Supplementary Tables

Table S1: Number of included patients per center

Study Center	Number of included patients
Czech Republic	
Prague	22
France	
Lyon	12
Toulouse	4
Germany	
Heidelberg	102
Essen	36
Hamburg	25
Tuebingen	24
Stuttgart	18
Muenster	16
Berlin	13
Hannover	10
Marburg	9
Freiburg	6
Cologne	5
Leipzig	4
Memmingen	2
Ulm	2
Frankfurt	1
Rostock	1
Greece	
Thessaloniki	4
Hungary	
Budapest	21
Ireland	
Dublin	46
Italy	
Rome	118
Padua	33
Milan	23
Turin	13
Netherlands	
Amsterdam	1
Poland	
Warsaw	64
Russia	
Moscow	19

Spain	
Barcelona	3
Switzerland	
Zurich	16
Turkey	
Ankara	38
Samsun	9
Istanbul	6
Gazi	2
Izmir	2
United Kingdom	
Manchester	56
Birmingham	13
Nottingham	2
London	1

Table S2: Infection subtypes in the first 2 years post-transplant

Infection subtype	**< 6 years (N=206)**	**6-12 years (N=278)**	**> 12 years (N=318)**
Gastroenteritis	83 (40.3%)	68 (24.5%)	48 (15.1%)
Gastritis	5 (2.43%)	9 (3.24%)	8 (2.52%)
Colitis	3 (1.46%)	8 (2.88%)	5 (1.57%)
Peritonitis	1 (0.49%)	1 (0.36%)	0 (0.00%)
Lower respiratory infection	52 (25.2%)	37 (13.3%)	26 (8.18%)
Pyelonephritis	50 (24.3%)	40 (14.4%)	35 (11.0%)
Cystitis	38 (18.5%)	51 (18.4%)	46 (14.5%)
BKPyV	43 (20.9%)	37 (13.3%)	30 (9.4%)
CMV	36 (17.5%)	39 (14.0%)	49 (15.4%)
EBV	65 (31.6%)	48 (17.3%)	32 (10.1%)
Sepsis	26 (12.6%)	19 (6.8%)	16 (5.03%)
Hepatitis	2 (0.97%)	3 (1.08%)	2 (0.62%)
HIV	0 (0.00%)	1 (0.36%)	0 (0.00%)
Pneumocystis jirovecii	2 (0.97%)	0 (0.00%)	1 (0.31%)
Other fungal infection	9 (4.37%)	7 (2.52%)	9 (2.83%)
Other viral infection	76 (36.9%)	62 (22.3%)	53 (16.7%)

BKPyV, BK polyomavirus; CMV, Cytomegalovirus; EBV, Epstein-Barr virus; HIV, Human immunodeficiency virus

Table S3: Outcome parameters in the first two years post-transplant for patients < 2 years (N=18)

Rejection episodes, N	
Year 1	0
Year 2	1
Infections, N	
Year 1	15
Year 2	10
Graft dysfunction, N	2
Diabetes mellitus, N	0
Death, N	0
Cumulative hospitalization days, mean (SD)	41.6 (40.5)
GFR, mean (SD)	
Month 3	77.8 (33.3)
Month 12	68.7 (24.4)
Month 24	73.5 (25.5)

GFR, estimated glomerular filtration rate.

Table S4: Tacrolimus exposure parameters in patients <2 years (N=18). Data are mean (SD).

Tacrolimus trough level (ng/mL)	
Month 1-3	8.2 (2.52)
Month 6-12	6.12 (1.74)
Month 18-24	5.08 (2.11)
TacIPV – CV (%)	24.0 (16.5)
TacIPV -MAD (%)	17.4 (12.6)
BSA-corrected C/D ratio	
Month 1-12	1.21 (0.60)
Month 1-3	1.16 (0.73)
Month 6-12	1.42 (0.73)
BW-corrected C/D ratio	
Month 1-12	26.0 (12.7)
Month 1-3	25.1 (15.4)
Month 6-12	32.4 (21.2)
BSA-1.73m^2-crrected C/D ratio	
Month 1-12	0.81 (0.36)
Month 1-3	0.67 (0.42)
Month 6-12	0.89 (0.45)

TacIPV, tacrolimus intrapatient variability; CV, coefficient of variation; MAD, mean absolute deviation; C/D ratio, concentration/dose ratio; BSA, body surface area; BW, body weight; BSA-1.73m^2, BSA scaled for 1.73 m^2

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	Line 1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3	Line 49-53
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	Line 69-85
Objectives	3	State specific objectives, including any prespecified hypotheses	4	Line 86-93
Methods				
Study design	4	Present key elements of study design early in the paper	5	Line 96-97
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	Line 96-109
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5	Line 110-115
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5	Line 116-153
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5	Line 116-153
Bias	9	Describe any efforts to address potential sources of bias	7	Line 154-171
Study size	10	Explain how the study size was arrived at	5	Line 110-115, Figure 1

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7	Line 154-171
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7	Line 154-171
		(*b*) Describe any methods used to examine subgroups and interactions	7	Line 154-171
		(*c*) Explain how missing data were addressed	7	Line 169-171
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	NA	
		(*e*) Describe any sensitivity analyses	NA	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	17	Figure 1
		(b) Give reasons for non-participation at each stage	17	Figure 1
		(c) Consider use of a flow diagram	17	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8	Line 173-188, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	7	Line 169-171
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	24	Table 1
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*NA*	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures		
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	3	Table 2
		(*b*) Report category boundaries when continuous variables were categorized	8	Line 184-185
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA	

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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA	
Discussion				
Key results	18	Summarise key results with reference to study objectives	11	Line 269-272
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13	Line 315-320
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13	Line 321-327
Generalisability	21	Discuss the generalisability (external validity) of the study results	13	Line 325-327
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14	Line 328-326

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.