SUPPLEMENTARY MATERIAL

Cefiderocol therapy among immunocompromised adult patients: a descriptive analysis from a prospective, multicentre cohort study

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Supplementary Table 1. 28-day clinical cure in patients receiving targeted cefiderocol therapy.

Infection*,[a]	Total	SOT	Haematology	Other IC	Non-IC
Enterobacterales infection [c]	17/22 (77.3)	-	4/5 (80.0)	5/7 (71.4)	8/10 (80.0)
Cefiderocol monotherapy	10/11 (90.9)	-	2/2 (100.0)	3/4 (75.0)	5/5 (100.0)
Combination therapy [b]	7/11 (63.6)	-	2/3 (66.7)	2/3 (66.7)	3/5 (60.0)
***Pseudomonas aeruginosa* infection** [d]	17/21 (81.0)	2/2 (100.0)	3/3 (100.0)	4/4 (100.0)	8/12 (66.7)
Cefiderocol monotherapy	9/11 (81.8)	1/1 (100.0)	2/2 (100.0)	4/4 (100.0)	2/4 (50.0)
Combination therapy [b]	8/10 (80.0)	1/1 (100.0)	1/1 (100.0)	-	6/8 (75.0)
***Acinetobacter baumannii* infection** [e] **(missing = 2)**	21/50 (42.00)	2/4 (50.0)	1/4 (25.0)	2/10 (20.0)	16/32 (50.0)
Cefiderocol monotherapy	13/25 (52.0)	2/4 (50.0)	0/1 (0.0)	2/4 (50.0)	9/16 (56.3)
Combination therapy [b], missing = 2	8/25 (32.0)	-	1/3 (33.3)	0/6 (0.0)	7/16 (43.8)
MBL-producing Gram-negative infection [f,g,h]	16/21 (76.2)	1/1 (100.0)	6/6 (100.0)	3/5 (60.0)	6/9 (66.7)
Cefiderocol monotherapy	10/12 (83.3)	1/1 (100.0)	4/4 (100.0)	2/3 (66.7)	3/4 (75.0)
Combination therapy [b]	6/9 (66.7)	-	2/2 (100.0)	1/2 (50.0)	3/5 (60.0)

Supplementary Table 1 legend. Results are presented as number of patients with 28-day clinical cure (percentage). Discharged patients excluded from denominator. MBL, metallo-β-lactamases.

***** Number of missing values, impacting frequency and percentage calculation, are reported.

[a] Infection by only one Gram-negative genus (with the exception of Enterobacterales infection, for which concomitant infection by more than one member of the Enterobacterales order was also considered).

[b] Anti-CR-GNB combination was defined as treatment with cefiderocol in combination with at least one of the following agents: aminoglycosides; fosfomycin; tigecycline (with the exception of targeted therapy of *P. aeruginosa* infections); polymyxins; sulbactam or ampicillin/sulbactam (as empirical treatment of as targeted therapy for *A. baumannii* infections).

[c] Site/s of Enterobacterales infection: bloodstream infection (n = 10); lower respiratory tract infection (n = 6); urinary tract infection (n = 1); skin and soft tissue infection (n = 1); intra-abdominal infection (n = 1); more than one indication (n = 3).

[d] Site/s of *P. aeruginosa* infection: lower respiratory tract infection (n = 11); bloodstream infection (n = 5); urinary tract infection (n = 2); intra-abdominal infection (n = 1); skin and soft tissue infection (n = 1); more than one indication (n = 1).

[e] Site/s of *A. baumannii* infection: lower respiratory tract infection (n = 25); bloodstream infection (n = 19); bone and joint infection (n = 2); urinary tract infection (n = 2); intra-abdominal infection (n = 1); more than one indication (n = 1).

[f] Site/s of MBL-producing Gram-negative infection: lower respiratory tract infection (n = 8); bloodstream infection (n = 5); urinary tract infection (n = 3); intra-abdominal infection (n = 2); skin and soft tissue infection (n = 2): more than one indication (n = 1).

[g] Type of MBL enzyme: VIM (n = 18); NDM (n = 3).

[h] Type of MBL-producing causative agent: *P. aeruginosa* (n = 11); Enterobacterales (n = 10).

Supplementary Table 2. Clinical outcomes in patients receiving targeted cefiderocol therapy, adjusted 28-day clinical cure**.

Infection*,[a]	Total	Haematology	Non-IC	Other IC	SOT
Enterobacterales infection [c]	20/25 (80.0)	4/5(80.0)	11/13 (84.6)	5/7 (71.4)	-
Cefiderocol monotherapy	12/13 (92.3)	2/2 (100.0)	7/7 (100.0)	3/4 (75.0)	-
Combination therapy [b]	8/12 (66.7)	2/3 (66.7)	4/6 (66.7)	2/3 (66.7)	-
***Pseudomonas aeruginosa* infection** [d]	19/23 (82.6)	3/3 (100.0)	9/13 (69.2)	4/4 (100.0)	3/3 (100.0)
Cefiderocol monotherapy	11/13 (84.6)	2/2 (100.0)	3/5 (60.0)	4/4 (100.0)	2/2 (100.0)
Combination therapy [b]	8/10 (80.0)	1/1 (100.0)	6/8 (75.0)	-	1/1 (100.0)
***Acinetobacter baumannii* infection** [e]**, missing = 2**	30/59 (50.9)	3/6 (50.0)	20/36 (55.6)	4/12 (33.3)	3/5 (60.0)
Cefiderocol monotherapy	15/27 (55.6)	0/1 (0.0)	10/17 (58.8)	3/5 (60.0)	2/4 (50.0)
Combination therapy [b], missing = 2	15/32 (46.9)	3/5 (60.0)	10/19 (52.6)	1/7 (14.3)	1/1 (100.0)
MBL-producing Gram-negative infection [f,g,h]	16/21 (76.2)	6/6 (100.0)	6/9 (66.7)	3/5 (60.0)	1/1 (100.0)
Cefiderocol monotherapy	10/12 (83.3)	4/4 (100.0)	3/4 (75.0)	2/3 (66.7)	1/1 (100.0)
Combination therapy [b]	6/9 (66.7)	2/2 (100.0)	3/5 (60.0)	1/2 (50.0)	-

Supplementary Table 2 legend. Results are presented as number of patients with adjusted 28-day clinical cure (percentage). MBL, metallo-β-lactamases.

* Number of missing values, impacting frequency and percentage calculation, are reported.

** Adjusted with inclusion of discharged patients in the denominator.

[a] Infection by only one Gram-negative genus (with the exception of Enterobacterales infection, for which concomitant infection by more than one member of the Enterobacterales order was also considered).

[b] Anti-CR-GNB combination was defined as treatment with cefiderocol in combination with at least one of the following agents: aminoglycosides; fosfomycin; tigecycline (with the exception of targeted therapy of *P. aeruginosa* infections); polymyxins; sulbactam or ampicillin/sulbactam (as empirical treatment of as targeted therapy for *A. baumannii* infections).

[c] Site/s of Enterobacterales infection: bloodstream infection (n = 11); lower respiratory tract infection (n = 7); urinary tract infection (n = 2); skin and soft tissue infection (n = 1); intra-abdominal infection (n = 1); more than one indication (n = 3).

[d] Site/s of *P. aeruginosa* infection: lower respiratory tract infection (n = 11); bloodstream infection (n = 6); urinary tract infection (n = 2); intra-abdominal infection (n = 1); skin and soft tissue infection (n = 1); more than one indication (n = 2)

[e] Site/s of *A. baumannii* infection: lower respiratory tract infection (n = 27); bloodstream infection (n = 24); bone and joint infection (n = 2); urinary tract infection (n = 2); intra-abdominal infection (n = 1); more than one indication (n = 2); site/s not reported (n = 1).

[f] Site/s of MBL-producing Gram-negative infection: lower respiratory tract infection (n = 8); bloodstream infection (n = 5); urinary tract infection (n = 3); intra-abdominal infection (n = 2); skin and soft tissue infection (n = 2): more than one indication (n = 1)

[g] Type of MBL enzyme: VIM (n = 18); NDM (n = 3)

[h] Type of MBL-producing causative agent: *P. aeruginosa* (n = 11); Enterobacterales (n = 10).

Supplementary Table 3. Multivariable model after backward selection (model C) and shared frailty analysis (model D) of factors associated with 30-day mortality in the study population receiving cefiderocol targeted therapy for Enterobacterales, *Pseudomonas aeruginosa* or *Acinetobacter baumannii* infection (n = 109).

	Multivariable model (Model C)[a]**		**Shared frailty model (Model D)[b]**	
Variable*	**HR (95% CI)**	**p-value**	**HR (95% CI)**	**p-value**
Age in years	1.02 (1.00-1.05)	**0.0466**	1.02 (1.00-1.05)	0.0728
Diabetes mellitus	2.14 (1.01-4.51)	**0.0464**	1.78 (0.82-3.88)	0.1470
Previous myocardial Injury	4.47 (1.98-10.11)	**0.0003**	3.76 (1.60-8.84)	**0.0024**
Previous steroid therapy	2.80 (1.32-5.95)	**0.0073**	2.60 (1.19-5.70)	**0.0168**
Presence of ARDS	3.05 (1.15-8.06)	**0.0246**	4.16 (1.43-12.06)	**0.0087**
Acinetobacter baumannii infection	2.61 (1.18-5.77)	**0.0174**	3.23 (1.30-8.04)	**0.0114**
Type of immunosuppression		0.1988		0.1497
SOT (vs. non-IC as ref.)	0.48 (0.10-2.12)	0.3443	0.46 (0.10-2.14)	0.3195
Haematology (vs. non-IC as ref.)	0.48 (0.14-1.71)	0.2587	0.50 (0.14-1.83)	0.2923
Other IC (vs. non-IC as ref.)	1.47 (0.65-3.34)	0.3559	1.66 (0.72-3.84)	0.2353

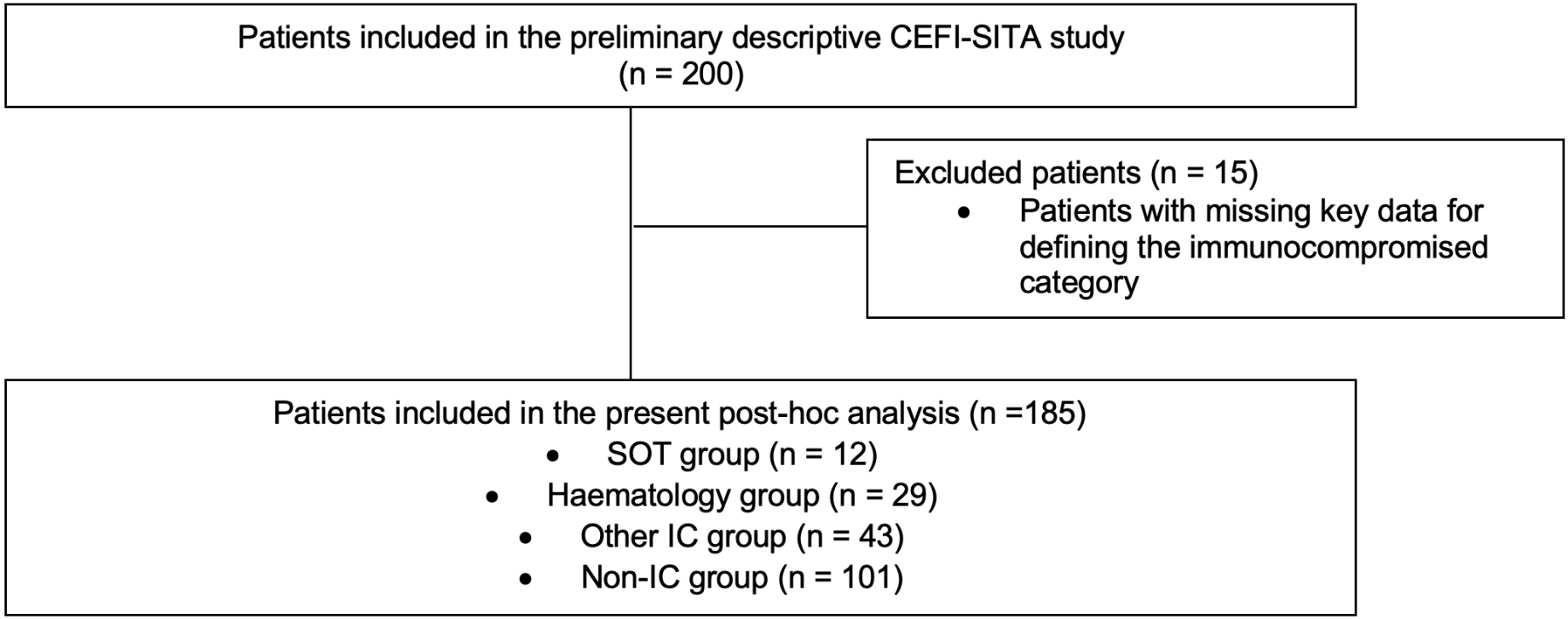
Supplementary Table 3 legend. Analyses conducted after multiple imputation. The reported p-values are from the Cox regression analysis. Bold values are significant at the selected level of significance (α = 0.05). ARDS, acute respiratory distress syndrome; CI, confidence interval. HR, hazard ratio; IC, immunocompromised; SOT, solid organ transplantation.

* Variable previous major surgery was included in the initial multivariable model as a time-dependent covariate, utilising an interaction term with time (significant: confirms that the association between the variable and the outcome varies over time, p = 0.0461). The variable was not selected by the backward procedure for the final model multivariable model.

[a] Final multivariable model after backward selection. Type of immunosuppression was forced to remain among the variables selected by the backward selection procedure (for details, see methods).

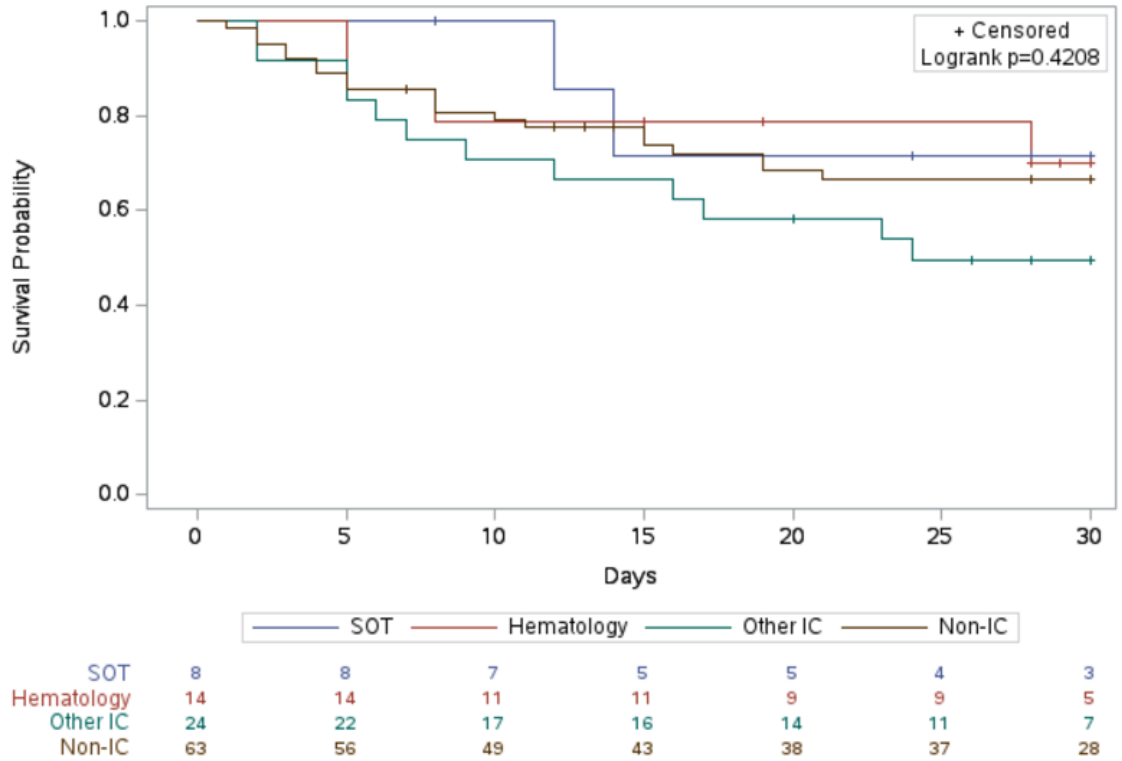
[b] Centre included as shared frailty.

Supplementary Figure 1. Flowchart of the patient inclusion process.



Supplementary Figure 1 legend. IC, immunocompromised; SOT, solid organ transplantation.

Supplementary Figure 2. Survival in patients with cefiderocol targeted treatment for Enterobacterales, *Pseudomonas aeruginosa*, or *Acinetobacter baumannii* infections (SOT vs. haematology vs. other IC vs. non-IC).



Supplementary Figure 2 legend. The time of origin was set at the day of cefiderocol initiation. Death was the event of interest and right-censoring was applied at the end of follow-up (hospital discharge or day 30, whichever came first). Site/s of *Enterobacterales* infection: bloodstream infection (n = 11); lower respiratory tract infection (n = 7); urinary tract infection (n = 2); skin and soft tissue infection (n = 1); intra-abdominal infection (n = 1); more than one indication (n = 3). Site/s of *P. aeruginosa* infection: lower respiratory tract infection (n = 11); bloodstream infection (n = 6); urinary tract infection (n = 2); intra-abdominal infection (n = 1); skin and soft tissue infection (n = 1); more than one indication (n = 2). Site/s of *A. baumannii* infection: lower respiratory tract infection (n = 27); bloodstream infection (n = 26); bone and joint infection (n = 2); urinary tract infection (n = 2); intra-abdominal infection (n = 1); more than one indication (n = 2); site/s not reported (n = 1). IC, immunocompromised; SOT, solid organ transplantation.