

SUPPLEMENTAL TABLE 1. Treatment indications of short-term FQ or non-FQ use in patients who received short-term (< 7 days) FQ or non-FQ antibiotics

	FQ use (n=23)		Non-FQ use (n=30)	
	No. of patients	No. of dead patients	No. of patients	No. of dead patients
Early switch to the first line anti-TB drugs	8	0	11	0
Empirical therapy for other infection	6	1	4	0
Rapid fatal due to progression of pneumonia during empirical antibiotics	4	4	1	1
Wrong prescription in emergency department	3	0	2	0
Hopeless discharge	1	1	0	0
Perioperative antibiotics	1 ^a	0	12 ^b	0
Total	30	1	30	1

^a Perioperative prophylaxis for cardiac window operation.

^b The 12 patients who received short-term non-FQ for perioperative antibiotics underwent the scheduled cancer surgery (lung cancer (n=3), hepatocellular carcinoma (n=2), urogenital cancer (n=1)) and the scheduled procedure (urogenital procedure (n=3), dental problem (n=1), CNS problem (n=1), lymph node excision (n=1)).

SUPPLEMENTAL TABLE 2. Demographics, clinical characteristics, treatments, and outcomes of the 57 immunocompromised patients who did not received empirical anti-TB treatment (missed TB group)

Variables	Long-term FQ		P
	group ^a (n = 15)	The comparator ^b (n = 42)	
Demographics			
Age, mean years ± SD	66 ± 11	64 ± 13	0.59
Male sex	10 (67)	27 (64)	0.87
Clinical diagnosis			
Pulmonary TB	13 (87)	38 (91)	0.65
Extrapulmonary TB	2 (13)	4 (10)	0.65
Disseminated TB	0 (0)	0 (0)	NA
Underlying disease			
Solid tumor	10 (67)	36 (86)	0.14
Transplantation	2 (13)	1 (2)	0.17
Hematologic malignancy	2 (13)	2 (5)	0.28
Chronic renal failure	0 (0)	1 (2)	>0.99
Liver cirrhosis	3 (20)	4 (10)	0.37
Connective tissue disease	1 (7)	3 (7)	>0.99
HIV infection	0 (0)	0 (0)	NA
Use of immunosuppressive agent (≤ 1 month)	7 (47)	11 (26)	0.20
Atypical chest image^c	11/13 (85)	28/38 (74)	0.70
Anti-TB drug susceptibility test			
Multidrug resistance	0/10 (0)	1/25 (4)	>0.99
Resistance to isoniazid	2/10 (20)	2/25 (8)	0.56
Resistance to rifampin	0/10 (0)	1/25 (4)	>0.99
Resistance to ethambutol	1/10 (10)	2/25 (8)	>0.99
Resistance to pyrazinamide	0/10 (0)	1/25 (4)	>0.99

Resistance to FQ	0/10 (0)	1/25 (4)	>0.99
Time from mycobacterial test to positive mycobacterial culture, median weeks (IQR)	6.8 (5.2-8.9)	5.1 (4.0-6.9)	0.42
Time from mycobacterial test to anti-TB therapy, median weeks (IQR)	8.7 (7.1-13.9)	5.4 (4.6-8.6)	0.02
Treatment			
Definitive anti-TB treatment ^d	8 (53)	23 (55)	0.92
Defaulted from anti-TB treatment ^e	4 (27)	7 (17)	0.46
Change of treatment regimen	1 (7)	0 (0)	0.26
AG exposure prior to TB diagnosis ^f	1 (7)	1 (2)	0.46
Duration of FQ use, median days (IQR)	18 (14-19)	2 (1-3) ^g	<0.001
Outcome			
Death before availability of positive mycobacterial culture	3 (20)	12 (29)	0.74
30-day all-cause mortality	2 (13)	7 (17)	>0.99
90-day all-cause mortality	2 (13)	13 (31)	0.31

NOTE. Data are no. (%) of patients unless indicated otherwise. AG, aminoglycoside; FQ, fluoroquinolone; HIV, human immunodeficiency virus; IQR, interquartile range; SD, standard deviation; TB, tuberculosis.

^a 10 (67%) were exposed to levofloxacin alone. In addition, 3 (20%) were exposed to ciprofloxacin and levofloxacin, and 2 (13%) were exposed to levofloxacin and moxifloxacin.

^b The comparator included the short-term FQ group (n=6), non-FQ group (n=15), and no antibiotics (n=21).

^c 6 patients (2 in the long-term FQ group and 4 in the comparator) had extrapulmonary manifestations of TB only.

^d 15 patients (3 in the long-term FQ group and 12 in the comparator) died before the availability of a positive mycobacterial culture, and 11 patients (4 in the long-term FQ group and 7 in the comparator) defaulted from anti-TB treatment.

^e Defined as treatment interruption for any reason.

^f No patients received AG for more than 7 days prior to TB diagnosis.

^g 6 (14%) patients in the comparator received FQ (< 7 days) prior to anti-TB treatment.

SUPPLEMENTAL TABLE 3. Univariate analysis of risk factors associated with 30-day mortality among the 57 immunocompromised patients who did not received empirical anti-TB treatment (missed TB group)

Variables	Died (n = 9)	Survived (n = 48)	OR (95% CI)	P
Demographics				
Age, mean years \pm SD	63 \pm 12	65 \pm 13	0.99 (0.94-1.05)	0.70
Male sex	6 (67)	31 (65)	1.10 (0.24-4.95)	>0.99
Clinical diagnosis				
Pulmonary TB	9 (100)	42 (88)	NA	0.58
Extrapulmonary TB	0 (0)	6 (13)	NA	0.58
Disseminated TB	0 (0)	0 (0)	NA	NA
Underlying disease				
Solid tumor	4 (44)	42 (88)	0.11 (0.02-0.55)	0.01
Transplantation	0 (0)	3 (6)	NA	>0.99
Hematologic malignancy	2 (22)	2 (4)	6.57 (0.79-54.48)	0.11
Chronic renal failure	0 (0)	1 (2)	NA	>0.99
Liver cirrhosis	2 (22)	5 (10)	2.46 (0.40-15.23)	0.30
Connective tissue disease	1 (11)	3 (6)	1.88 (0.17-20.36)	0.51
HIV infection	0 (0)	0 (0)	NA	NA
Immunosuppressive agent use (\leq 1 month)	6 (67)	12 (25)	6.00 (1.30-27.77)	0.02
Atypical chest image^a	7/9 (78)	33/42 (79)	0.98 (0.17-5.59)	>0.99
Anti-TB drug susceptibility test	2 (22)	33 (69)	0.13 (0.02-0.70)	0.02
Multidrug resistance	0/2 (0)	1/33 (3)	NA	>0.99
Resistance to isoniazid	0/2 (0)	4/33 (12)	NA	>0.99
Resistance to rifampin	0/2 (0)	1/33 (3)	NA	>0.99
Resistance to ethambutol	0/2 (0)	3/33 (9)	NA	>0.99
Resistance to pyrazinamide	0/2 (0)	1/33 (3)	NA	>0.99
Resistance to FQ	0/2 (0)	1/33 (3)	NA	>0.99

Time from mycobacterial test to positive

mycobacterial culture, median weeks (IQR)	5.6 (4.3-8.3)	6.8 (4.8-8.6)	0.86 (0.60-1.23)	0.51
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Time from mycobacterial test to anti-TB

therapy, median weeks (IQR)	NA	5.9 (4.7-9.4)	NA	NA
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Treatment

Definitive anti-TB treatment	0 (0)	31 (65)	NA	<0.001
Defaulted from anti-TB treatment	0 (0)	11 (23)	NA	0.18
Change of treatment regimen	0 (0)	1 (2)	NA	>0.99
AG use	0 (0)	2 (4)	NA	>0.99
FQ use	6 (67)	15 (31)	4.40 (0.97-20.00)	0.06
Short-term FQ use (< 7 days)	4 (44)	2 (4)	18.40 (2.67-127.03)	0.004
Long-term FQ use (≥ 7 days)	2 (22)	13 (27)	0.77 (0.14-4.19)	>0.99
Duration of FQ use	NA	NA	0.85 ^b (0.73-0.99)	0.04
Non-FQ use	3 (33)	12 (25)	1.50 (0.32-6.94)	0.69
Short-term non-FQ use (< 7 days)	1 (11)	6 (13)	0.88 (0.09-8.29)	>0.99
Non-FQ use (≥ 7 days)	2 (22)	6 (13)	2.00 (0.33-11.97)	0.60
No antibiotic use	0 (0)	21 (44)	NA	0.02

NOTE. Data are no. (%) of patients unless indicated otherwise. AG, aminoglycoside; CI, confidence interval; FQ, fluoroquinolone; HIV, human immunodeficiency virus; IQR, interquartile range; NA, not available; OR, odds ratio; SD, standard deviation; TB, tuberculosis.

^a 6 patients among those who survived had extrapulmonary manifestations of TB only.

^b The odds ratio for the duration of FQ use indicates that for every additional one day there is a 0.85 times lower risk of mortality in the patients (n=21) who received FQs.

SUPPLEMENTAL TABLE 4. Univariate analysis of risk factors associated with 30-day mortality excluding subjects who died within 3 days after antibiotic use

Variables	Died (n = 7)	Survived (n = 182)	OR (95% CI)	P
Demographics				
Age, mean years ± SD	60 ± 13	61 ± 15	1.00 (0.95-1.05)	0.89
Male sex	5 (71)	132 (73)	0.95 (0.18-5.04)	>0.99
Clinical diagnosis				
Pulmonary TB	7 (100)	148 (81)	NA	0.36
Extrapulmonary TB	0 (0)	23 (13)	NA	0.60
Disseminated TB	0 (0)	11 (6)	NA	>0.99
Underlying disease				
Solid tumor	3 (43)	119 (65)	0.40 (0.09-1.83)	0.25
Transplantation	0 (0)	13 (7)	NA	>0.99
Hematologic malignancy	1 (14)	12 (7)	2.36 (0.26-21.23)	0.40
Chronic renal failure	0 (0)	20 (11)	NA	>0.99
Liver cirrhosis	2 (29)	9 (5)	7.69 (1.31-45.21)	0.06
Connective tissue disease	1 (14)	15 (8)	1.86 (0.21-16.45)	0.47
HIV infection	0 (0)	1 (1)	NA	>0.99
Immunosuppressive agent use (≤ 1 month)	4 (57)	60 (33)	2.71 (0.59-12.50)	0.23
Atypical chest image^a	4/7 (57)	78/157 (50)	1.35 (0.29-6.23)	>0.99
Anti-TB drug susceptibility test	1 (14)	146 (80)	0.04 (0.01-0.35)	0.001
Multidrug resistance	0/1 (0)	3/146 (2)	NA	>0.99
Resistance to isoniazid	0/1 (0)	9/146 (6)	NA	>0.99
Resistance to rifampin	0/1 (0)	2/146 (1)	NA	>0.99
Resistance to ethambutol	0/1 (0)	5/146 (3)	NA	>0.99
Resistance to pyrazinamide	0/1 (0)	1/146 (1)	NA	>0.99
Resistance to FQ	0/1 (0)	3/146 (2)	NA	>0.99

Time from mycobacterial test to positive mycobacterial culture, median weeks (IQR)	7.7 (5.0-10.4)	7.6 (5.1-8.6)	1.14 (0.57-2.25)	0.51
Time from mycobacterial test to anti-TB therapy, median weeks (IQR)	1.0 (0.6-1.3)	3.0 (1.0-4.6)	0.56 (0.19-1.66)	0.26
Treatment				
Empirical anti-TB treatment	2 (29)	134 (74)	0.14 (0.03-0.76)	0.02
Definitive anti-TB treatment	2 (29)	165 (91)	0.04 (0.01-0.23)	<0.001
Defaulted from anti-TB treatment	0 (0)	11 (6)	NA	>0.99
Change of treatment regimen	0 (0)	13 (7)	NA	>0.99
AG use	0 (0)	5 (3)	NA	>0.99
FQ use	4 (57)	48 (26)	3.72 (0.80-17.24)	0.09
Short-term FQ use (< 7 days)	2 (29)	17 (9)	3.88 (0.70-21.55)	0.15
Long-term FQ use (≥ 7 days)	2 (29)	31 (17)	1.95 (0.36-10.50)	0.35
Duration of FQ use	NA	NA	0.98 ^b (0.87-1.10)	0.72
Non-FQ use	3 (43)	74 (41)	1.10 (0.24-5.03)	>0.99
Short-term non-FQ use (< 7 days)	0 (0)	29 (16)	NA	0.60
Non-FQ use (≥ 7 days)	3 (43)	45 (25)	2.28 (0.49-10.59)	0.37
No antibiotic use	0 (0)	60 (33)	NA	0.10

NOTE. Data are no. (%) of patients unless indicated otherwise. AG, aminoglycoside; CI, confidence interval; FQ, fluoroquinolone; HIV, human immunodeficiency virus; IQR, interquartile range; NA, not available; OR, odds ratio; SD, standard deviation; TB, tuberculosis.

^a 23 patients among those who survived had extrapulmonary manifestations of TB only. Of 11 patients with disseminated TB in the survival group, 9 had pulmonary plus extrapulmonary manifestations of TB and 2 had extrapulmonary manifestations of TB only.

^b The odds ratio for the duration of FQ use indicates that for every additional one day there is a 0.98 times lower risk of mortality in the patients (n=52) who received FQs.



SUPPLEMENTAL FIG 1. Stratified analysis according to FQ use and empirical anti-TB therapy