

0403

SUPPLEMENTARY DATA

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Supplementary Table S1. QT or QTcF prolongation 500ms predictors – mg per kg – all weight groups

	No Prolongation (N=251)	Prolongation (N=31)	P-Value	Overall (N=282)
Baseline Moxifloxacin per kg, Mean (SD)	13.7(1.4)	13.5(1.5)	0.644	13.7(1.4)
Week 4 Moxifloxacin per kg, Mean (SD)	13.6(1.4)	13.5(1.4)	0.814	13.6(1.4)
Week 8 Moxifloxacin per kg, Mean (SD)	13.5(1.5)	13.5(1.4)	0.961	13.5(1.5)
Week 12 Moxifloxacin per kg, Mean (SD)	13.4(1.5)	13.3(1.5)	0.615	13.4(1.5)
Week 16 Moxifloxacin per kg, Mean (SD)	13.3(1.4)	13.2(1.5)	0.862	13.3(1.4)
Baseline Clofazimine per kg, Mean (SD)	2.0(0.3)	1.9(0.4)	0.636	2.0(0.3)
Week 4 Clofazimine per kg, Mean (SD)	1.9(0.3)	1.9(0.4)	0.983	1.9(0.3)
Week 8 Clofazimine per kg, Mean (SD)	1.9(0.3)	1.9(0.4)	0.817	1.9(0.3)
Week 12 Clofazimine per kg, Mean (SD)	1.9(0.3)	1.9(0.4)	0.612	1.9(0.3)
Week 16 Clofazimine per kg, Mean (SD)	1.8(0.3)	1.9(0.4)	0.607	1.9(0.3)

Supplementary Table S2. QT or QTcF prolongation 500ms predictors – mg per kg – 33-50kg

	No Prolongation (N=114)	Prolongation (N=13)	P-Value	Overall (N=127)
Baseline Moxifloxacin per kg, Mean (SD)	13.5(1.2)	13.8(1.7)	0.444	13.5(1.3)
Week 4 Moxifloxacin per kg, Mean (SD)	13.4(1.3)	14.0(1.1)	0.131	13.5(1.2)
Week 8 Moxifloxacin per kg, Mean (SD)	13.3(1.2)	14.1(1.0)	0.026	13.3(1.2)
Week 12 Moxifloxacin per kg, Mean (SD)	13.2(1.2)	14.0(1.3)	0.050	13.3(1.3)
Week 16 Moxifloxacin per kg, Mean (SD)	13.1(1.1)	14.0(1.2)	0.013	13.2(1.2)
Baseline Clofazimine per kg, Mean (SD)	2.3(0.2)	2.3(0.3)	0.444	2.3(0.2)
Week 4 Clofazimine per kg, Mean (SD)	2.2(0.2)	2.3(0.2)	0.131	2.2(0.2)
Week 8 Clofazimine per kg, Mean (SD)	2.2(0.2)	2.3(0.2)	0.026	2.2(0.2)
Week 12 Clofazimine per kg, Mean (SD)	2.2(0.2)	2.3(0.2)	0.050	2.2(0.2)
Week 16 Clofazimine per kg, Mean (SD)	2.2(0.2)	2.3(0.2)	0.013	2.2(0.2)

Supplementary Table S3. QT or QTcF prolongation 500ms predictors – mg per kg – over 50kg

	No Prolongation (N=136)	Prolongation (N=18)	P-Value	Overall (N=154)
Baseline Moxifloxacin per kg, Mean (SD)	13.8(1.5)	13.4(1.4)	0.241	13.8(1.5)
Week 4 Moxifloxacin per kg, Mean (SD)	13.7(1.5)	13.2(1.6)	0.201	13.7(1.6)
Week 8 Moxifloxacin per kg, Mean (SD)	13.6(1.6)	13.1(1.5)	0.155	13.6(1.6)
Week 12 Moxifloxacin per kg, Mean (SD)	13.5(1.6)	12.7(1.4)	0.058	13.4(1.6)
Week 16 Moxifloxacin per kg, Mean (SD)	13.3(1.6)	12.7(1.5)	0.104	13.3(1.6)
Baseline Clofazimine per kg, Mean (SD)	1.7(0.2)	1.7(0.2)	0.241	1.7(0.2)
Week 4 Clofazimine per kg, Mean (SD)	1.7(0.2)	1.7(0.2)	0.201	1.7(0.2)
Week 8 Clofazimine per kg, Mean (SD)	1.7(0.2)	1.6(0.2)	0.155	1.7(0.2)
Week 12 Clofazimine per kg, Mean (SD)	1.7(0.2)	1.6(0.2)	0.058	1.7(0.2)
Week 16 Clofazimine per kg, Mean (SD)	1.7(0.2)	1.6(0.2)	0.104	1.7(0.2)

Supplementary Table S4. Univariable analysis of risk factors for QT/QTcF \geq 500 ms in the Short regimen arm

	No Prolongation (N=251)	Prolongation (N=31)	P-Value	Overall (N=282)
Age, Median (IQR)	31.8(25.0,41.5)	40.2(27.8,48.9)	0.011	32.8(25.6,42.2)
Age Group, N (%)			0.072	
18-24	61(95.3)	3(4.7)		64
25-34	87(91.6)	8(8.4)		95
35-44	57(85.1)	10(14.9)		67
45+	46(82.1)	10(17.9)		56
Sex, N (%)			0.629	
Male	149(89.8)	17(10.2)		166
Female	102(87.9)	14(12.1)		116
Country, N (%)			0.000	
Ethiopia	82(96.5)	3(3.5)		85
Vietnam	61(92.4)	5(7.6)		66
South Africa	96(88.1)	13(11.9)		109
Mongolia	12(54.5)	10(45.5)		22
HIV Status¹, N (%)			0.863	
Negative	85(91.4)	8(8.6)		93
Positive	93(92.1)	8(7.9)		101
Smoking Status, N (%)			0.746	
Never	162(88.5)	21(11.5)		183
Smoker	88(89.8)	10(10.2)		98
Diabetes, N (%)			0.810	
No	229(88.8)	29(11.2)		258
Yes	19(90.5)	2(9.5)		21
Height (cm), Mean (SD)	164.7(8.5)	163.4(11.0)	0.445	164.6(8.8)
Weight (kg), Mean (SD)	52.3(9.4)	53.6(10.2)	0.457	52.4(9.5)
BMI (kg/m²), N (%)			0.710	
<16	32(91.4)	3(8.6)		35
16-18.4	81(91.0)	8(9.0)		89
18.5-24.9	122(87.8)	17(12.2)		139
25+	15(83.3)	3(16.7)		18
Moxifloxacin Dose, N (%)			0.872	
800mg	136(88.3)	18(11.7)		154
600mg	114(89.8)	13(10.2)		127
400mg	1(100.0)	0(0.0)		1
Moxifloxacin (mg/kg), Mean (SD)	13.7(1.4)	13.5(1.5)	0.644	13.7(1.4)
Clofazimine (mg/kg), Mean (SD)	2.0(0.3)	1.9(0.4)	0.636	2.0(0.3)
QTcF, N (%)			0.000	
Less than 400ms	118(96.7)	4(3.3)		122
Greater than or equal to 400ms	133(83.1)	27(16.9)		160
ALT, Mean (SD)	20.5(16.3)	20.8(14.8)	0.903	20.5(16.1)
AST, Mean (SD)	27.5(19.0)	29.1(18.0)	0.649	27.7(18.9)
Creatinine, Mean (SD)	67.9(19.7)	59.1(20.0)	0.021	66.9(19.9)
Glucose, Mean (SD)	5.9(3.3)	5.6(2.7)	0.687	5.9(3.2)
Potassium, N (%)			0.613	
3.5mmol/L and above	221(88.8)	28(11.2)		249
Under 3.5mmol/L	17(85.0)	3(15.0)		20

¹ Ethiopia & South Africa only

Supplementary Table S5. Univariable analysis of risk factors for a QTcF ≥ 60 ms increase from baseline in the Short regimen arm

	No Prolongation (N=190)	Prolongation (N=92)	P-Value	Overall (N=282)
Age, Median (IQR)	32.0 (26.0,41.3)	33.8 (25.4,45.6)	0.353	32.8 (25.6,42.2)
Age Group, N (%)			0.369	
18-24	42 (65.6)	22 (34.4)		64
25-34	69 (72.6)	26 (27.4)		95
35-44	46 (68.7)	21 (31.3)		67
45+	33 (58.9)	23 (41.1)		56
Sex, N (%)			0.968	
Male	112 (67.5)	54 (32.5)		166
Female	78 (67.2)	38 (32.8)		116
Country, N (%)			0.000	
Ethiopia	68 (80.0)	17 (20.0)		85
Vietnam	39 (59.1)	27 (40.9)		66
South Africa	78 (71.6)	31 (28.4)		109
Mongolia	5 (22.7)	17 (77.3)		22
HIV Status¹, N (%)			0.319	
Negative	67 (72.0)	26 (28.0)		93
Positive	79 (78.2)	22 (21.8)		101
Smoking Status, N (%)			0.578	
Never	121 (66.1)	62 (33.9)		183
Smoker	68 (69.4)	30 (30.6)		98
Diabetes, N (%)			0.127	
No	177 (68.6)	81 (31.4)		258
Yes	11 (52.4)	10 (47.6)		21
Height (cm), Mean (SD)	165.0 (8.4)	163.6 (9.5)	0.212	164.6 (8.8)
Weight (kg), Mean (SD)	52.8 (9.8)	51.7 (8.8)	0.354	52.4 (9.5)
BMI (kg/m²), N (%)			0.349	
<16	27 (77.1)	8 (22.9)		35
16-18.4	56 (62.9)	33 (37.1)		89
18.5-24.9	92 (66.2)	47 (33.8)		139
25+	14 (77.8)	4 (22.2)		18
Moxifloxacin Dose, N (%)			0.271	
800mg	107 (69.5)	47 (30.5)		154
600mg	83 (65.4)	44 (34.6)		127
400mg	0 (0.0)	1 (100.0)		1
Moxifloxacin (mg/kg), Mean (SD)	13.7 (1.5)	13.6 (1.3)	0.900	13.7 (1.4)
Clofazimine (mg/kg), Mean (SD)	2.0 (0.3)	2.0 (0.3)	0.661	2.0 (0.3)
QTcF, N (%)			0.112	
Less than 400ms	76 (62.3)	46 (37.7)		122
Greater than or equal to 400ms	114 (71.3)	46 (28.7)		160
ALT, Mean (SD)	21.5 (17.8)	18.4 (11.9)	0.121	20.5 (16.1)
AST, Mean (SD)	28.3 (19.9)	26.3 (16.6)	0.409	27.7 (18.9)
Creatinine, Mean (SD)	67.2 (20.1)	66.2 (19.6)	0.688	66.9 (19.9)
Glucose, Mean (SD)	5.6 (2.6)	6.3 (4.1)	0.102	5.9 (3.2)
Potassium, N (%)			0.495	
3.5mmol/L and above	168 (67.5)	81 (32.5)		249
Under 3.5mmol/L	12 (60.0)	8 (40.0)		20

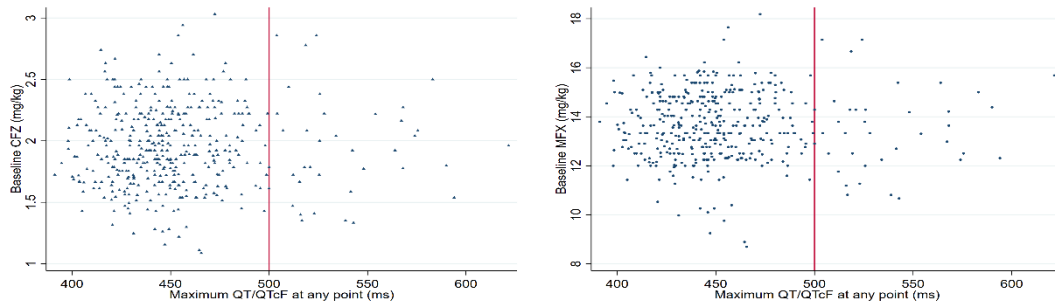
¹ Ethiopia & South Africa only

Supplementary Figure S1. Baseline clofazimine (A+C) and moxifloxacin (B+D) dose (mg/kg) and relationship to maximum QT/QTcF (A+B) and maximum QTcF increase (C+D) on the Short regimen.

A Baseline CFZ exposure by maximum QT/QTcF within one year

B Baseline MFX

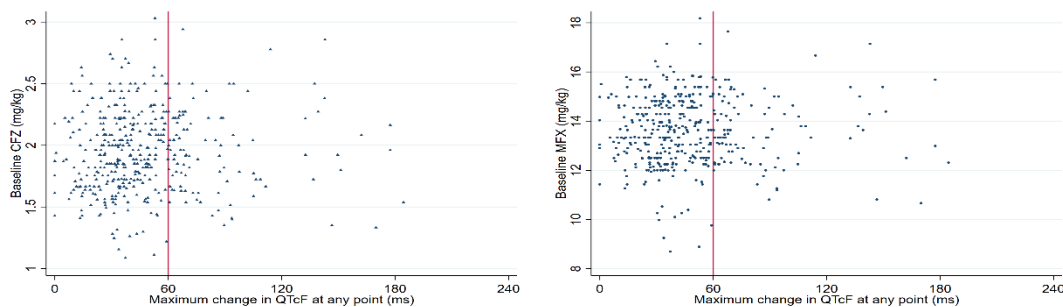
exposure by maximum QT/QTcF within one year



C Baseline CFZ exposure by maximum increase in QTcF within one year

D Baseline

MFX exposure by maximum increase in QTcF within one year



The red line indicates a maximum QT/QTcF of 500 ms (A+B) or a maximum increase in QTcF of 60 ms (C+D) within 52 weeks of follow-up, with patients to the right of this line exceeding the threshold. A non-linear relationship is seen in all four graphs plotting baseline mg/kg of clofazimine (A+C) and moxifloxacin (B+D) with maximum QT or QTcF value.