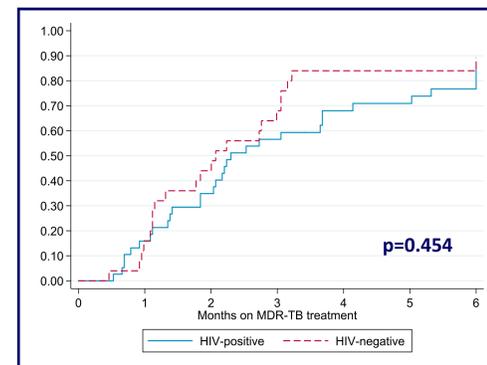
Patients characteristics (N=150 patients included)

	HIV-negative (N=55)	HIV-positive (N=95)	p-value	Total N(%)
Gender			0.061	
Male	37 (67.3)	49 (51.6)		86 (57.3)
Female	18 (32.7)	46 (48.4)		64 (42.7)
Age			<0.001	
Median [IQR]	26 [22 – 35]	33 [30 – 42]		32 [25 – 40]
<35	41 (74.5)	49 (52.1)		90 (60.4)
≥35	14 (25.5)	45 (47.9)		59 (39.6)
BMI			0.756	
Median [IQR]	18.4 [16.4 – 19.6]	17.6 [16.4– 19.9]		17.9 [16.4 – 19.8]
<18 kg/m ²	25 (45.4)	50 (53.2)		75 (50.3)
≥18 kg/m ²	30 (54.6)	44 (46.8)		74 (49.7)
DST at initiation				
Z resistant (N=78)	17 (54.8)	25 (53.2)	0.886	42 (53.8)
Km resistant (N=74)	0	1 (2.2)	-	1
Cm resistant (N=74)	0	0	-	0
Ofx resistant (N=74)	3 (10.3)	4 (8.9)	0.835	7 (9.5)

- 51 (53.7%) of HIV-positive were already on ART at MDR-TB treatment initiation
- Median time of ART: 7.8 months [IQR 1.2-52.7]
- Median CD4 count: 226 cells/μL [IQR 115-348]

Culture conversion: 63 patients eligible for this analysis

	Culture conversion at month 6, n(%)
Overall (N=63)	49 (77.8)
HIV	
Negative (N=25)	21 (84.0)
Positive (N=38)	28 (73.7)
Ofx resistance	
Susceptible (N=46)	36 (78.3)
Resistant (N=4)	2 (50.0)
Z resistance	
Susceptible (N=26)	22 (84.6)
Resistant (N=25)	16 (64.0)



Culture conversion according to HIV status

Treatment outcomes: 63 patients eligible for this analysis

	Success n (%)	Death n (%)	Failure n (%)	LFU n (%)
Overall (N=63)	45 (71.4)	6 (9.5)	7 (11.1)	5 (7.9)
HIV				
Negative (N=22)	18 (81.8)	0	2 (9.1)	2 (9.1)
Positive (N=41)	27 (65.9)	6 (14.6)	5 (12.2)	3 (7.3)
Ofx resistance				
Susceptible (N=39)	28 (71.8)	4 (10.3)	4 (10.3)	3 (7.7)
Resistant (N=4)	1 (25.0)	0	3 (75.0)	0
Z resistance				
Susceptible (N=23)	16 (69.6)	3 (13.0)	2 (8.7)	2 (8.7)
Resistant (N=21)	14 (66.7)	1 (4.8)	5 (23.8)	1 (4.8)

Among HIV-positive patients, 6 died:

- 3 died < 1 month of treatment: 1 not on ART and 1 received ART < 1 month
- 3 died after 6 months of MDR-TB treatment
- Median BMI: 19.1 kg/m² [IQR 17.0-22.0]

Discussion

- High rate of culture conversion and higher success rate than the conventional MDR-TB treatment are reported
- HIV-positive patients seem to have a lower success rate mainly due to a higher death rate and a slightly higher failure rate
- High proportion of treatment failure among fluoroquinolone-resistant patients stresses the need to use rapid molecular testing in order to adapt their treatment and exclude them from the shortened regimen