

Vaccination and Immunisation Status in European Paediatric Renal Transplant Recipients

An Analysis of the CERTAIN Registry

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Rationale

- Increased risk of both common and opportunistic infections after Tx due to immunosuppressive therapy
- Course of infections often more severe after Tx
- Protection against many infections by vaccinations pre-transplant, for some pathogens also by post-transplant vaccinations
- Vaccination response depends also on type and intensity of immunosuppressive treatment
- Few data available on vaccination and immunisation status in paediatric RTx



Aims

- Analysis of **vaccination status and vaccination titres** pre- and post-transplant and evaluation according to country-specific vaccination schedules and era
- Documentation of **a secondary antibody loss** after RTx and **the efficacy of re-vaccination**
- Analysis of the clinical efficacy of vaccinations, i.e. **the prevalence of vaccination-preventable diseases post-transplant**
- Determination of the impact of post-transplant vaccinations on **the development of HLA antibody levels** (in a subset of patients where data on HLA antibody levels are available)

Results

254 patients from 14 centres in 4 countries

- **Germany** (Essen, Freiburg, Hamburg, Hanover, Heidelberg, Munster, Rostock, Stuttgart, Tübingen)
- **Italy** (Rome)
- **Turkey** (Samsun, Hacettepe)
- **United Kingdom** (London, Manchester)

Patient and Transplant Characteristics (n = 254)

Age at RTx (yrs)	10.0 ± 5.6
Male gender	158 (62.2%)
Caucasian, n (%)	237 (93.3%)
Living donation, n (%)	98 (38.6%)
Second RTx or more, n (%)	21 (8.3%)
HLA mismatches	2.4 ± 1.3
Cold ischemia time (hrs)	9.9 ± 7.6
eGFR (ml/min·1.73 m ²)*	80.5 ± 27.2

*On day 30 post-transplant

Vaccination Titres after Renal Transplantation



All patients
(n = 254)

Complete vaccination data set
(n = 181)

Titre measurement prior to RTx
(n = 150)

Titre measurement before and after RTx
(n = 105)

Tetanus
(n = 41)

Diphtheria
(n = 41)

Pertussis
(n = 35)

Hepatitis A
(n = 53)

Hepatitis B
(n = 87)

Pneumococcal
(n = 31)

Measles
(n = 51)

Mumps
(n = 47)

Rubella
(n = 47)

Varicella
(n = 56)

Vaccination Titres before RTx

Inactivated Vaccines

Vaccine	Positive	Borderline	Negative
Tetanus (n = 65)	39 (60.0%)	22 (33.8%)	4 (6.2%)
Complete vacc. (n = 43)	27 (62.8%)	14 (32.6%)	2 (4.7%)
Incomplete vacc. (n = 22)	12 (54.5%)	8 (36.4%)	2 (9.1%)
Diphtheria (n = 65)	25 (38.5%)	29 (44.6%)	12 (18.5%)
Complete vacc. (n = 43)	19 (44.2%)	18 (41.9%)	6 (13.9%)
Incomplete vacc. (n = 22)	6 (27.3%)	10 (45.5%)	6 (27.3%)
Pertussis (n = 47)	10 (21.3%)	6 (12.8%)	31 (65.9%)
Complete vacc. (n = 35)	8 (22.9%)	5 (14.3%)	22 (62.8%)
Incomplete vacc. (n = 12)	2 (16.7%)	1 (8.3%)	9 (75.0%)
Hepatitis B (n = 155)	90 (58.6%)	39 (25.2%)	26 (16.8%)
Complete vacc. (n = 133)	80 (60.2%)	34 (25.6%)	19 (14.3%)
Incomplete vacc. (n = 22)	10 (45.5%)	5 (22.7%)	7 (31.8%)
Pneumococcal (n = 36)	25 (69.4%)	-	11 (30.6%)
Complete vacc. (n = 34)	25 (73.5%)	-	9 (26.5%)
Incomplete vacc. (n = 2)	-	-	2 (100%)
Hepatitis A (n = 62)	40 (64.5%)	7 (11.3%)	15 (24.2%)
Complete vacc. (n = 44)	30 (68.2%)	6 (13.6%)	8 (18.2%)
Incomplete vacc. (n = 18)	10 (55.6%)	1 (5.6%)	7 (38.9%)



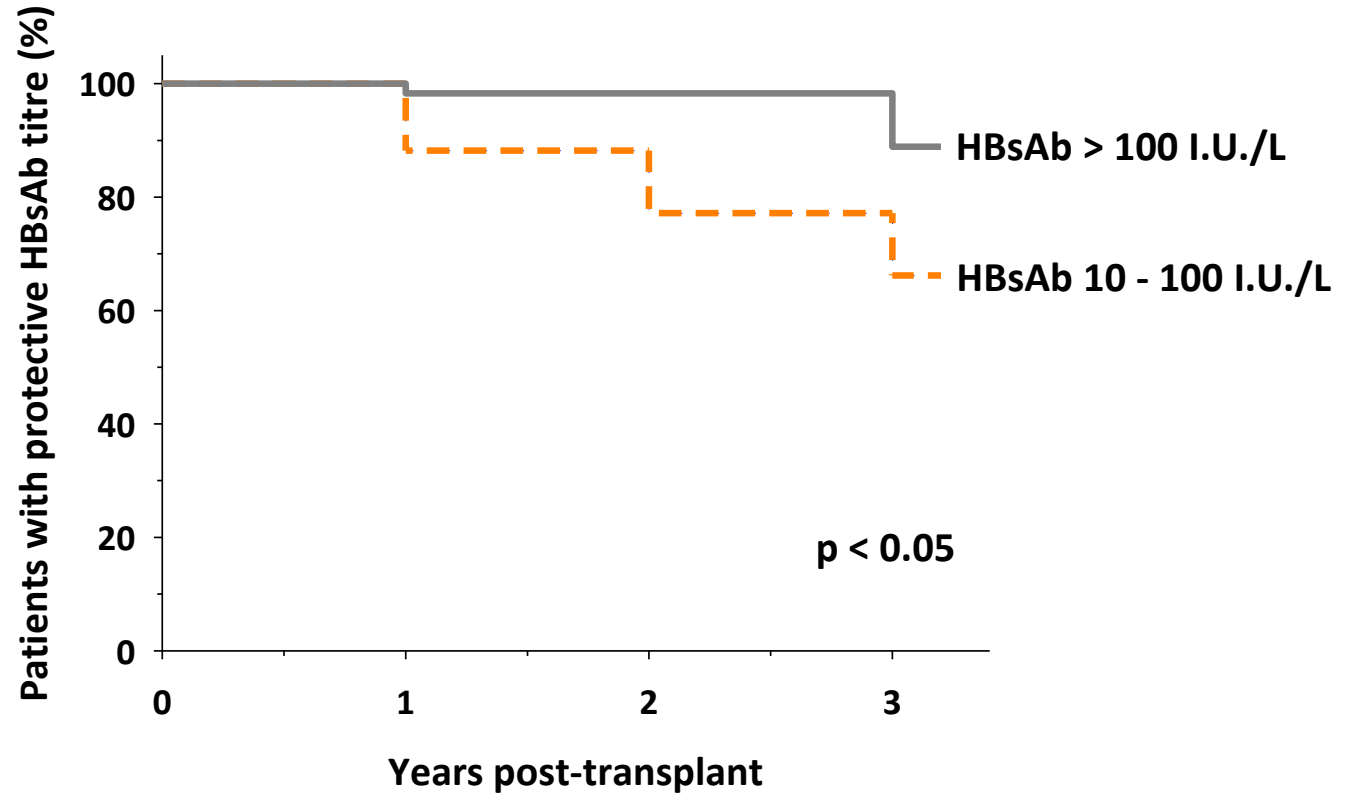
Am J Transplant
2009; 9(S3): 1-155

Vaccine	After RTx	Titre Control	Evidence Grade
Tetanus	+		1D
Diphtheria	+		1D
Pertussis	+		1D
HiB	+		1D
Hepatitis B	Titre <10 U/l Europe <100 U/l	6 - 12 weeks after vaccination, yearly after RTx	2D
Poliovirus (IPV)	+		1D
Influenza A und B	Yearly*		1D
Pneumococcus	Every 3 – 5 years?		2D
Hepatitis A, Meningococcus, Rabies, FSME, Japan. Encephalitis (inact.), Salmonella typhi (inact.)	In case of increased risk		2D
Measles	In case of epidemia?		2C
Mumps	-		2C
Rubella	-		2C
Varicella	-		2C
Poliovirus (OPV)	-		2C
Intranasal influenza	-		2C
Yellow Fever	-		2C
Japan. Encephalitis (Live vacc.)	-		2C
Salmonella typhi (Live vacc.)	-		2C

No vaccinations within first 6 months after RTx except

***Influenza - 1 month post-transplant at the earliest**

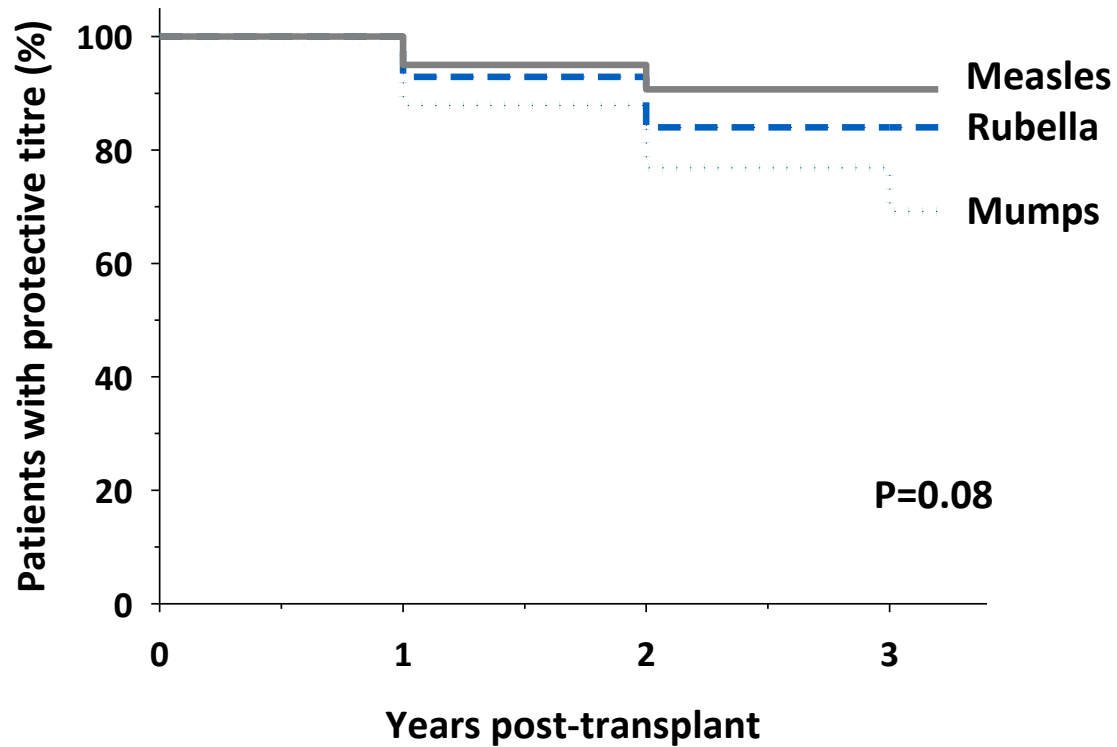
Hepatitis B Titre



Patients at risk:

HBsAb > 100 I.U./L	58	57	30	21	19
HBsAb > 10 I.U./L	17	15	8	7	6

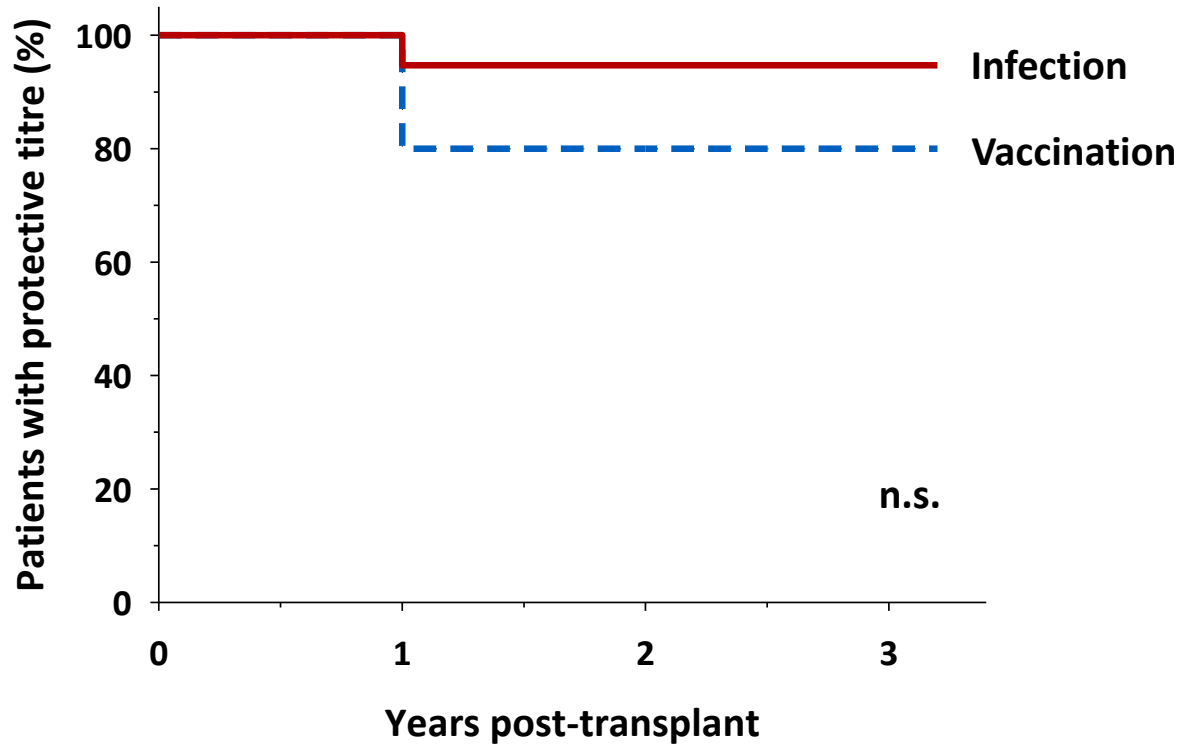
MMR Titres



Patients at risk:

Measles	40	38	22	15	15
Rubella	42	39	21	14	14
Mumps	33	29	16	10	9

VZV Titre



Patients at risk:

Infection	19	18	13	9	9
Vaccination	25	20	13	10	10

Live Virus Vaccinations after RTx

Vaccine	Patients (n = 254)
Measles	3 (1.2%)
Mumps	2 (0.8%)
Rubella	3 (1.2%)
Varicella	3 (1.2%)

Comparison of pre-transplant Vaccination Status with Healthy Population

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Seroprevalence of Measles-, Mumps- and Rubella-Specific IgG Antibodies in German Children and Adolescents and Predictors for Seronegativity

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Summary

- **Hepatitis B:** A pre-transplant titre > 100 U/L is associated post-transplant with a significantly lower loss of protective antibody status compared to a titre $< 100 > 10$ U/L.
- **Measles:** In the long run (> 6 years since vaccination), two shots are more effective than one shot in children post-transplant.
- **Mumps:** There is a tendency for a more pronounced loss of protective antibodies against mumps compared to measles and rubella both in healthy children and in children post-transplant.
- **Rubella:** The antibody response is more robust compared to measles and mumps both in healthy children and in children post-transplant.



Work in Progress

- Post-transplant vaccination status and additional sequential vaccination titres (tetanus, diphtheria, pertussis, hepatitis A, pneumococci)
- Impact of immunosuppressive regimen on vaccination titres
- Prevalence of vaccination-preventable diseases post-transplant
- Impact of post-transplant vaccinations on the development of HLA antibodies

Thank you!

