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BACKGROUND

Setting



- Mozambique is a country with a high prevalence of both HIV and TB
 - HIV prevalence among adults in 2015: 10.5% [8.3% - 13.3%]
 - TB incidence in 2015: 551/100000 population
- Prevalence of MDR-TB is not very high but the burden of DR-TB is high due to the number of patients with TB, and the country has a very limited capacity to respond
- Regions where MSF has projects
- Cities, towns or villages where MSF works

Current standard treatment for MDR-TB

- Current standard treatment scheme for MDR-TB:
 - 8 months of Kanamycin, Levofloxacin, Ethionamide, Cycloserine, Pyrazinamide, Ethambutol, followed by
 - 12 months of Levofloxacin, Ethionamide, Cycloserine, Ethambutol
- Patients with XDR-TB receive a similar regimen with Capreomycin instead of Kanamycin, Prothionamide instead of Ethionamide, and PAS

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

- The results from an observational study in a cohort of patients with MDR-TB without previous treatment with second-line drugs in Bangladesh showed very high rates of MDR-TB treatment success using a standardized regimen of 9-11 months of duration
- A standardized short-course 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 the Health Districts of Chamanculo, Mavalane and Jose Macamo in Maputo, Mozambique
- 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 will be excluded from the study even if they have also pulmonary TB because of the different complexity of their management
 - Baseline contraindications to any medications where benefits of the regimen do not outweigh the risks as judged by the study doctor (including ventricular arrhythmia or QTcF interval >450ms)
 - 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 2, 4 and 6 months of treatment stratified by HIV-status and fluoroquinolone baseline resistance
- Treatment outcomes of the first patients enrolled in the study stratified by HIV-status and fluoroquinolone baseline resistance

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RESULTS

Patients characteristics

Characteristics (N=126)	HIV-negative (N=42)	HIV-positive (N=84)	P-value	Total N(%)
Gender			0.002	
Male	33 (78.6)	42 (50.0)		75 (59.5)
Female	9 (21.4)	42 (50.0)		51 (40.5)
Age			0.002	
Median [IQR]	26 [22 - 37]	33 [30 - 41]		32 [26 - 41]
<35	31 (73.8)	45 (53.6)		76 (60.3)
≥35	11 (26.2)	39 (56.4)		50 (39.7)
BMI			0.995	
Median [IQR]	17.9 [16.1 - 19.5]	17.7 [16.96 - 20.3]		17.8 [16.4 - 19.8]
<18 kg/m ²	22 (52.4)	43 (52.4)		65 (52.4)
≥18 kg/m ²	20 (47.6)	39 (47.6)		59 (47.6)

DST at treatment initiation

	HIV-negative (N=42)	HIV-positive (N=84)	P-value	Total N(%)
Z-resistant (N=48)	11 (57.9)	12 (41.4)	0.263	23 (47.9)
Eto-resistant (N=43)	9 (60.0)	12 (42.9)	0.284	21 (48.8)
SLIDs-resistant (N=44)				
Km	0	1 (3.6)		1 (2.3)
Cm	0	0		0
Both Km and Cm	0	0		0
FQ-resistant			0.552	
Ofx (N=44)	2 (12.5)	2 (7.1)		4 (9.1)
Mfx (N=41)	0	0		0

- 59 (70.2%) of HIV-positive received ART at MDRTB treatment start

Culture conversion

- Patients eligible for this analysis:**
 - Started treatment at least 8 months before censoring date of database (≤31 December 2016)
 - Culture positive at treatment initiation
- 54 patients eligible for culture conversion analysis**

	Culture conversion at month 2 n(%)	Culture conversion at month 4 n(%)	Culture conversion at month 6 n(%)
Overall (N=54)	16 (29.6)	31 (57.4)	34 (63.0)
HIV			
Negative (N=18)	6 (33.3)	13 (72.2)	14 (77.8)
Positive (N=36)	10 (27.8)	18 (50.0)	20 (55.6)
Ofx resistance			
Susceptible (N=39)	13 (33.3)	24 (61.5)	26 (66.7)
Resistant (N=4)	1 (25.0)	2 (50.0)	2 (50.0)
Z resistance			
Susceptible (N=24)	8 (33.3)	14 (58.3)	17 (70.8)
Resistant (N=20)	6 (30.0)	12 (60.0)	12 (60.0)
Eto resistance			
Susceptible (N=22)	5 (22.7)	13 (59.1)	15 (68.2)
Resistant (N=20)	8 (40.0)	12 (60.0)	12 (60.0)

Treatment outcomes

- Eligible for analysis:
 - Started treatment at least 10 months before censoring date of database (≤31 October 2016)
 - Have an outcome assessed
- 43 patients eligible for treatment outcome analysis**

	Success n (%)	Death n (%)	Failure n (%)	LFU n (%)	p-value
Overall	29 (65.9)	4 (9.1)	6 (13.6)	5 (11.4)	
HIV					0.068
Negative (N=17)	14 (82.3)	0	1 (5.9)	2 (11.8)	
Positive (N=27)	15 (55.6)	4 (14.8)	5 (18.5)	3 (11.1)	
Ofx resistance					0.096
Susceptible (N=31)	21 (67.7)	3 (9.7)	3 (9.1)	4 (12.9)	
Resistant (N=4)	1 (25.0)	0	3 (75.0)	0	

Treatment outcomes Excluding lost to follow-up

	Success n (%)	Death n (%)	Failure n (%)	p-value
Overall	29 (74.4)	4 (10.3)	6 (15.4)	
HIV				0.032
Negative (N=15)	14 (93.3)	0	1 (6.7)	
Positive (N=24)	15 (62.5)	4 (16.7)	5 (30.8)	
Ofx resistance				0.030
Susceptible (N=27)	21 (77.8)	3 (11.1)	3 (11.1)	
Resistant (N=4)	1 (25.0)	0	3 (75.0)	

DISCUSSION

- This study on the first MDR-TB patients receiving short course regimen in Mozambique shows a high rate of culture conversion and a higher success rate (65.9%) than the standard MDR-TB treatment
- However, HIV-positive patients seem to have a slower conversion, and a lower success rate mainly due to early deaths and treatment failures
- Resistance to fluoroquinolone seems also to be associated with a lower success rate. This confirms the WHO recommendation to exclude them from the short course regimen and stresses the need to use rapid molecular testing for FQ resistance