A regimen containing bedaquiline and delamanid compared to bedaquiline alone in patients with drug resistant tuberculosis with poor prognosis

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Table S1: Culture conversion status of patients who received bedaquiline-based and those who received bedaquiline-delamanid combination regimens at different time points during treatment. Data is n (%).

	Patients who received bedaquiline-based regimen (n=82)	Patients who received delamanid-bedaquiline combination regimen (n=40)	p-values
Positive at baseline	52/82 (63.4)	26/40 (65.0)	0.86
Culture Conversion at 2 months	25/38 (65.8)	13/23 (56.5)	0.47
Culture Conversion at 6 months	33/36 (92.5)	18/22 (81.8)	0.26
Culture Conversion at 12 months	27/31 (87.1)	13/15 (86.7)	0.97

Patients who were culture negative at the point of recruitment were excluded from the analysis at 2, 6 and 12 months.

Table S2: Comparison of treatment outcomes between patients who received bedaquiline-based regimen and those who received delamanid-bedaquiline combination regimen. Data is (n)%

	Patients who received bedaquiline-based regimen (n=82)	Patients who received delamanid-bedaquiline combination regimen (n=40)	p-values
XDR-TB	n=67	n=19	
Favourable outcome	44 (65.7)	14 (73.7)	0.51
Unfavourable Outcome	23 (34.3)	5 (26.3)	
PRE-XDRTB	n=10	n=15	
Favourable outcome	4 (40)	9 (60)	0.32
Unfavourable Outcome	6 (60)	6 (40)	
MDR-TB	n=5	n=6	
Favourable outcome	4 (80)	4 (66.67)	0.62
Unfavourable Outcome	1 (20)	2(33.33)	

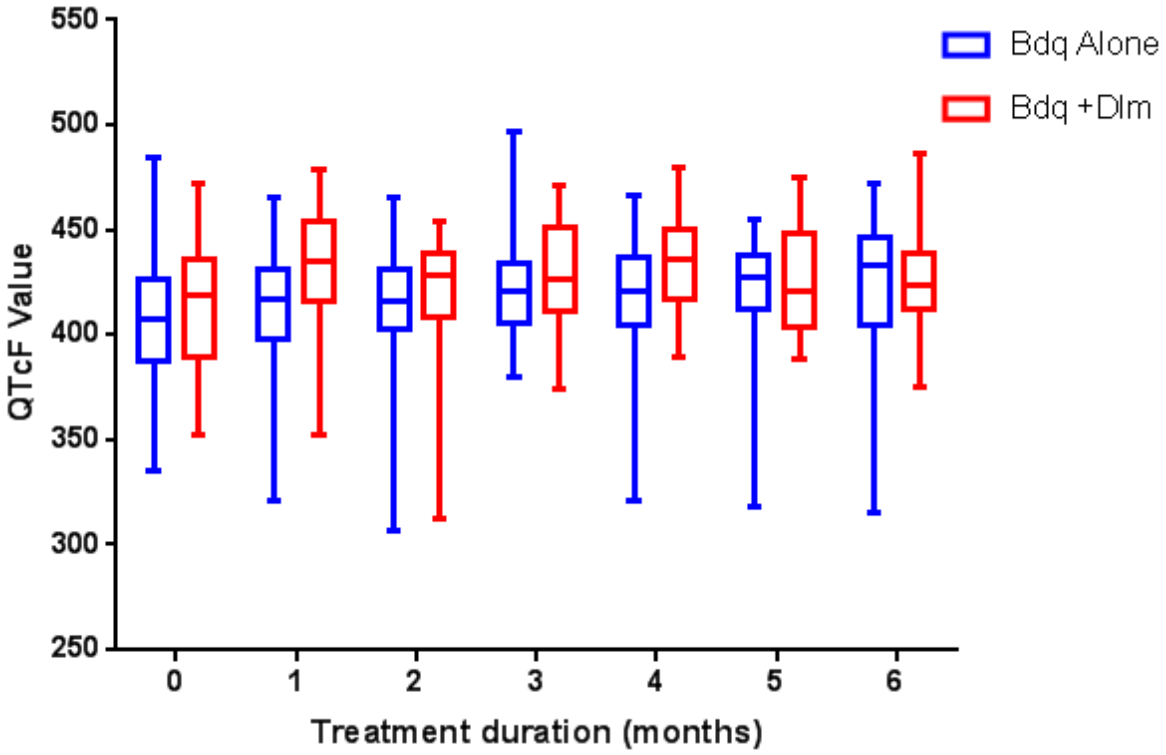


Figure S1: QTcF values at different time points during treatment with either bedaquiline-based regimen or delamanid-bedaquiline combination regimen. Boxes represent the median and IQR, while error bars represent range values

Table S3: (A) Univariate Cox proportional hazard model for developing unfavourable outcome in the HIV-infected patients

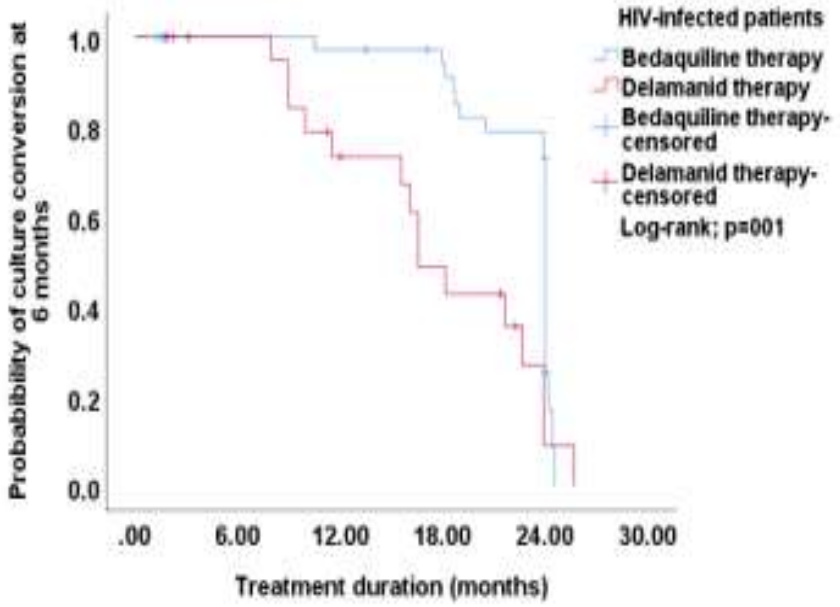
Variables	Hazard ratio (95% C.I)	p-value
Age (years)	1.013 (0.960- 1.068)	0.64
Gender (male)	1.173 (0.479- 2.871)	0.73
Weight (kg)	0,981 (0.945- 1.018)	0.31
Age at admission < 50 years	0.206 (0.058- 0.734)	0.02
Previous TB treatment	1.808 (0.748- 4.367)	0.19
Days of admission	0.993 (0.986- 0.999)	0.03
Clofazimine treatment	0.596 (0.080- 4.467)	0.62
Delamanid treatment	0.785 (0.485- 1.269)	0.32
Moxifloxacin treatment	1.262 (0.484- 3.293)	0.64
Levofloxacin treatment	0.883 (0.116- 6.717)	0.88
Any fluoroquinolone	0.047 (0.000-10560)	0.63
Linezolid treatment	0.416 (0.056- 3.109)	0.39
Delamanid-bedaquiline treatment	0.651 (0.248- 1.706)	0.38
Number of medications	1.099 (0.847- 1.426)	0.48
Number of adverse events	1.137 (0.960-1.347)	0.14
5 likely effective drugs	0.684 (0.395- 1.183)	0.17
Resistant to >5 drugs	2.688 (0.762- 9.482)	0.12
TTP* < 7 days	1.709 (0.570- 5.119)	0.34
SMG$^{\#}$ > 2 plusses	2.270 (0.752- 6.847)	0.15
(B) Multivariate Cox proportional hazard model for unfavourable outcome		
Age at admission < 50 years	0.333 (0.079-1.396)	0.13
Resistant to >5 drugs	4.725 (1.041-21.43)	0.04
Previous TB treatment	2.181 (0.810- 5.871)	0.12
Days of admission	0.990 (0.982- 0.998)	0.02
5 likely effective drugs	0.465 (0.142- 1.520)	0.21
Number of adverse events	1.173 (0.949- 1.449)	0.14
SMG$^{\#}$ > 2 plusses	2.442 (0.690- 8.640)	0.17

Table S4: Adverse events reported by HIV-infected patients who received bedaquiline-based regimen and those who received delamanid-bedaquiline combination regimen. Data is n (%).

Adverse event	Patients who received bedaquiline alone (n=42)	Patients who received bedaquiline and delamanid (n=22)	p-values
Dizziness/disorientation	5 (11.9)	4 (18.2)	0.49
Psychosis	2 (4.8)	4 (18.2)	0.08
Blurred vision	1 (2.4)	2 (9.1)	0.23
Hearing loss	20 (47.6)	8 (36.4)	0.39
Hypothyroidism	4 (9.5)	2 (9.1)	0.96
Peripheral neuropathy	6 (14.3)	7 (31.8)	0.098
Anaemia	7 (16.7)	11 (50)	0.005*
Diarrhoea	3 (7.1)	4 (18.2)	0.18
Abdominal pain	8 (19.0)	1 (4.5)	0.11
Vomiting	11 (26.2)	4 (18.2)	0.47
Nausea	9 (21.4)	3 (13.6)	0.45
Elevated liver enzyme	15 (35.7)	8 (36.4)	0.96
Deranged renal function	12 (28.6)	8 (36.4)	0.52
Arthralgia	8 (19)	3 (13.6)	0.59

*95.5% of patients in the bedaquiline-delamanid group received linezolid in their regimen compared to 88.1% in the bedaquiline group; linezolid is associated with increased risk of developing anaemia.

A



B

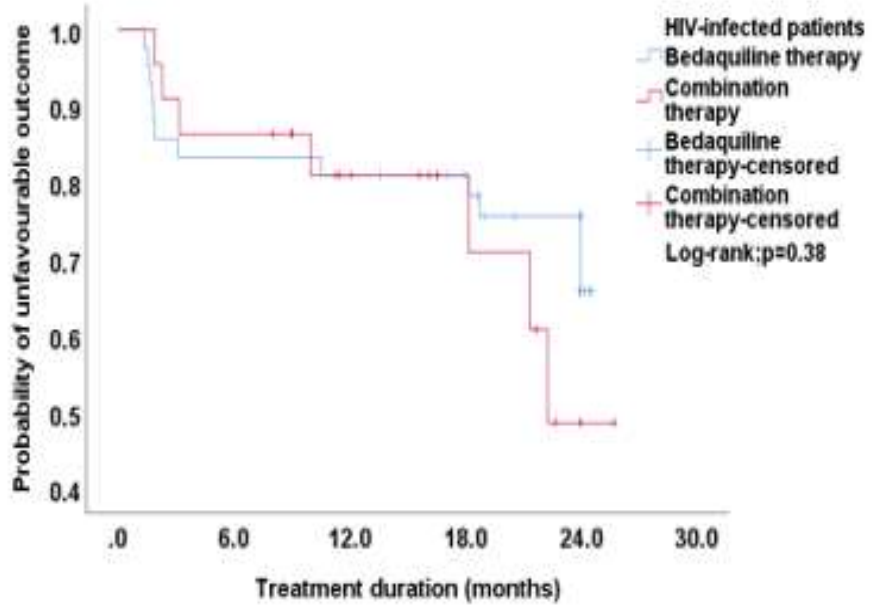


Figure S2 (A): Kaplan Meier estimate for the probability of culture conversion and (B) the probability of achieving an unfavourable outcome in HIV-infected patients who received bedaquiline-alone regimen and those who received delamanid-bedaquiline combination regimen.