SUPPLEMENTAL DATA

SUPPLEMENTARY FIGURES

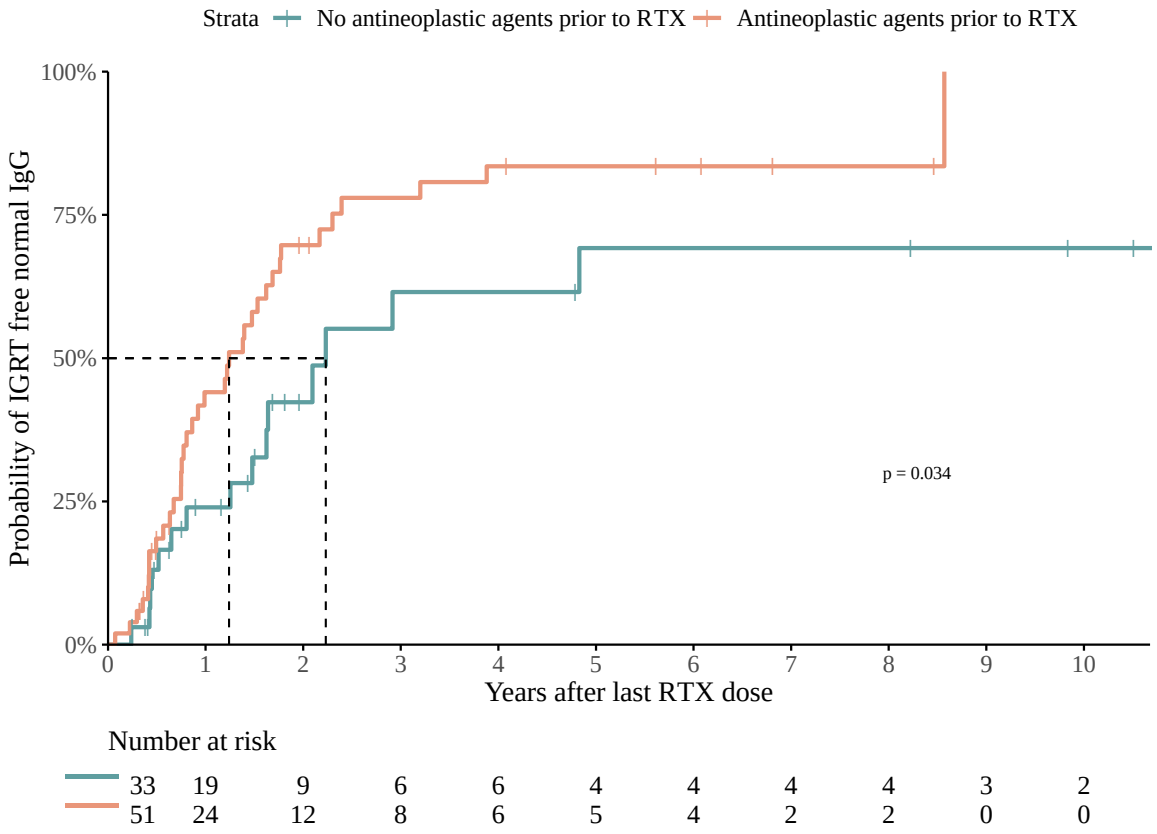

Figure S1. Time to IGRT-free normal IgG stratified by antineoplastic agent exposure. Time to IGRT-free normal IgG level after last RTX dose in patients with HG and a minimum of 3 months of IgG follow-up measurements. Kaplan Meier curves are stratified per antineoplastic agent exposure prior RTX therapy. Patients were classified as still having HG when (1) IgG levels were below -2SD compared to age matched reference values, or (2) during IGRT for any indication. A log-rank test was performed, which showed a significant difference in Kaplan Meier curves (p=0.034).

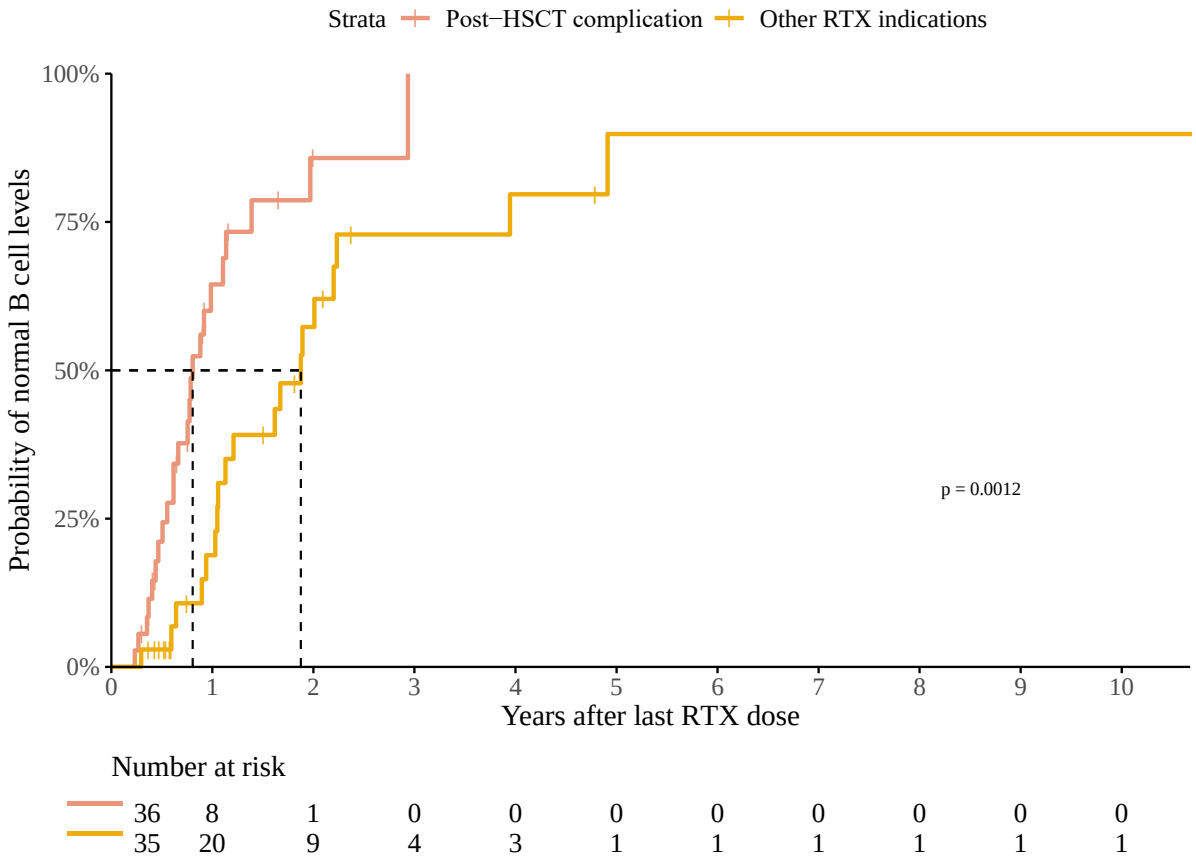

Figure S2. CD19$^+$ B cell reconstitution stratified by RTX indication. CD19$^+$ B cell reconstitution after last RTX dose in patients receiving RTX therapy for post-HSCT complications compared to other indications. Normal B cell levels were defined as measurements above -2SD from reference for age. A log-rank test was performed, which showed a significant difference in Kaplan Meier curves (p=0.001).

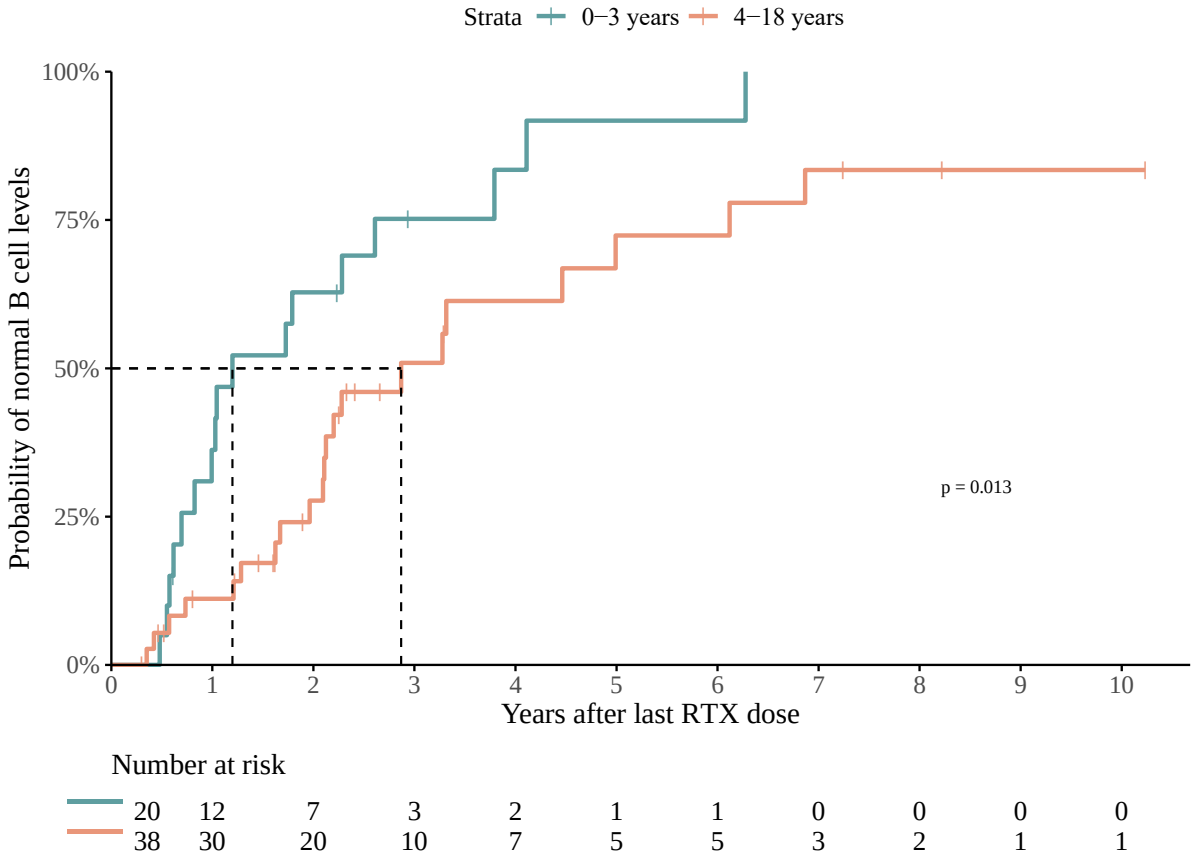

Figure S3. CD19^{+}CD27^{+}IgG^{+} switched memory B cell reconstitution stratified by age group. CD19^{+}CD27^{+}IgG^{+} memory B cell reconstitution after last RTX dose in patients aged 0-3 years compared to aged 4-18 years. A minimum of 3 months of CD19^{+}CD27^{+}IgG^{+} memory B cell follow-up measurements was implemented. Normal B cell levels were defined as measurements above -2SD from reference for age. A log-rank test was performed, which showed a significant difference in Kaplan Meier curves (p=0.013).

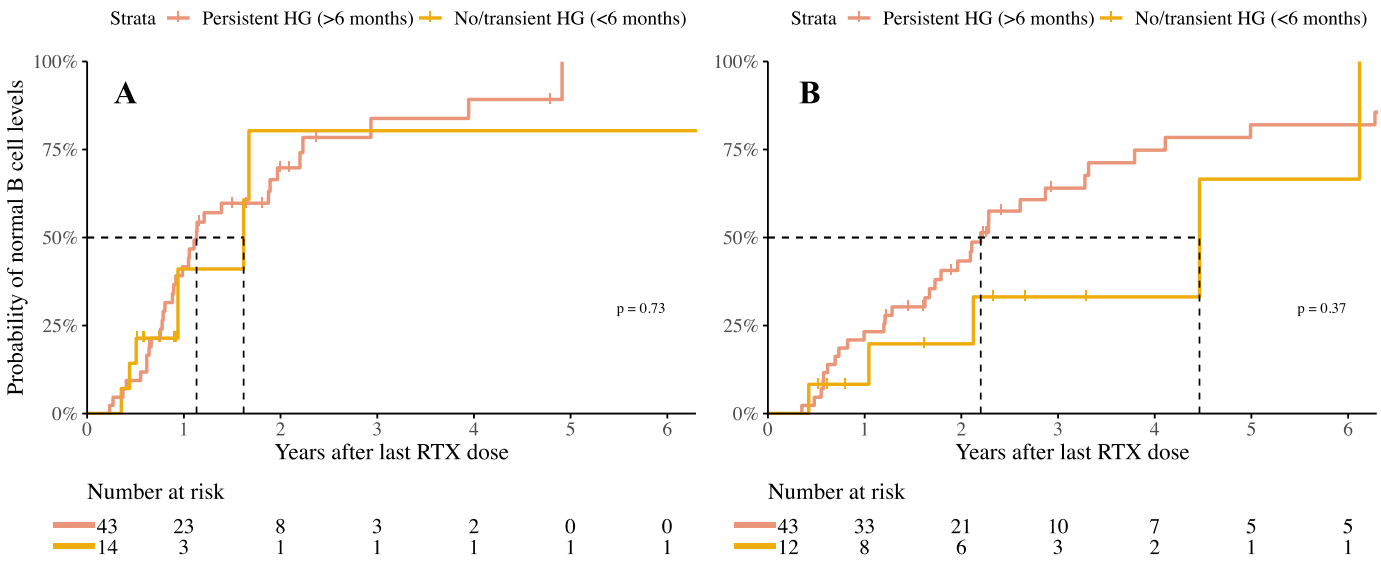

Figure S4. CD19⁺ B cell and CD19⁺CD27⁺IgG⁺ switched memory B cell reconstitution stratified by persistent HG. (A) CD19⁺ B cell reconstitution and (B) CD19⁺CD27⁺IgG⁺ memory B cell reconstitution after last RTX dose in patients with persistent HG (>6 months) compared to patients with transient (<6 months) or no HG after last RTX dose. A minimum of 3 months follow-up measurements was implemented in both panels shown. Normal B cell levels were defined as measurements above -2SD from reference for age. Log rank tests found no association between persistent HG and (A) CD 19⁺ B cell reconstitution times (p=0.73); and/or (B) IgG⁺ memory B cell reconstitution times (p=0.37).

SUPPLEMENTARY TABLES

Table S1. Baseline characteristics by RTX indication

RTX indication	Autoimmune diseases	Immunodeficiencies	Hematological malignancies	Nephrotic syndrome	Post-HSCT complication	Post-solid organ transplantation complication	**Overall**	P*
Number of patients	42	4	13	9	67	6	**141**	
Female sex (n (%))	26 (61.9)	1 (25.0)	4 (30.8)	1 (11.1)	28 (41.8)	1 (16.7)	**61 (43.3)**	**0.024**
Age in years (mean ±*SD*)	11.5 (4.92)	9.75 (6.40)	12.0 (4.12)	10.4 (5.10)	6.82 (5.89)	13.0 (4.43)	**9.26 (5.80)**	**<0.001**
Baseline immunoglobulins and B cell count								
IgG (median (IQR) [SD])	-0.40 [-1.58, 1.57]	-0.96 [-1.24, -0.69]	-1.96 [-2.59, -1.60]	-3.01 [-3.15, -2.17]	-1.27 [-1.86, -0.47]	-0.87 [-1.74, 0.58]	**-1.27 [-2.04, -0.34]**	**0.001**
IgA (median (IQR) [SD])	-1.00 [-1.84, -0.62]	-1.60 [-2.01, -1.23]	-1.83 [-2.13, -1.65]	-1.17 [-1.68, -0.36]	-1.55 [-2.11, -0.74	-1.31 [-1.76, -0.62]	**-1.48 [-2.02, -0.64]**	0.468
IgM (median (IQR) [SD])	-0.54 [-1.25, 0.18]	-1.66 [-2.17, 20.11]	-1.69 [-1.98, -0.11]	-0.90 [-1.12, 1.40]	-1.03 [-1.71, 1.09]	-1.03 [-1.16, -0.26]	**-0.90 [-1.67, 0.46]**	0.555
$CD19^+$ B cell counts (median (IQR) [SD])	-0.37 [-1.67, 1.69]	-3.24 [-3.29, -3.20]	NA [NA, NA]	-0.02 [-0.04, 0.78]	-1.65 [-2.50, -0.27]	-1.98 [-2.34, -1.77]	**-1.71 [-2.97, 0.11]**	**0.033**
$CD19^+CD27^+IgG^+$ memory B cell counts (median (IQR) [SD])	1.06 [-0.50, 1.23]	-1.67 [-1.67, -1.67]	NA [NA, NA]	-0.45 [-0.83, 0.51]	1.10 [0.48, 2.98]	-1.31 [-1.83, 0.37]	**-0.95 [-2.03, 0.89]**	0.057
RTX therapy regimen								
Number of RTX cycles (median [min, max]) [a]	1 [1, 6]	1 [1, 1]	1[1, 2]	1 [1, 3]	1 [1, 4]	1 [1, 2]	**1 [1, 6]**	0.144
Number of RTX doses (median [min, max])	4 [2, 15]	4 [4, 4]	6 [1, 8]	2 [1, 5]	3 [1, 12]	3 [2, 4]	**3 [1, 15]**	**0.005**
Relative cumulative dose in mg/m^2 (median [*IQR*])	1390 [1116, 1509]	1481 [1343, 1507]	2200 [783, 2260]	851 [750, 1112]	1138 [760, 1434]	840 [377, 1885]	**1171 [784, 1518]**	**0.026**
Medication prior to RTX [b]								
Corticosteroids (n (%)) [c]	30 (71.4)	2 (50.0)	10 (76.9)	8 (88.9)	61 (91.0)	6 (100.0)	**117 (83.0)**	**0.036**
Antineoplastic agents (n (%)) [d]	3 (7.1)	0 (0.0)	12 (92.3)	0 (0.0)	56 (83.6)	0 (0.0)	**71 (50.4)**	**<0.001**
Immunosuppressants or immunomodulators (n (%)) [e]	30 (71.4)	2 (50.0)	10 (76.9)	8 (88.9)	62 (92.5)	6 (100.0)	**118 (83.7)**	**0.019**
(Other) biological DMARDs (n (%)) [f]	3 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)	29 (43.3)	4 (66.7)	**36 (25.5)**	**<0.001**
IGRT within five months prior to RTX (n, %)	10 (23.8)	2 (50.0)	1 (7.7)	0 (0.0)	36 (53.7)	2 (33.3)	**51 (36.2)**	**0.001**
Medication during or after RTX[b]								
Corticosteroids (n (%))	38 (90.5)	4 (100.0)	13 (100.0)	7 (77.8)	66 (98.5)	5 (83.3)	**133 (94.3)**	0.066
Antineoplastic agents (n (%))	5 (11.9)	1 (25.0)	13 (100.0)	0 (0.0)	28 (41.8)	0 (0.0)	**47 (33.3)**	**<0.001**
Immunosuppressants or immunomodulators (n (%))	38 (90.5)	4 (100.0)	13 (100.0)	7 (77.8)	66 (98.5)	6 (100.0)	**134 (95.0)**	0.064
(Other) biological DMARDs (n (%))	4 (9.5)	2 (50.0)	0 (0.0)	0 (0.0)	13 (19.4)	0 (0.0)	**19 (13.5)**	**0.042**
IGRT during or after RTX(n (%))	18 (42.9)	4 (100.0)	6 (46.2)	0 (0.0)	60 (89.6))	1 (16.7)	**89 (63.1)**	**<0.001**
Pre-RTX HG (n/total available (%))	5/32 (15.6)	0/2 (0.0)	6/11 (54.5)	7/8 (87.5)	14/64 (21.8)	1/5 (20.0)	**33/122 (27.0)**	**<0.001**

**P-values were calculated using Chi-squared test for categorical and One-way ANOVA for continuous variables; Kruskal-Wallis and Fisher test were used for non-normally distributed and low (expected) count variables, respectively.*

[a] *A cycle was defined as: one or more rituximab doses with no more than 45 days between courses.*
[b] *Medication was classified according to the ATC/DDD Index 2021*
[c] *Prednisone, dexamethasone, triamcinolone, hydrocortisone*
[d] *Cyclophosphamide and other alkylating agents, methotrexate and other antimetabolites, protein kinase inhibitors, miscellaneous*
[e] *Mycophenolic acid, sirolimus, leflunomide, everolimus, cyclosporine, tacrolimus, azathioprine, methotrexate*
[f] *Thymoglobulin, abatacept, infliximab, adalimumab, tocilizumab, miscellaneous*

Table S2. RTX indications in detail

RTX indication	Diagnosis	Number of patients
Autoimmune diseases	Autoimmune cytopenia	12
	Autoimmune CNS disease	8
	Juvenile Dermatomyositis (JDM)	5
	Hematological diseases, development of inhibitory antibodies[a]	5
	Vasculitis	3
	Systemic Lupus Erythematosus (SLE)	3
	Autoimmune hepatitis	2
	Juvenile Idiopathic Arthritis	1
	Miscellaneous	3
Immunodeficiencies	Immunodeficiencies with autoimmunity	4
Hematological malignancies	Burkitt lymphoma	5
	Non-Hodgkin lymphoma	3
	Hodgkin lymphoma	2
	Miscellaneous	3
Nephrotic syndrome	Nephrotic syndrome	9
Post-HSCT complication	Autoimmune cytopenia	23
	EBV infection or reactivation	22
	Post-transplant lymphoproliferative disease (PTLD)	5
	Humoral transplant rejection	1
	Prophylaxis for autoimmune cytopenia[b]	10
	HSCT conditioning regimen[c]	6
Post-solid organ transplantation complication	Post-transplant lymphoproliferative disease (PTLD)	4
	Humoral transplant rejection	2
Total		141

[a]*Treatment and/or transfusion related inhibitory antibodies (e.g. factor VIII antibodies)*
[b]*RTX was prophylactically administered pre- and/or post-HSCT. Both were classified as post-HSCT complication.*
[c]*RTX administered pre-HSCT as a part of HSCT conditioning, was also classified as post-HSCT complication.*