Non-Hodgkin lymphoma and pre-existing conditions: spectrum, clinical characteristics and outcome in 213 children and adolescents

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Invitation Letter:

Padua, 23 May, 2014

Dear Colleagues,

During the last international BFM (i-BFM) meeting in Prague, it was decided to perform a collaborative study among i-BFM countries (members) and centres to collect retrospective data of patients with non-Hodgkin's Lymphomas (NHL) who have been affected by constitutional (genetic) syndromes. We all know that incidence of cancer in patients with confirmed of suspected genetic syndromes is higher than in the healthy population. In addition, patients with concomitant genetic disorders are often not eligible for standard treatment and/or therapy is reduced/modified by individual decisions of the treating physicians. Solid outcome data are not available yet, although some groups have reported that NHL patients with underlying genetic syndromes perform quite well.

The aim of this multi-national study is to gather broad information on the clinical characteristics, treatment and outcome of this specific patient population. We would like to restrict this study to patients who have been treated in the period from 1984 until end of 2013 and to standard data that should be available for most of the patients.

In the attachment you will find an excel file with the listed information/parameters that we would like to collect for every patient. It would be great if we could get the data until the end of October 2014 which then will be analysed in Padua.

If you have any questions concerning the project or the data needed by us, please feel free to contact me at the e-mail address marta.pillon@unipd.it or Andishe Attarbaschi at the email address andishe.attarbaschi@stanna.at. We hope that after the successful project on follicular lymphoma we can have another fruitful cooperation allowing us both to learn more about the spectrum of constitutional syndromes involved in children and adolescents with NHL and to have a nice publication under the umbrella of i-BFM (and EICNHL). As for the follicular lymphoma project, countries and study groups being members of EICNHL (if it is ok for you Denise?) but not of NHL i-BFM will also be invited to take part, being another step forward in bringing both cooperative groups closer to each other.

Thank you for your cooperation.

Sincerely,

Marta Pillon
Coordinator of the AIEOP NHL Working Group
and of the i-BFM project on NHL in genetic syndromes

Andishe Attarbaschi
NHL i-BFM Chair
St. Anna Children's Hospital

Suppl. Table 1. Questionnaire sent out to the groups and centers

Country/Group/Center
Patient No.
Date of birth
Gender
Date of diagnosis
Histological subtype
Immunology
Associated genetic condition
Pre-treatment LDH
Stage of disease
Sites of involvement
Risk group
Treatment protocol
Modifications from protocol
Date of complete remission
Event (yes/no)
Type of event
Date of event
Second-line therapy
Radiotherapy (yes/no); dose
Stem cell transplantation (yes/no); type
Death
Date of death
Cause of death
Date of last follow-up
Remarks

Suppl. Table 2. Clinical and laboratory characteristics and outcome of NHL patients in cancer predisposition syndromes (n<3 patients)

Pre-existing condition	Gender	Age at dg.	Histology	LDH	Stage of disease	Relapse/ progression	SML	Death	Disease-related death	Therapy-related death	Follow-up
Abernethy malformation type I	male	6.92	B-NHL n. f. sp.	452	I	no	no	no			2.98 & CR
ALPS	male	0.19	T-LBL	320	n. a.	no	no	yes	no	yes	
DNA ligase deficiency	female	2.33	DLBCL	1827	IV	yes	no	yes	yes	no	
IL7R-α deficiency	female	0.59	DLBCL	1379	III	no	no	no			5.98 & CR
Cartilage hair syndrome	female	1.77	DLBCL	n. a.	III	no	no	yes	no	yes	
Cartilage hair syndrome	female	4.28	DLBCL	n. a.	n. a.	no	no	no			9.02 & CR
Common gamma chain deficiency	male	0.44	ALCL	426	n. a.	no	no	no			17.67& CR
Fanconi anemia	male	12.93	T-LBL	871	III	yes	no	yes	no	Yes	
Hyper-IgE syndrome	female	3.50	Burkitt	316	IV	no	no	no			7.75 & CR
Hyper-IgE syndrome	male	13.57	DLBCL	299	II	yes	no	no			5.56 & CR
Hyper-IgM syndrome	female	11.73	MZL	353	III	yes	no	no			5.11 & CR
Hyper-IgM syndrome	female	14.60	DLBCL	502	III	no	no	yes	no	yes	
IL-2 inducible T-cell kinase deficiency	male	0.77	DLBCL	n. a.	III	no	no	no			1.66 & CR
Li-Fraumeni syndrome	male	6.10	DLBCL	1246	III	no	no	no			5.29 & CR
Noonan-like syndrome	male	7.00	Burkitt	n. a.	II	no	no	no			5.87 & CR
Rothmund-Thomson syndrome	female	3.30	T-NHL	390	II	no	no	yes	no	yes	
Sotos syndrome	male	12.88	T-LBL	224	IV	no	no	no			9.23 & CR
STK4 deficiency	female	11.79	MALT lymphoma	n. a.	II	no	no	no			0.33 & CR

Abbreviations: dg., diagnosis; LDH, lactate dehydrogenase; SML, secondary malignancy; ALPS, autoimmune lymphoproliferative syndrome; B-NHL, mature B-cell non-Hodgkin's lymphoma; T-LBL, T-cell lymphoblastic lymphoma; BCP-LBL, B-cell precursor lymphoblastic lymphoma; ALCL, anaplastic large cell lymphoma; DLBCL, diffuse large B-cell lymphoma; MZL, marginal zone lymphoma; MALT, mucosa-associated lymphoid tissue lymphoma; n. a., not available; n. f. sp., not further specified; CR, in complete remission

Suppl. Table 3. Clinical and laboratory characteristics and outcome of NHL patients in each one category of genetic diseases and syndromes not further specified (n>2 patients)

	G6PD deficiency	Developmental delay
No. of patients	4	8
Gender		
male	3	7
female	1	1
Age (years) at dg.		
median	8.66	13.06
range	2.94-15.55	4.34-16.7
Histology		
Mature B-NHL	4	5
Burkitt lymphoma	2	3
DLBCL	2	2
T-LBL	0	2
BCP-LBL	0	0
ALCL	0	1
Stage of disease		
I	0	0
II	2	3
III	2	4
IV	0	1
LDH		
≥500 U/l	3	5
<500 U/l	1	2
not available	0	1
Relapse/progression	0	2
Second malignancy	0	0
Death	0	2
disease-related	0	2
therapy-related	0	0
in CR	4	6
Follow-up (years)		
median	2.9	5.92
range	1.05-4.95	1.39-11.78

Abbreviations: G6PH, Glucose-6-phosphate dehydrogenase; No., number; dg., diagnosis; B-NHL, B-cell non-Hodgkin's lymphoma; T-LBL, T-cell lymphoblastic lymphoma; BCP-LBL, B-cell precursor lymphoblastic lymphoma; ALCL, anaplastic large cell lymphoma; PTCL, peripheral T-cell lymphoma; DLBCL, diffuse large B-cell lymphoma; LDH, lactate dehydrogenase; SML, secondary malignancy; CR, complete remission

Suppl. Table 4. Clinical and laboratory characteristics and outcome of NHL patients in genetic diseases not known to be associated with an increased cancer risk (n<3 patients)

Pre-existing condition	Gender	Age at dg.	Histology	LDH	Stage of disease	Relapse/ progression	SML	Death	Disease-related death	Therapy-related death	Follow-up
α-1-antitrypsin deficiency	male	2.48	PTCL	624	III	yes	no	yes	yes	no	
α-1-antitrypsin deficiency	male	2.19	Burkitt	888	IV	yes	no	yes	no	yes	
Baller-Gerold syndrome	female	2.42	PTCL*	550	n. a.	no	no	no			11.35 & in CR
Bare lymphocyte syndrome	female	18.70	DLBCL	243	III	no	no	yes	no	yes	
Congenital dyserythropoetic anemia	female	6.03	B-NHL n. f. sp.	99	IV	yes	no	no			8.35 & in CR
Charcot-Marie-Tooth disease	male	10.21	Burkitt	337	II	no	no	no			4.96 & in CR
CTP synthase 1 deficiency	male	1.05	DLBCL	n. a.	n. a.	yes	no	no			2.61 & in CR
Cystic fibrosis	female	14.67	DLBCL	658	II	no	no	yes	no	yes	
Cystic fibrosis	female	7.43	Burkitt	245	I	no	no	no			0.40 & in CR
Duane syndrome	male	16.55	DLBCL	339	I	no	no	no			1.23 & in CR
Factor VII deficiency	female	14.54	PMLBCL	3417	IV	yes	no	yes	yes	no	
Factor XII deficiency	male	6.60	Burkitt	384	II	no	no	no			6.77 & in CR
Gaucher syndrome	male	9.83	DLBCL	680	II	no	no	no			0.87 & in CR
Hemophilia A	male	14.41	Burkitt	345	I	no	No	no			12.08 & in CR
Hemophilia A	male	14.67	Burkitt	1524	IV	no	No	no			1.30 & in CR
Hirschsprung's disease	male	4.99	DLBCL	598	III	yes	No	yes	yes	no	
Kabuki syndrome	male	5.93	Burkitt	1075	III	no	No	no			0.39 & in CR
Kartagener syndrome	male	4.66	T-LBL	552	III	yes	No	yes	yes	no	
Marfan syndrome	male	13.90	DLBCL	616	III	no	No	no			1.53 & in CR
Duchenne muscular dystrophy	male	5.27	ALCL	954	II	yes	No	no			3.55 & in CR
Myotonic dystrophy Curschmann-Steinert	male	4.15	BCP-LBL	n. a.	III	no	No	no			5.91 & in CR
Congenital Finish nephrosis	female	12.91	ALCL	n. a.	III	no	No	no			8.68 & in CR
Rett syndrome	female	11.56	ALCL	312	III	no	No	no			12.62 & in CR
Waardenburg syndrome	female	14.07	B-NHL	1652	III	yes	No	yes	no	yes	
Smith-Magenis syndrome	male	12.51	T-LBL	342	IV	yes	No	yes	no	yes	
Silver-Russell syndrome	male	16.86	DLBCL	224	II	no	No	no			4.64 & in CR

Williams-Beuren syndrome	male	5.80	Burkitt	11937	III	yes	No	no			5.50 & in CR
Williams-Beuren syndrome	male	3.94	Burkitt	5589	III	no	No	no			9.51 & in CR
Cri-du-chat syndrome	male	11.44	Burkitt	1030	III	no	No	no			3.89 & in CR
Chromosomal aberrations n. f. sp.	male	4.93	Burkitt	743	IV	no	No	no			13.76 & in CR
22q11.2 deletion syndrome	female	8.30	PTCL	n. a.	IV	yes	No	yes	yes	no	
Turner syndrome	female	11.04	T-LBL	582	II	no	No	no			18.80 & in CR
Triple X syndrome	female	11.24	ALCL	248	II	no	No	no			2.24 & in CR
Klinefelter syndrome	male	14.76	ALCL	173	II	no	No	no			18.38 & in CR
Prader-Labhart-Willi syndrome	female	17.21	BCP-LBL	n. a.	II	no	No	no			5.05 & in CR
Prader-Labhart-Willi syndrome	male	7.46	other**	2910	n. a.	no	No	no			8.59 & in CR

Abbreviations: dg., diagnosis; LDH, lactate dehydrogenase; SML, secondary malignancy; B-NHL, mature B-cell non-Hodgkin's lymphoma; T-LBL, T-cell lymphoblastic lymphoma; BCP-LBL, B-cell precursor lymphoblastic lymphoma; ALCL, anaplastic large cell lymphoma; PTCL, peripheral T-cell lymphoma; DLBCL, diffuse large B-cell lymphoma; PMLBCL, primary mediastinal large B-cell lymphoma; n. a., not available; n. f. sp., not further specified; CR, complete remission

*NK-cell lymphoma

**biphenotypic lymphoblastic lymphoma

Suppl. Table 5. Clinical and laboratory characteristics and outcome of NHL patients with underlying multifactorial diseases (n=7 patients), organ malformations (n=5 patients) and syndromes not further specified (n=2 patients)

Type of condition	Pre-existing condition	Gender	Age at dg.	Histology	LDH	Stage of disease	Relapse/ progression	SML	Death	Disease-related death	Therapy-related death	Follow-up
Multifactorial disease	Congenital hearing loss	male	15.97	PMLBCL	197	IV	no	no	no			1.95 & CR
Multifactorial disease	autism	male	6.08	Burkitt	5313	IV	no	no	no			7.50 & CR
Multifactorial disease	autism	female	9.73	DLBCL	854	III	yes	no	yes	yes	no	
Multifactorial disease	Autoimmune enteropathy	male	1.28	DLBCL	n. a.	n. a.	yes	no	yes	no	yes	
Multifactorial disease	Familial myoclonic epilepsy	female	17.83	Burkitt	1141	III	no	no	no			2.23 & CR
Multifactorial disease	Familial myoclonic epilepsy	male	3.41	Burkitt	1917	III	yes	no	yes	yes	no	
Multifactorial disease	Gilles de la Tourette syndrome	female	10.90	Burkitt	294	IV	no	no	yes	no	yes	
Organ malformation	Polymicrogyria	male	13.12	T-LBL	1308	III	no	no	no			4.95 & CR
Organ malformation	Congenital heart disease	male	4.04	T-LBL	n. a.	n. a.	yes	no	yes	yes	no	
Organ malformation	Partial agenesis of corpus callosum	male	9.67	T-LBL	1000	IV	no	no	no			2.76 &CR
Organ malformation	Kidney agenesis	male	8.93	Burkitt	226	IV	yes	no	yes	no	yes	
Organ malformation	Agenesis of the phalanges of hand and foot	female	13.61	DLBCL	332	III	no	no	no			6.78 & CR
Syndrome n. f. sp.	Prematurity, single kidney, dysmorphic spinal vertebrae	male	3.21	T-LBL	n. a.	III	no	no	no			14.7 & CR
Syndrome n. f. sp.	Congenital heart disease, facial dysmorphism, deafness	female	5.81	ALCL	313	III	no	no	yes*	no	no	

Abbreviations: dg., diagnosis; LDH, lactate dehydrogenase; SML, secondary malignancy; n. f. sp., not further specified; T-LBL, T-cell lymphoblastic lymphoma; ALCL, anaplastic large cell lymphoma; DLBCL, diffuse large B-cell lymphoma; PMLBCL, primary mediastinal large B-cell lymphoma; n. a., not available; CR; in complete remission

*heart failure while waiting for heart transplantation

Suppl. Table 6. Clinical and laboratory characteristics and outcome of NHL patients with a pre-existing condition who developed a secondary malignancy (n=21)

Pre-existing condition	Gender	Age at dg.	Histology	LDH	Stage of disease	Secondary malignancy	Death	Disease-related death	Treatment-related death	SML-related death	Follow-up
NBS	female	12.78	T-NHL	1200	III	DLBCL	yes	no	yes	no	
CMMRD	male	7.66	T-LBL	n. a.	III	colorectal carcinoma	no				9.26 & in CR
NBS	male	4.69	T-LBL	378	IV	other lymphoma*	yes	yes	no	no	
CMMRD	male	4.35	T-LBL	1310	III	brain tumor n. f. sp.	no				4.10 & in CR
CMMRD	male	5.13	T-LBL	648	III	clonally diverse T-NHL	yes	no	no	yes	
CMMRD	male	17.97	Burkitt	2697	III	colorectal carcinoma	yes	no	no	yes	
CMMRD	female	13.60	T-LBL	489	III	colorectal carcinoma	yes	no	no	yes	
CMMRD	male	6.28	T-LBL	n. a.	III	brain tumor (glioblastoma)	yes	no	no	yes	
CMMRD	male	4.62	T-LBL	n. a.	III	brain tumor (glioblastoma)	yes	no	no	yes	
WAS	male	6.32	Burkitt	285	III	clonally diverse mature B-NHL	yes	n. a.	n. a.	n.a.	
NBS	female	10.93	DLBCL	1157	III	NHL n. f. sp.	yes	no	no	yes	
CMMRD	male	3.03	BCP-LBL	751	IV	brain tumor (glioblastoma)	yes	no	no	yes	
CMMRD	female	7.75	T-LBL	n. a.	III	myelodysplastic syndrome	yes	no	no	yes	
AT	male	8.91	DLBCL	224	III	hepatoblastoma	yes	no	no	yes	
NF1	male	3.38	T-LBL	213	III	acute myeloid leukemia	yes	no	no	yes	
AT	male	11.90	DLBCL	193	II	clonally diverse mature B-NHL	yes	no	n. a.	n. a.	
AT	male	5.53	DLBCL	322	III	clonally diverse mature B-NHL	yes	no	no	yes	
NBS	female	9.48	plasmablastic B-NHL	204	III	acute lymphatic leukemia	yes	no	no	yes	
CMMRD	female	6.47	T-LBL	206	III	colorectal carcinoma	yes	no	no	yes	
CMMRD	male	16.21	T-LBL	n. a.	III	brain tumor (glioblastoma)	yes	no	no	yes	
XLP	male	4.77	DLBCL	355	II	clonally diverse mature B-NHL	no				9.19 & in CR

Abbreviations: dg., diagnosis; NBS, Nijmegen breakage syndrome; CMMRD, constitutional mismatch repair disease; WAS, Wiskott-Aldrich syndrome; AT, ataxia telangiectasia; NF1, neurofibromatosis type 1; XLP, X-linked lymphoproliferative syndrome; LDH, lactate dehydrogenase; SML, secondary malignancy; n. f. sp., not further specified; B-NHL, mature B-cell non-Hodgkin's lymphoma; T-LBL, T-cell lymphoblastic lymphoma; DLBCL, diffuse large B-cell lymphoma; n. a., not available; CR, complete remission

*blastic plasmacytoid dendritic cell lymphoma

Suppl. Table 7. Outcome of the 3 major histological subgroups among the 5 largest distinct groups of pre-existing conditions (>20 patients)

A) Number of patients with and without events

AT

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
event				
no	7	1	0	8
yes	20	1	3	24
				32

NBS

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
event				
no	5	2	0	7
yes	6	2	11	19
				26

CMMRD

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
event				
no	1	2	0	3
yes	2	16	0	18
				21

PID n. f. sp.

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
event				
no	9	0	3	12
yes	12	1	2	15
				27

Genetic diseases

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
event				
no	17	3	5	25
yes	9	2	4	15
				40

B) Number of patients with and without relapse/progression

AT

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
relapse/progression				
no	24	2	1	27
yes	3	0	2	5
				32

NBS

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
relapse/progression				
no	9	4	3	16
yes	3	1	6	10
				26

CMMRD

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
relapse/progression				
no	2	12	0	14
yes	1	6	0	7
				21

PID n. f. sp.

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
relapse/progression				
no	18	0	5	23
yes	3	1	0	4
				27

Genetic diseases

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
relapse/progression				
no	19	3	6	28
yes	7	2	3	12
				40

C) Number of patients with and without a toxic death as a first event

AT

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
toxic death as first event				
no	15	1	2	18
yes	12	1	1	14
				32

NBS

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
toxic death as first event				
no	10	4	6	20
yes	2	1	3	6
				26

CMMRD

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
toxic death as first event				
no	3	18	0	21
yes	0	0	0	0
				21

PID n. f. sp.

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
toxic death as first event				
no	12	1	4	17
yes	9	0	1	10
				27

Genetic diseases

	mature B-NHL	T- and BCP-LBL	other NHL	all NHLs
toxic death as first event				
no	24	5	9	38
yes	2	0	0	2
				40

Abbreviations: B-NHL, B-cell non-Hodgkin's lymphoma; T- and BCP-LBL, T-cell and B-cell precursor lymphoblastic lymphoma; NHL, non-Hodgkin's lymphoma; AT, ataxia telangiectasia; NBS, Nijmegen breakage syndrome; CMMRD, constitutional mismatch repair deficiency; PID n. f. sp.; primary immunodeficiency not further specified

Suppl. Table 8. Outcome of the 3 major histological subgroups across the 5 largest distinct groups of pre-existing conditions (>20 patients)

A) Number of patients with and without events

mature B-NHL

	AT	NBS	CMMRD	PID n. f. sp.	genetic diseases	all disorders
event						
no	7	5	1	9	17	39 (44%)
yes	20	7	2	12	9	50 (56%)
						89

T- and BCP-LBL

	AT	NBS	CMMRD	PID n. f. sp.	genetic diseases	all disorders
event						
no	1	2	2	0	3	8 (26%)
yes	1	3	16	1	2	23 (74%)
						31

other NHLs

	AT	NBS	CMMRD	PID n. f. sp.	genetic diseases	all disorders
event						
no	0	0	0	3	5	8 (31%)
yes	3	9	0	2	4	18 (69%)
						26

B) Number of patients with and without relapse/progression

mature B-NHL

	AT	NBS	CMMRD	PID n. f. sp.	genetic diseases	all disorders
relapse/progression						
no	24	9	2	18	19	72 (81%)
yes	3	3	1	3	7	17 (19%)
						89

T- and BCP-LBL

	AT	NBS	CMMRD	PID n. f. sp.	genetic diseases	all disorders
relapse/progression						
no	2	4	12	0	3	21 (68%)
yes	0	1	6	1	2	10 (32%)
						31

other NHLs

	AT	NBS	CMMRD	PID n. f. sp.	genetic diseases	all disorders
relapse/progression						
no	1	3	0	5	6	15 (58%)
yes	2	6	0	0	3	11 (42%)
						26

C) Number of patients with and without a toxic death as a first event

mature B-NHL

	AT	NBS	CMMRD	PID n. f. sp.	genetic diseases	all disorders
toxic death as first event						
no	15	10	3	12	24	54 (61%)
yes	12	2	0	9	2	35 (39%)
						89

T- and BCP-LBL

	AT	NBS	CMMRD	PID n. f. sp.	genetic diseases	all disorders
toxic death as first event						
no	1	4	18	1	5	29 (94%)
yes	1	1	0	0	0	2 (6%)
						31

other NHLs

	AT	NBS	CMMRD	PID n. f. sp.	genetic diseases	all disorders
toxic death as first event						
no	2	6	0	4	9	21 (81%)
yes	1	3	0	1	0	5 (19%)
						26

Abbreviations: B-NHL, B-cell non-Hodgkin's lymphoma; T- and BCP-LBL, T-cell and B-cell precursor lymphoblastic lymphoma; NHL, non-Hodgkin's lymphoma; AT, ataxia telangiectasia; NBS, Nijmegen breakage syndrome; CMMRD, constitutional mismatch repair deficiency; PID n. f. sp.; primary immunodeficiency not further specified

Suppl. Table 9. Comparison of the initial characteristics of the 3 major histological subgroups (including the 151 patients with cancer predisposition syndromes and PIDs not further specified only) with a representative cohort of patients without pre-existing conditions,

A) Comparison of the 96 mature B-NHL patients with the NHL-BFM 95 trial[34]

	NHL-BFM 95 trial	cancer predisposition syndromes and PIDs
No. of patients	505	96
Recruitment period	04/1996 - 03/2001	1984 - 2015
Gender		
male	386 (76%)	60 (62.5%)
female	119 (24%)	36 (37.5%)
Age (years) at dg.		
median	9.3	8.7
range	1.4 - 19.7	0.6 - 18.2
Histology		
Burkitt lymphoma	283 (56%)	18 (19%)
DLBCL	97 (19%)	57 (59%)
PMLBCL	15 (3%)	1 (1%)
others	31 (6%)	20 (21%)
mature B-cell leukemia	79 (16%)	/
Stage		
I	53 (10%)	6 (6%)
II	119 (24%)	20 (21%)
III	221 (44%)	43 (45%)
IV	33 (7%)	14 (15%)
mature B-cell leukemia	79 (16%)	/
not available	/	13 (14%)

B) Comparison of the 31 LBL patients with the NHL-BFM 95 trial[31]

	NHL-BFM 95 trial	cancer predisposition syndromes and PIDs
No. of patients	156	31
Recruitment period	04/1995 - 03/2001	1984 - 2015
Gender		
male	98 (63%)	24 (77%)
female	58 (37%)	7 (23%)
Age (years) at dg.		
<10	91 (58%)	18 (58%)
10 - 14	48 (31%)	6 (19%)
>14	17 (11%)	7 (23%)
Histology		
T-LBL	126 (81%)	28 (90%)
BCP-LBL	26 (17%)	3 (10%)
others	4 (3%)	/
Stage		
I	/	1 (3%)
II	/	1 (3%)
III	116 (74%)	23 (74%)
IV	40 (26%)	5 (16%)
not available	/	1 (3%)

C) Comparison of the 8 ALCL patients with the EICNHL ALCL99 trial[43]

	EICNHL ALCL99 trial	cancer predisposition syndromes and PIDs
No. of patients	352	8
Recruitment period	11/1999 - 12/2005	1984 - 2015
Gender		
male	211 (60%)	3
female	141 (40%)	5
Age (years) at dg.		
<3	19 (5%)	3
3 - 16	308 (88%)	4
>16	25 (7%)	1
Stage		
I	24 (7%)	1
II	66 (19%)	0
III	222 (63%)	5
IV	40 (11%)	1
not available	/	1

Abbreviations: NHL-BFM 95 trial, non-Hodgkin's lymphoma Berlin-Frankfurt-Münster 95 trial; EICNHL ALCL99 trial, European Intergroup for Childhood non-Hodgkin's lymphoma anaplastic large cell lymphoma 99 trial; PIDs, primary immunodeficiencies; No., number; dg., diagnosis; DLBCL, diffuse large B-cell lymphoma; PMLBCL, primary mediastinal large B-cell lymphoma; T-LBL, T-cell lymphoblastic lymphoma; BCP-LBL, B-cell precursor lymphoblastic lymphoma

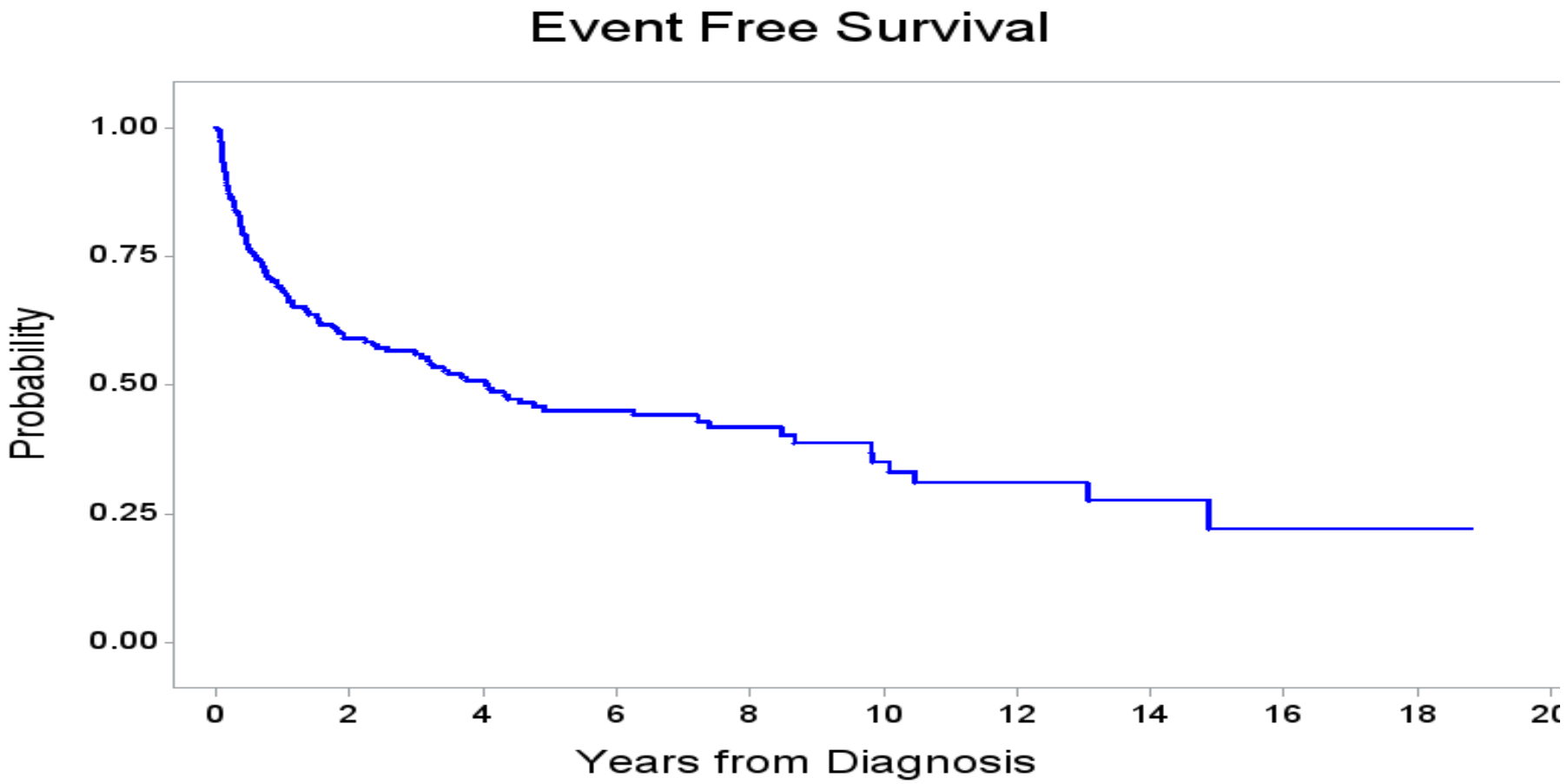
Supplemental Figures

Suppl. Figure 1. 5-year event-free and overall survival rates (1-A) and 5-year cumulative incidence rates of relapse and treatment-related death (1-B) of the 213 patients with pre-existing conditions and NHL.

Suppl. Figure 2. 10-years cumulative incidence of secondary malignancies of the 151 patients with cancer predisposition syndromes (n=124) and PIDs not further specified (n=27): overall (2-A) and according to the pre-existing conditions (2-B).

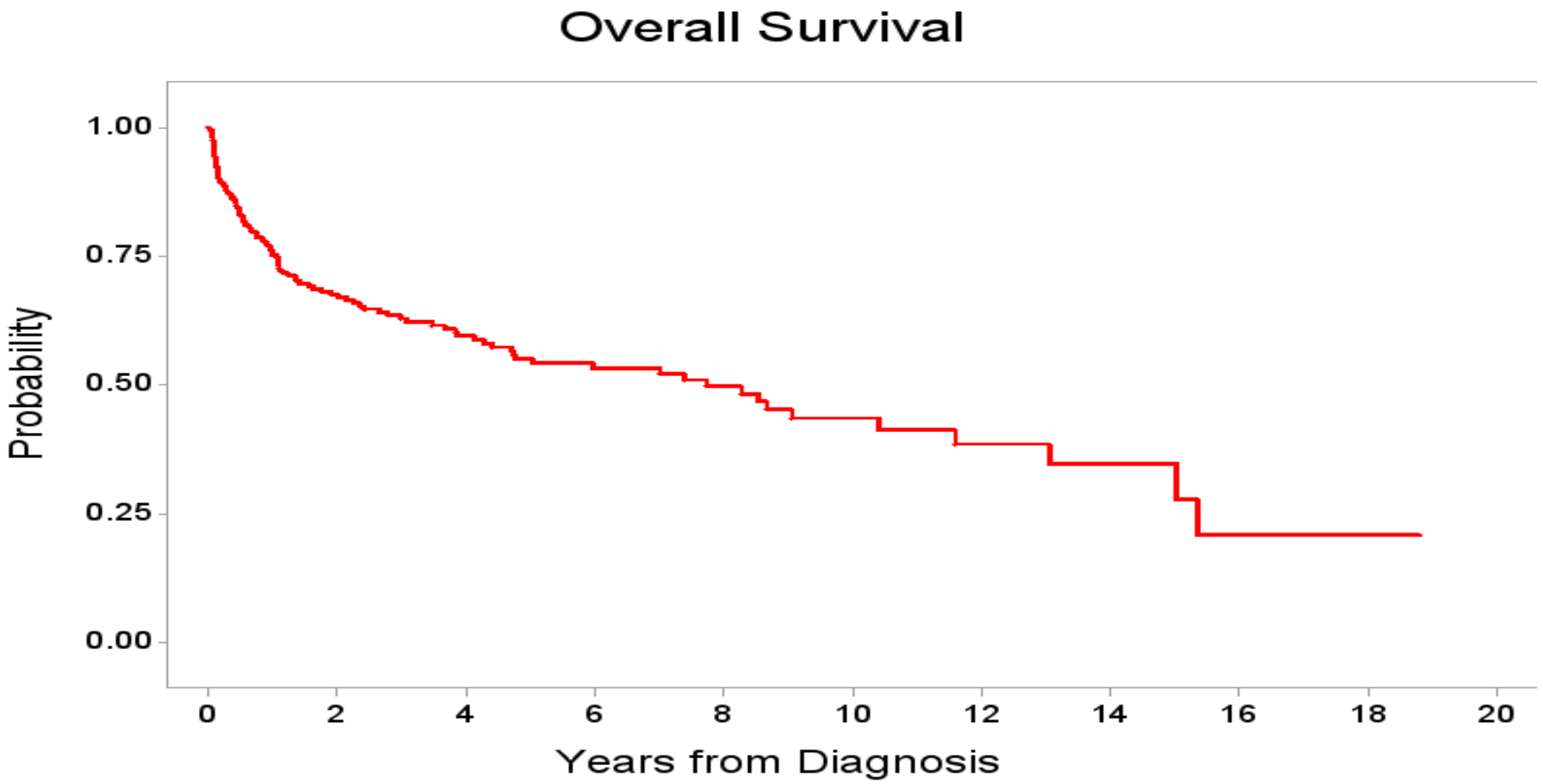
Suppl. Figure 3. 7-year overall survival rate of the 21 patients with a secondary malignancy.

Suppl. Figure 1-A



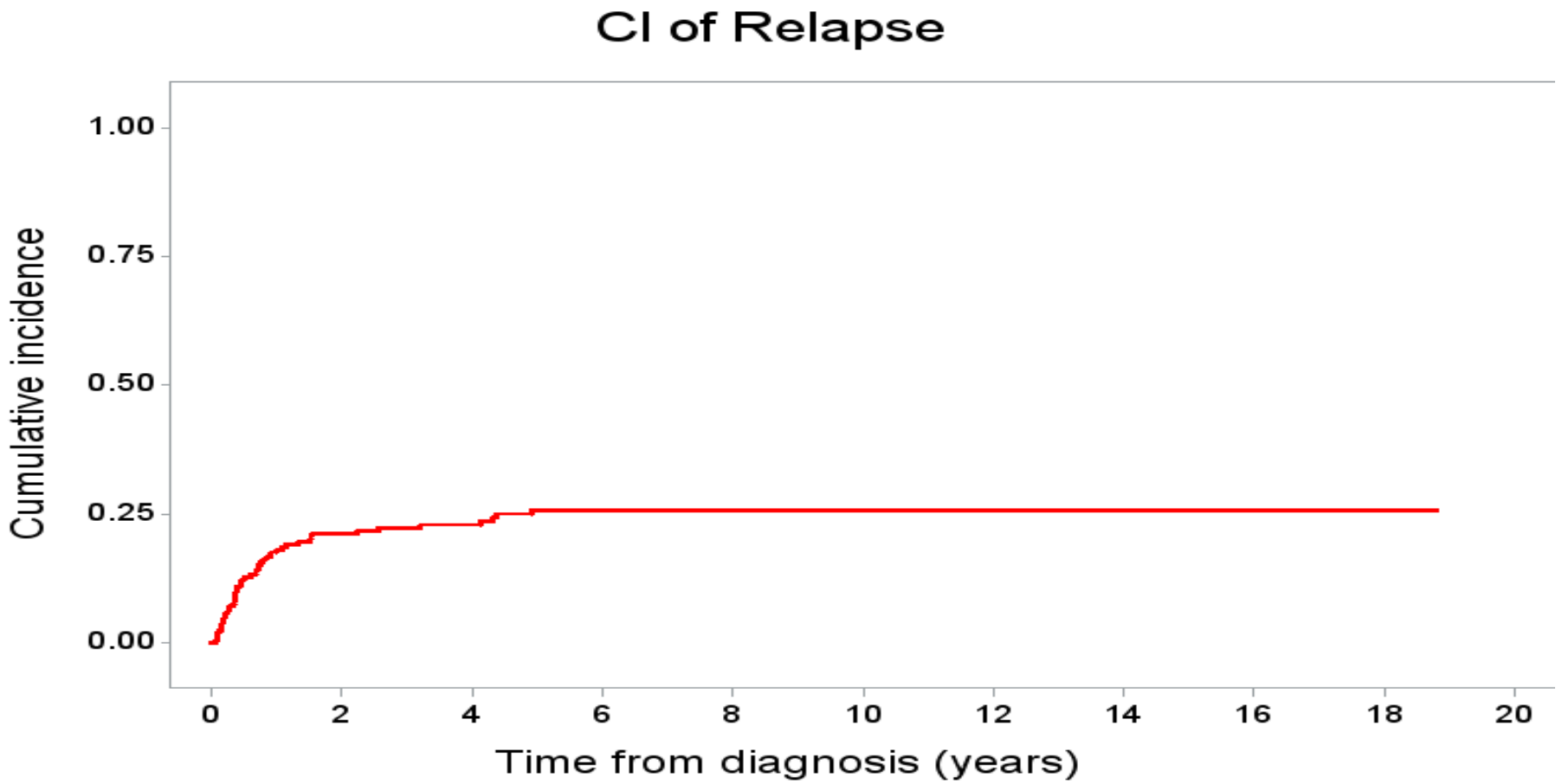
5-year probability of event-free survival (EFS): n=213, 117 events: 45%±4%

Suppl. Figure 1-B



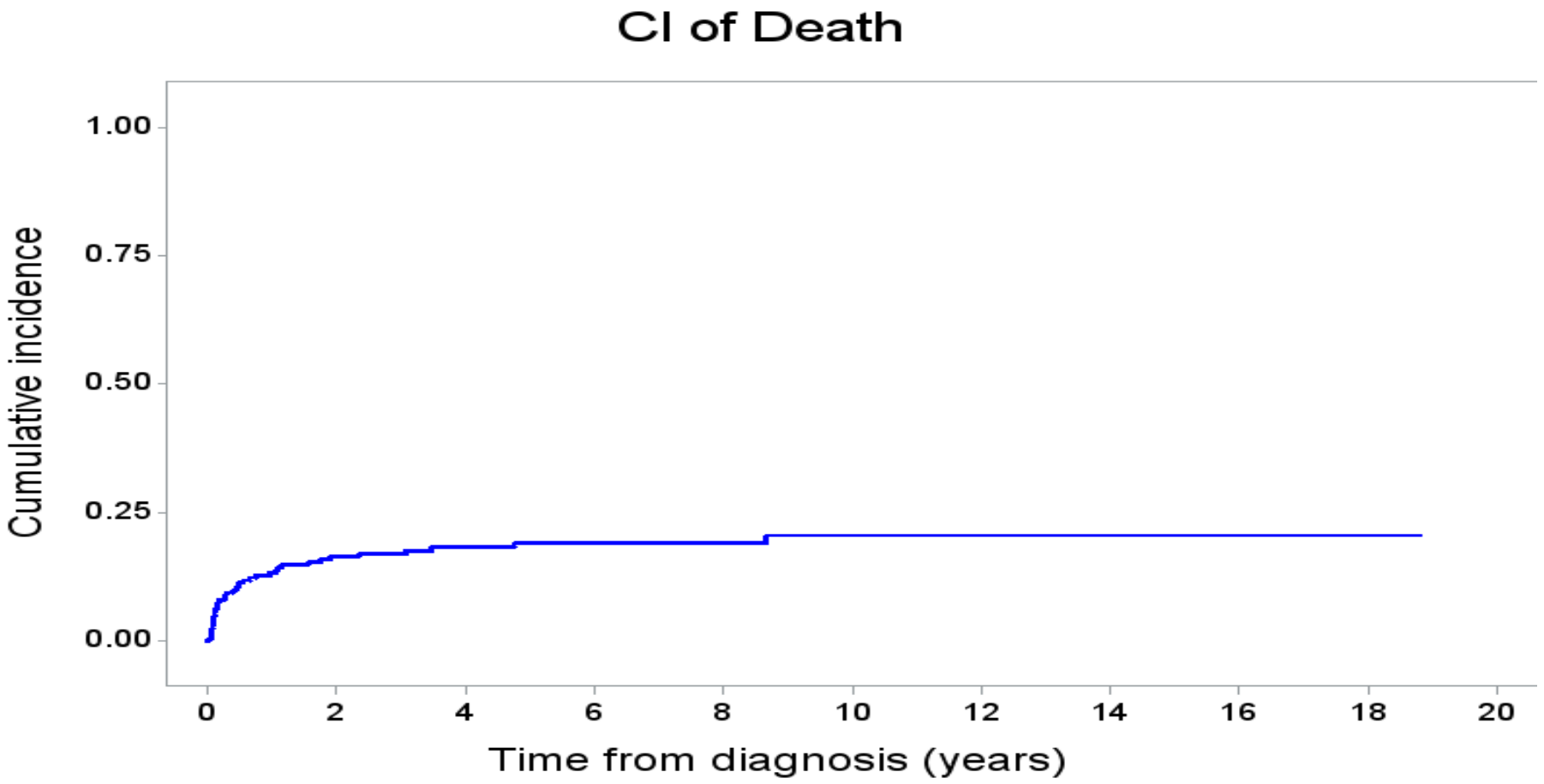
5-year probability of overall survival (OS): n=213, 100 events: 54%±4%

Suppl. Figure 1-C



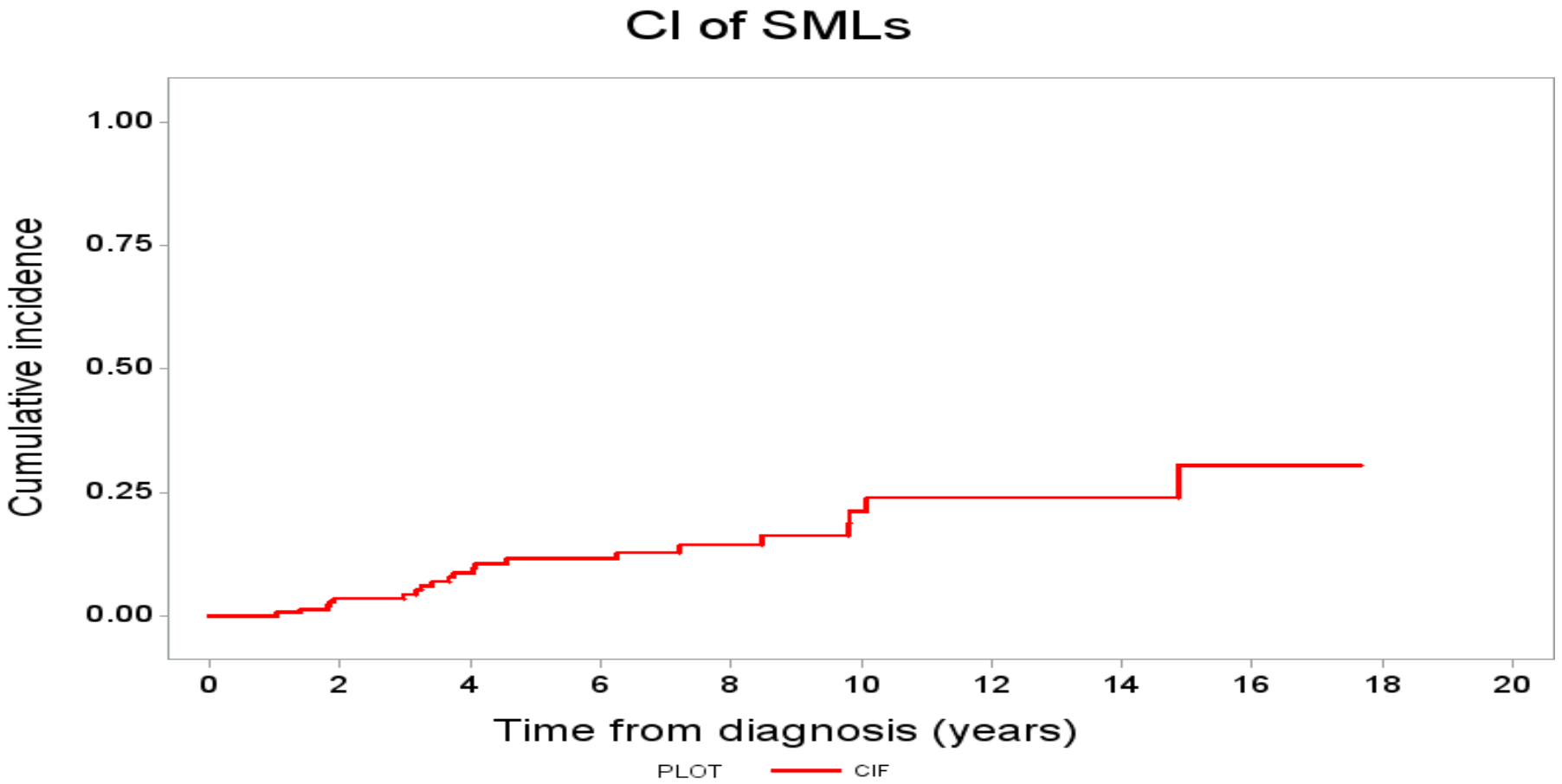
5-year cumulative incidence of relapse (CIR): n=213, 51 events: 26%±3%

Suppl. Figure 1-D



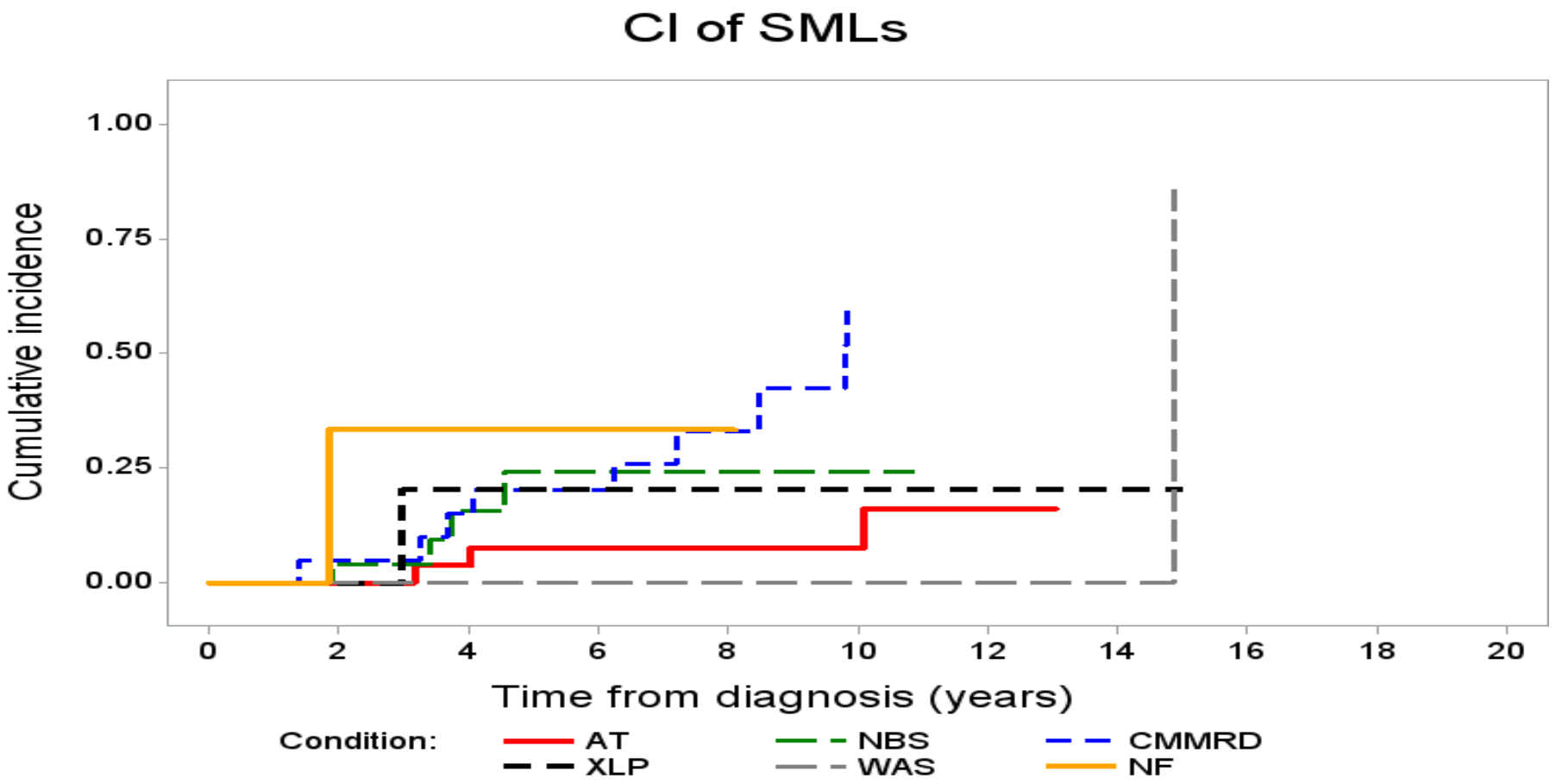
5-year cumulative incidence of death (CID) as a first event: n=213, 39 events: 19%3±%

Suppl. Figure 2-A



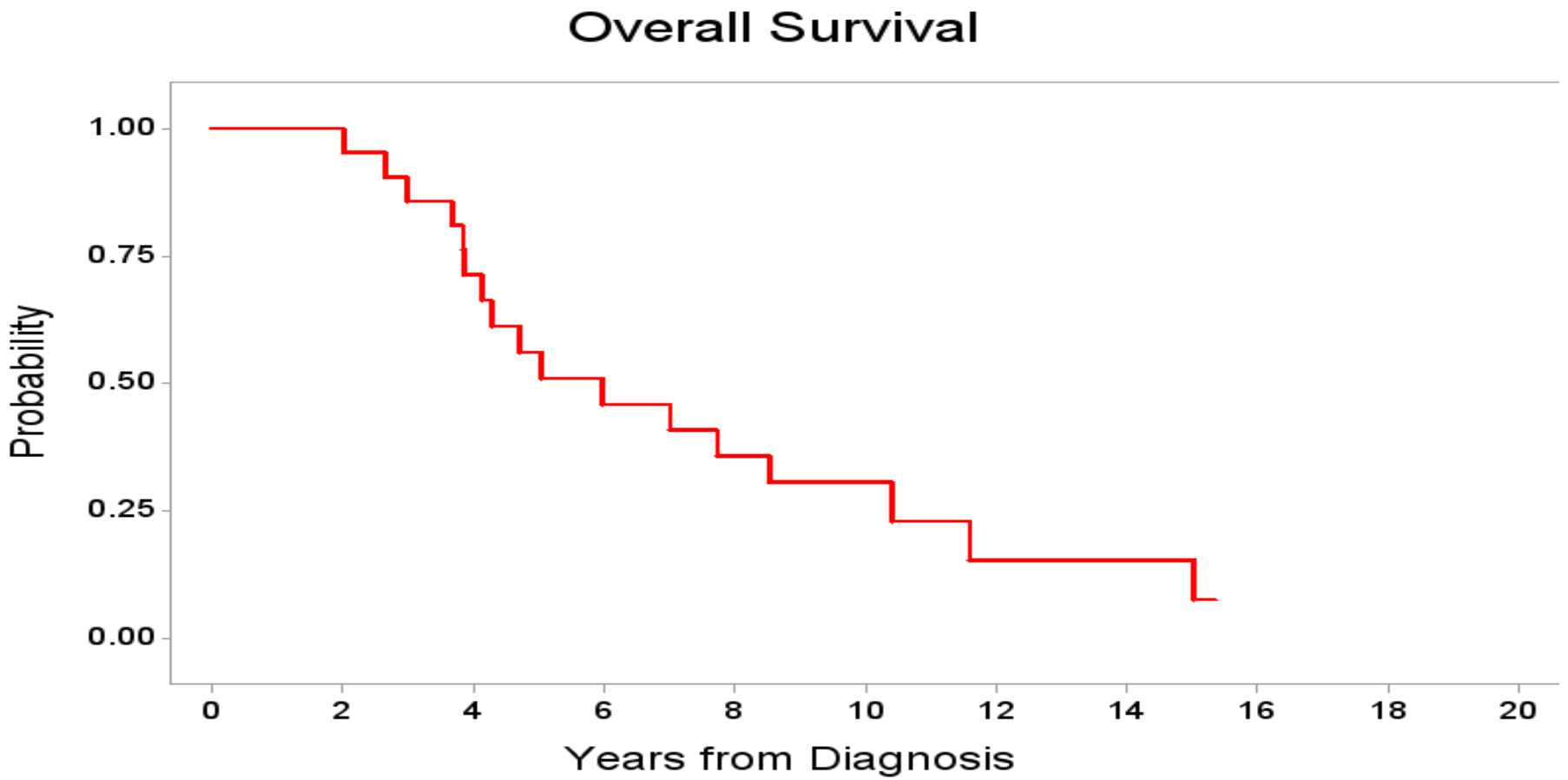
10-years cumulative incidence of secondary malignancies: n=151, 21 events: 24%±5%

Suppl. Figure 2-B



10-years cumulative incidence of SML in AT:	**n=32,**	**3 events:**	**16%±11%**	
10-years cumulative incidence of SML in NBS:	**n=26,**	**4 events:**	**24%±12%**	
10-years cumulative incidence of SML in CMMRD:	**n=21,**	**9 events:**	**61%±15%**	
10-years cumulative incidence of SML in XLP:	**n=11,**	**1 event:**	**20%±21%**	
10-years cumulative incidence of SML in WAS:	**n=7,**	**1 event:**	**0%**	
10-years cumulative incidence of SML in NF:	**n=3,**	**1 event:**	**33%±33%**	**P=0.075**

Suppl. Figure 3



7-year probability of overall survival: n=21, 18 events: 41%±11%