Supplement to: Long-term self-administered outpatient parenteral antimicrobial therapy in the treatment of tuberculosis

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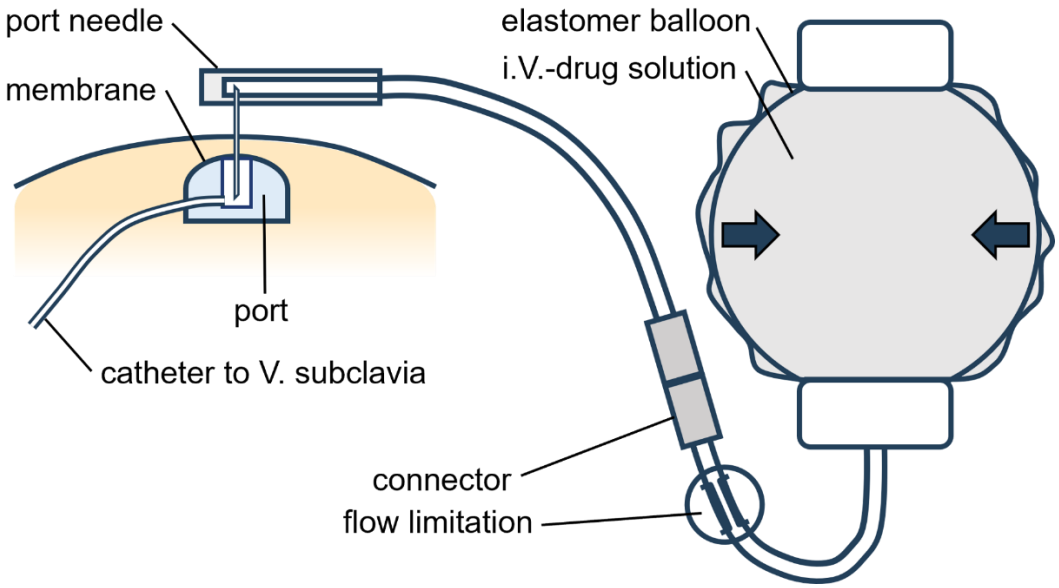
Supplement Table 1. WHO-recommended for drug-resistant tuberculosis since 2014.

WHO 2014 20 months [1]	**WHO 2016** 18 months [2]	**WHO 2018** 18 months [3]	**WHO 2022** 6 / 18 months [4]
G2 Amikacin Capreomycin **G3** Levofloxacin Moxifloxacin **G4** Terizidone /Cycloserine PAS Prothionamide /Ethionamide **G1** Pyrazinamide Ethambutol **G5** Bedaquiline Delamanid Linezolid Clofazimine Meropenem + Amo/Clav High-dose isoniazid	**A** Levofloxacin Moxifloxacin **B** Amikacin Capreomycin **C** Prothionamide /Ethionamide Terizidone /Cycloserine Linezolid **D1** Clofazimine Pyrazinamide Ethambutol **D2** High-dose isoniazid Bedaquiline **D3** Delamanid PAS Meropenem + Amo/Clav	**A** Levofloxacin Moxifloxacin Bedaquiline Linezolid **B** Clofazimine Terizidone /Cycloserine **C** Ethambutol Delamanid Pyrazinamide Meropenem + Amo/Clav Amikacin Prothionamide /Ethionamide PAS	**6-month regimens** **RR/MDR** Moxifloxacin Bedaquiline Linezolid Pretomanid **pre-XDR** Bedaquiline Linezolid Pretomanid **18-month regimens** **XDR** →2018 priority grouping

Obligatorily parenteral drugs and underlined. However, parenteral formulations are available for every drug except for pyrazinamide. Regimens are composed by taking either one or all drugs from a drug group, according to the respective guideline. A, B, C, D1-3, as well as G1-5: Drug groups. WHO: World Health Organization. PAS: Para-amino salicylic acid. Amo/Clav: amoxicillin/clavulanic acid. RR/MDR: rifampicin-resistant/multi-drug resistant tuberculosis. pre-XDR: pre-extensively drug-resistant tuberculosis

Supplement Figure S1



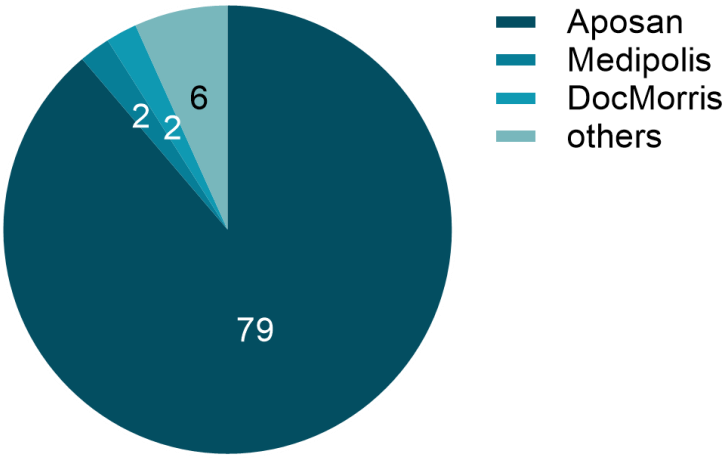
Supplement Figure S1: Schematic figure of an OPAT system. Patients connect a drug solution-filled elastomer balloon to an indwelling port-needle. The drug solution flows through the port needle and the port catheter system into the upper central vein. A flow limitation device determines the infusion duration. Patients are trained in the handling and disinfection of the OPAT systems by a specialized nurse. Elastomer balloons are discarded after infusion, port needles are changed regularly (normally every two weeks) by trained personnel.

Supplement Table S2. Outcome definitions by WHO and TBnet as well as long-term outcome definitions.

Outcome	WHO	TBnet	long-term
evaluation	at end of treatment, no follow-up-period	1 year follow-up after end of treatment	Health status at the time of follow-up evaluation (as long as possible - at least 6 months after end of treatment
favorable			
cure	Treatment completed without evidence of failure AND - for rif-resistant-/MDR-/XD TB patients: three or more consecutive cultures taken at least 30 days apart are negative after the first 8 months of treatment - for all other patients: negative smear or culture in the last month of treatment and on at least one previous occasion	Negative culture status 6 months after treatment initiation, no positive culture thereafter, no relapse within 1 year after treatment completion	-
treatment completed	Treatment completed as recommended by the national policy without evidence of failure but conditions for cure are not met	-	-
relapse free	-	-	Alive and no relapse
unfavorable			
failed	- for RIF-RESISTANT-/MDR-/XDR-patients: treatment terminated or need for permanent regime change of at least two anti-tuberculosis-drugs because of: - lack of conversion by the end of month 8 of treatment or - bacteriological reversion after month 8 after conversion to negative or - evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs or - adverse drug reactions - for all other patients: positive sputum or culture at month 5 or later during treatment	Positive culture status 6 months after treatment initiation or thereafter or relapse within 1 year after treatment completion	Relapse after end of treatment
died	Death during treatment	Death during treatment or follow-up	Death during treatment or follow-up
lost to follow-up	Treatment interruption of 2 or more consecutive months	Nonreceipt of care 6 months after treatment initiation	-
not available	Transferred out to another treatment unit or unknown outcome	Transferred out to another treatment unit or unknown outcome (no culture status at 6 months/ no post-treatment assessment)	No health status obtainable (lost to follow-up/ transferred out)

Long-term outcome definitions as defined previously [5]. WHO: World Health Organization. TBnet: Tuberculosis Network European Trials group. Rif-resistant TB: rifampicin-resistant tuberculosis; MDR TB: multidrug-resistant tuberculosis; pre-XDR TB: pre-extensively drug-resistant tuberculosis; XDR TB: extensively drug-resistant tuberculosis.

Supplement Figure S2

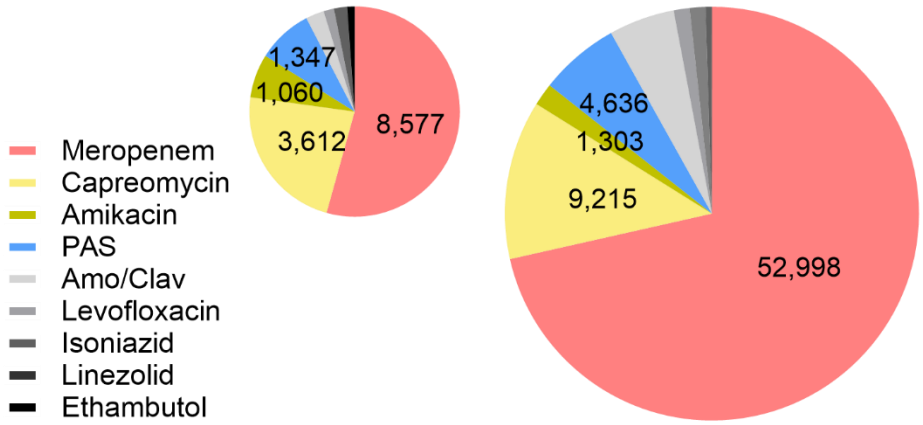


Supplement Figure S2. Enrolment into OPAT programs. OPAT programs were provided by specialized pharmacies. The majority of patients were enrolled into programs provided by Aposan GmbH, Cologne, Germany. Medipolis: Medipolis Intensiv Care & Service GmbH, Jena, Germany; DocMorris: DocMorris Apotheke am UKE, Hamburg, Germany.

Supplement Table S3. OPAT in patients with pan-susceptible or poly-resistant TB.

Patient ID	Drug resistance	Drug regimen	Reason for parenteral application
P18	isoniazid, rifampicin genotypic but not phenotypic	rifampicin, moxifloxacin, prothionamide, terizidone, ethambutol, pyrazinamide, capreomycin	reactivation of tuberculous spondylitis nine months after end of previous therapy (fourth relapse); TB of lung, pleura, lymph nodes and bones
P24	isoniazid, prothionamide	levofloxacin, terizidone, linezolid, capreomycin	severe adverse drug events (DRESS, acute liver failure) under rifampicin-moxifloxacin-ethambutol
P28	None	high dose rifampicin, levofloxacin, clofazimine, linezolid, meropenem, amoxicillin/clavulanic acid	therapy escalation because of mixed response after one year of previous therapy: cerebral, pleural, pulmonary TB, massive mediastinal and abdominal lymphadenopathy, possible hepatic affection
P87	none	rifampicin, isoniazid, ethambutol, levofloxacin	repeatedly subtherapeutic drug levels under oral administration; HIV
P88	none	rifampicin, levofloxacin, terizidone, clofazimine, meropenem, amoxicillin/clavulanic acid	tuberculous meningoencephalitis

Supplement Figure S3



Supplement Figure S4. Total parenteral drug administrations in the in- and outpatient setting. Left: total parenteral drug administrations in the inpatient setting, right: total parenteral drug administrations in OPAT. Meropenem and Amoxicillin/Clavulanic acid were administered three times per day, all other drugs once daily. PAS: Para-amino salicylic acid. Amo/Clav: amoxicillin/clavulanic acid.

Supplement Table S4. Port system-associated complications, causative pathogens and management.

Patient		Pathogen	Management	
inpatient setting				
P69	bloodstream infection	*Candida parapsylosis*	explantation	+ Voriconazole
P70	thrombosis	-	explantation	
P71	local infection	n.d.	explantation	
P72	local infection	n.d.	explantation	
P73	bloodstream infection	*Candida albicans*	explantation	+ Caspofungin
P88	local infection	1st infection: n.d.	explantation	
outpatient setting				
P82	bloodstream infection	*Stenotrophomonas maltophila*	explantation	+ Thrimetoprim/sulfamethoxazole
P83	local infection	n.d.	explantation	
P84	bloodstream infection	*Stenotrophomonas maltophila, Candida albicans, Candida parapsylosis*	explantation	+ Caspofungin
P85	bloodstream infection	*Pseudomonas aeruginosa*	explantation	+ Piperacillin/tazobactam
P86	bloodstream infection	*Candida albicans, Staphylococcus aureus*	explantation	+ Voriconazole, caspofungin, flucloxacillin
P87	thrombosis	-	explantation	
P88	bloodstream infection	2nd infection: *Staphylococcus aureus*	explantation	+ Flucloxacillin
P89	bloodstream infection	*Escherichia coli, Klebsiella oxytoca*	explantation	+ Ampicillin/sulbactam

P69-P89: Patient identifiers. n.d.: not determined.

Supplement Table S5. Inpatient and OPAT complication rates.

	inpatient treatment	OPAT
patients	89	89
port system infections	5	7
port system thrombosis	1	1
complication rate (%)	6.7	9.0
total treatment days	8,276	29,129
complication rate (%)	1 per 1,379.3 0.7 per 1000 days	1 per 3,641.1 0.3 per 1000 days
total administrations	15,497	71,128
complication rate (%)	1 per 2,582.8 0.4 per 1000 adm.	1 per 8,891.0 0.1 per 1000 adm.

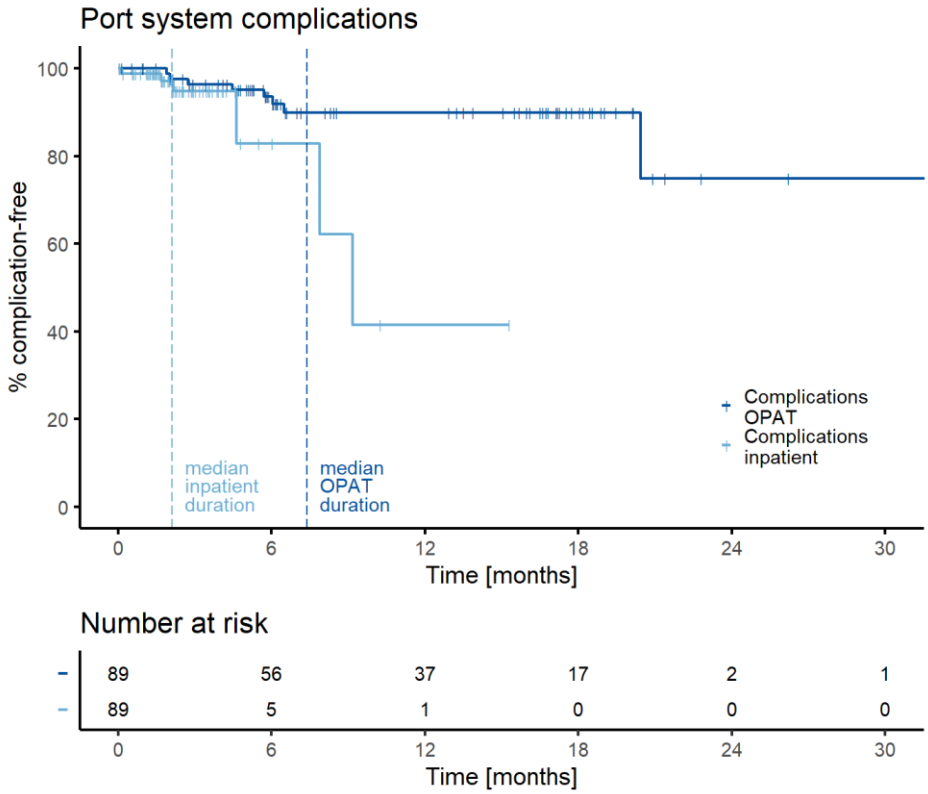
OPAT: outpatient parenteral antimicrobial therapy; adm.: administrations.

Supplement Table S6: Baseline parameters and patient characteristics, stratified by inpatient port system-associated complications.

	total	no inpatient port-assoc. complication	inpatient port-assoc. complication	odds ratio	p-value
Total	89 (100.0%)	83 (93.3%)	6 (6.7%)		
Sex					
female	30 (33.7 %)	28 (33.7 %)	2 (33.3 %)	0.98 (0.13-5.35)	>0.9
male	59 (66.3 %)	55 (66.3 %)	4 (66.7 %)	1.02 (0.19-7.66)	>0.9
Migration history	86 (96.6 %)	80 (96.4 %)	6 (100.0 %)		>0.9
Age at discharge	33.6 (26.2-42.8)	33.6 (25.9-43.0)	33.1 (26.6-41.1)		0.9
BMI	21.0 (18.6-23.9)	21.0 (18.5-23.9)	20.7 (20.3-23.5)	1.04 (0.82-1.29)	0.7
Underweight	22 (24.7 %)	21 (25.3 %)	1 (16.7 %)	0.59 (0.03-3.94)	>0.9
Diabetes	1 (1.1 %)	1 (1.2 %)	0 (0.0 %)		>0.9
Smoker	35 (39.3 %)	32 (38.6 %)	3 (50.0 %)	1.59 (0.28-9.07)	0.7
Alcohol abuse	5 (5.6 %)	4 (4.8 %)	1 (16.7 %)		0.3
IV-drug abuse	6 (6.7 %)	5 (6.0 %)	1 (16.7 %)	3.12 (0.15-25.17)	0.4
HIV positive	8 (9.0 %)	6 (7.2 %)	2 (33.3 %)	6.42 (0.78-41.02)	0.089
HepB positive	8 (9.0 %)	8 (9.6 %)	0 (0.0 %)		>0.9
HepC positive	17 (19.1 %)	15 (18.1 %)	2 (33.3 %)	2.27 (0.3-12.78)	0.3
Previous TB	31 (34.8 %)	28 (33.7 %)	3 (50.0 %)	1.96 (0.34-11.22)	0.4
Cavitary disease	50 (56.2 %)	45 (54.2 %)	5 (83.3 %)	4.22 (0.64-82.77)	0.2
Miliary disease	4 (4.5 %)	3 (3.6 %)	1 (16.7 %)	5.33 (0.24-51.73)	0.2
Extrapulmonary disease	11 (12.4 %)	10 (12.0 %)	1 (16.7 %)	1.46 (0.07-10.36)	0.6
Drug-resistance					
pan-susceptible	4 (4.5 %)	3 (3.6 %)	1 (16.7 %)	5.33 (0.24-51.73)	0.2
poly-resistant	1 (1.1 %)	1 (1.2 %)	0 (0.0 %)		>0.9
rifampicin-resistant	2 (2.2 %)	2 (2.4 %)	0 (0.0 %)		>0.9
MDR	56 (62.9 %)	54 (65.1 %)	2 (33.3 %)	0.27 (0.04-1.46)	0.2
pre-XDR	21 (23.6 %)	20 (24.1 %)	1 (16.7 %)	0.63 (0.03-4.22)	>0.9
XDR	5 (5.6 %)	3 (3.6 %)	2 (33.3 %)	13.33 (1.46-107.86)	0.035
Number of drugs					
1	58 (65.2 %)	53 (63.9 %)	5 (83.3 %)	2.83 (0.43-55.57)	0.7
2	24 (27.0 %)	24 (28.9 %)	0 (0.0 %)		0.2
3 and more	7 (7.9 %)	6 (7.2 %)	1 (16.7 %)	2.57 (0.12-19.82)	0.4
median	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-1.0)	1.37 (0.45-3.16)	0.5
Use in drug regimens					
Amikacin	22 (24.7 %)	19 (22.9 %)	3 (50 %)	3.37 (0.58-19.54)	0.2
Capreomycin	60 (67.4 %)	58 (69.9 %)	2 (33.3 %)	0.22 (0.03-1.18)	0.085
Meropenem	39 (43.8 %)	34 (41 %)	5 (83.3 %)	7.21 (1.1-141.36)	0.082
PAS	24 (27 %)	21 (25.3 %)	3 (50 %)	2.95 (0.51-17.05)	0.3
Drug administrations					
Amikacin	31.0 (16.0-96.0)	34.5 (17.5-89.5)	16.0 (12.5-98.5)	1 (0.98-1.01)	0.5
Capreomycin	71.0 (58.5-102.5)	71.0 (59.3-101.8)	141.5 (82.8-200.3)	1.02 (0.99-1.04)	0.9
Meropenem	286.5 (228.0-361.5)	286.5 (228.0-354.0)	427.5 (222.8-688.5)	1.01 (1-1.01)	0.4
PAS	51.5 (13.3-77.3)	55.0 (17.0-78.0)	4.0 (3.5-29.5)	0.97 (0.91-1)	0.2
Total	149.0 (77.0-294.0)	144.0 (73.5-290.0)	217.5 (186.0-559.5)	1 (1-1)	0.3

Drug administrations until occurrence of port system-associated complications. Categorial variables as n (%), continuous variables as median (IQR); Assoc.: associated; yrs: years; BMI: body-mass index; i.v.: intravenous; HIV: human immunodeficiency virus; HepB: hepatitis B virus; HepC: hepatitis C virus; Poly-resistant TB: resistant to two or more anti-tuberculosis-drugs, non-MDR, non-rif-resistant. Rif-resistant TB: rifampicin-resistant tuberculosis; MDR TB: multidrug-resistant tuberculosis; pre-XDR TB: pre-extensively drug-resistant tuberculosis; XDR TB: extensively drug-resistant tuberculosis; PAS: Para-amino salicylic acid.

Supplement Figure S4



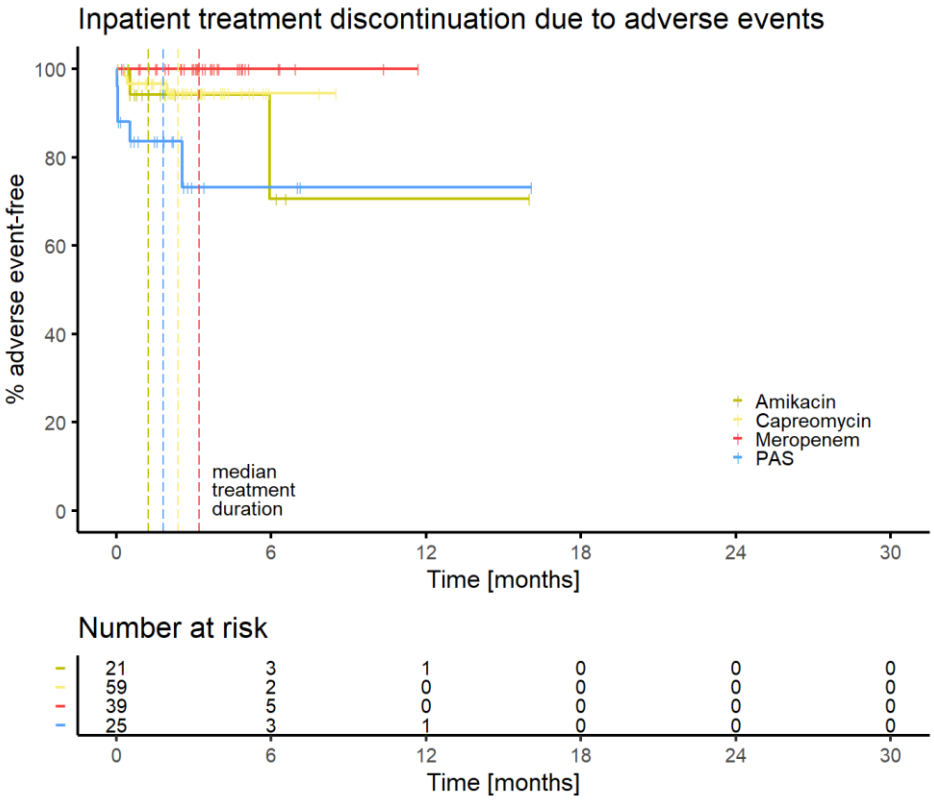
Supplement Figure S5. Port system complications over time during inpatient treatment and sOPAT. Complications comprise port system infection and -thrombosis. sOPAT complications are displayed for better clarity. Complication rates were low, at a median treatment duration of 2.1 months, 97.1 % of inpatients had no complication and at median sOPAT duration of 7.4 months, 89.9 % of patients in sOPAT were free of complications. Complication rates were very similar in the sOPAT and the inpatient setting over these seven and a half months with an inpatient complication-free survival of 82.9 %.

Supplement Table S7. Baseline parameters and patient characteristics, stratified by sOPAT drug discontinuation due to adverse drug events.

	total	no drug discontinuation	drug discontinuation due to adverse events	odds ratio	p-value
Total	89 (100.0%)	77 (86.5%)	12 (13.5%)		
Sex					
female	30 (33.7 %)	24 (31.2 %)	6 (50.0 %)	2.21 (0.63-7.76)	0.2
male	59 (66.3 %)	53 (68.8 %)	6 (50.0 %)	0.45 (0.13-1.58)	0.2
Migration history	86 (96.6 %)	75 (97.4 %)	11 (91.7 %)		0.4
Age at discharge	33.6 (26.2-42.8)	33.6 (25.2-42.4)	35 (27.8-43.3)		0.7
BMI	21.0 (18.6-23.9)	20.9 (18.6-23.8)	22.6 (19.4-26.1)	1.09 (0.93-1.29)	0.4
Underweight	22 (24.7 %)	19 (24.7 %)	3 (25.0 %)	1.02 (0.21-3.83)	>0.9
Diabetes	1 (1.1 %)	1 (1.3 %)	0 (0.0 %)		>0.9
Smoker	35 (39.3 %)	31 (40.3 %)	4 (33.3 %)	0.74 (0.18-2.57)	0.8
Alcohol abuse	5 (5.6 %)	5 (6.5 %)	0 (0.0 %)		>0.9
IV-drug abuse	6 (6.7 %)	4 (5.2 %)	2 (16.7 %)	3.65 (0.46-21.42)	0.2
HIV positive	8 (9.0 %)	6 (7.8 %)	2 (16.7 %)		0.3
HepB positive	8 (9.0 %)	6 (7.8 %)	2 (16.7 %)	2.37 (0.32-12.04)	0.3
HepC positive	17 (19.1 %)	15 (19.5 %)	2 (16.7 %)	0.83 (0.12-3.57)	>0.9
Previous TB	31 (34.8 %)	27 (35.1 %)	4 (33.3 %)	0.93 (0.23-3.23)	>0.9
Cavitary disease	50 (56.2 %)	42 (54.5 %)	8 (66.7 %)	1.67 (0.48-6.67)	0.5
Miliary disease	4 (4.5 %)	2 (2.6 %)	2 (16.7 %)		0.086
Extrapulmonary disease	11 (12.4 %)	10 (13.0 %)	1 (8.3 %)	0.61 (0.03-3.69)	>0.9
Drug-resistance					
pan-susceptible	4 (4.5 %)	3 (3.9 %)	1 (8.3 %)		0.4
poly-resistant	1 (1.1 %)	1 (1.3 %)	0 (0.0 %)		>0.9
rifampicin-resistant	2 (2.2 %)	1 (1.3 %)	1 (8.3 %)	6.91 (0.26-183.48)	0.3
MDR	56 (62.9 %)	51 (66.2 %)	5 (41.7 %)	0.36 (0.1-1.25)	0.12
pre-XDR	21 (23.6 %)	18 (23.4 %)	3 (25.0 %)	1.09 (0.22-4.13)	>0.9
XDR	5 (5.6 %)	3 (3.9 %)	2 (16.7 %)	4.93 (0.6-33.5)	0.13
Number of drugs					
1	58 (65.2 %)	55 (71.4 %)	3 (25.0 %)	0.13 (0.03-0.49)	0.003
2	24 (27.0 %)	19 (24.7 %)	5 (41.7 %)	2.18 (0.59-7.66)	0.3
3 and more	7 (7.9 %)	3 (3.9 %)	4 (33.3 %)	12.33 (2.34-72.97)	0.006
median	1.0 (1.0-2.0)	1.0 (1.0-2.0)	2.0 (1.8-3.0)	3.6 (1.7-8.97)	<0.001
Use in drug regimens					
Amikacin	9 (10.1 %)	6 (7.8 %)	3 (25.0 %)	3.94 (0.74-18.01)	0.10
Capreomycin	53 (59.6 %)	48 (62.3 %)	5 (41.7 %)	0.43 (0.12-1.47)	0.2
Meropenem	44 (49.4 %)	36 (46.8 %)	8 (66.7 %)	2.28 (0.66-9.12)	0.2
PAS	15 (16.9 %)	11 (14.3 %)	4 (33.3 %)	3 (0.71-11.4)	0.11
Drug administrations					
Amikacin	159.0 (53.0-180.0)	169.0 (156.0-195.5)	45.0 (33.0-112.5)	0.98 (0.95-1)	0.3
Capreomycin	159.0 (99.0-187.0)	157.5 (100.0-187.0)	159.0 (99.0-170.0)	1 (0.98-1)	0.8
Meropenem	1,359.0 (546.8-1,648.5)	1,359.0 (525.8-1,609.5)	1,413.0 (1,066.5-1,648.5)	1 (1-1)	0.8
PAS	325.0 (156.5-484.5)	186.0 (119.5-401.0)	484.5 (476.8-516.3)	1.01 (1-1.03)	0.056
Total	380.0 (153.0-1,413.0)	334.0 (153.0-1,365.0)	1,024.0 (195.0-1,768.5)	1 (1-1)	0.2

Drug administrations until occurrence of port system-associated complications. Categorial variables as n (%), continuous variables as median (IQR); Assoc.: associated; yrs: years; BMI: body-mass index; i.v.: intravenous; HIV: human immunodeficiency virus; HepB: hepatitis B virus; HepC: hepatitis C virus; Poly-resistant TB: resistant to two or more anti-tuberculosis-drugs, non-MDR, non-rif-resistant. Rif-resistant TB: rifampicin-resistant tuberculosis; MDR TB: multidrug-resistant tuberculosis; pre-XDR TB: pre-extensively drug-resistant tuberculosis; XDR TB: extensively drug-resistant tuberculosis; PAS: Para-amino salicylic acid; *omitted due to redundancy.

Supplement Figure S5



Supplement Figure S6. Inpatient treatment discontinuation due to adverse drug events over time. Median inpatient treatment durations for amikacin, capreomycin, PAS, and meropenem were 1.2, 2.4, 1.8, and 3.2 months, respectively. Like in sOPAT, capreomycin and meropenem were least often stopped due to adverse drug events during inpatient treatment: At the median inpatient 100.0 % of patients on meropenem treatment as well as 93.6 % of patients on capreomycin treatment had not discontinued treatment due to adverse drug events.

Supplement Table S8. Baseline parameters and patient characteristics, stratified by inpatient drug discontinuation due to adverse drug events.

	total	no drug discontinuation	drug discontinuation due to adverse events	odds ratio	p-value
Total	89 (100.0%)	80 (89.9%)	9 (10.1%)		
Sex					
female	30 (33.7 %)	25 (31.3 %)	5 (55.6 %)	2.75 (0.67-11.95)	0.2
male	59 (66.3 %)	55 (68.8 %)	4 (44.4 %)	0.36 (0.08-1.48)	0.2
Migration history	86 (96.6 %)	77 (96.3 %)	9 (100.0 %)		>0.9
Age at discharge	33.6 (26.2-42.8)	34.3 (26.1-43.3)	29 (27.9-32.9)		0.4
BMI	21.0 (18.6-23.9)	21.2 (18.9-24.1)	20.2 (17.3-23.8)	0.89 (0.72-1.07)	0.4
Underweight	22 (24.7 %)	18 (22.5 %)	4 (44.4 %)	2.76 (0.63-11.51)	0.2
Diabetes	1 (1.1 %)	1 (1.3 %)	0 (0.0 %)		>0.9
Smoker	35 (39.3 %)	32 (40.0 %)	3 (33.3 %)	0.75 (0.15-3.06)	>0.9
Alcohol abuse	5 (5.6 %)	5 (6.3 %)	0 (0.0 %)		>0.9
IV-drug abuse	6 (6.7 %)	5 (6.3 %)	1 (11.1 %)	1.88 (0.09-13.73)	0.5
HIV positive	8 (9.0 %)	7 (8.8 %)	1 (11.1 %)	1.3 (0.07-8.79)	0.6
HepB positive	8 (9.0 %)	8 (10.0 %)	0 (0.0 %)		>0.9
HepC positive	17 (19.1 %)	16 (20.0 %)	1 (11.1 %)	0.5 (0.03-3.02)	>0.9
Previous TB	31 (34.8 %)	29 (36.3 %)	2 (22.2 %)	0.5 (0.07-2.24)	0.5
Cavitary disease	50 (56.2 %)	46 (57.5 %)	4 (44.4 %)	0.59 (0.14-2.39)	0.5
Miliary disease	4 (4.5 %)	2 (2.5 %)	2 (22.2 %)	11.14 (1.19-105.68)	0.049
Extrapulmonary disease	11 (12.4 %)	10 (12.5 %)	1 (11.1 %)	0.88 (0.04-5.56)	>0.9
Drug-resistance					
pan-susceptible	4 (4.5 %)	4 (5.0 %)	0 (0.0 %)		>0.9
poly-resistant	1 (1.1 %)	1 (1.3 %)	0 (0.0 %)		>0.9
rifampicin-resistant	2 (2.2 %)	2 (2.5 %)	0 (0.0 %)		>0.9
MDR	56 (62.9 %)	47 (58.8 %)	9 (100.0 %)		0.024
pre-XDR	21 (23.6 %)	21 (26.3 %)	0 (0.0 %)		0.11
XDR	5 (5.6 %)	5 (6.3 %)	0 (0.0 %)		>0.9
Number of drugs					
1	58 (65.2 %)	50 (62.5 %)	8 (88.9 %)	4.8 (0.82-91.3)	0.2
2	24 (27.0 %)	24 (30.0 %)	0 (0.0 %)		0.11
3 and more	7 (7.9 %)	6 (7.5 %)	1 (11.1 %)	1.54 (0.08-10.76)	0.5
median	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-1.0)	0.97 (0.31-2.18)	0.2
Use in OPAT regimens					
Amikacin	22 (24.7 %)	17 (21.3 %)	5 (55.6 %)	4.63 (1.11-20.58)	0.038
Capreomycin	60 (67.4 %)	53 (66.3 %)	7 (77.8 %)	1.78 (0.4-12.52)	0.7
Meropenem	39 (43.8 %)	35 (43.8 %)	4 (44.4 %)	1.03 (0.24-4.17)	>0.9
PAS	24 (27.0 %)	19 (23.8 %)	5 (55.6 %)	4.01 (0.97-17.69)	0.056
OPAT administrations					
Amikacin	31.0 (16.0-96.0)	31.0 (15.8-96.3)	38.0 (24.0-39.0)	1 (0.98-1.01)	0.8
Capreomycin	71.0 (58.5-102.5)	79.0 (61.0-104.0)	60.0 (14.0-64.5)	0.98 (0.95-1)	0.048
Meropenem	286.5 (228.0-361.5)	294.0 (228.8-412.5)	234.0 (144.8-282.8)	0.99 (0.98-1)	0.15
PAS	51.5 (13.3-77.3)	55.0 (23.5-78.0)	2.0 (2.0-4.0)	0.96 (0.91-1)	0.023
Total	149.0 (77.0-294.0)	148.5 (75.3-311.8)	185.0 (84.0-255.0)		0.3

OPAT administrations until occurrence of port system-associated complications. Categorial variables as n (%), continuous variables as median (IQR); Assoc.: associated; yrs: years; BMI: body-mass index; i.v.: intravenous; HIV: human immunodeficiency virus; HepB: hepatitis B virus; HepC: hepatitis C virus; Poly-resistant TB: resistant to two or more anti-tuberculosis-drugs, non-MDR, non-rif-resistant. Rif-resistant TB: rifampicin-resistant tuberculosis; MDR TB: multidrug-resistant tuberculosis; pre-XDR TB: pre-extensively drug-resistant tuberculosis; XDR TB: extensively drug-resistant tuberculosis; PAS: Para-amino salicylic acid.

Supplement Table S9. Therapy response and outcome parameters, stratified by sOPAT port system-associated complications.

	total	no OPAT port-assoc. complication	OPAT port-assoc. complication	p-value
Treatment response				
Time to culture conversion [days]	38.5 (14.0-89.3)	38.5 (13.8-83.3)	55.0 (20.5-121.8)	0.5
Total therapy duration [months]	20.0 (19.7-21.0)	20.0 (19.8-21.0)	20.0 (17.5-23.6)	0.8
Outcome				
WHO				
cure	24 (27.0 %)	24 (29.6 %)	0 (0.0 %)	0.10
completed	33 (37.1 %)	30 (37.0 %)	3 (37.5 %)	>0.9
failed	21 (23.6 %)	18 (22.2 %)	3 (37.5 %)	0.4
died	2 (2.2 %)	2 (2.5 %)	0 (0.0 %)	>0.9
lost to follow-up	2 (2.2 %)	2 (2.5 %)	0 (0.0 %)	>0.9
not available	7 (7.9 %)	5 (6.2 %)	2 (25.0 %)	0.12
TBnet				
cure	64 (71.9 %)	61 (75.3 %)	3 (37.5 %)	0.037
failed	3 (3.4 %)	2 (2.5 %)	1 (12.5 %)	0.2
died	4 (4.5 %)	3 (3.7 %)	1 (12.5 %)	0.3
lost to follow-up	2 (2.2 %)	2 (2.5 %)	0 (0.0 %)	>0.9
not available	16 (18.0 %)	13 (16.0 %)	3 (37.5 %)	0.2
Long-term				
relapse free	56 (62.9 %)	52 (64.2 %)	4 (50.0 %)	0.5
relapse	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
died	4 (4.5 %)	3 (3.7 %)	1 (12.5 %)	0.3
NA / lost to follow-up	29 (32.6 %)	26 (32.1 %)	3 (37.5 %)	0.7

Outcome definitions according to Supplement Table S2. OPAT: outpatient parenteral antimicrobial therapy. WHO: World Health Organization. TBnet: Tuberculosis Network European Trials group. NA: Not available.

Supplement Table S10. Therapy response and outcome parameters, stratified by sOPAT parenteral drug discontinuation due to adverse drug events.

	total	no drug discontinuation	drug discontinuation due to adv. events	p-value
Therapy response				
Time to culture conversion [days]	38.5 (14.0-89.3)	36.0 (14.0-69.0)	135.0 (89.0-220.0)	0.042
Total therapy duration [months]	20.0 (19.7-21.0)	20.0 (19.8-21.2)	19.9 (18.4-20.0)	0.2
Outcome				
WHO				
cure	24 (27.0 %)	22 (27.8 %)	2 (20.0 %)	0.7
completed	33 (37.1 %)	31 (39.2 %)	2 (20.0 %)	0.3
failed	21 (23.6 %)	16 (20.3 %)	5 (50.0 %)	0.052
died	2 (2.2 %)	2 (2.5 %)	0 (0.0 %)	>0.9
lost to follow-up	2 (2.2 %)	2 (2.5 %)	0 (0.0 %)	>0.9
not evaluated	7 (7.9 %)	6 (7.6 %)	1 (10.0 %)	0.6
TBnet				
cure	64 (71.9 %)	56 (70.9 %)	8 (80.0 %)	0.7
failed	3 (3.4 %)	3 (3.8 %)	0 (0.0 %)	>0.9
died	4 (4.5 %)	3 (3.8 %)	1 (10.0 %)	0.4
lost to follow-up	2 (2.2 %)	2 (2.5 %)	0 (0.0 %)	>0.9
not evaluated	16 (18.0 %)	15 (19.0 %)	1 (10.0 %)	0.7
Long-term				
relapse free	56 (62.9 %)	48 (60.8 %)	8 (80.0 %)	0.3
relapse	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
died	4 (4.5 %)	3 (3.8 %)	1 (10.0 %)	0.4
NA / lost to follow-up	29 (32.6 %)	28 (35.4 %)	1 (10.0 %)	0.2

Outcome definitions according to Supplement Table S2. OPAT: outpatient parenteral antimicrobial therapy. WHO: World Health Organization. TBnet: Tuberculosis Network European Trials group. NA: Not available.

Supplement Table S11. Therapy response and outcome parameters, stratified by inpatient port system-associated complications.

	total	no inpatient port-assoc. complication	inpatient port-assoc. complication	p-value
Therapy response				
Time to culture conversion [days]	38.5 (14.0-89.3)	36.0 (13.5-69.0)	116.0 (109.0-196.0)	0.018
Total therapy duration [months]	20.0 (19.7-21.0)	20.0 (19.5-21.0)	28.3 (20.9-34.4)	0.017
Outcome				
WHO				
cure	24 (27.0 %)	22 (26.5 %)	2 (33.3 %)	0.7
completed	33 (37.1 %)	32 (38.6 %)	1 (16.7 %)	0.4
failed	21 (23.6 %)	18 (21.7 %)	3 (50.0 %)	0.14
died	2 (2.2 %)	2 (2.4 %)	0 (0.0 %)	>0.9
lost to follow-up	2 (2.2 %)	2 (2.4 %)	0 (0.0 %)	>0.9
not evaluated	7 (7.9 %)	7 (8.4 %)	0 (0.0 %)	>0.9
TBnet				
cure	64 (71.9 %)	60 (72.3 %)	4 (66.7 %)	>0.9
failed	3 (3.4 %)	1 (1.2 %)	2 (33.3 %)	0.011
died	4 (4.5 %)	4 (4.8 %)	0 (0.0 %)	>0.9
lost to follow-up	2 (2.2 %)	2 (2.4 %)	0 (0.0 %)	>0.9
not evaluated	16 (18.0 %)	16 (19.3 %)	0 (0.0 %)	0.6
Long-term				
relapse free	56 (62.9 %)	54 (65.1 %)	2 (33.3 %)	0.2
relapse	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
died	4 (4.5 %)	4 (4.8 %)	0 (0.0 %)	>0.9
NA / lost to follow-up	29 (32.6 %)	25 (30.1 %)	4 (66.7 %)	0.085

Outcome definitions according to Supplement Table S2. OPAT: outpatient parenteral antimicrobial therapy. WHO: World Health Organization. TBnet: Tuberculosis Network European Trials group. NA: Not available.

Supplement Table S12. Therapy response and outcome parameters, stratified by inpatient parenteral drug discontinuation due to adverse drug events.

	total	no drug discontinuation	drug discontinuation due to adv. events	p-value
Therapy response				
Time to culture conversion [days]	38.5 (14.0-89.3)	38.5 (14.5-78.3)	55.0 (9.5-101.3)	>0.9
Total therapy duration [months]	20.0 (19.7-21.0)	20.0 (19.8-21.0)	20.0 (19.4-22.0)	0.9
Outcome				
WHO				
cure	24 (27.0 %)	22 (27.5 %)	2 (22.2 %)	>0.9
completed	33 (37.1 %)	30 (37.5 %)	3 (33.3 %)	>0.9
failed	21 (23.6 %)	18 (22.5 %)	3 (33.3 %)	0.4
died	2 (2.2 %)	2 (2.5 %)	0 (0.0 %)	>0.9
lost to follow-up	2 (2.2 %)	2 (2.5 %)	0 (0.0 %)	>0.9
not evaluated	7 (7.9 %)	6 (7.5 %)	1 (11.1 %)	0.5
TBnet				
cure	64 (71.9 %)	57 (71.3 %)	7 (77.8 %)	>0.9
failed	3 (3.4 %)	3 (3.8 %)	0 (0.0 %)	>0.9
died	4 (4.5 %)	4 (5.0 %)	0 (0.0 %)	>0.9
lost to follow-up	2 (2.2 %)	2 (2.5 %)	0 (0.0 %)	>0.9
not evaluated	16 (18.0 %)	14 (17.5 %)	2 (22.2 %)	0.7
longterm				
relapse free	56 (62.9 %)	49 (61.3 %)	7 (77.8 %)	0.5
relapse	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
died	4 (4.5 %)	4 (5.0 %)	0 (0.0 %)	>0.9
NA / lost to follow-up	29 (32.6 %)	27 (33.8 %)	2 (22.2 %)	0.7

Outcome definitions according to Supplement Table S2. OPAT: outpatient parenteral antimicrobial therapy. WHO: World Health Organization. TBnet: Tuberculosis Network European Trials group. NA: Not available.

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