Terms definition:

BSIs: any positive result of bacterial culture with automated blood culture system (BD BACTEC™) excluding those which considered contamination based on repeated control cultures (in asymptomatic patients and those with mix bacterial culture results)

FN: calculated absolute neutrophil count less than 500 cells/mm^3 and temperature above 38.3^oC on at least one occasion or above 38^oC sustained over a 1-h period [1].

IFIs: diagnosis of fungal infections by direct and indirect mycological tests (including mannan test and galactomannan test, blood (PCR) polymerase chain reaction), histopathology, PCR and imaging studies based on the criteria developed and revised by European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) [2].

RTX maintenance therapy: patients receiving RTX for at least 375mg/m^2/week for four consequent weeks [3, 4].

Protocol escalation: change of the standard-risk protocol to high-risk protocol.

Follow up period: time from the last dose of RTX to the end of the follow-up period. Close follow up was considered to be continued for different endpoints for at least 36 months since the last dose of RTX.

Reference:

1. Freifeld, A.G., et al., Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. Clinical infectious diseases, 2011. 52(4): p. e56-e93.
2. Donnelly, J.P., et al., Revision and update of the consensus definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. Clinical infectious diseases, 2020. 71(6): p. 1367-1376.
3. Plosker, G.L. and D.P. Figgitt, Rituximab: a review of its use in non-Hodgkin's lymphoma and chronic lymphocytic leukaemia. Drugs, 2003. 63(8): p. 803-843.
4. Dotan, E., C. Aggarwal, and M.R. Smith, Impact of rituximab (Rituxan) on the treatment of B-cell non-Hodgkin's lymphoma. Pharmacy and Therapeutics, 2010. 35(3): p. 148.

Appendix 1. Demographics and clinical characteristics of 183 patients with malignancy, ITP, and hematologic disorders

Variables	Exposed group (61) N（%）	Unexposed group (122) N（%）	p. value
Gender			
Male	46 (75.4)	68 (55.7)	0.010*
Female	15 (24.6)	54 (44.3)	
Age, mean ±SD	7.83 ±4.56	7.13 ±5.09	0.209**
Underlying disease			
Malignancy	42 (68.9)	116 (95.1)	<0.001*
ITP/hematologic disorders	19 (31.1)	6 (4.9)	
Baseline protocol risk[a]			
Standard-risk	9 (14.8)	72 (59.0)	<0.001*
High-risk	33 (54)	44 (36)	
Change to high-risk protocol[a]	8 (13.1)	33 (27)	<0.001*
RTX dose (mg), mean (±SD)	1928.57 (1947.40)	-	-
Infectious events	32 (52.5)	103 (84.4)	0.013*
FN	30 (49.2)	95 (77.9)	<0.001*
BSI	7 (11.5)	34 (27.9)	0.012*
IFI	6 (9.8)	19 (15.6)	0.287
All-cause mortality	15 (24.6)	31 (25.4)	0.904

ITP: immune thrombocytopenic purpura, RTX: Rituximab, FN: febrile neutropenia, BSI: bloodstream infection, IFI: invasive fungal infection.

* Statistically significant by Chi-Square test

** Statistically nonsignificant by Mann-Whitney Test

a. excluding ITP and non-malignant cases

Appendix 2. The adjusted effect of RTX treatment on the patient's survival, results of the Cox proportional hazards model

Variable	HR	Robust SE	z	P>|z|	95% conf.	interval
RTX treatment	3.269	1.962	1.97	0.048*	1.008	10.599
Lymphoma [a]	1.708	0.979	0.93	0.350	0.555	5.253
Change to high-risk protocol	4.821	2.422	3.13	0.002*	1.800	12.908
Protocol risk [b]						
High-risk	1.406	0.693	0.69	0.489	0.535	3.697
Male gender	1.252	0.414	0.68	0.497	0.654	2.397
Age						
<2 years	1.966	1.263	1.05	0.293	.557	6.929
2-5 years	1.790	0.901	1.16	0.247	.667	4.803
5-10 years	0.795	0.347	-0.52	0.600	.337	1.871

HR: hazard ratio, SE: standard error, RTX: Rituximab

a. other childhood malignancies (reference)

b. non-high-risk protocol (reference)

c. >10 years (reference)

* Statistically significant

Appendix 3. The adjusted effect of RTX treatment on the febrile neutropenic events, results of the Cox proportional hazards model

Variable	HR	Robust SE	z	P>|z|	95% conf.	interval
RTX treatment	1.686	0.607	1.45	0.147	0.832	3.414
Lymphoma [a]	1.167	0.368	0.49	0.625	0.628	2.168
Change to high-risk protocol	1.074	0.224	0.35	0.729	0.714	1.617
Protocol risk [b]						
High-risk	1.658	0.340	2.47	0.014*	1.109	2.480
Female gender	1.161	0.226	0.77	0.441	0.793	1.701
Age						
2-5 years	1.701	0.688	1.31	0.189	0.770	3.759
5-10 years	1.297	0.503	0.67	0.502	0.606	2.774
> 10 years	1.437	0.580	0.90	0.370	0.650	3.173

HR: hazard ratio, SE: standard error, RTX: Rituximab

a. other childhood malignancies (reference)

b. non-high-risk protocol (reference)

c. <2 years (reference)
* Statistically significant

Appendix 4. The adjusted effect of RTX treatment on bloodstream infections, results of the Cox proportional hazards model

Variable	HR	Robust SE	z	P>|z|	95% conf.	interval
RTX treatment	1.599	1.425	0.53	0.598	0.278	9.171
Lymphoma [a]	2.433	2.003	1.08	0.280	0.484	12.218
Change to high-risk protocol	4.078	1.743	3.29	0.001*	1.764	9.425
Protocol risk [b]						
Standard-risk	1.811	0.749	1.44	0.151	0.805	4.076
Male gender	1.243	0.469	0.58	0.563	0.593	2.608
Age						
<2 years	3.612	2.227	2.08	0.037*	1.079	12.096
2-5 years	1.747	0.862	1.13	0.258	0.664	4.598
5-10 years	0.386	0.227	-1.61	0.107	0.121	1.227

HR: hazard ratio, SE: standard error, RTX: Rituximab
a. other childhood malignancies (reference)
b. non-standard-risk protocol (reference)
c. >10 years (reference)
* Statistically significant

Appendix 5. The adjusted effect of RTX treatment on invasive fungal infections, results of the Cox proportional hazards model

Variable	HR	Robust SE	z	P>|z|	95% conf.	interval
RTX treatment	4.339	2.821	2.26	0.024*	1.213	15.520
Lymphoma [a]	2.260	1.144	1.61	0.107	0.838	6.098
Change to high-risk protocol	4.865	2.954	2.61	0.009*	1.480	15.993
Protocol risk [b]						
High-risk	1.006	0.575	0.01	0.991	0.328	3.085
Female gender	3.374	1.728	2.37	0.018*	1.236	9.207
Age						
<2 years	1.306	0.878	0.40	0.691	0.349	4.880
2-5 years	0.627	0.351	-0.83	0.406	0.209	1.880
5-10 years	0.506	0.337	-1.02	0.307	0.137	1.867

HR: hazard ratio, SE: standard error, RTX: Rituximab
a. other childhood malignancies (reference)
b. non-high-risk protocol (reference)
c. >10 years (reference)
* Statistically significant

Appendix 6. Dose-dependent effect of RTX on death in children with malignancy, results of multivariable logistic regression models adjusted for the patient's covariates

Variable	OR	Robust Std. error	z	P>|z|	95% conf. interval	
RTX dose [a]						
2nd quartile	2.289	3.386	0.56	0.575	0.126	41.567
3rd quartile	5.719	6.222	1.60	0.109	0.678	48.241
4th quartile	11.831	15.176	1.93	0.054	0.957	146.16
Change to high-risk protocol	2.863	3.599	0.84	0.403	0.243	33.636
BSI	1.344	2.085	0.19	0.849	0.064	28.105
FN	2.058	3.374	0.44	0.660	0.082	51.178
IFI	1.462	1.668	0.33	0.739	0.156	13.684
Diagnosis (lymphoma) [b]	0.193	0.278	-1.14	0.253	0.011	3.224

OR: odds ratio, RTX: Rituximab, BSI: bloodstream infection, FN: febrile neutropenia, IFI: invasive fungal infection

a. the first quartile (reference)

b. other malignancies (reference)

Appendix 7. Dose-dependent effect of RTX on infectious events in children with malignancy, results of multivariable logistic regression models adjusted for the patient's covariates

Variable	OR	Robust Std. error	z	P>|z|	95% conf. interval	
RTX dose [a]						
2nd quartile	2.458	3.179	0.70	0.487	0.195	30.998
3rd quartile	3.173	4.370	0.84	0.402	0.213	47.180
4th quartile	6.370	6.958	1.70	0.090	0.748	54.198
Diagnosis (lymphoma) [b]	10.937	10.567	2.48	0.013*	1.646	72.661
Change to high-risk protocol	1.827	2.041	0.54	0.590	0.204	16.325
Age	0.826	0.101	-1.55	0.122	0.648	1.052
High-risk protocol [c]	1.683	1.924	0.46	0.649	0.179	15.823

OR: odds ratio, RTX: Rituximab

a. the first quartile (reference)

b. other malignancies (reference)

c. standard-risk protocol (reference)

* Statistically significant

Appendix 8. The adjusted effect of RTX treatment on the patient's survival, results of the logistic regression model

Variable	OR	Std. error	z	P>|z|	95% conf. interval	
RTX treatment	1.544	1.027	0.65	0.514	0.419	5.692
Change to high-risk protocol	12.330	5.739	5.40	<0.001*	4.951	30.705
Protocol risk [a]						
Intermediate-risk	1.489	1.096	0.54	0.588	0.352	6.301
High-risk	2.351	1.216	1.65	0.099	0.852	6.483
Infectious complications	2.614	2.274	1.10	0.269	0.474	14.389
Male gender	1.691	0.800	1.11	0.267	0.668	4.274
Age	1.018	0.044	0.42	0.676	0.934	1.109

OR: odds ratio, RTX: Rituximab

a. Standard-risk protocol (reference)

* Statistically significant

Appendix **9. Life Table** [a]

Interval Start Time	Number Entering Interval	Number Withdrawing during Interval	Number Exposed to Risk	Number of Terminal Events	Proportion Terminating	Proportion Surviving	Cumulative Proportion Surviving at End of Interval	Std. Error of Cumulative Proportion Surviving at End of Interval	Probability Density	Std. Error of Probability Density	Hazard Rate	Std. Error of Hazard Rate
0	42	24	30.000	7	.23	.77	.77	.08	.019	.006	.02	.01
12	11	3	9.500	4	.42	.58	.44	.13	.027	.011	.04	.02
24	4	0	4.000	1	.25	.75	.33	.14	.009	.008	.02	.02
36	3	3	1.500	0	.00	1.00	.33	.14	.000	.000	.00	.00

a. The median survival time is 21.91 months