Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article.

Appendix

This appendix has been provided by the authors to give readers additional information about the study.

Supplement to: ***Multimodal Safety Assessment of Measles-Mumps-Rubella Vaccination after Pediatric Liver Transplantation***

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Supplement to Introduction

Table S1: Published studies on measles immunization after liver transplantation

Reference	Number of patients and study type	Treatment	History of measles vaccine before LT	Time from LT to first measles-containing vaccine study dose	Method of measles-specific IgG concentration measuring and protection cut-off used	Seroconversion rate	Long-term seroprotection	Clinical data available: complication/s following vaccination or occurrence of measles breakthrough disease
Rand 1993[1] Chicago, USA	18 patients (retrospective study)	CSA+SCS (n=13) CSA+AZA+SCS (n=4) TAC (n=1)	none	1.5 - 65 m (median, 16.5)	Solid-phase fluorescent immunoassay >12	7/17 = 41% (after 1 dose)	4/14 = 29% (6 m after vaccination)	1 rejection episode 3 weeks after vaccine. Breakthrough NA.
Kano 2002[2] Tokyo, Japan	13 patients (prospective study)	TAC or CSA	13/13 (1dose)	> 1 year	ELISA >2.0 EIA unit	11/13 = 85% (after 1 dose)	7/11 = 64% (6 m after vaccination)	No complication. 3 breakthrough diseases: 2 primary vaccine failures, 1 secondary vaccine failure
Khan 2006[3] Philadelphia, USA	31 patients (retrospective study)	TAC (n=22) CSA (n=9)	none	4-20 m (median, 26)	ELISA protective cut-off definition NA ("individual laboratory reference data")	19/26 = 73% (after 1-3 doses: 1 dose (n=13); 2 doses (n=15); 3 doses (n=3))	NA	No complications. Breakthrough NA.
Shinjoh 2008[4] 2015[5] Tokyo, Japan	37 patients (prospective study)	TAC or CSA	18/37 (number of doses NA)	> 2 years	Hemagglutinin inhibition test >1:8 ELISA index >2.0 EIA index >4.0	36/36 = 100% (after 1 dose, some patients received booster, total of 48 doses administered)	10/16 = 63% (5 years after vaccination)	No complications, 2 cases of fever without origin 2 to 3 weeks after vaccination. No breakthrough disease.
Kawano 2015[6] Nagoya, Japan	26 patients (prospective study)	TAC	8/26 (number of doses NA)	> 1 year	EIA index >2.5 (correlated to 120 IU/L)	11/25=44% (after 1 dose) 8/8=100% (after 2 dose)	4/8=50% (0.4-3.6 years after vaccination)	No complications. Breakthrough NA.

AZA: azathioprine; CSA: cyclosporine; EIA: enzyme immunoassay; ELISA: enzyme-linked immunosorbent assay; EVR: everolimus; LT: liver transplantation; m: month; MMF: mycophenolate mofetil; MPA: mycophenolic acid; NA: not available; SRL: sirolimus; SCS: systemic corticosteroid; TAC: tacrolimus; wk: week.

Supplement to Methods

Patient enrollment

All pediatric liver transplant recipients followed at Geneva University Hospitals (Geneva, Switzerland) who were at least 1 year post-transplantation were eligible. Patients were identified by the investigators who contacted them by telephone 1 week before a routine follow-up visit. Information sheets for parents adapted to the child's age were then sent to interested families and reviewed together with an investigator during the routine visit at the Geneva University Hospitals. Consent forms were signed at that time. Patients were enrolled in the study between April 2013 and October 2016. Primary vaccination occurred between April 2013 and March 2016. Booster doses were administered between April 2014 and November 2016. The follow-up for the present study ended in December 2016. Data were collected throughout this period at each patient visit to Geneva University Hospitals.

Methods for quantification of antigen-specific antibody concentration

Measles- and mumps-specific IgG antibodies were assessed using enzyme-linked immunosorbent assays (ELISA) on the platform DSX® (Dynex® Technologies, VA, USA) and rubella-specific IgG antibodies were assessed on the platform ARCHITECT i2000SR® (Abbott Laboratories®, IL, USA) at the vaccinology and virology laboratories of Geneva University Hospitals.

Serum was tested at baseline for all patients and 4 weeks following each measles-mumps-rubella (MMR) immunization in vaccinated patients. Measles-specific antibodies were monitored yearly thereafter in all patients, as recommended for routine liver transplant (LT) recipient follow-up.

The lowest limit of quantification of the ELISA measles test is 50 IU/L. Therefore, titers below this limit are reported as a value of 25 IU/L (half of the lowest limit). Assay **seropositivity cut-offs** were experimentally established as follows: measles-specific IgG antibody concentration >20 IU/L; rubella-specific IgG antibody >10 IU/L; mumps-specific IgG index >0.2. These cut-off values were established and validated using sera from immune and non-immune individuals according to the Good Laboratory Practice guidelines. **Seroconversion** was defined as a rise in IgG concentration above the seropositivity cut-off following immunization in previously seronegative patients.

For measles, a "**seroprotective concentration**" (>150 IU/L) was experimentally defined as the lowest concentration associated with the presence of neutralizing antibodies in a series of independent sera from healthy subjects. The validation of this cut-off was made with the collaboration of the Caen University Hospital Center, which is the French National Reference Center for measles virus. By extension, **seroprotection** was defined as a concentration >150 IU/L.

Primary vaccine failure was defined as the inability to reach the seropositivity cut-off after immunization. The inability to maintain seropositive IgG concentration after seroconversion due to waning immunity was called "**loss of seropositivity**". **Secondary vaccine failure** was defined as the occurrence of measles (disease), despite prior immunization.

Safety criteria for MMR vaccine administration

Criteria for MMR immunization were defined as follows:
1) Age ≥ 12 months
2) Non-seroprotective measles-specific IgG antibodies concentration (<150 IU/L)
3) Being ≥ 12 months after LT and ≥ 2 months from the time of an acute rejection episode
4) Low immunosuppression, defined as steroids < 2 mg/kg/day, tacrolimus < 0.3mg/kg/day and tacrolimus level < 8 ng/ml for > 1 month
5) Total lymphocyte count ≥ 0.75 G/L at time of immunization
6) No measles-containing immunoglobulins within the last 5 months
7) No known exposure to wild-type measles in the last 4 weeks
8) No live attenuated vaccine immunization within the last 4 weeks
9) No antiviral agents within the last 4 weeks
10) No febrile illness (>38.5°C) within the last 72 hours
11) No pregnancy: female patients of childbearing age had a pregnancy test before each vaccine dose and were asked to avoid pregnancy from the time of enrollment until 1 month after the last vaccine dose.
The selection of these criteria was driven by experts' opinion, based on clinical consideration. Only non-seroprotected patients were eligible for vaccination because seroprotected patients have high levels of measles-specific antibodies that rapidly neutralize the vaccine-strain, and the virus cannot replicate sufficiently.

Vaccine safety monitoring

Lot number and expiration date were both recorded on the patient's case report form.

Local and systemic adverse events were reported by the patients and caregiver on a standardized diary card at weeks 1, 2, 4, 6, and 8 after immunization; cards were then sent by mail to the study center. The following information were collected:

1) Administration site reaction:

a) Redness: If present, when did it start? What was the maximal size? How long did it last?
b) Induration: If present, when did it start? What was the maximal size? How long did it last?
c) Pain: If present, how long did it last?
d) Localized cutaneous rash

2) Systemic adverse event:

a) Fever (>38°C): If present, what was the maximal temperature?
b) Generalized cutaneous rash: If present, how long did it last?
c) Irritability
d) Anorexia
e) Fatigue
f) Headache
g) Nausea, vomiting
h) Diarrhea
i) Arthralgia
j) Myalgia
k) Parotiditis, cheek swelling
l) Conjunctivitis

Immunized patients were called at least three times (7-10 days, 20 days, and 1 month) after each immunization and standardized questions were asked:

1) How is the patient doing since vaccination / last call? What happened?
2) Did the patient have a febrile episode (>38°C) since vaccination / last call? If yes, when did it start? What was the maximum temperature? How long did it last? Were antipyretic drugs given? If yes, which one and how many dose(s)?
3) Did the patient have an episode of cutaneous rash since vaccination / last call?
4) Were there administration-site adverse events (redness, induration, pain) following vaccination? If yes, when did it start? What was the maximal size? How long did it last?
5) Were there any other averse events since vaccination / last call? What happened?
6) Overall, did the patient consulted since vaccination / last call? Was a treatment prescribed?

During each phone call, the patient and its caregivers were reminded to fill the diary cards, do the urine collection (see below) and arrange the blood sampling for assessment of vaccine responses.

Duration of viral replication following MMR immunization

Patients were asked to collect a sample of first-voided morning urine around days 7-10, 20, and 30 following MMR immunization. Collection was made by the patient (with the help of his/her parents/guardians) at home in a special recipient that can preserve RNA at room temperature until shipment to the study center's laboratory. The viral copy numbers of measles were then quantified by an in-house real-time polymerase chain reaction assay (RT-PCR) following a standardized protocol.[7] The same procedure was conducted in a cohort of healthy children following their first dose of MMR vaccine, acting as control population.

Breakthrough disease monitoring

Parents were asked to call the study center or contact the patient's physician in the case of rash. Physicians were given precise management guidelines and the rash was documented by a picture. In the presence of a measles-like rash, urine specimens, as well as cutaneous and oropharyngeal swabs, were immediately collected in order to determine whether a wild-strain or vaccine-strain of measles or another virus was the cause. Breakthrough diseases were also actively asked for at least annually during the routine follow-up visit of LT recipients.

Statistics: logistic regressions

Factors associated with seroprotection against measles at inclusion were identified using univariate logistic regression with the following variables: liver disease (biliary atresia or other), age at LT, history of rejection (number, timing), and prior history of MMR vaccine before inclusion (number, age, and timing). When appropriate, continuous variables were further divided into subgroups, based on clinical relevance. For the age at transplantation, we chose <1 year (very early transplantation), 1-3 years (early transplantation), and >3 years (transplantation during childhood). For the age at first MMR dose, we chose <9 months (very accelerated schedule), 9-12 months (accelerated schedule), and >12 months (universal recommendation for healthy children). For the delay between last MMR and LT, we chose <4 months (rapidly after immunization), 4-12 months (reasonable delay), >12 months (long delay).

All significant predictors ($P<0.20$) were then included in a stepwise backward multivariate analysis. In order to obtain a better estimate of the possible effect of each factor independently, we adjusted for age at first LT as it is the variable that best includes all other variables associated with the absence of seroprotection against measles at baseline (transplantation at younger age is linked to more severe disease and a lower chance to be immunized with two or any MMR doses before transplantation).

We then studied factors associated with seroprotection at 1-year follow-up using univariate logistic regression with the following variables: liver disease (biliary atresia or other), age at transplantation, history of rejection (number, timing), prior history of MMR vaccine before inclusion (number, age, and timing), and intensity of sero-response to study primary vaccination (> or <400 IU/L). We used backward stepwise multivariate logistic regression model. All significant predictors ($P<0.20$) were then included in a stepwise backward multivariate analysis to determine independent predictive factors.

The study protocol did not plan any interim analysis.

Sample size

The trial was designed to be a descriptive study of the influence of immunosuppression on measles-specific immunity resulting from immunization before transplantation and the safety and immunogenicity of MMR vaccine in children after LT. The influence of anti-rejection drugs on the maintenance of vaccine-driven antibody responses was unknown at the time of writing of the study protocol, thus precluding calculation of sample size estimates. All parents/guardians of children undergoing LT in Switzerland were approached for study inclusion.

Study monitoring

The study was independently monitored by the Clinical Research Center (CRC) of Geneva University Hospitals according to a pre-established plan and Good Clinical Practice recommendations. The monitor ensured that the trial was conducted in compliance with the approved protocol, oversaw the trial and evaluated progress, verified that the rights and safety of participants were protected, and that the reported data were complete, accurate, and verifiable from source documents.

Supplement to Results

Table S2: Patient characteristics at the time of study inclusion

	All patients N=90	Inclusion				Study immunization	
		Non-seroprotected N=46			Seroprotected N=44	Immunized with MMR study N=44	Non-immunized with MMR study N=46
		All patients N=46	MMR-naïve N=28	MMR non-naïve N=18			
Age at inclusion (years), median (IQR)	10.3 (5.7-13.6)	7.4 (5.2-13.1)	8.5 (5.4-12.9)	7.0 (4.0-13.4)	12.2 (7.7-14.7)	7.2 (4.9-12.3)	12.2 (8.1-14.9)
Duration of study follow-up (years), median (IQR)	2.1 (1.6-3.0)	2.4 (2.0-3.0)	2.8 (2.0-3.0)	2.3 (2.0-2.9)	2.0 (1.9-2.9)	2.5 (2.0-3.0)	2.0 (0.9-2.8)
Gender							
Male, n(%)	47 (52%)	21 (46%)	12 (43%)	9 (50%)	26 (59%)	21 (48%)	25 (57%)
Female, n(%)	43 (48%)	25 (54%)	16 (57%)	9 (50%)	18 (41%)	23 (52%)	19 (43%)
Diagnostic							
Biliary atresia, n(%)	**51 (57%)**	**31 (67%)**	**19 (68%)**	**12 (67%)**	**20 (45%)**	**32 (73%)**	**19 (41%)**
Other cholestatic disease, n(%)	**13 (14%)**	**5 (11%)**	**5 (18%)**	**0**	**8 (18%)**	**4 (9%)**	**9 (20%)**
- Alagille syndrom, n (%)	5 (6%)	0	0	0	5 (13%)	0	5 (11%)
- Progressive familial intrahepatic cholestasis type 1, n (%)	2 (2%)	1 (2%)	1 (4%)	0	1 (2%)	0	2 (5%)
- Progressive familial intrahepatic cholestasis type 3, n (%)	2 (2%)	2 (4%)	2 (7%)	0	0	2 (5%)	0
- Hemochromatosis, n (%)	1 (1%)	1 (2%)	1 (4%)	0	0	1 (2%)	0
- Sclerosing cholangitis, n (%)	1 (1%)	0	0	0	1 (2%)	0	1 (2%)
- Cholestatic hepatopathy of indeterminate causis, n (%)	2 (2%)	1 (2%)	1 (4%)	0	1 (2%)	1 (2%)	1 (2%)
Wilson disease, n (%)	**1 (1%)**	**0**	**0**	**0**	**1 (2%)**	**0**	**1 (2%)**
Alpha1-antitrypsin deficiency, n (%)	**2 (2%)**	**1 (2%)**	**0**	**1 (6%)**	**1 (2%)**	**1 (2%)**	**1 (2%)**
Acute liver failure (ALF), n (%)	**4 (4%)**	**2 (4%)**	**1 (4%)**	**1 (6%)**	**2 (5%)**	**2 (5%)**	**2 (4%)**
- Autoimmune ALF, n (%)	1 (1%)	0	0	0	1 (3%)	0	1 (2%)
- Acetaminophen-induced ALF, n (%)	1 (1%)	0	0	0	1 (3%)	0	1 (2%)
- ALF of indeterminate causes, n (%)	2 (2%)	2 (4%)	1 (4%)	1 (6%)	0	2 (5%)	0
Inherited metabolic disorder, n (%)	**4 (4%)**	**1 (2%)**	**0**	**1 (6%)**	**3 (7%)**	**1 (2%)**	**3 (7%)**
- Crigler-Najjar syndrome type 2, n (%)	1 (1%)	0	0	0	1 (2%)	0	1 (2%)
- Ornithine transcarbamylase deficiency, n (%)	1 (1%)	1 (2%)	0	1 (6%)	0	1 (2%)	0
- Glycogen storage disease type 3, n (%)	1 (1%)	0	0	0	1 (2%)	0	1 (2%)
- Branched-chain ketoaciduria, n (%)	1 (1%)	0	0	0	1 (2%)	0	1 (2%)
Oncologic disorder, n (%)	**4 (4%)**	**1 (2%)**	**0**	**1 (6%)**	**3 (7%)**	**1 (2%)**	**3 (7%)**
- Hepatoblastoma, n (%)	2 (2%)	1 (2%)	0	1 (6%)	1 (2%)	1 (2%)	1 (2%)
- Embryonal sarcoma of the liver, n (%)	1 (1%)	0	0	0	1 (2%)	0	1 (2%)
- Malignant mixed tumor of the liver, n (%)	1 (1%)	0	0	0	1 (2%)	0	1 (2%)
Other diagnosis, n (%)	**11 (12%)**	**5 (11%)**	**3 (11%)**	**2 (11%)**	**6 (14%)**	**3 (7%)**	**8 (17%)**
- Cryptogenic cirrhosis, n (%)	5 (6%)	4 (9%)	2 (7%)	2 (11%)	1 (2%)	2 (5%)	3 (7%)
- Cystic fibrosis, n (%)	1 (1%)	0	0	0	1 (2%)	0	1 (2%)
- Hepatic veno-occlusive disease, n (%)	1 (1%)	1 (2%)	1 (4%)	0	0	1 (3%)	0
- Hepatopathy of indeterminate causes, n (%)	1 (1%)	0	0	0	1 (2%)	0	1 (2%)
- Caroli syndrom, n (%)	1 (1%)	0	0	0	1 (2%)	0	1 (2%)
- Overlap syndrome, n (%)	1 (1%)	0	0	0	1 (2%)	0	1 (2%)

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continued	All patients N=90	Inclusion				Study immunization	
		Non-seroprotected N=46			Seroprotected N=44	Immunized with MMR study N=44	Non-immunized with MMR study N=46
		All patients N=46	MMR-naïve N=28	MMR non-naïve N=18			
Transplant							
Number of liver transplantations/patients							
- 1 transplantation, n (%)	85 (94%)	43 (93%)	26 (93%)	17 (94%)	42 (95%)	42 (95%)	43 (93%)
- 2 transplantations, n (%)	4 (4%)	3 (7%)	2 (7%)	1 (6%)	1 (2%)	2 (5%)	2 (4%)
- 3 transplantations, n (%)	1 (1%)	0	0	0	1 (2%)	0	1 (2%)
Living donor transplantation, n (% all transplantations)	12(13%)	8 (16%)	7 (23%)	1 (5%)	4 (9%)	9 (20%)	3 (6%)
Age at first LT (years), median (IQR)	1.4 (0.8-4.1)	0.9 (0.7-1.3)	0.8 (0.6-0.9)	1.2 (0.8-1.8)	4.0 (1.7-10.5)	0.9 (0.7-1.3)	3.8 (1.4-10.4)
Time since last LT							
- at inclusion (years), median (IQR)	5.0 (1.8-9.9)	6.1 (3.9-12.0)	7.2 (4.4-12.0)	5.6 (2.0-11.8)	2.2 (1.1-8.3)	6.1 (3.7-10.9)	2.6 (1.1-9.0)
- at first MMR study dose (years), median (IQR)	6.3 (4.0-10.9)	6.5 (4.3-11.9)	7.6 (5.0-12.1)	6.3 (3.1-11.8)	3.0 (2.7-5.6)	6.3 (4.0-10.9)	-
Rejection							
History of transplant rejection, n (%)	**43 (51%)**	**26 (57%)**	**18 (64%)**	**8 (44%)**	**19 (43%)**	**24 (55%)**	**21 (45%)**
- 1 episode, n (%)	36 (40%)	19 (41%)	12 (43%)	7 (39%)	17 (39%)	16 (36%)	20 (44%)
- 2 episodes, n (%)	6 (7%)	5 (11%)	4 (14%)	1 (6%)	1 (2%)	6 (14%)	0
- 3 episodes, n (%)	3 (3%)	2 (4%)	2 (7%)	0	1 (2%)	2 (5%)	1 (2%)
Time since last rejection episode							
- at inclusion (years), median (IQR)	5.7 (1.9-9.9)	6.5 (2.8-10.5)	5.7 (2.8-9.2)	10.3 (4.2-12.0)	2.1 (1.0-8.9)	5.7 (2.6-9.6)	3.7 (1.2-9.9)
- at first MMR study dose (years), median (IQR)	6.4 (3.0-9.6)	6.7 (3.9-10.0)	6.2 (3.9-9.0)	10.9 (7.2-11.7)	1.7 (1.6-1.8)	6.4 (3.0-9.6)	-
Treatment							
- Tacrolimus, n (%)	85 (94%)	43 (93%)	26 (93%)	17 (94%)	42 (95%)	41 (93%)	44 (96%)
- doses (mg/kg/day), median (IQR)	0.07 (0.05-0.13)	0.06 (0.04-0.11)	0.08 (0.05-0.11)	0.06 (0.04-0.08)	0.08 (0.06-0.14)	0.06 (0.05-0.11)	0.08 (0.05-0.14)
- Everolimus, n (%)	5 (6%)	1 (2%)	0	1 (6%)	4 (9%)	1 (2%)	4 (9%)
- doses (mg/kg/day), median (IQR)	0.09 (0.05-0.10)	0.19	-	0.19	0.07 (0.04-0.09)	0.19	0.07 (0.04-0.09)
- Cyclosporin, n (%)	4 (4%)	2 (4%)	2 (7%)	0	2 (5%)	2 (5%)	2 (4%)
- doses (mg/kg/day), median (IQR)	0.03 (0.02-0.03)	0.03 (0.02-0.03)	0.03 (0.02-0.03)	-	0.03 (0.02-0.03)	0.03 (0.02-0.03)	0.03 (0.02-0.03)
- Mycophenolate mofetil, n (%)	15 (17%)	6 (13%)	4 (14%)	2 (11%)	9 (20%)	4 (9%)	11 (24%)
- doses (mg/kg/day), median (IQR)	20.8 (15.4-27.3)	17.3 (5.6-21.7)	17.3 (10.8-23.5)	13.7 (5.6-21.7)	24.9 (18.3-27.3)	17.3 (10.8-20.1)	24.9 (15.4-28.6)
- Prednisone, n (%)	3 (3%)	1 (2%)	0	1 (6%)	2 (6%)	1 (2%)	2 (4%)
- doses (mg/kg/day), median (IQR)	0.23 (0.17-0.39)	0.17	-	0.2	0.31 (0.23-0.39)	0.17	0.31 (0.23-0.39)
Two anti-rejection drugs at inclusion, n (%)	22 (24%)	7 (15%)	4 (14%)	3 (17%)	15 (34%)	5 (11%)	17 (37%)
Measles							
History of measles disease, n (%)	0	0	0	0	0	0	0
History of measles exposure, n (%)	1 (1%)	1 (2%)	1 (4%)	0	0	1 (2%)	0
History of measles vaccine before or after LT, n (%)	**62 (69%)**	**18 (39%)**	**0**	**18 (100%)**	**44 (100%)**	**20 (45%)**	**42 (91%)**
- Before LT, n (%)	**58 (64%)**	**17 (37%)**	**-**	**17 (94%)**	**41 (93%)**	**18 (41%)**	**40 (87%)**
- 1 dose, n (%)	17 (19%)	8 (17%)	-	8 (44%)	9 (20%)	8 (18%)	9 (20%)
- 2 doses, n (%)	39 (43%)	9 (20%)	-	9 (50%)	30 (68%)	10 (23%)	29 (63%)
- 3 doses, n (%)	1 (1%)	0	-	0	1 (2%)	0	1 (2%)
- After LT, n (%)	**6 (7%)**	**2 (4%)**	**-**	**2 (11%)**	**4 (9%)**	**3 (7%)**	**3 (7%)**
- 1 dose, n (%)	4 (4%)	2 (4%)	-	2 (11%)	2 (5%)	3 (7%)	1 (2%)
- 2 doses, n (%)	1 (1%)	0	-	0	1 (2%)	0	1 (2%)
- 3 doses, n (%)	1 (1%)	0	-	0	1 (2%)	0	1 (2%)
Age at first measles vaccine before LT (year), median (IQR)	1.0 (0.8-1.3)	0.8 (0.7-1.0)	-	0.8 (0.7-1.0)	1.1 (1.0-1.4)	0.7 (0.6-1.0)	1.1 (1.0-1.4)
Time after LT at first measles vaccine dose (off-label) (years), median (range)	3.9 (0.8-13.7)	1.5 (0.8-2.1)	-	1.5 (0.8-2.1)	6.1 (2.7-13.7)	2.1 (0.8-7.1)	5.1 (2.7-13.7)

ALF: Acute liver failure; IQR: interquartile range; LT: liver transplantation; MMR: measles-mumps-rubella vaccine; n: number.

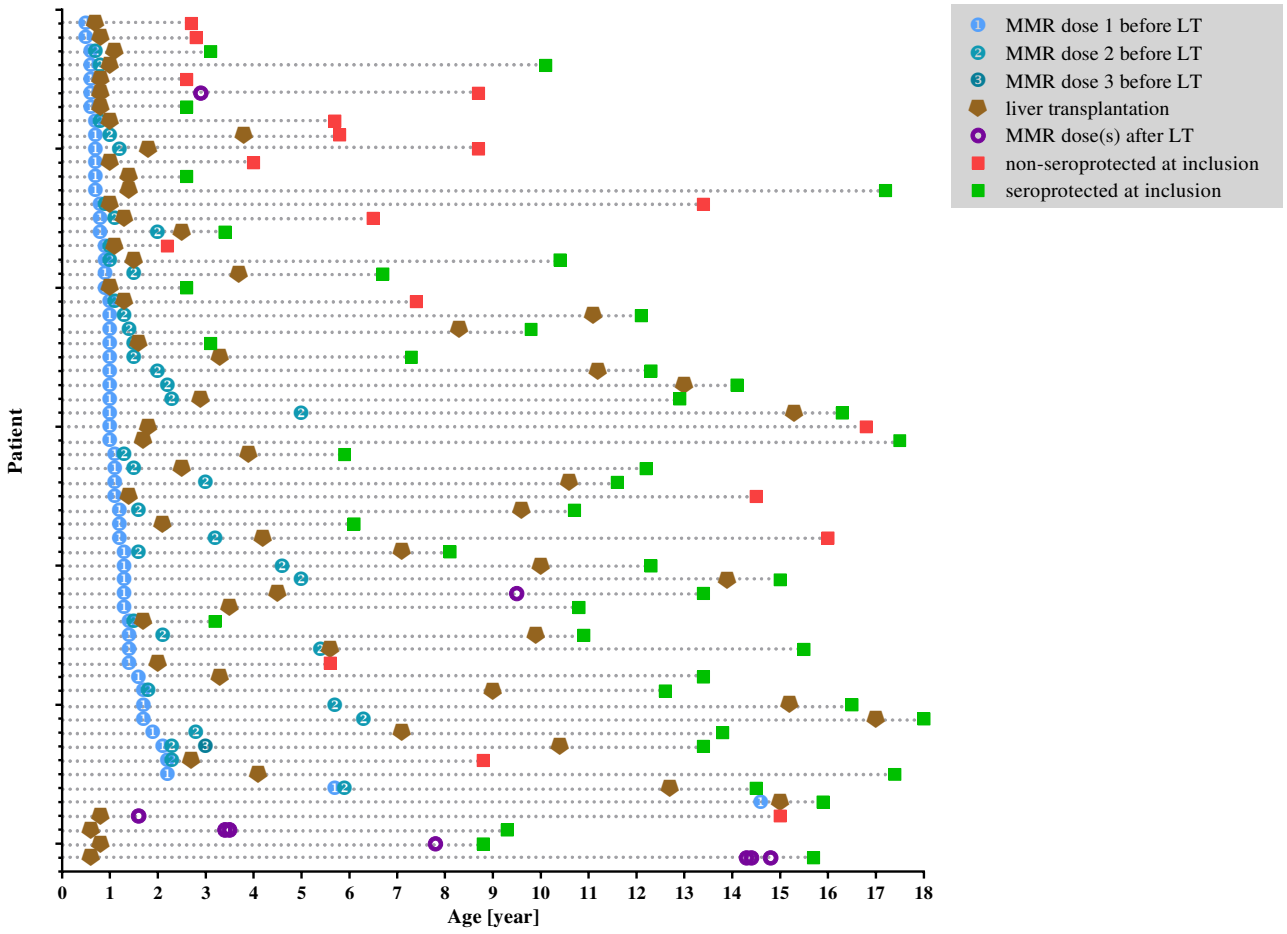
Table S3: Patient MMR immunization status before study inclusion

Subject number	Diagnosis	Treatment at inclusion	Previous history of MMR vaccine	Before LT			Age at first LT (years)	After LT			Age at inclusion (years)
				Age at dose 1 (years)	Age at dose 2 (years)	Age at dose 3 (years)		Age at dose 1 (years)	Age at dose 2 (years)	Age at dose 3 (years)	
PATIENTS NON-SEROPROTECTED AT STUDY INCLUSION											
51	Biliary atresia	TAC+SCS	1 dose before LT	0.5			0.7				2.7
38	Biliary atresia	TAC	1 dose before LT	0.5			0.8				2.8
5	Biliary atresia	TAC	1 dose before LT	0.6			0.8				2.6
57	Biliary atresia	TAC	1 dose before LT and 1 dose after LT	0.6			0.8	2.9			8.7
35	Biliary atresia	TAC	1 dose before LT	0.7			1.0				4.0
26	Biliary atresia	TAC+MMF	2 doses before LT	0.7	0.8		1.0				5.7
12	ALF of IC	TAC	2 doses before LT	0.7	1.0		3.8				5.8
49	Alpha1-antitrypsin deficiency	TAC	2 doses before LT	0.7	1.2		1.8				8.7
68	Cryptogenic cirrhosis	TAC	2 doses before LT	0.8	0.9		1.0				13.4
71	Biliary atresia	EVR	2 doses before LT	0.8	1.1		1.3				6.5
82	Biliary atresia	TAC+MMF	2 doses before LT	0.9	1.0		1.1				2.2
15	Biliary atresia	TAC	1 dose before LT	1.0			1.8				16.8
20	Cryptogenic cirrhosis	TAC	2 doses before LT	1.0	1.1		1.3				7.4
42	Biliary atresia	TAC	1 dose before LT	1.1			1.4				14.5
54	OTC deficiency	TAC	2 doses before LT	1.2	3.2		4.2				16.0
32	Hepatoblastoma	TAC	1 dose before LT	1.4			2.0				5.6
67	Biliary atresia	TAC	2 doses before LT	2.2	2.3		2.7				8.8
7	Biliary atresia	TAC	1 dose after LT				0.8	1.6			15.0
PATIENTS SEROPROTECTED AT STUDY INCLUSION											
73	Biliary atresia	TAC	2 doses before LT	0.6	NA		0.8				2.6
60	Biliary atresia	CSA	2 doses before LT	0.6	0.8		1.0				10.1
80	Biliary atresia	TAC	2 doses before LT	0.6	0.7		1.1				3.1
65	Biliary atresia	TAC	1 dose before LT	0.7			1.4				2.6
79	Biliary atresia	TAC	1 dose before LT	0.7			1.4				17.2
81	Autoimmune ALF	TAC	2 doses before LT	0.8	2.0		2.5				3.4
72	Hepatopathy of IC	TAC	1 dose before LT	0.9			1.0				2.6
22	Biliary atresia	TAC+MMF	2 doses before LT	0.9	1.0		1.5				10.4
33	Hepatoblastoma	TAC	2 doses before LT	0.9	1.5		3.7				6.7
11	Biliary atresia	TAC	2 doses before LT	1.0	1.4		8.3				9.8
78	Cystic fibrosis	TAC	2 doses before LT	1.0	5.0		15.3				16.3
61	Biliary atresia	TAC	2 doses before LT	1.0	2.3		2.9				12.9
90	Cystic fibrosis	TAC+MMF	2 doses before LT	1	2.2		13				14.1
70	Biliary atresia	TAC	2 doses before LT	1.0	1.5		1.6				3.1
17	Alagille syndrome	TAC	2 doses before LT	1.0	1.5		3.3				7.3

84	Overlap syndrome	TAC	2 doses before LT	1.0	2.0		11.3				12.3
19	Biliary atresia	TAC	1 dose before LT	1.0			1.7				17.5
89	Biliary atresia	TAC	2 doses before LT	1	1.3		11.1				12.1
53	Embryonal sarcoma of the liver	TAC+EVR	2 doses before LT	1.1	3.0		10.6				11.6
36	Branched-chain ketoaciduria	TAC	2 doses before LT	1.1	1.3		3.9				5.9
1	Cholestatic hepatopathy of IC	TAC	2 doses before LT	1.1	1.5		2.5				12.2
88	Biliary atresia	TAC	2 doses before LT	1.2	1.6		9.6				10.7
2	Acetaminophen-induced ALF	TAC+MMF	2 doses before LT	1.2	2.1		2.1				6.1
63	Crigler-Najjar syndrome type 2	TAC	1 dose before LT and 1 dose after LT	1.3			4.5	9.5			13.4
85	Sclerosing cholangitis	TAC+SCS	2 doses before LT	1.3	5.0		13.9				15.0
27	Biliary atresia	TAC+SCS	2 doses before LT	1.3	1.6		7.1				8.1
34	Alagille syndrome	TAC	2 doses before LT	1.3	4.6		10.0				12.3
37	Alagille syndrome	TAC+MMF	1 dose before LT	1.3			3.5				10.8
16	Biliary atresia	CSA	2 doses before LT	1.4	5.4		5.6				15.5
76	Biliary atresia	TAC	2 doses before LT	1.4	1.5		1.7				3.2
58	Alpha1-antitrypsin deficiency	TAC+EVR	2 doses before LT	1.4	2.1		9.9				10.9
13	Alagille syndrome	TAC+MMF	1 dose before LT	1.6			3.3				13.4
21	Malignant mixed tumor of the liver	TAC+EVR	2 doses before LT	1.7	1.8		9.0				12.6
77	Biliary atresia	TAC	2 doses before LT	1.7	6.3		17.0				18.0
75	Biliary atresia	TAC+EVR	2 doses before LT	1.7	5.7		15.2				16.5
8	PFIC type 1	TAC	2 doses before LT	1.9	2.8		7.1				13.8
55	Alagille syndrome	TAC+MMF	3 doses before LT	2.1	2.3	3.0	10.4				13.4
87	Caroli syndrome	TAC+MMF	1 dose before LT	2.2			4.1				17.4
9	Glycogen storage disease type 3	TAC+MMF	2 doses before LT	5.7	5.9		12.7				14.5
83	Cryptogenic cirrhosis	TAC	1 dose before LT	14.6			15.0				15.9
64	Biliary atresia	TAC	2 doses after LT				0.6	3.4	3.5		9.3
4	Biliary atresia	TAC	1 dose after LT				0.8	7.8			8.8
25	Biliary atresia	TAC	3 doses after LT				0.6	14.3	14.4	14.8	15.7
66	Wilson's disease	TAC+MMF	Immunization unknown				10.9				16.6

ALF: acute liver failure; CSA: cyclosporin; EVR: everolimus; IC: indeterminate causes; LT: liver transplantation; MMF: mycophenolate mofetil; NA: not available; OTC: ornithine transcarbamylase deficiency; PFIC: progressive familial intrahepatic cholestasis; SCS: systemic corticosteroids; TAC: tacrolimus.

Figure S1: Effect of MMR vaccination on seroprotection against measles at study inclusion



LT: liver transplantation; MMR: measles-mumps-rubella vaccine.

Each dotted horizontal line represents the life of a single patient included in the study that had received at least one dose of measles vaccine before inclusion. The brown pentagons represent LT. The circles stand for MMR administration before inclusion. Doses received before transplantation are in blue and those received after transplantation are in purple. The square is the time of inclusion (green, seroprotected; red, non-seroprotected).

MMR immunization study procedure

Forty of the 46 patients not protected against measles at study inclusion were immunized (Table 2 of the main manuscript). Thirteen patients received the MMR vaccine at inclusion (patient numbers 3, 14, 23, 31, 32, 42, 43, 45, 52, 54, 57, 59, 62, 69) and 15 patients were immunized by their pediatrician in the 1.3 months (IQR, 0.8-1.9) following inclusion due to personal preference (patient numbers 5, 6, 7, 10, 12, 18, 20, 29, 35, 38, 39, 40, 47, 49, 67). Vaccination was postponed in 11 patients that received the vaccine 14.2 months after inclusion (IQR, 6.9-18.6) for the following reasons: required varicella zoster virus immunization (n=3; patient numbers 28, 41, 74); initial refusal of the vaccine (n=3; patient numbers 30, 46, 56); investigation for post-transplant lymphoproliferative disorder (n=1; patient number 71); alloimmune pancytopenia (n=1; patient number 5); difficulties in adjusting tacrolimus treatment (n=1; patient number 15); graft instability with suspicion of rejection (n=2; patients numbers 26, 51).

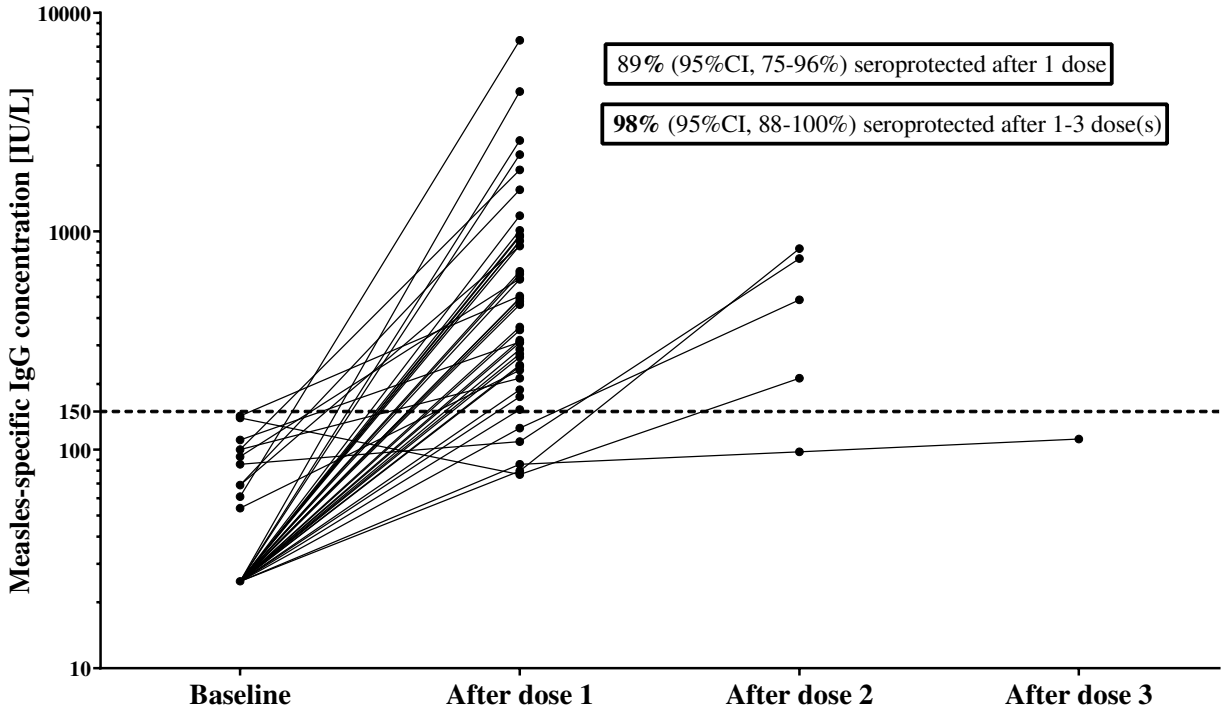
One patient received a MMR dose at inclusion by mistake (patient number 4). He had no documented MMR immunization in his vaccination record and previous measles serology monitored yearly at our center had always been negative. When the baseline serology showed that he was seroprotected at inclusion, further investigation revealed that he had received a MMR dose 7.1 years after transplantation, i.e. 11 months before study inclusion in an off-label setting as a primary prevention in the context of a measles outbreak in his home town.

During follow-up, we identified four patients who lost seroprotection against measles between inclusion and 1-year follow-up. Three were immunized at a median of 12.4 months (range, 11.5 to 13.1) after inclusion (patient numbers 70, 73, 80). The fourth patient had a contraindication to vaccination because of graft dysfunction and required a new LT (patient number 72).

Seroresponse to primary MMR immunization

Interestingly, all 3 patients not protected at inclusion and who did not reach seroprotective concentration after the first dose were MMR-naïve before inclusion, and transplanted at a younger age (range, 0.5 to 0.7 months; P=0.02) for biliary atresia. One patient did not reach seroprotective concentration despite immunization with a total of 3 MMR doses and was the only primary vaccine response failure of our study (patient number 39). This 10 year-old girl had been transplanted at 6 months of age for biliary atresia. She received tacrolimus treatment during the entire study and was clinically stable. She had never received any MMR vaccine before inclusion. The maximal concentration of vaccine response was 116 IU/L after the third dose and was maintained at 118 IU/L one year after. Surprisingly, her 2- and 3-year follow-up IgG concentration were above the seroprotective threshold at 153 IU/L and 158 IU/L, respectively, without receiving any further MMR vaccine dose, nor being in contact with someone with measles disease. Her vaccine responses were otherwise normal.

Figure S2: Seroresponse to primary MMR immunization after transplantation



Measles-specific	Baseline	After primary dose(s)			
IgG concentration [IU/L] Median (IQR)	(n=44)	after dose 1 (n=44)	after dose 2 (n=5)	after dose 3 (n=1)	**overall (n=44)**
All patients	**25 (25-25)**	**486 (243-902)**	**486 (213-752)**	**112 (-)**	**501 (282-902)**
MMR-naive	25 (25-25)	414 (243-902)	486 (98-835)	112 (-)	482 (292-902)
MMR non-naive	25 (25-93)	501 (249-1204)	483 (213-752)		557 (277-1204)

IgG: immunoglobulins G; IQR: interquartile range; MMR: measles-mumps-rubella vaccine; n: number of patients;
Values are given as medians (IQR) if there are more than 2 patients in the category.
"MMR-naïve patients" include patients with no previous history of MMR vaccination (before and/or after transplantation) at inclusion.

Maintenance of seroprotection against measles after MMR vaccination at 1-year follow-up

Table S4: Factors associated with maintenance of seroprotection against measles at 1-year follow-up

	Maintenance of protection against measles at 1-year follow-up		Multivariate model	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Diagnostic of biliary atresia	0.85 (0.20-3.56)	0.8	-	
Number of MMR dose before inclusion - None - 1 dose - ≥ 2 doses	 Reference 0.17 (0.03-0.95) 0.28 (0.05-1.53)	0.08 (Overall) Reference 0.04 0.1	-	
Number of MMR dose before inclusion - None - 1 dose - ≥ 2 doses	 6.0 (1.05-34.2) Reference 1.67 (0.23-12.2)	0.08 (Overall) 0.04 Reference 0.6	-	
MMR vaccination before inclusion	0.22 (0.05-0.88)	0.03	0.05 (0-0.66)	0.02
Age at first MMR vaccine before LT - <12 months - >12 months	 Reference 0.53 (0.06-4.91)	0.6 (Overall) Reference 0.6	-	
Age at first MMR vaccine before LT (year, continuous variable)	0.37 (0.02-8.38)	0.5	-	
Age at last MMR vaccine before LT (year, continuous)	1.77 (0.37-8.54)	0.5	-	
Delay between last MMR and LT - <4 months (rapidly after immunization) - 4-12 months (reasonable delay) - >12 months (long delay)	 0.22 (0.02-2.45) Reference 1	0.2 (Overall) 0.3 Reference 0.7	-	
Delay between last MMR and LT (year, continuous)	0.84 (0.15-4.71)	0.8	-	
Age at first LT - < 1-year-old (very early transplantation) - 1-3-years-old (early transplantation) - >3-years-old (transplantation during childhood)	 2.43 (0.58-10.2) Reference 0.43 (0.03-5.98)	0.3 (Overall) 0.2 Reference 0.5	-	
Age at first LT (year, continuous)	0.53 (0.24-1.17)	0.1	-	
Delay between last LT and study vaccination (year, continuous)	1.30 (1.05-1.63)	0.02	1.39 (1.03-1.89)	0.03
Previous history of rejection	3.20 (0.82-12.5)	0.09	-	
Number of rejection episodes - None - 1 episode - 2 episodes - 3 episodes	 Reference 3.3 (0.68-16.3) 2.0 (0.29-13.8) 1	0.3 (Overall) Reference 0.1 0.5 -	-	
Delay between last rejection episode and inclusion (year, continuous)	1.01 (0.77-1.31)	0.9	-	
Age at study inclusion (year, continuous)	1.22 (1.01-1.48)	0.03	-	
Peak of seroresponse to primary vaccination - Measles concentration <400 IU/L - Measles concentration >400 IU/L	 Reference 5.70 (1.37-23.8)	0.01 (Overall) Reference 0.02	 Reference 26.5 (1.91-368)	 Reference 0.02

OR: odds ratio; CI: confidence interval; MMR: measles-mumps-rubella vaccine; LT: liver transplantation.

Vaccine efficacy

No breakthrough measles disease was reported throughout the follow-up (median, 2.1 years; IQR, 1.6 to 3.0) or any contact with wild-type measles in the community. Therefore, no conclusion can be drawn on the vaccine efficacy in our population.

Vaccine response to the rubella component of the vaccine

At the time of inclusion, 48% of patients (43/90) were seroprotected against rubella, including 68% of patients with a history of MMR vaccine before inclusion (42/62).

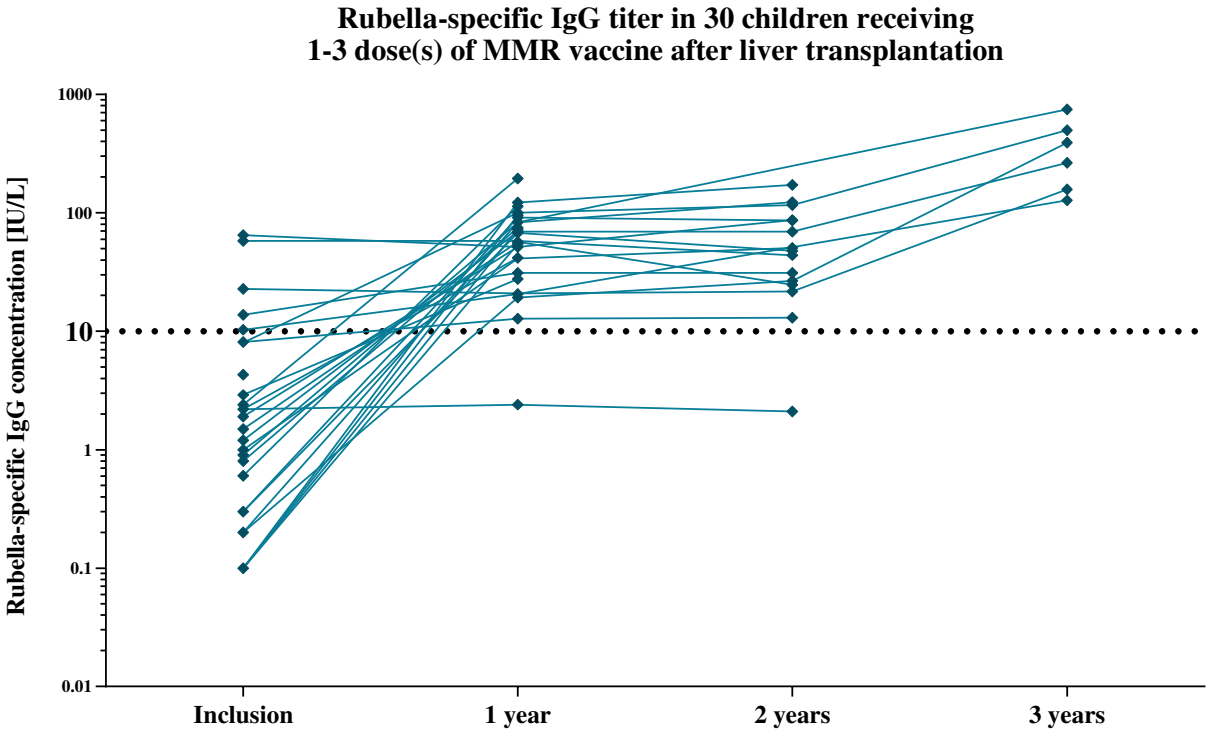
Among the 44 patients immunized with MMR in the setting of the present study, 7 patients (16%) were already seroprotected against rubella at inclusion, but received MMR vaccine since they were not seroprotected against measles (patient numbers 4, 7, 15, 35, 49, 70, 73). They maintained their protection against rubella throughout follow-up with a slight increase in rubella-specific IgG concentration in some cases (Figure A3).

Thirty-six patients were not seroprotected against rubella before study vaccination. Vaccine responses were not measured directly after primary vaccination, but the 1-year follow-up serology is available for 31 patients: 81% (25/31; 95% CI, 63 to 93) were seroprotected one year after 1-3 MMR doses, namely, 79% (23/29; 95% CI, 60 to 92) in patients who received 1 dose, and 100% in those who received 2-3 doses (97.5% CI, 16 to 100; patient numbers 39 and 44). Further serological follow-up is available at 2- and/or 3-year follow-up for 16 patients, with a 94% persistence of seroprotection (95% CI, 70 to 99.8). Of note, 4 children had received 1 or 2 MMR booster doses at 1-year follow-up, with 2 patients receiving another booster at 2-year follow-up (Figure A3). These boosters were administered due to the loss of seroprotection against measles. Interestingly, the only patient who was no longer seroprotected against rubella during follow-up had also lost seroprotection against measles and needed a MMR booster at 1- and 2-year follow-up (patient number 20).

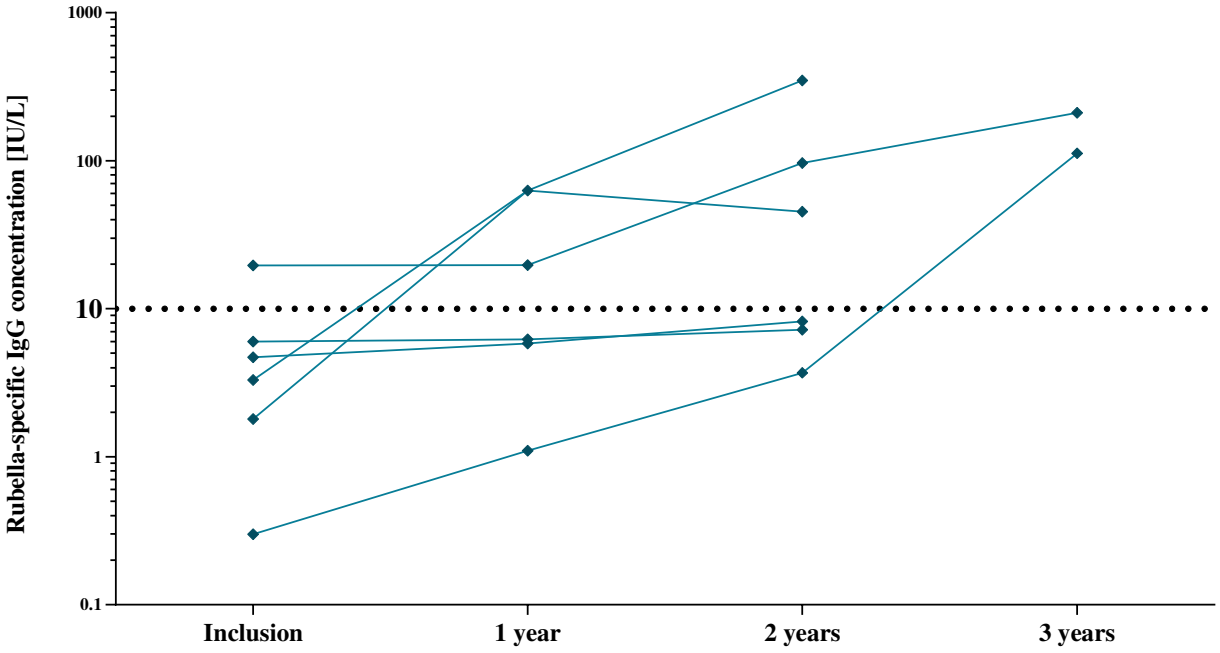
Six patients were not seroprotected against rubella 1 year after 1 dose of primary vaccination (19% non-response to one dose; 95% CI, 7 to 37). Interestingly, all had received the MMR vaccine before transplantation. Five were not seroprotected against measles at 1-year follow-up and subsequently received 1 to 2 booster doses. The 2-year serology is available for 4 of these patients; none were seroprotected against rubella (Figure A3).

Data were missing throughout follow-up for two patients (numbers 56 and 80).

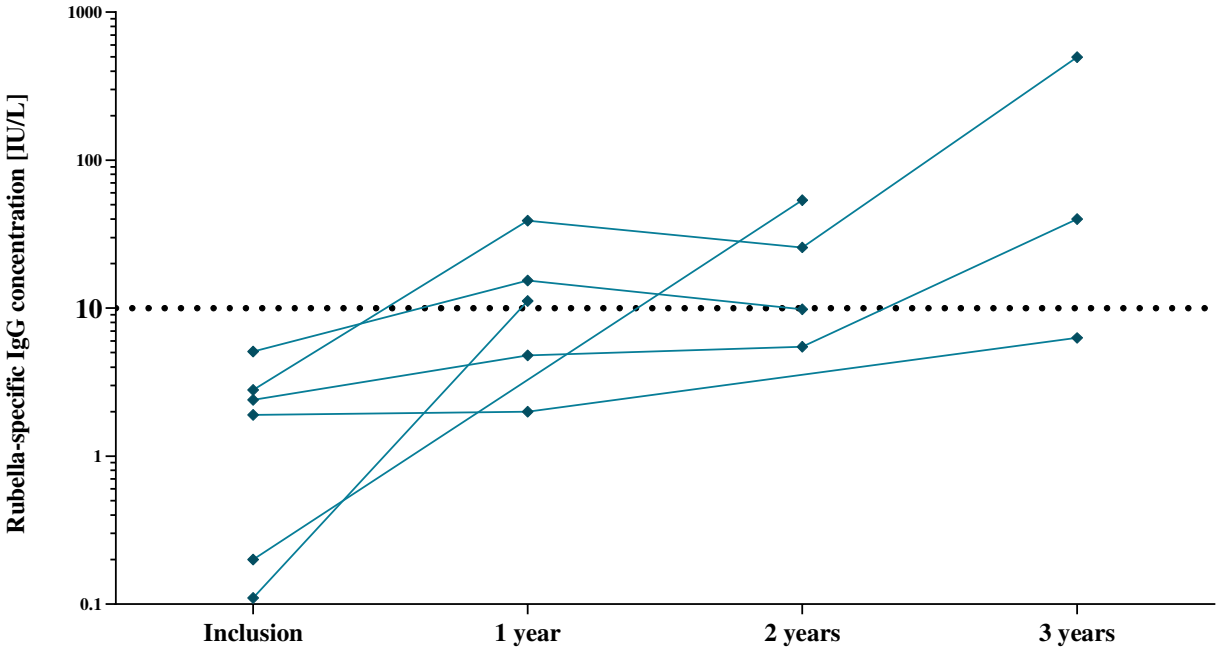
Figure S3: Evolution of rubella-specific igg concentration following MMR vaccination after liver transplantation



Rubella-specific IgG titer in 6 children receiving 1 dose and 1-2 booster(s) of MMR vaccine after liver transplantation



Rubella-specific IgG titer in 6 children receiving 1 dose and 2 boosters (1 and 2 year) of MMR vaccine after liver transplantation



Rubella-specific IgG concentration [IU/L]	**Baseline**	**1-year follow-up**	**2-year follow-up**	**3-year follow-up**
All immunized patients	**1.9 (0.3-5.1)**	**51.5 (19.3-74.9)**	**44.0 (13.0-85.8)**	**211.1 (112.5-496.7)**
MMR-naive	0.8 (0.2-1.9)	71.1 (54.6-94.8)	53.5 (26.6-116.2)	496.7 (391-500.0)
MMR non-naive	4.7 (2.2-19.6)	17.6 (5.3-29.4)	9.0 (5.5-31.1)	119.9 (39.9-157.7)
Non-immunized patients	**26.3 (10.2-59.0)**	**20.2 (10.0-40.3)**	**34.3 (13.9-56.3)**	**116.0 (5.8-259.3)**
MMR-naive	0.7 (0.3-7.15)	1.9 (0.5-3.2)	-	-
MMR non-naive	32.2 (13.1-60.7)	21.9 (14.8-46.6)	34.3 (13.9-56.3)	116.0 (5.8-259.3)

IgG: immunoglobulins G; MMR: measles-mumps-rubella vaccine. Values are given as medians (IQR).
"Immunized patients" are those who received MMR vaccine after transplantation in the context of the study.
"MMR-naïve patients" are patients with no previous history of MMR vaccination (before and/or after transplantation) at inclusion.

Vaccine response to the mumps component

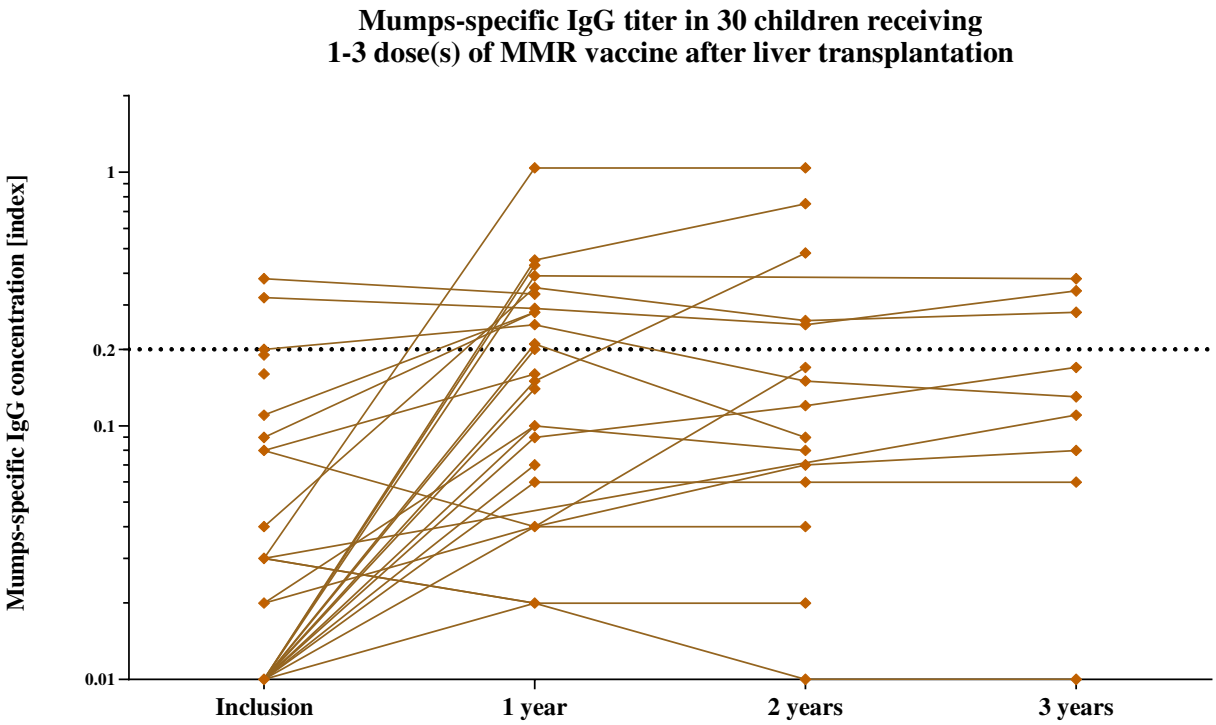
As mentioned in the Methods section, there is no established cut-off for mumps-specific antibody concentration predicting seroprotection. We arbitrarily defined seroprotection in patients as a mumps-specific IgG index >0.2, given that it is the cut-off used by the manufacturer, which reports index values <0.1 as seronegative, 0.11 to 0.19 as indeterminate, and >0.2 as seropositive.

At inclusion, 30/90 patients (33%) had a mumps-specific IgG index >0.2, representing 30/62 patients (48%; 95% CI, 36 to 61) with a previous history of MMR vaccine (before and/or after transplantation). Among the 44 patients immunized with MMR in the context of the study, 4 patients (9%) already had a mumps-specific IgG index >0.2 before vaccination (patient numbers 4, 49, 67, 71). All but one maintained a mumps-specific IgG index >0.2 throughout follow-up, the remaining patient had a mumps-specific IgG index waning at 0.15 and 0.13 at 2- and 3-year follow-up (patient number 4).

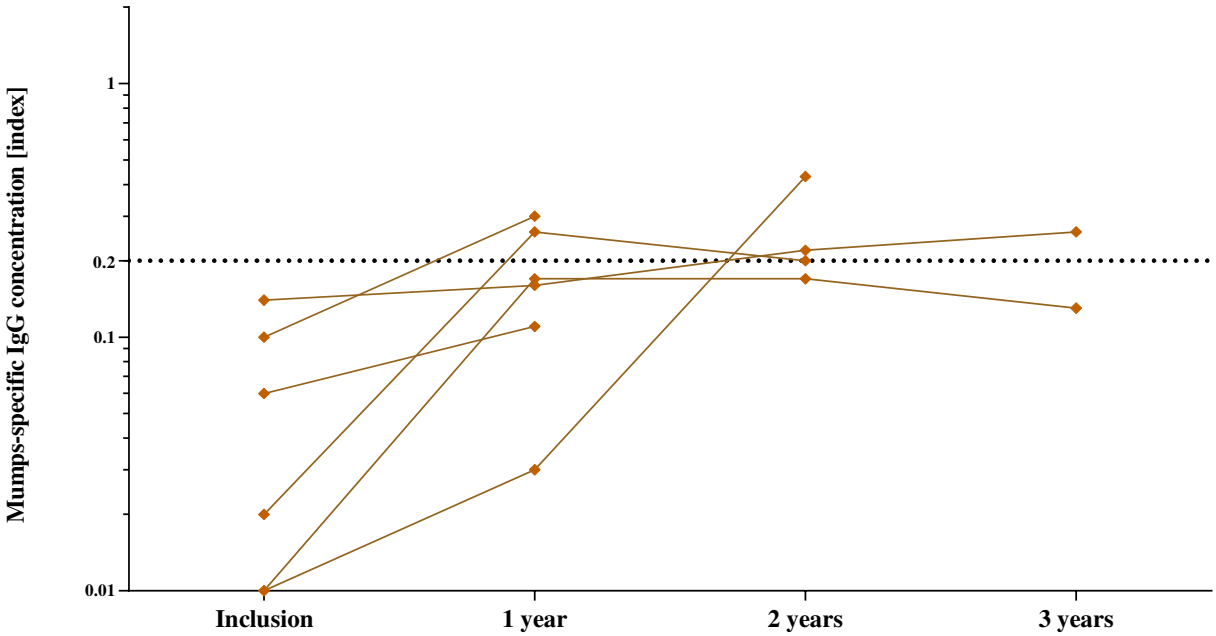
The remaining 38 patients had a mumps-specific IgG index <0.2 before study vaccination. Mumps serology were not measured directly after primary vaccination, but the 1-year follow-up serology is available for 33 patients. Among these, there is a 36% (12/33; 95% CI, 20 to 55) rate of mumps-specific IgG index >0.2 at 1 year after 1 to 3 MMR doses, namely 32% (95% CI, 17 to 51) of the 31 patients who received 1 dose, and 100% of the remaining cases who received 2 or 3 doses (97.5% CI, 16 to 100; patient numbers 39 and 44). Further serological follow-up was available at the 2- and/or 3-year follow-up for 7 patients, with a 71% persistence of mumps-specific IgG index >0.2 (95% CI, 29 to 96). Of note, 5/7 patients had only received 1 MMR dose in the context of the study. One had received 2 MMR booster doses at 1 year (patient number 62), although the mumps-specific IgG index remained >0.2 throughout follow-up. The remaining patient had received MMR booster doses at 1- and 3-year follow-up, with mumps-specific IgG index waning <0.2 (patient number 12). These boosters were administered due to loss of seroprotection against measles as mumps-specific IgG index <0.2 was not an indication for further MMR doses in our protocol.
Twenty-one of 31 patients did not have a mumps-specific IgG index >0.2 at 1 year after 1 dose of primary vaccination. Interestingly, 6/21 had received the MMR vaccine before transplantation and 15/21 had not. Seven were not seroprotected against measles at 1 year and subsequently received 1 to 2 booster doses. The 2- and/or 3-year serology is available for 6 of these patients. Of these, only 2 reached a mumps-specific IgG index >0.2 (patient numbers 30 and 35).

Data were missing throughout follow-up for two patients (numbers 56 and 80).

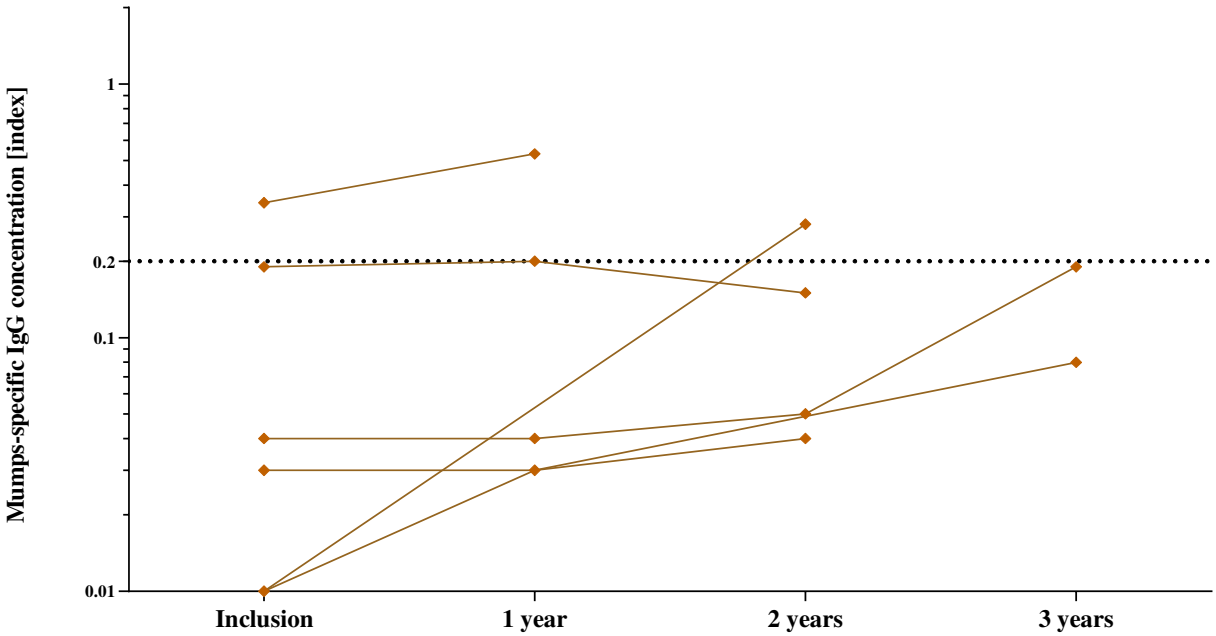
Figure S4: Evolution of mumps-specific IgG concentration following MMR vaccination after liver transplantation



Mumps-specific IgG titer in 6 children receiving 1 dose and 1-2 booster(s) of MMR vaccine after liver transplantation



Mumps-specific IgG titer in 6 children receiving 1 dose and 2 boosters (1 and 2 year) of MMR vaccine after liver transplantation



Mumps-specific IgG concentration (index)	**Baseline**	**1-year follow-up**	**2-year follow-up**	**3-year follow-up**
All immunized patients	**0.03 (0.01-0.09)**	**0.16 (0.04-0.28)**	**0.15 (0.06-0.26)**	**0.13 (0.08-0.26)**
MMR-naïve	0.01 (0.01-0.02)	0.10 (0.04-0.21)	0.11 (0.06-0.27)	0.17 (0.06-0.28)
MMR non-naïve	0.10 (0.03-0.19)	0.25 (0.16-0.30)	0.17 (0.15-0.25)	0.13 (0.11-0.26)
Non-immunized patients	**0.21 (0.08-0.41)**	**0.16 (0.06-0.33)**	**0.16 (0.09-0.28)**	**0.24 (0.18-0.47)**
MMR-naïve	0.01 (0.01-0.02)	0.04 (0-0.08)	0.02 (-)	-
MMR non-naïve	0.23 (0.10-0.52)	0.16 (0.06-0.39)	0.16 (0.09-0.28)	0.24 (0.18-0.47)

IgG: immunoglobulins G; MMR: measles-mumps-rubella vaccine.
Values are given as medians (IQR) if there are 2 or more patients in the category.
"Immunized patients" are those who received MMR vaccine after transplantation in the context of the study.
"MMR-naïve patients" are patients with no previous history of MMR vaccination (before and/or after transplantation) at inclusion.

Vaccine safety monitoring

Measles shedding was not detected after MMR vaccination in LT children. Among the 33 patients and the 6 healthy controls with available urine at days 7-10, 20, and 30 after MMR administration, measles vaccine strain was detected only once in a 1-year-old healthy control at day 10 following his first dose of MMR vaccine.

Table S5: Frequencies of self-reported side-effect on standardized diary cards

ALL PATIENTS					
N=49	Week 1	Week 2	Week 4	Week 6	Week 8
Any reaction at injection site	**9 (18%)**	**2 (4%)**	**2 (4%)**	**3 (6%)**	**0**
Redness	3 (6%)	0	0	0	0
Induration	3 (6%)	1 (2%)	1 (2%)	1 (2%)	0
Pain	4 (8%)	0	0	1 (2%)	0
Rash	1 (2%)	1 (2%)	1 (2%)	1 (2%)	0
Any general effect	**16 (33%)**	**11 (22%)**	**9 (18%)**	**5 (10%)**	**6 (12%)**
Fever	3 (6%)	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Rash	0	1 (2%)	0	1 (2%)	0
Irritability	6 (12%)	5 (10%)	3 (6%)	1 (2%)	1 (2%)
Anorexia	2 (4%)	1 (2%)	1 (2%)	0	2 (4%)
Fatigue	5 (10%)	7 (14%)	5 (10%)	0	4 (8%)
Headache	4 (8%)	3 (6%)	2 (4%)	1 (2%)	1 (2%)
Nausea, vomiting	3 (6%)	1 (2%)	3 (6%)	0	2 (4%)
Diarrhea	2 (4%)	3 (6%)	3 (6%)	2 (4%)	1 (2%)
Arthralgia	1 (2%)	0	1 (2%)	1 (2%)	1 (2%)
Myalgia	2 (4%)	0	1 (2%)	0	0
Parotiditis, cheek swelling	1 (2%)	2 (4%)	2 (4%)	0	0
Conjunctivitis	0	1 (2%)	0	0	0
PATIENTS MMR-NAÏVE AT VACCINATION					
N=18	Week 1	Week 2	Week 4	Week 6	Week 8
Any reaction at injection site	**5 (28%)**	**1 (6%)**	**0**	**1 (6%)**	**0**
Redness	2 (11%)	0	0	0	0
Induration	1 (6%)	0	0	1 (6%)	0
Pain	3 (17%)	0	0	0	0
Rash	0	1 (6%)	0	0	0
Any general effect	**7 (39%)**	**3 (17%)**	**3 (17%)**	**3 (17%)**	**2 (11%)**
Fever	1 (3%)	0	1 (6%)	0	0
Rash	0	0	0	0	0
Irritability	2 (11%)	0	0	1 (6%)	0
Anorexia	1 (6%)	0	0	0	1 (6%)
Fatigue	1 (6%)	2 (11%)	1 (6%)	0	1 (6%)
Headache	3 (17%)	2 (11%)	1 (6%)	1 (6%)	1 (6%)
Nausea, vomiting	2 (11%)	1 (3%)	2 (11%)	0	0
Diarrhea	1 (6%)	0	2 (11%)	2 (11%)	0
Arthralgia	0	0	0	1 (6%)	1 (6%)
Myalgia	1 (6%)	0	0	0	0
Parotiditis, cheek swelling	0	0	0	0	0
Conjunctivitis	0	0	0	0	0
PATIENTS NON-NAÏVE FOR MMR AT VACCINATION					
N=31	Week 1	Week 2	Week 4	Week 6	Week 8
Any reaction at injection site	**4 (13%)**	**1 (3%)**	**2 (6%)**	**2 (7%)**	**0**
Redness	1 (3%)	0	0	0	0
Induration	2 (6%)	1 (3%)	1 (3%)	0	0
Pain	1 (3%)	0	0	1 (3%)	0
Rash	1 (3%)	0	1 (3%)	1 (3%)	0
Any general effect	**9 (29%)**	**8 (26%)**	**6 (19%)**	**2 (6%)**	**4 (13%)**
Fever	2 (11%)	1 (3%)	1 (3%)	1 (3%)	1 (3%)
Rash	0	1 (3%)	0	1 (3%)	0
Irritability	4 (13%)	5 (16%)	3 (10%)	0	1 (3%)
Anorexia	1 (3%)	1 (3%)	1 (3%)	0	1 (3%)
Fatigue	4 (13%)	5 (16%)	4 (13%)	0	3 (10%)
Headache	1 (3%)	1 (3%)	1 (3%)	0	0
Nausea, vomiting	1 (3%)	0	1 (3%)	0	2 (6%)
Diarrhea	1 (3%)	3 (10%)	1 (3%)	0	1 (3%)
Arthralgia	1 (3%)	0	1 (3%)	0	0
Myalgia	1 (3%)	0	1 (3%)	0	0
Parotiditis, cheek swelling	1 (3%)	2 (6%)	2 (6%)	0	0
Conjunctivitis	0	1 (3%)	0	0	0

Frequencies of local and systemic adverse events reported by the patients on the standardized diary cards are expressed according to the number of patients returning symptom diaries. The patients are then divided into two groups according to their history of MMR vaccination (naïve or not). The occurrence of each adverse event was compared between the two groups using Chi-squared

or Fischer's exact tests depending on sample sizes. None of the difference observed was statistically significant.

Table S6: Safety monitoring following MMR immunization after liver transplantation

Patient number	MMR dose	Local side-effects	Other side-effects	Patient paper questionnaire available	Final diagnosis	Previous history of MMR vaccine
PATIENTS MMR-NAÏVE AT VACCINATION						
3	1	Pain D0	Fatigue D9	Yes		No MMR vaccine
6	1	None	Fever, vomiting, diarrhea, fatigue at D28-31	Yes	Gastroenteritis	No MMR vaccine
10	1	None	None	Yes		No MMR vaccine
14	1	Redness D0-1	- Diarrhea W4-6 - Headache W6-8 - Arthralgia W6-8	Yes	Gastroenteritis	No MMR vaccine
18	1	None	None	No		No MMR vaccine
23	1	None	Coryza D20	No		No MMR vaccine
28	1	None	Worsening of alloimmune hepatitis 4.5 months after vaccination	No		No MMR vaccine
29	1	None	Recurrence of PTLD 18 months after vaccination	Yes		No MMR vaccine
30	1	None	None	Yes		No MMR vaccine
31	1	None	Headache, fatigue, chilling (no fever) D11-21	Yes		No MMR vaccine
39	1	None	Fatigue, headache D3	Yes		No MMR vaccine
40	1	Pain D0-2	- Vomiting D0 - Exanthema with 3 itching lesions (thorax, nose) D14-20 - Diarrhea D35-36	Yes		No MMR vaccine
41	1	None	- Coryza, cough, ocular pruritus D8-9 - Fever D9	Yes		No MMR vaccine
43	1	None	Fatigue, anorexia W8	Yes		No MMR vaccine
44	1	None	- Irritability W1 + W6 - Headache, abdominal pain D13 + D22	Yes		No MMR vaccine
45	1	Redness, induration D0-6	Subfebrile, headache, diarrhea W1	Yes		No MMR vaccine
46	1	Pain D0-3	Fatigue D0-3	Yes		No MMR vaccine
47	1	None	None	No		No MMR vaccine
51	1	None	- Irritability W1 - Diarrhea, fatigue W2 (D14-15) - Irritability and fatigue W8	Yes		No MMR vaccine
52	1	None	None	Yes		No MMR vaccine
56	1	None	- Fever D1 - Headache, nausea, vomiting D1-2 - Fatigue W1	Yes		No MMR vaccine
59	1	None	Irritability D1-2	Yes		No MMR vaccine
62	1	Pain D0	- Fatigue D0-4 - Fever D11-12 (PCR measles-negative) - Coryza D34	No		No MMR vaccine
69	1	None	None	Yes		No MMR vaccine
74	1	None	None	No		No MMR vaccine
PATIENTS NON-NAÏVE FOR MMR AT VACCINATION						
4	1	None	None	No		1 dose after LT
5	1	None	Fever, fatigue, anorexia D3-7	Yes	Otitis	1 dose before LT
	2	Induration D0	None	Yes		
7	1	None	None	Yes		1 dose after LT
12	1	None	- Irritability D0-8 - Cheek swelling D2-3 - Conjunctivitis, coryza D21 - Buttock rash D21	No	Upper respiratory tract infection	2 doses before LT
	2	None	- Irritability D0-7 - Cheek swelling W2-4 - Buttock rash D14-19 - Coryza D18-20	Yes	Upper respiratory tract infection	
	3	Induration W2-4	- Irritability fatigue W1-4 - Cheek swelling W1-4	Yes		
14	2	None	- Vomiting W1 - Fever, irritability, headache, anorexia, diarrhea, vomiting, myalgia, arthralgia D20	Yes	Gastroenteritis	1 dose after LT (during this study)
	3	None	Fever max 40.6°C with abdominal pain and constipation D31-40	Yes	Gastroenteritis	
15	1	None	None	No		1 dose before LT
20	1	None	None	Yes		2 doses before LT

	2	None	None	No		
	3	Redness D1	- Irritability W1-2 - Fever max 39°C on D29 with flu-like symptoms	No	Upper respiratory tract infection	
26	1	None	None	Yes		2 doses before LT
30	2	None	None	No		1 dose after LT (during this study)
32	1	None	Itching rash (limited to lower extremity) D19	Yes		1 dose before LT
	2	Redness, induration D1	None	Yes		
	3	None	None	Yes		
35	1	None	Fatigue, irritability, nausea W2-4	Yes		1 dose before LT
	2	Induration D1-4 max 1cm	Fatigue W4	Yes		
38	1	None	- Diarrhea D0-3 - Fever, fatigue, anorexia, conjunctivitis, coryza, cough D8-12 (NP PCR negative for measles) - Diarrhea D29-31	Yes	Otitis	1 dose before LT
	2	None	None	Yes		
39	2	None	Headache D0-1	Yes		1 dose after LT (during this study)
	3	None	None	Yes		
41	2	None	None	No		1 dose after LT (during this study)
	3	None	- Fever max 38.5°C D1 with headache and irritability	No		
42	1	None	- Irritability W1-2 - Fatigue W1-4 - Transplant rejection 9 months after vaccination	Yes		1 dose before LT
	2	None	- Rash D11 - Headache D13	Yes	Migraine	
	3	None	- Headache D2-4 - Fever D12, max 38°C	Yes	Migraine	
44	2	None	None	No		1 dose after LT (during this study)
49	1	Redness, rash D2-3	None	Yes		2 doses before LT
54	1	None	None	Yes		2 doses before LT
56	2	None	None	No		1 dose after LT (during this study)
57	1	None	None	Yes		1 dose before and 1 dose after LT
62	2	None	None	No		1 dose after LT (during this study)
	3	None	None	No		
67	1	None	None	Yes		2 doses before LT
	2	Redness D1-4 max 1 cm, pain D1	Headache D5	No		
	3	Pain D1-2 & W6	None	Yes		
70	1	None	None	Yes		2 doses before LT
71	1	None	None	No		2 doses before LT
73	1	None	None	No		2 doses before LT
	2	None	Fatigue, anorexia, vomit W7	Yes	Intestinal obstruction	
80	1	Cutaneous rash for 1 day	- Irritability W1-2 - Fever max 38.8°C, fatigue W8	Yes	Picornavirus upper respiratory tract infection	2 doses before LT
	2	None	- Coryza D12-17 - Diarrhea D17-21	Yes		

D: day; W: week; PTLD: post-transplant lymphoproliferative disease; PCR: polymerase chain reaction.

Table S7: Side-effects occurring around day 10 post-MMR administration

Patient number	MMR study dose	Side-effect	Final diagnosis (after medical consultation)
PATIENTS MMR-NAÏVE AT VACCINATION			
3	1	Fatigue D9	
31	1	Headache, fatigue, chilling (no fever) D11-21	
40	1	Exanthema with 3 itching lesions (thorax, nose) D14-20	Non-specific viral rash (not compatible with measles)
41	1	- Coryza, cough, ocular pruritus D8-9 - Fever D9	
44	1	- Irritability W1 + W6 - Headache, abdominal pain D13 + D22	
51	1	Diarrhea, fatigue W2 (D14-15)	
62	1	- Fever D11-12 (PCR measles negative) - Coryza D34	
PATIENTS NON-NAÏVE FOR MMR AT VACCINATION			
12	1	- Irritability D0-8 - Cheek swelling D2-3 - Conjunctivitis, rhinorrhea D21 - Buttock rash D21	Upper respiratory tract infection
14	2	- Vomiting W1 - Fever, irritability, headache, anorexia, diarrhea, vomiting, myalgia, arthralgia D20	Gastroenteritis (contact with infected cases)
20	3	- Irritability W1-2 - Fever max 39°C on D29 with flu-like symptoms	Upper respiratory tract infection
32	1	Itching rash (limited to lower extremity) D19	
35	1	Fatigue, irritability, nauseous W2-4	
38	1	Fever, fatigue, anorexia, conjunctivitis, coryza, cough D8-12 (NP PCR negative for measles)	Otitis
42	1	- Irritability W1-2 - Fatigue W1-4	
42	2	- Rash D11 (small 3 macular lesion not itching, periombilical) - Headache D13	Migraine
42	3	Fever D12, max 38°C	
80	1	Irritability W1-2	

D: day; W: week.

Table S8: Serious adverse events occurring after MMR administration

Patient number	MMR study dose	Serious adverse event	Evolution
PATIENTS MMR-NAÏVE AT VACCINATION			
28	1	Worsening of alloimmune hepatitis 4.5 months after vaccination	Successfully treated by prednisone
29	1	Recurrence of PTLD 18 months after vaccination	Treatment with rituximab
PATIENTS NON-NAÏVE FOR MMR AT VACCINATION			
4	1	Transplant rejection 3 years after vaccination	Successfully treated by mycophenolate mofetil
42	1	Transplant rejection 9 months after vaccination	Successfully treated by mycophenolate mofetil and prednisone
70	1	PTLD 4 months after vaccination	Treatment with rituximab, substitution with IVIG
70	1	Acute rejection 6 months after vaccination	Treatment with prednisone and everolimus
73	2	Intestinal obstruction 7 weeks after vaccination	Successfully managed with surgery

PTLD: post-transplant lymphoproliferative disease; IVIG: intravenous immunoglobulin

Narrative report of relevant side-effects

Fever

Four patients experienced fever around day 10 after immunization (numbers 38, 41, 42 and 62) and one patient at day 20 (number 14). Other cases of fever started on day 1 (numbers 41 and 56), day 3 (number 5), day 28 (number 6), day 29 (number 20), day 31 (number 14), and day 60 (number 80).

- **Patient number 5** presented with fever and anorexia on day 3. He consulted his pediatrician who diagnosed acute otitis media and prescribed amoxicillin. Symptoms were resolved on day 7.
- **Patient number 6** reported fever, fatigue and gastrointestinal symptoms from days 28 to 31, which were diagnosed as gastroenteritis.
- **Patient number 14** reported fever at day 20 after a second dose, accompanied by headache, irritability, myalgia, arthralgia and gastrointestinal symptoms, and after contact with a person with diagnosed gastroenteritis. She received only one dose of paracetamol and all symptoms resolved within a few days. After the third dose, she had fever on day 31 in the setting of gastroenteritis.
- **Patient number 20** presented with fever and flu-like symptoms on day 29, which were diagnosed as a benign upper respiratory tract infection and treated with paracetamol.
- **Patient number 38** presented fever with fatigue, anorexia, coryza, coughing and conjunctivitis starting at day 8 after vaccination. Ear examination revealed acute otitis media, which was successfully treated by amoxicillin. Measles strain was not identified by PCR in any biological sample.
- **Patient number 41** complained of upper respiratory tract infection symptoms with coryza and cough, as well as ocular pruritus without any other sign of conjunctivitis starting on day 8 after the first dose. Fever started at day 9 and spontaneously resolved. The attending pediatrician diagnosed upper respiratory tract infection. No side-effect was observed after the second dose. After the third dose, he developed fever at day 1 post-vaccine, with a headache and irritability that responded well to paracetamol and ibuprofen without any recurrence.
- **Patient number 42** was sub-febrile (maximum 38°C) at day 12 after the third dose without any other symptoms, with spontaneous resolution after one day.
- **Patient number 56** reported fever on day 1 with a 2-day episode of nausea and headache.
- **Patient number 62** was febrile without any other symptoms at day 11, 4 hours after a surgical procedure. The fever did not recur. A measles strain was not identified par PCR in any biological sample.
- **Patient number 80** reported fever 2 months after vaccination in the setting of a documented picornavirus upper respiratory tract infection.

Other systemic symptoms

Three patients reported increased fatigue around day 10 (patient numbers 3, 31 and 35), two patients reported headache at day 13 (patient numbers 42 and 44), one patient had diarrhea with fatigue and irritability at day 14 (patient number 51), and one patient was irritable during 2 weeks following vaccination (patient number 80).

- **Patient number 3** was more tired than usual on day 9, without any other complaint.
- **Patient number 31** had intense headaches with fatigue and a few episodes of chills without fever between days 11 and 21. Headaches were relieved by paracetamol.
- **Patient number 35** reported being tired, irritable and nauseous between weeks 2 and 4 in the standardized diary card, although this was not revealed during the telephone interviews.
- **Patient number 44** complained of a 1-day duration episode of headache with abdominal pain on days 13 and 22.
- **Patient number 42** reported an episode of headache on day 13, 2 days after a localized cutaneous rash (see below).
- **Patient number 51** had an episode of diarrhea with fatigue and irritability without fever on days 14 and 15.
- **Patient number 80** was irritable during 2 weeks following vaccination.

Cutaneous rash

Four patients experienced localized rash starting at days 11 (patient number 42), 14 (patient number 40), 19 (patient number 32) and 21 (patient number 12).

- **Patient number 42** presented three small non-pruriginous macula lesions near the ombilicus from day 11, accompanied by headache from day 13.
- **Patient number 40** presented three isolated pruriginous macular-papular lesions on both thorax and nose between days 14 and 20 without any other symptoms.
- **Patient number 32** presented diffuse pruriginous lesions on the lower extremities at day 19 that resolved spontaneously.
- **Patient number 12** presented a buttock rash on day 21 after the first dose with no other lesion, as well as conjunctivitis and coryza, which was diagnosed as upper respiratory tract infection. Interestingly, he presented exactly the same rash on days 14 to 19 after the second dose, together with coryza.

Cheek swelling

Only 1 patient (patient number 12) reported cheek swelling that occurred 3 times: from day 2 after the first dose, and from week 2 after the second and third dose. According to the patient's mother, the patient always experiences cheek swelling following vaccination.

Arthralgia

Only one patient (patient number 14) reported arthralgia on day 20 after the second dose in the context of a viral infection diagnosed as gastroenteritis (see Fever).

Serious adverse events in immunized patients

Six patients developed serious adverse events after vaccination (patient numbers 4, 28, 29, 42, 70 and 73) and 2 before vaccination (patient numbers 26 and 51).

- **Patient number 4** experienced a third acute cellular rejection episode 3 years after vaccination that was successfully managed by mycophenolate mofetil. He already had a first rejection episode 3 weeks after transplantation and a second episode 6.5 years after transplantation, which was 1.5 years before inclusion and MMR vaccination.
- **Patient number 26** experienced an episode of acute cellular rejection before vaccination, 1 year after inclusion, possibly due to a human herpes virus 6 (HHV6) infection, which was successfully treated with valganciclovir, high-dose corticosteroids, and by increasing immunosuppression with tacrolimus and mycophenolate mofetil. She was then immunized with MMR 1.5 years after this episode without any complications.
- **Patient number 28** had liver test abnormalities before immunization. As he was clinically stable with no contraindication, MMR was administered a few months later. Liver tests did not improve over time and he underwent a liver biopsy 4.5 months after immunization, which revealed alloimmune hepatitis. He was then successfully treated with corticosteroids with no recurrence. Given that the perturbation of liver function tests preceded immunization, the causality of the vaccine remains uncertain.
- **Patient number 29** was diagnosed with recurrence of PTLD 18 months after immunization, which was successfully treated with rituximab. She received IVIG substitution for 6 months.
- **Patient number 42** experienced an acute cellular rejection 9 months after the first dose of MMR vaccine, which was successfully treated by increasing immunosuppressive therapy with prednisone and mycophenolate mofetil. As she was found to be no longer seroprotected at follow-up, she received two further doses of MMR vaccine, starting at 11 months after the rejection episode, without any further complications.
- **Patient number 51** experienced a rejection episode 1.5 years after inclusion that was successfully managed by steroids. She was immunized 11 months after this episode without any complications.
- **Patient number 70** was diagnosed with PTLD 4 months after immunization, which was treated with rituximab and he received IVIG substitution. He then had an episode of acute graft rejection 6 months after vaccination that was managed with triple immunosuppression including steroids, everolimus, and tacrolimus.
- **Patient number 73** was hospitalized 7 weeks after his second dose of MMR for intestinal obstruction. After 48 h of conservative treatment, he was successfully managed surgically.

Serious adverse events in non-immunized patients

Among the non-immunized patients, there were 8 serious adverse events of graft dysfunction (patient numbers 16, 22, 25, 50, 72, 75, 82 and 85) and one PTLD (number 76).

- **Patient number 16** experienced a late acute cellular rejection episode that was successfully treated with mycophenolate mofetil.
- **Patient number 22** was diagnosed with chronic graft rejection and an acute exacerbation, possibly secondary to adenoviral infection.
- **Patient number 25** unfortunately died of chronic graft dysfunction while waiting for a new donor.
- **Patient number 50** experienced an episode of graft dysfunction with no histological criteria for acute rejection.
- **Patient number 72** underwent a second transplantation.
- **Patient number 75** had an episode of graft rejection that was managed by steroids and by increasing her treatment of tacrolimus and everolimus.
- **Patient number 76** developed PTLD.
- **Patient number 82** experienced acute cellular rejection due to liver infection by Human herpesvirus 6, which was successfully managed with corticosteroids and a higher doses of tacrolimus and mycophenolate mofetil.
- **Patient number 85** experienced a worsening of her rejection episode, which was managed with corticosteroids and higher doses of tacrolimus, as well as rituximab and immunoglobulins. Since the response was suboptimal, mycophenolate mofetil was added.

Supplement to Discussion

Vaccine response to the rubella and mumps components

We observed an 81% seroprotection rate against rubella after 1 to 3 doses of primary vaccination after LT, similar to previous reports (Table A9). Regarding the rate of 36% of patients with a mumps-specific index >0.2 after 1 to 3 MMR doses, which is lower than the 48 to 100% rate reported in the literature, we attributed it to the high cut-off set by our laboratory. Of note, this cut-off is designed to diagnose mumps disease, rather than evaluating vaccine responses. Since there is no established cut-off for seroprotection in the literature, the clinical relevance of these results in unknown.

TableS9: Rate of seroprotection following MMR vaccination after liver transplantation

Antigen	Literature data	Reference	This study
Measles	**39-100%**	[1-3, 5, 6]	**98%; 95% CI, 93-100% (43/44 patients)**
	7/18 (39%)	Rand 1993 [1]	89%; 95% CI, 75-96% (39/44 patients) after 1 dose
	11/13 (85%)	Kano 2002 [2]	80%; 95% CI, 28-99% (4/5 patients) after 2-3 doses
	19/26 (73%)	Khan 2006 [3]	
	36/36 (100%)	Shinjoh 2015 [5]	
	11/25 (44%) after 1 dose	Kawano 2015 [6]	
	8/8 (100%) after 2 doses		
Rubella	**50-100%**	[2, 5, 6]	**81%; 95% CI, 63-93% (27/33 patients)**
	6/6 (100%)	Kano 2002 [2]	79%; 95% CI, 60-92% (25/31 patients) after 1 dose
	35/35 (100%)	Shinjoh 2015 [5]	100%; 95% CI, 16-100% (2/2 patients) after 2-3 doses
	19/27 (70%) after 1 dose	Kawano 2015 [6]	
	1/2 (50%) after 2 doses		
Mumps	**48-100%**	[2, 5, 6]	**53%; 95% CI,34-72% (16/30 patients)**
	2/2 (100%)	Kano 2002 [2]	50%; 95% CI, 31-69% (14/28 patients) after 1 dose
	24/35 (69%)	Shinjoh 2015 [5]	100%; 95% CI,16-100% (2/2 patients) after 2-3 doses
	12/25 (48%) after 1 dose	Kawano 2015 [6]	
	5/7 (71%) after 2 doses		

However, our study was designed to increase protection after LT against measles, rather than rubella and mumps, and the protocol was based on measles serology for the administration of MMR vaccine doses. Therefore, some patients have received MMR doses while they already had high IgG concentrations against rubella and/or mumps. Others would probably have benefitted from subsequent booster doses to enhance seroprotection against rubella and/or mumps, which was not administered as the goal of seroprotection against measles was achieved. Our results on rubella and mumps need to be interpreted with caution as secondary outcomes.

The risk and benefit of choosing between MMR and a single-antigen measles vaccine was carefully evaluated. As discussed above, the primary aim of our study was the immunogenicity of measles immunization after LT as mumps and rubella infections seem to be less significant threats for transplanted children. However, even in healthy individuals, mumps encephalitis and congenital rubella syndrome can be life-threatening events. Therefore, patients can directly benefit from the trivalent vaccine. The use of the MMR vaccine was very well accepted by parents/guardians and the childrens' pediatricians as it is routinely used in Switzerland and has a long track-record of efficacy and safety in the healthy population.

The incidence of vaccine-related adverse events is remarkably similar between MMR and monovalent measles vaccine. Most adverse events reported following MMR vaccine (such as fever and rash) are attributable to the measles component, and hardly any adverse event is secondary to the mumps part of the vaccine. The rubella strain can affect joints, but since this reaction is secondary to an immune overreaction, it is less likely to occur in immunosuppressed individuals. As observed in our study, only one patient (patient number14) reported diffuse arthralgia, together with myalgia and other systemic symptoms, which could be attributed to an ongoing gastroenteritis episode rather than to the rubella component of the vaccine.

Based on our results, it appears reasonable to administer MMR rather than single-antigen measles vaccine after transplantation when considering the high immunogenicity of the mumps and rubella component and the absence of an increased safety concern.

Monitoring of measles shedding following MMR vaccination

Measles viral shedding was not prolonged after MMR vaccination in LT children. These findings contrast with previous data on viral shedding after measles vaccine or disease. Measles RNA is known to be detected following **measles infection** using reverse transcriptase polymerase chain reaction RT-PCR in various clinical specimens such as urine, nasopharyngeal aspirate or throat swab [7]. Viral shedding may last longer in immunocompromised patient, since their immune system is less able to clear the virus. In a study conducted in Zambia among children hospitalized with measles infection, the authors showed a prolonged measles virus shedding in 91% of HIV-infected children (10/11) compared to 53% of HIV-uninfected children (19/36). In this study, measles strains were detected by RT-PCR in urine and nasopharyngeal swab collected 1-2 months after the measles rash onset [8].

Rota et al. have shown that measles virus RNA could also be detected following **MMR vaccination**. In this study, viral shedding was identified at least once in the urine sample of 83% healthy children (10/12) and 100% healthy young adults (4/4) during the 2-week period after MMR vaccination [9].In our study we measured measles vaccine-strains in urine since it was the most convenient, easy to explain to patients, and less invasive than aspirate or swab. Samples were collected at the time of presumed viral replication peak, namely around day 10 following MMR vaccination. The same procedure was conducted in a cohort of healthy children following their first dose of MMR vaccine, acting as control population. Overall, measles vaccine strain was detected only once in a 1-year-old healthy control at day 10 following his first dose of MMR vaccine. We did not document viral shedding in LT patient, nor in the other young healthy children.

Our results are consistent with those by Frenkel at al. who failed to detect measles, mumps, nor rubella from peripheral blood mononuclear cells, polymorphonuclear leukocytes, or plasma in 10 HIV-infected children following MMR vaccination [10]. Our results contrast with previous findings by Rota et al. mentioned earlier. However, the two studies differ by the type of MMR vaccine used and the number of urine sampling. In the study by Rota et al., the authors used the measles vaccine strain Moraten (Attenuvax®; Merck, Sharp and Dohme, West Point, Pa.), and urine samples were collected every day from day 1 to day 14.

Technical issues are unlikely in our study since we followed a standardized protocol for the RT-PCR assay with valid positive and negative controls. Furthermore, measles vaccine-strain was detected in one of our healthy controls at day 10 following MMR vaccine. One can question the timing of the urine sampling, and earlier or repeated urine samples would have maybe identified viral shedding in more subjects. Absence of viral shedding in non-naïve patients could be explained by inhibition of viral replication by preexisting antibody; but the 10 to 20-fold increase in antibody concentration observed in these patients after vaccination (Figure S2) suggests a limited little replication. Moreover, measles vaccine strain was not detected either in the 24 MMR-naïve patients who lacked preexisting measles antibody. In conclusion, our results show the absence of prolonged viral shedding following MMR vaccine in LT recipients (MMR-naïve or not), decreasing the hypothetical fear of uncontrolled viral vaccine-strain replication.

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