Outcomes with a shorter multidrug-resistant tuberculosis regimen from Karakalpakstan, Uzbekistan

Online Supplementary Appendix

Table S1: Standardised shorter MDR-TB regimen and weight-based dosing

	Intensive Phase (4-6 months)	Continuation Phase (5 months)
Duration	Pyrazinamide + ethambutol + isoniazid + moxifloxacin + capreomycin (kanamycin) + prothionamide + clofazimine for at least four months and smear negative. If smear positive at four months, continue until first sputum culture is negative, maximum six months (when five-month culture result becomes available.)	Pyrazinamide + ethambutol + moxifloxacin + prothionamide + clofazimine for five months, starting after four months or first negative culture, whichever is later.
Description	Seven drugs; includes injectable & high dose isoniazid	Five drugs; only oral drugs in standard dosages.

Dosing of standardised MDR-TB drugs for adults and adolescents >25 kg

Drug	**Frequency**	**Weight range in Kg**			
		<25	**25-32**	**33-50**	**>50***
Isoniazid (H)	Once daily	15-20 mg/kg	300mg	400mg	600mg*
Pyrazinamide (Z)	Once daily	30-40 mg/kg	1000mg	1600mg	2000mg
Ethambutol (E)	Once daily	15-25 mg/kg	600mg	800mg	1200mg
Moxifloxacin (Mfx)	Once daily	7.5-10 mg/kg	400mg	400mg	400mg
Prothionamide (Pto)	Once daily #	15/25 mg/kg	250mg	500mg	750mg*
Clofazimine (Cfz)	Once daily	2-3 mg/kg	100mg	100mg	100mg
Capreomycin (Cm)$	Once daily		15mg/kg		

*For Prothionamide and isoniazid highest doses are given above 55kg

Prothionamide can be given in divided doses in the intensive phase if maximum doses are used and the patient has major gastrointestinal side effects not responding to anti-emetics.

$ If sensitive to kanamycin and not taken kanamycin previously then change to kanamycin at the same dose.

Table S2: Outcome definitions for shorter MDR-TB regimen

Outcome	Definition
Cure	Cure was defined as an MDR-TB patient who completed the treatment according to protocol and has at least four negative cultures from samples collected at least 30 days apart within the final five months of treatment. If there was a positive culture then a minimum of three consecutive negative cultures taken at least 30 days apart in the final 3 months of treatment was required for cure.
Treatment complete	Defined as an MDR-TB patient who completed treatment according to the protocol, but did not meet the definition for cure because of lack of sufficient bacteriological results.
Death	Defined as a patient who died for any reason during the course of MDR-TB treatment, or during one year's follow-up, and not already classified as having treatment failure prior to death.
Treatment failure	Failure was defined if a patient met one of three criteria: 1. Failure to culture convert: did not achieve negative culture by the end of month five, had two positive cultures during the continuation phase or one positive culture during the last three months of treatment. 2. Resistance amplification: amplification of resistance to either ofloxacin or to two injectables (capreomycin and kanamycin) on a sputum sample collected 30 days or more after the start of treatment. 3. Clinical decision due to lack of clinical response, drug toxicity or intolerance.
Lost to follow-up (LTFU) during treatment	Defined as treatment interruption for two or more consecutive months, for any reason.
LTFU post treatment	An MDR-TB patient with an outcome at the end of treatment of either treatment cure, complete, treatment outcome "other", or transfer out, who is non-contactable during the twelve-month post-treatment period (as assessed at the end of 12 +/-3 months).
Recurrence-free cure	An MDR-TB patient who meets the criteria of cured, or completed short course of treatment, and remains asymptomatic at the end of the follow-up period (one year after treatment completion).
Recurrence	An MDR-TB patient who meets the criteria of cured, or completed SR, and at any time during the follow up period (first year after treatment completion) is subsequently diagnosed with at least one sample of bacteriologically positive RR-TB by culture and DST.