



Terapia di prima linea nel linfoma di Hodgkin a predominanza linfocitaria

The young side of
LYMPHOMA

gli under 40 a confronto

11-12 ottobre 2024
Auditorium Petruzzi
Pescara

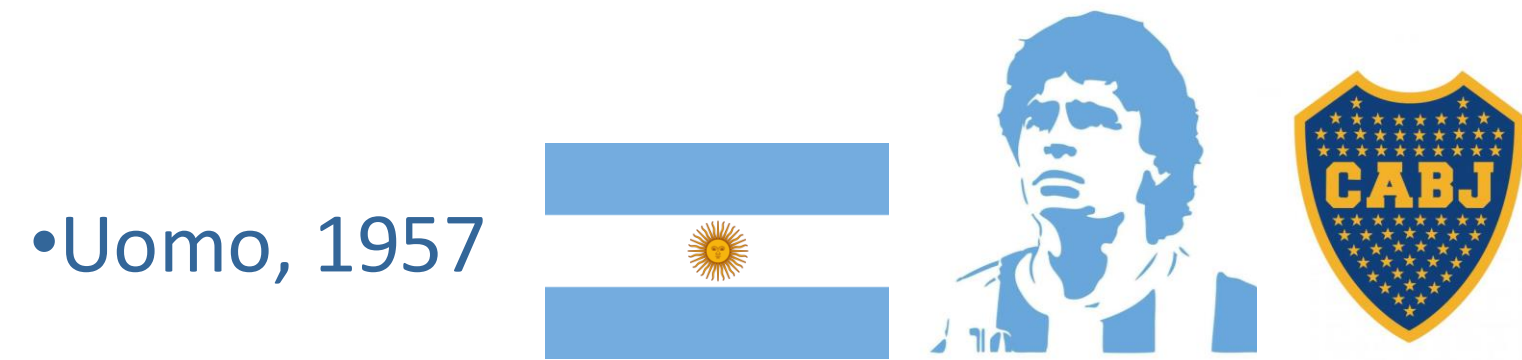
The Radioncologist point of view

Fabio Matrone

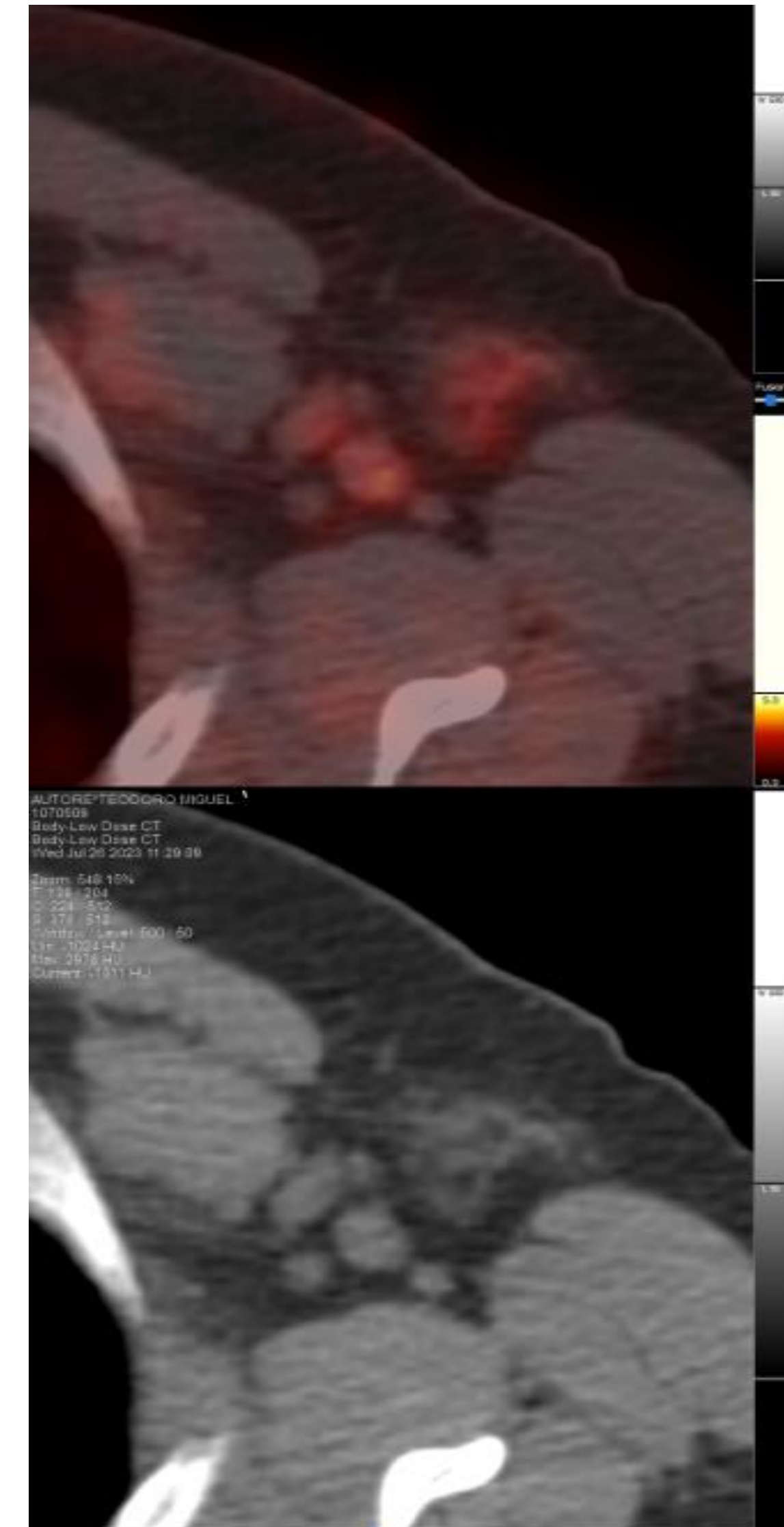
Dept. of Radiation Oncology
Centro di Riferimento Oncologico di Aviano CRO IRCCS
Aviano (PN), Italy

Disclosures of Fabio Matrone

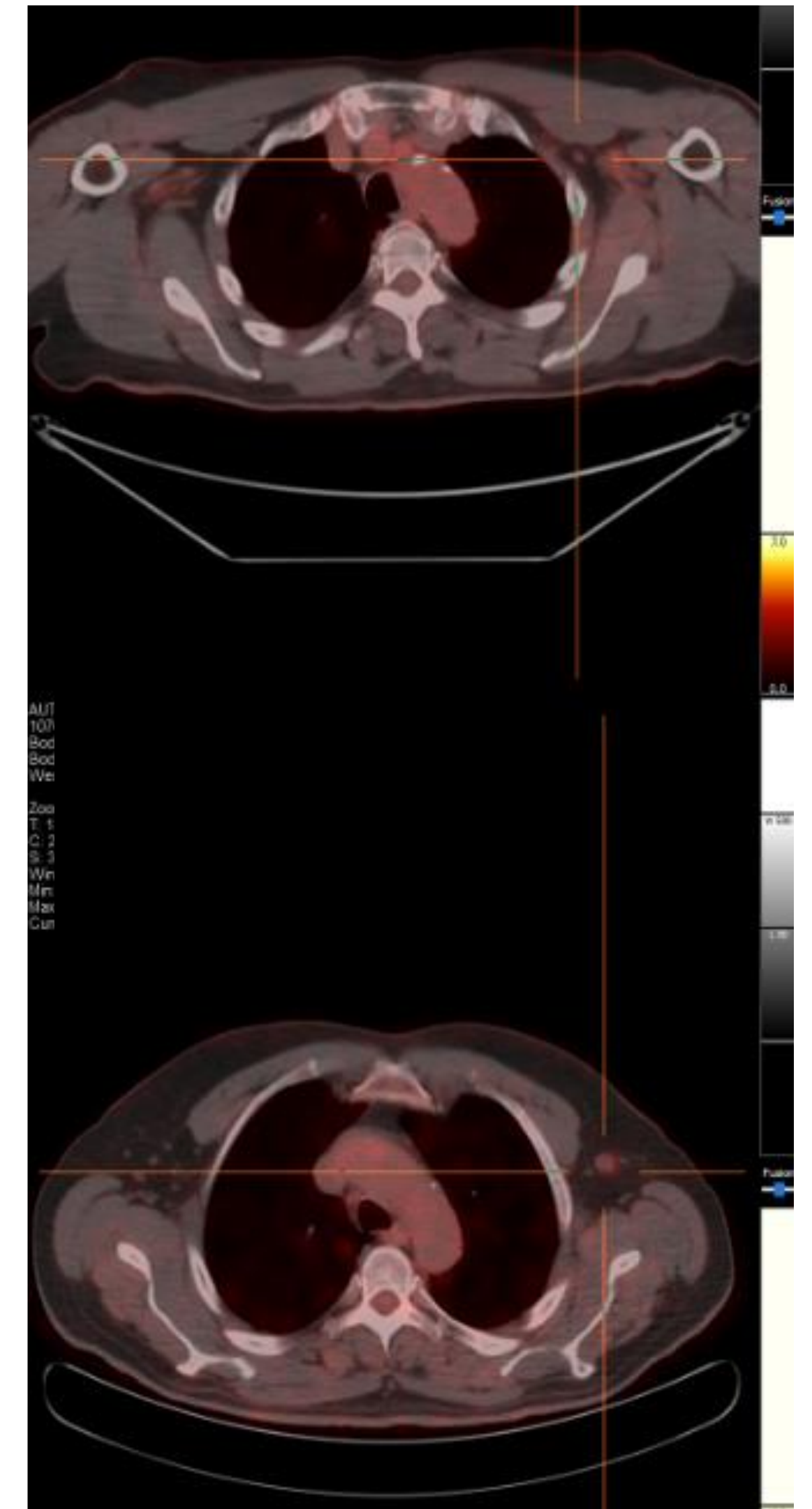
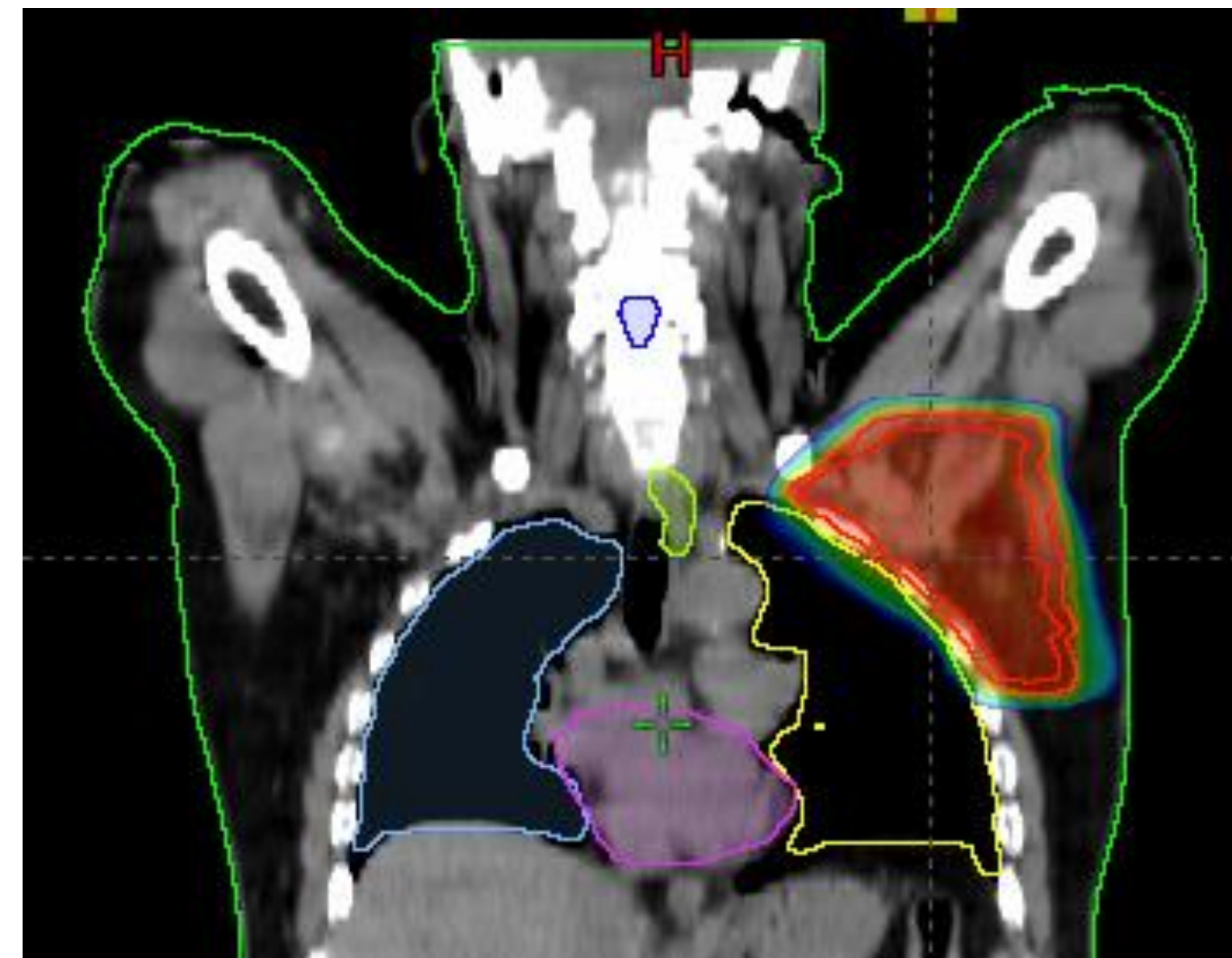
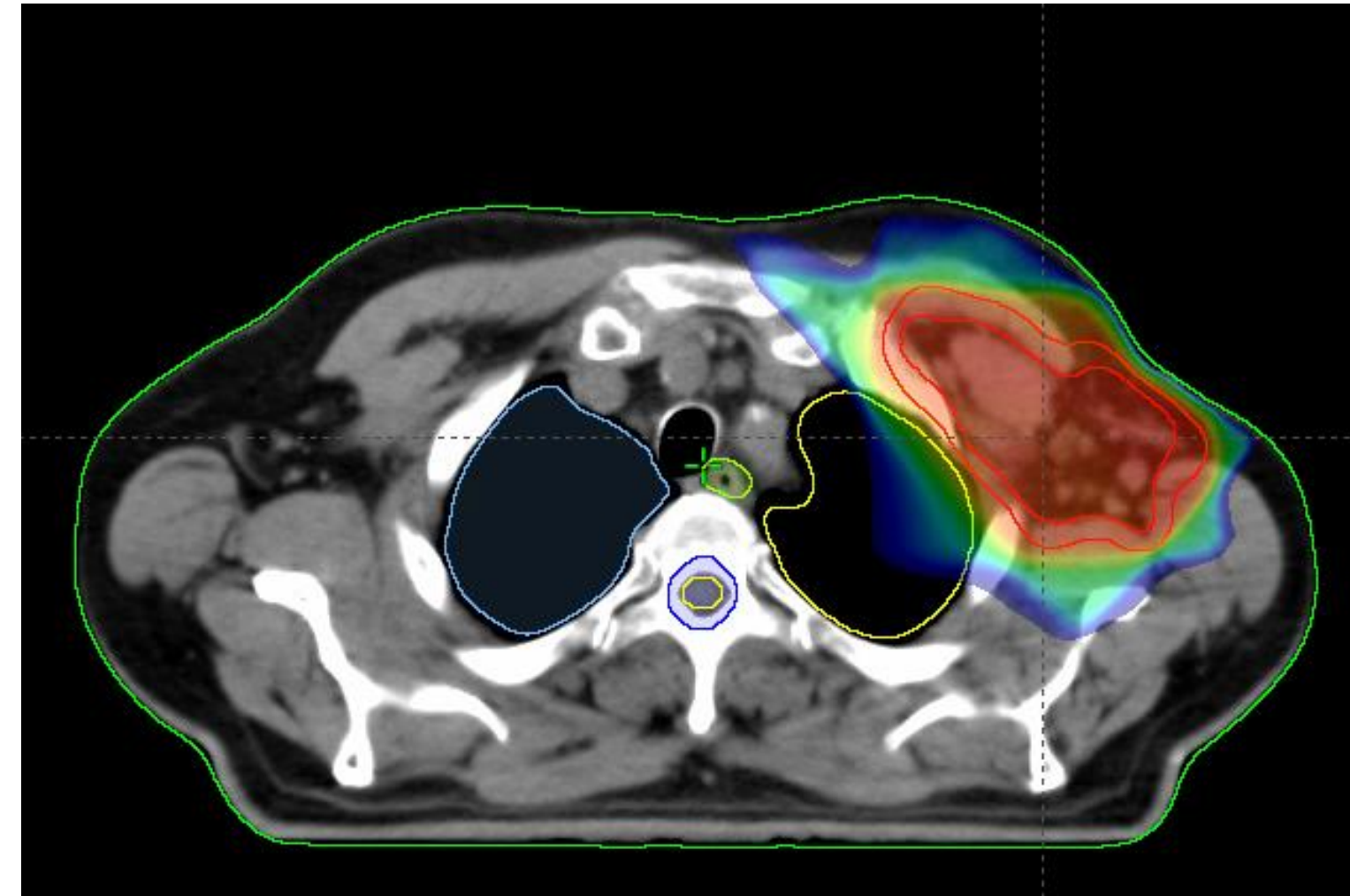
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
none							



- Uomo, 1957
- 2003: NPLHD inguine dx. RT esclusiva,TD 36 Gy in 18 frx.
- 2023: comparsa di adenopatia ascellare sx 4.3x2 cm. Benessere, non sint B
- 06.06.2023 **biopsia escissionale**: linfoma di Hodgkin, predominanza linfocitaria nodulare
- 12.07.2023 **BOM**: Midollo osseo cellulato (50% circa) con normale rappresentazione delle linee emopoietiche,indenne da evidente infiltrazione neoplastica
- 26.07.2023 **PET FDG**: moderato iperaccumulo del tracciante FDG incorispondenza di tre reperti linfonodali localizzati nel cavo ascellare di sinistra (SUVmax 2.8 vs SUVepatico 2.6)



- 16.10.2023-06.11.2023: **ISRT esclusiva su ascella sx**, TD 30 Gy in 15 frazioni
- 13.02.2024 **PET FDG**: completa scomparsa del modesto iperaccumulo del 18FDG, precedentemente segnalato alle formazioni linfonodali dell'ascella sinistra.
- 04.10.2024 **ultimo FU**: ned



Do you agree with the management of this clinical case?

a) Absolutely yes!

b) Yes...but...maybe...

c) Absolutely not! Damn radioncologists!

d)



For b) and c): what would you have done in this clinical case?

a) Asportation only

b) Rituximab alone

c) CT exclusive

d) CMT



National
Comprehensive
Cancer
Network®

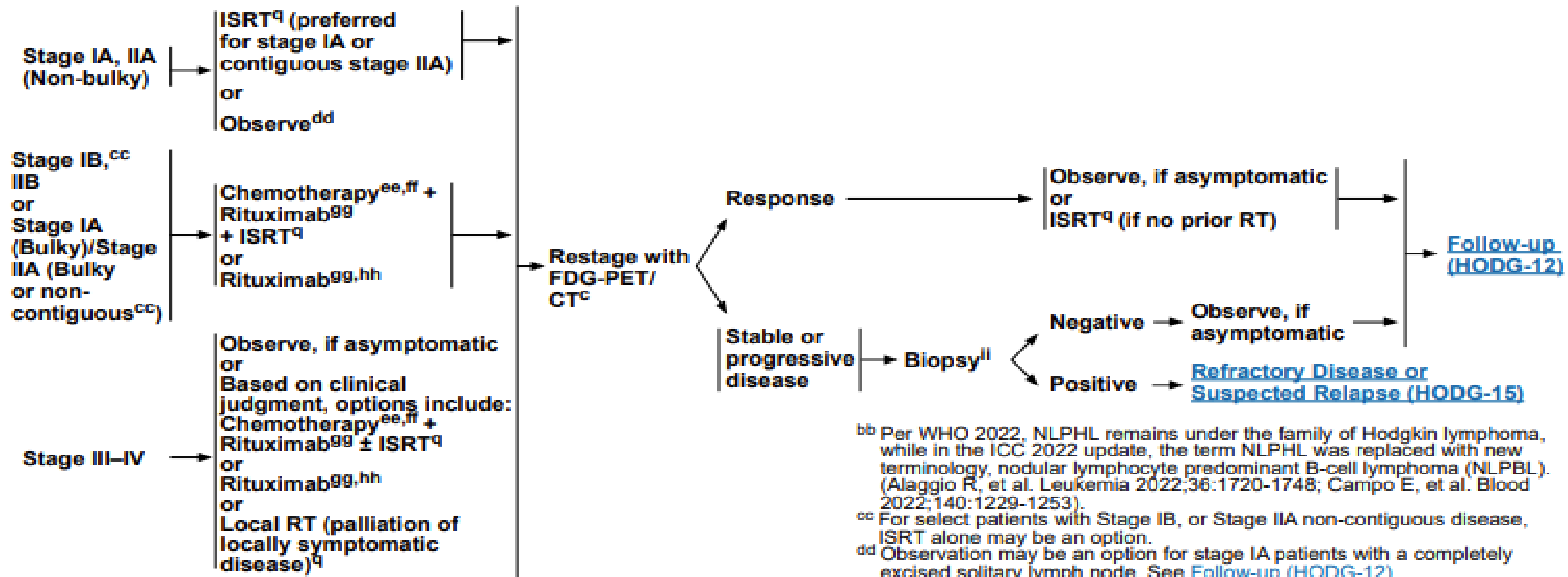
NCCN Guidelines Version 3.2024 Hodgkin Lymphoma (Age ≥18 years)

[NCCN Guidelines Index](#)
[Table of Contents](#)
[Discussion](#)

CLINICAL PRESENTATION:

Nodular Lymphocyte Predominant Hodgkin Lymphoma^{aa,bb}

PRIMARY TREATMENT



^c [Principles of FDG-PET/CT \(HODG-A\)](#).

^q [Principles of Radiation Therapy \(HODG-C\)](#).

^{aa} NLPBL has a different natural history and response to therapy than CHL, especially stages I–II. For that reason, separate guidelines are presented for NLPBL. Patients who present with bulky disease, subdiaphragmatic disease, or splenic involvement have a high risk for initial or later transformation to large cell lymphoma. Data suggest outcomes differ for typical immunohistochemical patterns (A/B) versus variant patterns (C/D/E/F). (Swerdlow SH, Campo E, Harris NL, et al. WHO classification of tumours of haematopoietic and lymphoid tissues. Lyon, France: IARC; 2017).

^{bb} Per WHO 2022, NLPBL remains under the family of Hodgkin lymphoma, while in the ICC 2022 update, the term NLPBL was replaced with new terminology, nodular lymphocyte predominant B-cell lymphoma (NLPBL). (Alaggio R, et al. Leukemia 2022;36:1720-1748; Campo E, et al. Blood 2022;140:1229-1253).

^{cc} For select patients with Stage IB, or Stage IIA non-contiguous disease, ISRT alone may be an option.

^{dd} Observation may be an option for stage IA patients with a completely excised solitary lymph node. See [Follow-up \(HODG-12\)](#).

^{ee} [Principles of Systemic Therapy \(HODG-B, 3 of 7\)](#).

^{ff} Generally, a brief course of chemotherapy (2–4 mo) would be given with RT.

^{gg} An FDA-approved biosimilar is an acceptable substitute for rituximab. Rituximab and hyaluronidase human injection for subcutaneous use may be substituted for rituximab after patients have received the first full dose of rituximab by intravenous infusion.

^{hh} Rituximab monotherapy can be used for palliation in select cases.

ⁱⁱ Biopsy is recommended for sites of progressive disease, especially subdiaphragmatic sites, to rule out transformation.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.



National
Comprehensive
Cancer
Network®

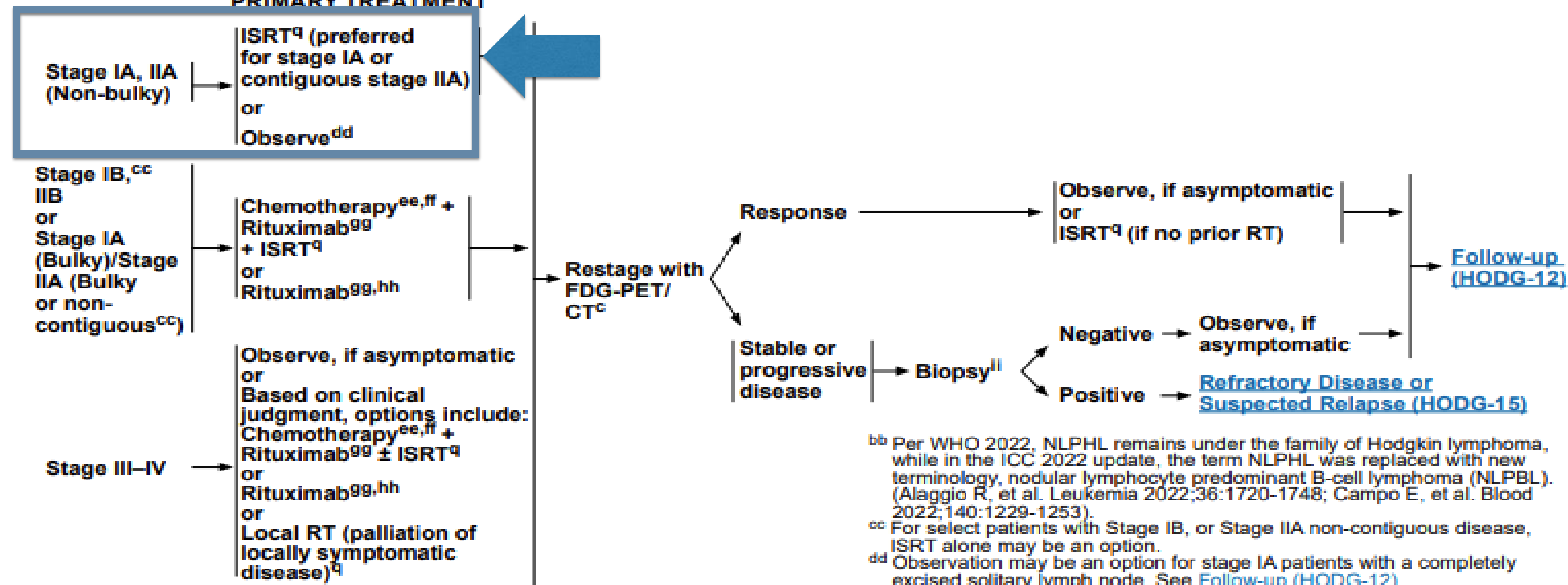
NCCN Guidelines Version 3.2024 Hodgkin Lymphoma (Age ≥18 years)

[NCCN Guidelines Index](#)
[Table of Contents](#)
[Discussion](#)

CLINICAL PRESENTATION:

Nodular Lymphocyte Predominant Hodgkin Lymphoma^{aa,bb}

PRIMARY TREATMENT



^c [Principles of FDG-PET/CT \(HODG-A\)](#).

^q [Principles of Radiation Therapy \(HODG-C\)](#).

^{aa} NLPBL has a different natural history and response to therapy than CHL, especially stages I–II. For that reason, separate guidelines are presented for NLPBL. Patients who present with bulky disease, subdiaphragmatic disease, or splenic involvement have a high risk for initial or later transformation to large cell lymphoma. Data suggest outcomes differ for typical immunohistochemical patterns (A/B) versus variant patterns (C/D/E/F). (Swerdlow SH, Campo E, Harris NL, et al. WHO classification of tumours of haematopoietic and lymphoid tissues. Lyon, France: IARC; 2017).

^{bb} Per WHO 2022, NLPBL remains under the family of Hodgkin lymphoma, while in the ICC 2022 update, the term NLPBL was replaced with new terminology, nodular lymphocyte predominant B-cell lymphoma (NLPBL). (Alaggio R, et al. Leukemia 2022;36:1720-1748; Campo E, et al. Blood 2022;140:1229-1253).

^{cc} For select patients with Stage IB, or Stage IIA non-contiguous disease, ISRT alone may be an option.

^{dd} Observation may be an option for stage IA patients with a completely excised solitary lymph node. See [Follow-up \(HODG-12\)](#).

^{ee} [Principles of Systemic Therapy \(HODG-B, 3 of 7\)](#).

^{ff} Generally, a brief course of chemotherapy (2–4 mo) would be given with RT.

^{gg} An FDA-approved biosimilar is an acceptable substitute for rituximab. Rituximab and hyaluronidase human injection for subcutaneous use may be substituted for rituximab after patients have received the first full dose of rituximab by intravenous infusion.

^{hh} Rituximab monotherapy can be used for palliation in select cases.

ⁱⁱ Biopsy is recommended for sites of progressive disease, especially subdiaphragmatic sites, to rule out transformation.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Outcome of RT in early stage

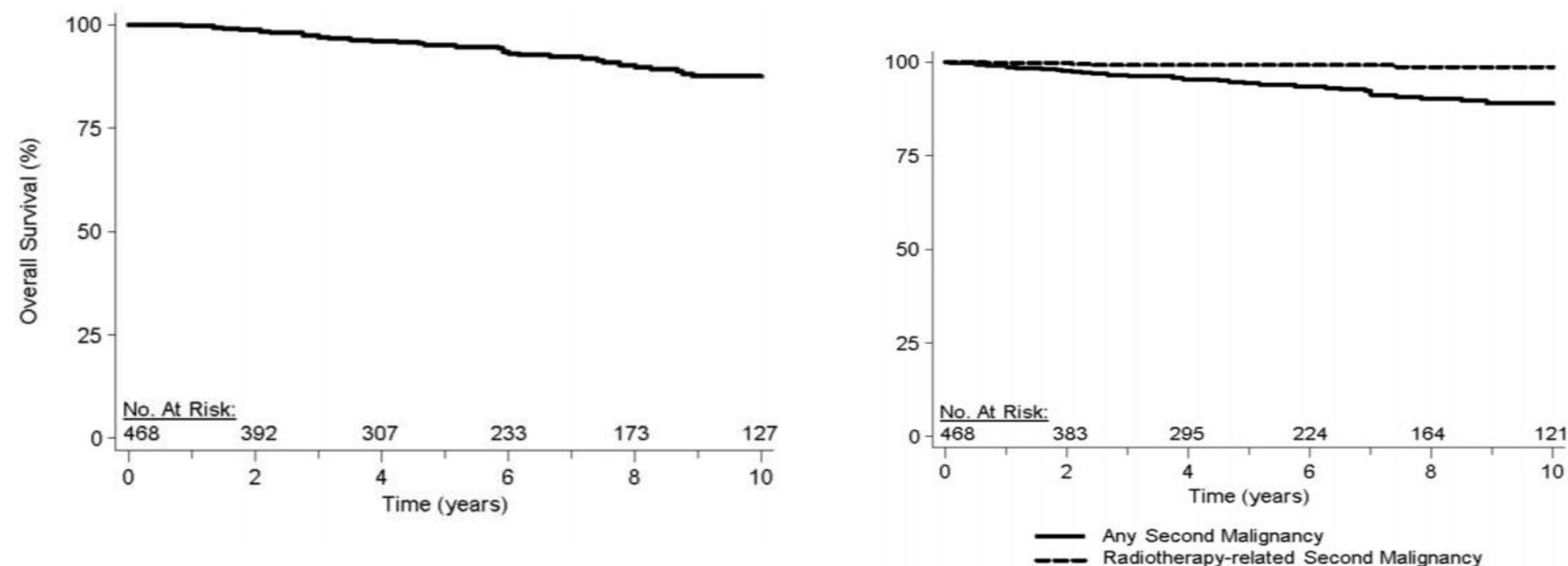
Second malignancies of RT in early stage

Long-Term Outcomes in Patients with Early Stage Nodular Lymphocyte-Predominant Hodgkin's Lymphoma Treated with Radiotherapy



Abhishek A. Solanki¹, Melissa Horoschak LeMieux¹, Brian C.-H. Chiu², Usama Mahmood³, Yasmin Hasan¹, Matthew Koshy^{1,4}

¹ Department of Radiation and Cellular Oncology, University of Chicago, Chicago, Illinois, United States of America, ² Department of Health Studies, University of Chicago, Chicago, Illinois, United States of America, ³ Division of Radiation Oncology, University of Texas M. D. Anderson Cancer Center, Houston, Texas, United States of America, ⁴ Department of Radiation Oncology, University of Illinois Hospital, Chicago, Illinois, United States of America



469 patients, median age 37y.

68% stage I disease, 7% had B-symptoms.

Median follow-up was 6 years.

10y CSS and OS were 98% and 88%, respectively.

10y freedom from SM and freedom from RT-related SM were 89% and 99%, respectively.

Long-Term Course of Patients With Stage IA Nodular Lymphocyte-Predominant Hodgkin Lymphoma: A Report From the German Hodgkin Study Group

Dennis A. Eichenauer, Annette Plütschow, Michael Fuchs, Bastian von Tresckow, Boris Böll, Karolin Behringer, Volker Diehl, Hans Theodor Eich, Peter Borchmann, and Andreas Engert

JOURNAL OF CLINICAL ONCOLOGY

2015

Table 1. Characteristics of Patients With Stage IA NPLHL

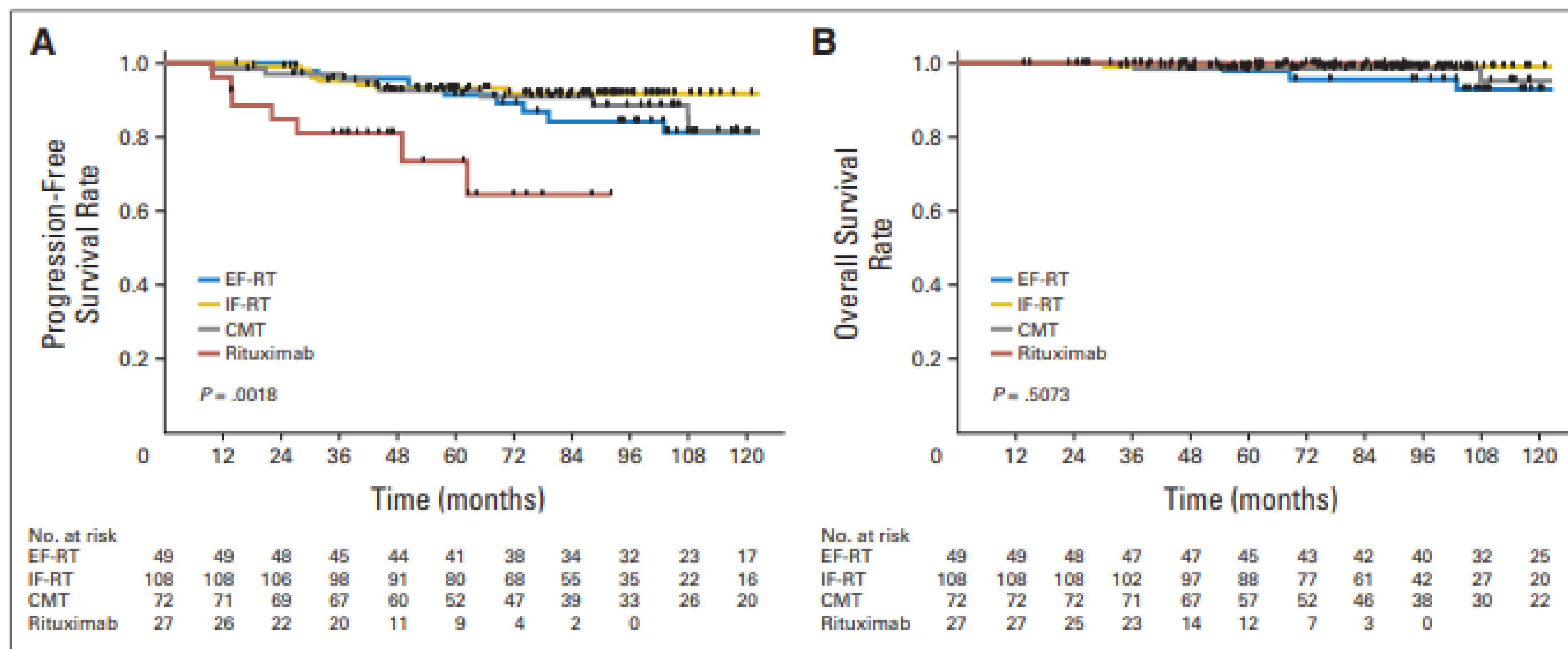
Characteristic	CMT (n = 72) No. of Patients (%)	EF-RT (n = 49) No. of Patients (%)	IF-RT (n = 108) No. of Patients (%)	Rituximab (n = 27) No. of Patients (%)	Total (n = 256) No. of Patients (%)
Age at diagnosis, years					
Median	36	38	39	39	39
Range	16-73	17-70	16-75	19-68	16-75
Mean	40.5	39.7	41.5	40.7	40.8
SD	13.9	14.7	14.5	14.9	14.3
16-20	3 (4)	2 (4)	11 (10)	2 (7)	18 (7)
21-40	39 (54)	24 (49)	47 (44)	12 (44)	122 (48)
41-60	22 (31)	18 (37)	35 (32)	8 (30)	83 (32)
61-75	8 (11)	5 (10)	15 (14)	5 (19)	33 (13)
Sex					
Female	22 (31)	11 (22)	21 (19)	8 (30)	62 (24)
Male	50 (69)	38 (78)	87 (81)	19 (70)	194 (76)
WHO performance status					
Missing	14	48	3	0	65
0	56 (97)	1 (100)	97 (92)	27 (100)	181 (95)
1	2 (3)	0 (0)	8 (8)	0 (0)	10 (5)
Localization of disease					
Supradiaphragmatic	56 (78)	36 (73)	84 (78)	21 (78)	197 (77)
Infradiaphragmatic	16 (22)	13 (27)	24 (22)	6 (22)	59 (23)
Treatment outcome					
Missing	0	0	1	0	1
Complete remission	33 (46)	43 (88)	7 (7)	15 (56)	98 (38)
Unconfirmed complete remission	39 (54)	6 (12)	100 (93)	12 (44)	157 (62)
Observation time, months					
Median	95	110	87	49	91
Range	17-239	15-222	18-174	14-92	14-239

Long-Term Course of Patients With Stage IA Nodular Lymphocyte-Predominant Hodgkin Lymphoma: A Report From the German Hodgkin Study Group

JOURNAL OF CLINICAL ONCOLOGY

2015

Dennis A. Eichenauer, Annette Plütschow, Michael Fuchs, Bastian von Tresckow, Boris Böll, Karolin Behringer, Volker Diehl, Hans Theodor Eich, Peter Borchmann, and Andreas Engert



8y-PFS rate for the whole patient group excluding patients treated with rituximab was 88.9%

The whole patient group had an estimated 8y-OS rate of 98.2%

Long-Term Course of Patients With Stage IA Nodular Lymphocyte-Predominant Hodgkin Lymphoma: A Report From the German Hodgkin Study Group

Dennis A. Eichenauer, Annette Plütschow, Michael Fuchs, Bastian von Tresckow, Boris Böll, Karolin Behringer, Volker Diehl, Hans Theodor Eich, Peter Borchmann, and Andreas Engert

JOURNAL OF CLINICAL ONCOLOGY

2015

Table 3. Four-Year PFS of Patients Treated for Stage IA NLPHL

Variable	No. of Patients	No. of Events (%)	4-Year PFS Rate (%; 95% CI)	Log-Rank <i>P</i>	Cox Univariate Hazard Ratio (95% CI)
Total	256	45 (18)	92.3 (89.0 to 95.6)	.0018	—
Treatment modality					
EF-RT	49	15 (31)	95.8 (90.2 to 100.0)		1.56 (0.68 to 3.58)
IF-RT	108	11 (10)	93.2 (88.4 to 98.1)		—
CMT	72	12 (17)	92.9 (86.8 to 98.9)		1.00 (0.43 to 2.35)
Rituximab	27	7 (26)	81.0 (66.0 to 96.0)	4.99 (1.88 to 13.21)	

Abbreviations: CMT, combined-modality treatment; EF-RT, extended-field radiotherapy; IF-RT, involved-field radiotherapy; NLPHL, nodular lymphocyte-predominant Hodgkin lymphoma; PFS, progression-free survival.

Table 2. Eight-Year PFS of Patients Treated for Stage IA NLPHL

Variable	No. of Patients	No. of Events (%)	8-Year PFS Rate (%; 95% CI)	Log-Rank <i>P</i>	Cox Univariate Hazard Ratio (95% CI)
Total	229	38 (17)	88.9 (84.5 to 93.4)	.4305	—
Treatment modality					
EF-RT	49	15 (31)	84.3 (73.6 to 95.0)		—
IF-RT	108	11 (10)	91.9 (86.5 to 97.3)		0.64 (0.28 to 1.47)
CMT	72	12 (17)	88.5 (80.3 to 96.8)		0.64 (0.30 to 1.39)

Abbreviations: CMT, combined-modality treatment; EF-RT, extended-field radiotherapy; IF-RT, involved-field radiotherapy; NLPHL, nodular lymphocyte-predominant Hodgkin lymphoma; PFS, progression-free survival.

Long-Term Course of Patients With Stage IA Nodular Lymphocyte-Predominant Hodgkin Lymphoma: A Report From the German Hodgkin Study Group

Dennis A. Eichenauer, Annette Plütschow, Michael Fuchs, Bastian von Tresckow, Boris Böll, Karolin Behringer, Volker Diehl, Hans Theodor Eich, Peter Borchmann, and Andreas Engert

8/72 (11.1%) treated with CMT, 3/49 (6.1%) treated with EF-RT, 4/108 (3.7%) treated with IF-RT, and 2/27 (7.4%) treated with rituximab developed a second malignancy

Table 4. Characteristics of Second Malignancies After Treatment for Stage IA NLP HL

Secondary Malignancy	Chronic Myeloid Leukemia (n = 1)	Non-Hodgkin Lymphoma (N = 7)	Solid Tumor (N = 9)	Total (n = 17)
Time to secondary malignancy, years				
Median	16.6	6.2	5.7	6.2
Range	16.6-16.6	1.0-15.8	2.0-16.4	1.0-16.6
Secondary solid tumors according to localization, No.				
Missing			0	
Colorectal cancer			2	
Lung cancer			2	
Breast cancer			1	
Stomach cancer			1	
Bladder cancer			1	
Salivary gland cancer			1	
Unknown localization			1	
Secondary non-Hodgkin lymphoma according to histology, No.				
Missing		0		
Diffuse large B-cell lymphoma		3		
T-cell-rich B-cell lymphoma		2		
Follicular lymphoma		1		
Marginal zone lymphoma		1		

Abbreviation: NLP HL, nodular lymphocyte-predominant Hodgkin lymphoma.

NLP HL was the cause of death in only 1 pt

2 pts died for second malignancies

The young side of LYMPHOMA

gli under 40 a confronto

Stage I-II nodular lymphocyte-predominant Hodgkin lymphoma: a multi-institutional study of adult patients by ILROG

Michael S. Binkley,^{1,2} M. Shahzad Rauf,³ Sarah A. Milgrom,⁴ Chelsea C. Pinnix,⁴ Richard Tsang,⁵ Michael Dickinson,⁶ Andrea K. Ng,^{7,8} Kenneth B. Roberts,⁹ Sarah Gao,⁹ Alex Balogh,¹⁰ Umberto Ricardi,¹¹ Mario Levis,¹¹ Carla Casulo,¹² Michael Stolten,¹³ Lena Specht,¹⁴ John P. Plastaras,¹⁵ Christopher Wright,¹⁵ Christopher R. Kelsey,¹⁶ Jessica L. Brady,¹⁷ N. George Mikhael,¹⁷ Bradford S. Hoppe,^{18,19} Stephanie A. Terezakis,²⁰ Marco Picardi,²¹ Roberta Della Pepa,²¹ Youlia Kirova,²² Saad Akhtar,³ Irfan Maghfoor,³ Julie L. Koenig,^{1,2} Christopher Jackson,⁹ Erin Song,¹⁶ Shuchi Sehgal,²⁰ Ranjana H. Advani,²³ Yasodha Natkunam,²⁴ Louis S. Constine,¹³ Hans T. Eich,²⁵ Andrew Wirth,²⁶ and Richard T. Hoppe^{1,2}



559 eligible patients treated at 18 participating institutions from 1995 through 2018

Parameter	Total (n = 559)	RT (n = 257)	CMT (n = 184)*	CT (n = 47)†	Observation (n = 37)	Rituximab and RT (n = 19)	Rituximab alone (n = 15)	P‡
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Age at diagnosis								
Median (years)	39	42	36	36	43	33	57	.01
IQR	27-52	29-53	25-49	25-48	22-59	21-42	31-72	
Range	16-90	17-90	16-75	17-76	16-81	18-65	16-82	
Sex								
Male	404 (72.3)	187 (72.8)	140 (76.1)	30 (63.8)	24 (64.9)	15 (78.9)	8 (53.3)	.21
Female	155 (27.7)	70 (27.2)	44 (23.9)	17 (36.2)	13 (35.1)	4 (21.1)	7 (46.7)	
ECOG PS								
0-1	486 (86.9)	205 (79.8)	173 (94.0)	44 (93.6)	34 (91.9)	18 (94.7)	12 (80.0)	.002
>1	8 (6.0)	2 (0.8)	2 (1.1)	0 (0.0)	2 (5.4)	0 (0.0)	2 (13.3)	
Unreported	65 (11.6)	50 (19.4)	9 (4.9)	3 (6.4)	1 (2.7)	1 (5.3)	1 (6.7)	
Stage								
Stage I	307 (54.9)	175 (68.1)	77 (41.8)	11 (23.4)	32 (86.5)	9 (47.4)	3 (20.0)	<.0001
Extranodal	12 (2.1)	3 (1.2)	4 (2.2)	2 (4.3)	3 (8.1)	0 (0.0)	0 (0.0)	
B symptoms	13 (2.3)	6 (2.3)	2 (1.1)	4 (8.5)	1 (2.7)	0 (0.0)	0 (0.0)	
Stage II	252 (45.1)	82 (31.9)	107 (58.2)	36 (76.6)	5 (13.5)	10 (52.6)	12 (80.0)	
Extranodal	20 (3.6)	9 (3.5)	8 (4.3)	1 (2.1)	1 (2.7)	0 (0.0)	1 (6.7)	
B symptoms	25 (4.5)	8 (3.1)	11 (6.0)	4 (8.5)	0 (0.0)	1 (5.3)	1 (6.7)	
Spleen	4 (0.7)	2 (0.8)	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Disease location								
Above diaphragm	439 (78.5)	206 (80.2)	151 (82.1)	31 (66.0)	25 (67.6)	15 (78.9)	11 (73.3)	.17
Below diaphragm	116 (20.8)	50 (19.5)	32 (17.4)	14 (29.8)	12 (32.4)	4 (21.1)	4 (26.7)	
Unknown	4 (0.7)	1 (0.4)	1 (0.5)	2 (4.3)	0 (0.0)	0 (0.0)	0 (0.0)	
Immunoarchitecture								
A/B Typical	166 (29.7)	86 (33.5)	59 (32.1)	10 (21.3)	6 (16.2)	3 (15.8)	2 (13.3)	.01
C/D/E/F Variant	43 (7.7)	14 (5.4)	17 (9.2)	3 (6.4)	3 (8.1)	1 (5.3)	5 (33.3)	
Unknown	350 (62.6)	157 (61.1)	108 (58.7)	34 (72.3)	28 (75.7)	15 (78.9)	8 (53.3)	
Follow up, years								
Median	5.5	5.4	5.9	5.0	4.1	3.8	6.3	.02
IQR	3.1-10.1	3.0-10.1	3.8-10.8	2.8-8.6	1.9-5.8	2.4-10.9	3.1-7.4	
GHSg clinical criteria								
Favorable	473 (84.6)	234 (91.1)	152 (82.6)	31 (66.0)	35 (94.6)	13 (68.4)	8 (53.3)	<.0001
Unfavorable	77 (13.8)	21 (8.2)	27 (14.7)	14 (29.8)	2 (5.4)	6 (31.6)	7 (46.7)	
Unknown	9 (1.6)	2 (0.8)	5 (2.7)	2 (4.3)	0 (0.0)	0 (0.0)	0 (0.0)	
Treatment dates (range)	1995-2018	1995-2018	1995-2018	1996-2017	2003-2018	2002-2017	2000-2018	

Pescara, 11-12 ottobre 2024

The young side of LYMPHOMA

gli under 40 a confronto

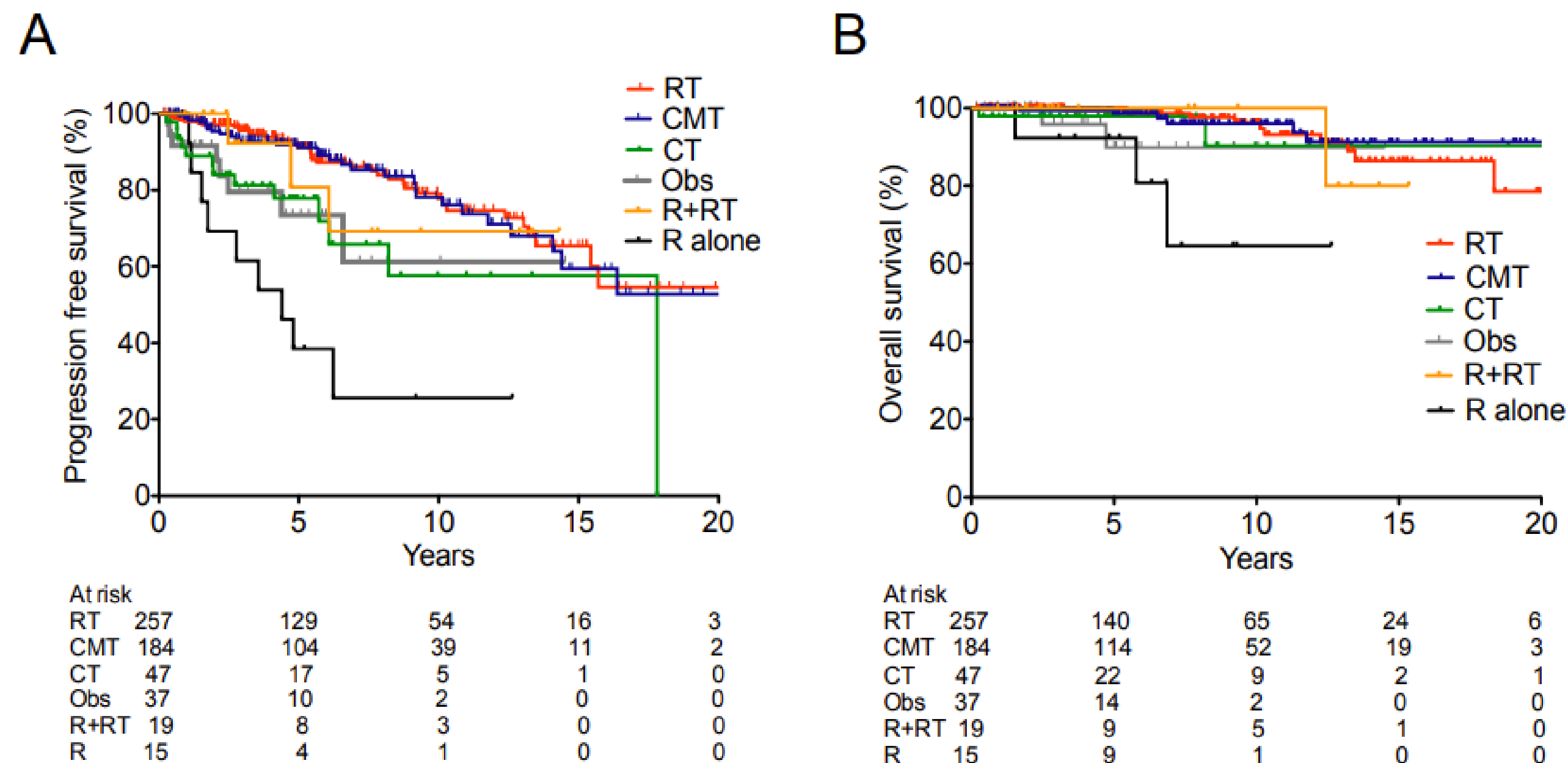
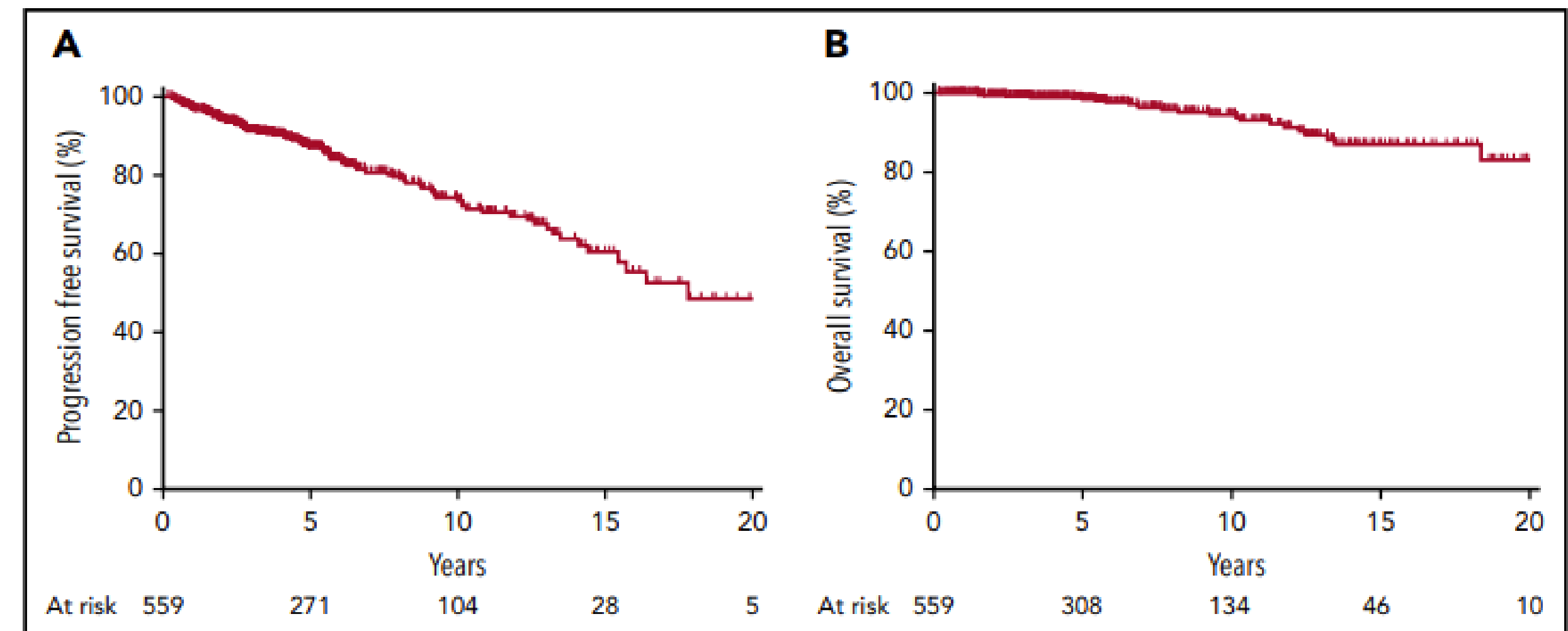
Stage I-II nodular lymphocyte-predominant Hodgkin lymphoma: a multi-institutional study of adult patients by ILROG

Michael S. Binkley,^{1,2} M. Shahzad Rauf,³ Sarah A. Milgrom,⁴ Chelsea C. Pinnix,⁴ Richard Tsang,⁵ Michael Dickinson,⁶ Andrea K. Ng,^{7,8} Kenneth B. Roberts,⁹ Sarah Gao,⁹ Alex Balogh,¹⁰ Umberto Ricardi,¹¹ Mario Levis,¹¹ Carla Casulo,¹² Michael Stolten,¹³ Lena Specht,¹⁴ John P. Plastaras,¹⁵ Christopher Wright,¹⁵ Christopher R. Kelsey,¹⁶ Jessica L. Brady,¹⁷ N. George Mikhael,¹⁷ Bradford S. Hoppe,^{18,19} Stephanie A. Terezakis,²⁰ Marco Picardi,²¹ Roberta Della Pepa,²¹ Youlia Kirova,²² Saad Akhtar,³ Irfan Maghfoor,³ Julie L. Koenig,^{1,2} Christopher Jackson,⁹ Erin Song,¹⁶ Shuchi Sehgal,²⁰ Ranjana H. Advani,²³ Yasodha Natkunam,²⁴ Louis S. Constine,¹³ Hans T. Eich,²⁵ Andrew Wirth,²⁶ and Richard T. Hoppe^{1,2}

The 5y PFS and OS in the entire cohort were 87.1% and 98.3%

The 5y PFS were 91.1% with RT, 90.5% with CMT, 77.8% with CT, 73.5% with observation, 80.8% with rituximab and RT, and 38.5% with rituximab alone.

5y OS were 99.4% with RT, 99.4% with CMT, 97.9% with CT, 89.8% with observation, 100% with rituximab and RT, and 92.3% with rituximab alone

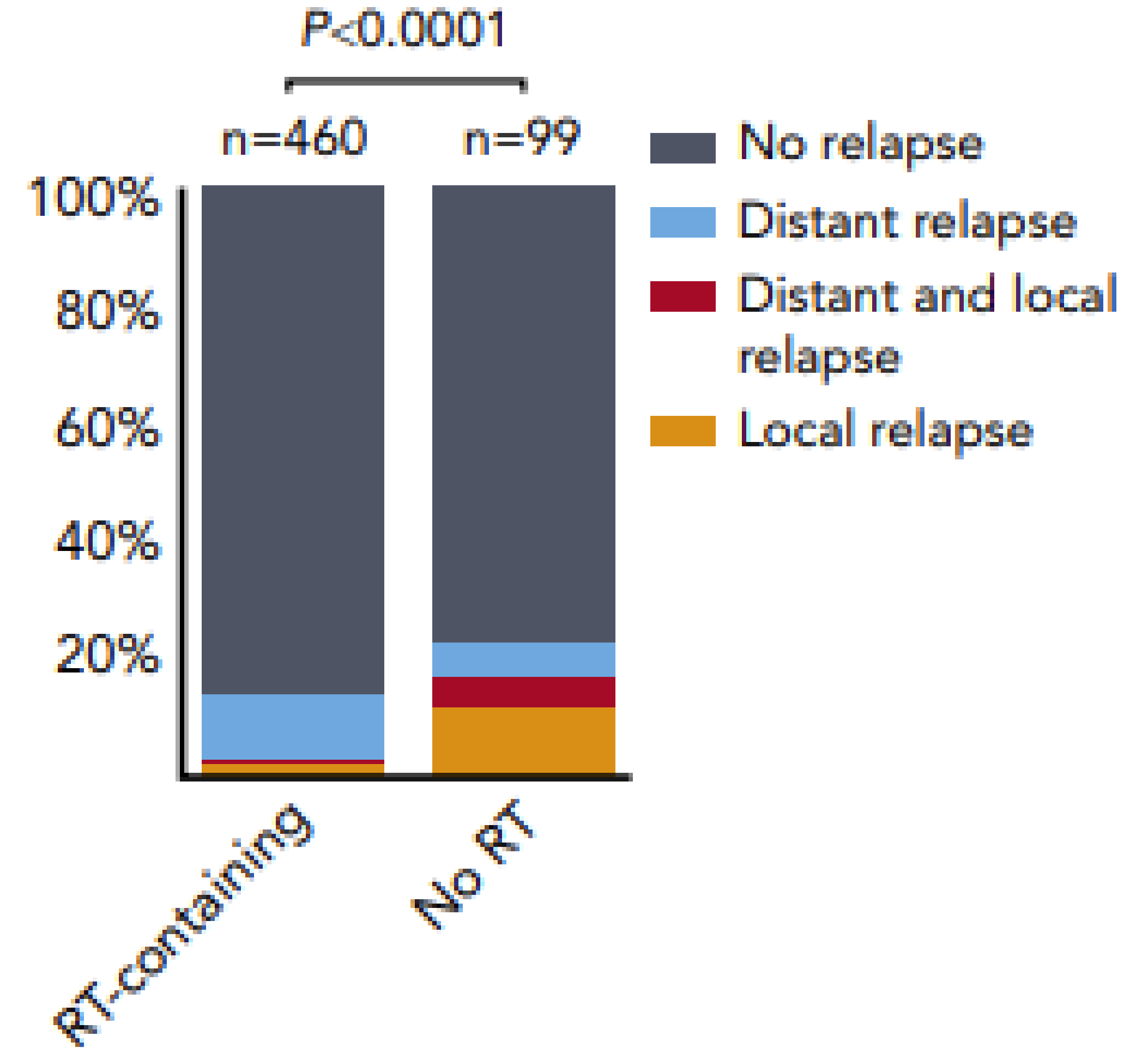


Stage I-II nodular lymphocyte-predominant Hodgkin lymphoma: a multi-institutional study of adult patients by ILROG

Michael S. Binkley,^{1,2} M. Shahzad Rauf,³ Sarah A. Milgrom,⁴ Chelsea C. Pinnix,⁴ Richard Tsang,⁵ Michael Dickinson,⁶ Andrea K. Ng,^{7,8} Kenneth B. Roberts,⁹ Sarah Gao,⁹ Alex Balogh,¹⁰ Umberto Ricardi,¹¹ Mario Levis,¹¹ Carla Casulo,¹² Michael Stolten,¹³ Lena Specht,¹⁴ John P. Plastaras,¹⁵ Christopher Wright,¹⁵ Christopher R. Kelsey,¹⁶ Jessica L. Brady,¹⁷ N. George Mikhael,¹⁷ Bradford S. Hoppe,^{18,19} Stephanie A. Terezakis,²⁰ Marco Picardi,²¹ Roberta Della Pepa,²¹ Youlia Kirova,²² Saad Akhtar,³ Irfan Maghfoor,³ Julie L. Koenig,^{1,2} Christopher Jackson,⁹ Erin Song,¹⁶ Shuchi Sehgal,²⁰ Ranjana H. Advani,²³ Yasodha Natkunam,²⁴ Louis S. Constine,¹³ Hans T. Eich,²⁵ Andrew Wirth,²⁶ and Richard T. Hoppe^{1,2}



There was a significantly higher rate of local-only progression in patients who did not receive RT as part of primary management



Stage I-II nodular lymphocyte-predominant Hodgkin lymphoma: a multi-institutional study of adult patients by ILROG

Michael S. Binkley,^{1,2} M. Shahzad Rauf,³ Sarah A. Milgrom,⁴ Chelsea C. Pinnix,⁴ Richard Tsang,⁵ Michael Dickinson,⁶ Andrea K. Ng,^{7,8} Kenneth B. Roberts,⁹ Sarah Gao,⁹ Alex Balogh,¹⁰ Umberto Ricardi,¹¹ Mario Levis,¹¹ Carla Casulo,¹² Michael Stolten,¹³ Lena Specht,¹⁴ John P. Plataras,¹⁵ Christopher Wright,¹⁵ Christopher R. Kelsey,¹⁶ Jessica L. Brady,¹⁷ N. George Mikhael,¹⁷ Bradford S. Hoppe,^{18,19} Stephanie A. Terezakis,²⁰ Marco Picardi,²¹ Roberta Della Pepa,²¹ Youlia Kirova,²² Saad Akhtar,³ Irfan Maghfoor,³ Julie L. Koenig,^{1,2} Christopher Jackson,⁹ Erin Song,¹⁶ Shuchi Sehgal,²⁰ Ranjana H. Advani,²³ Yasodha Natkunam,²⁴ Louis S. Constine,¹³ Hans T. Eich,²⁵ Andrew Wirth,²⁶ and Richard T. Hoppe^{1,2}

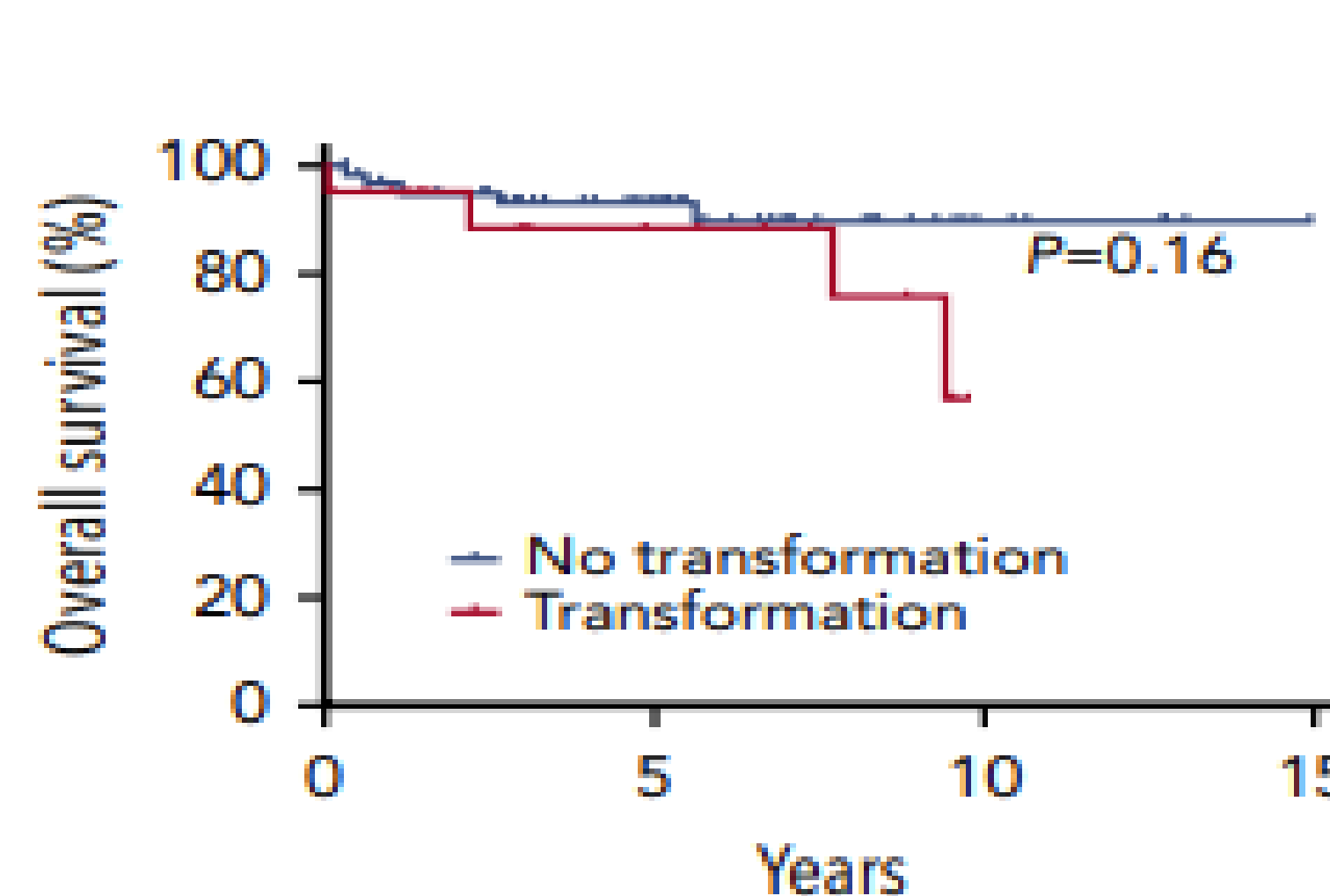


There were 24 reported deaths with 7 confirmed lymphoma-specific deaths.

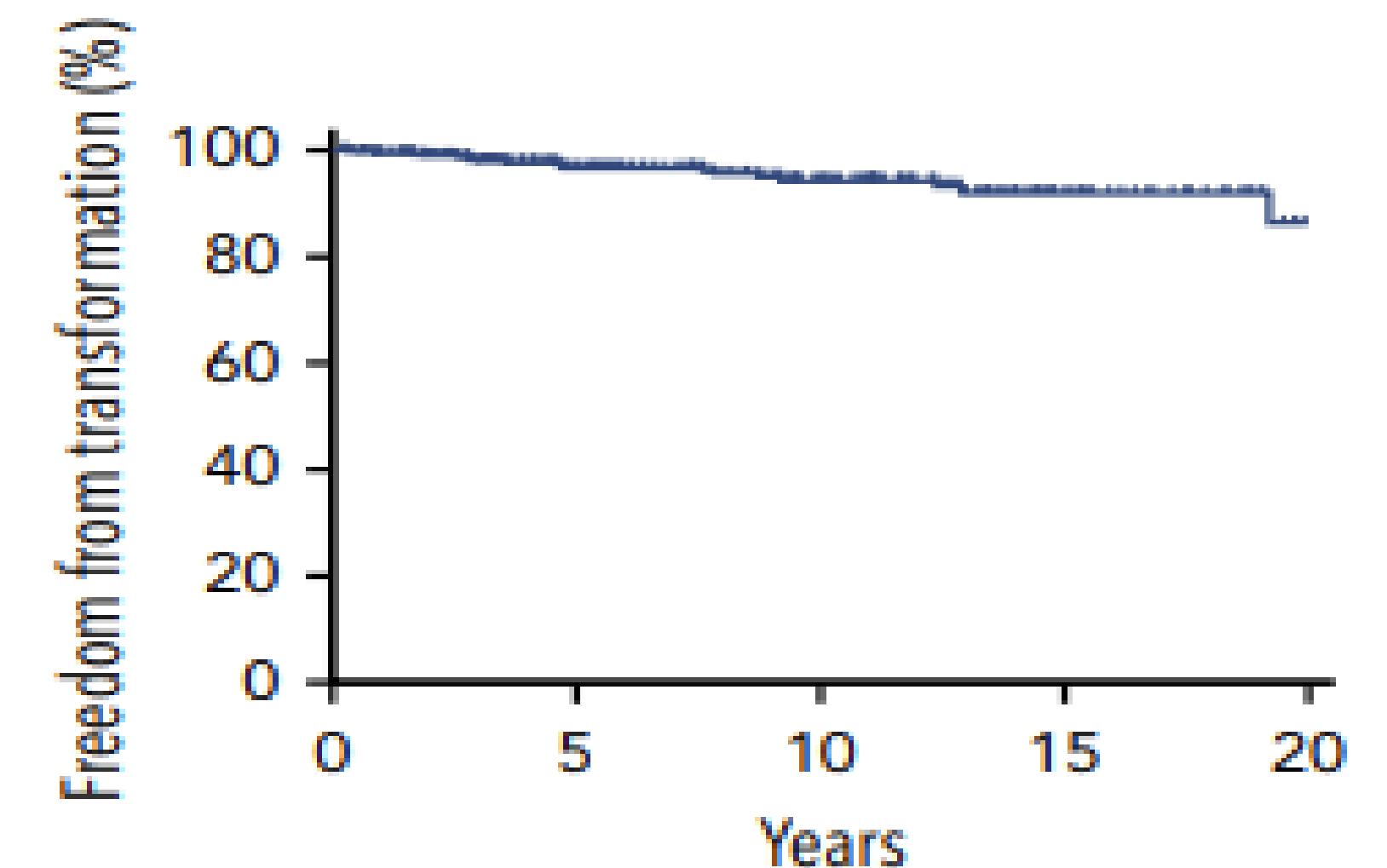
Nonlymphoma-specific deaths: 2 CV (1 CMT [ABVD + BEACOPP + med RT] and 1 med IFRT), 1 bleomycin lung toxicity, 1 gastrointestinal bleed, 1 secondary to thrombocytopenia, 1 AML, 1 pancreatic cancer, 1 pneumonia, and 5 noncancer deaths not specified. 4 deaths were of unknown cause.

21 pts (3.8%) underwent transformation at a median of 3.6 years. 5y-FFT was 96.7%

4 lymphoma-specific deaths occurred in patients who experienced transformation



At risk	0	5	10	15
No trans.	65	35	7	1
Trans.	21	10	0	0



At risk	0	5	10	15	20
	559	296	127	43	10



National
Comprehensive
Cancer
Network®

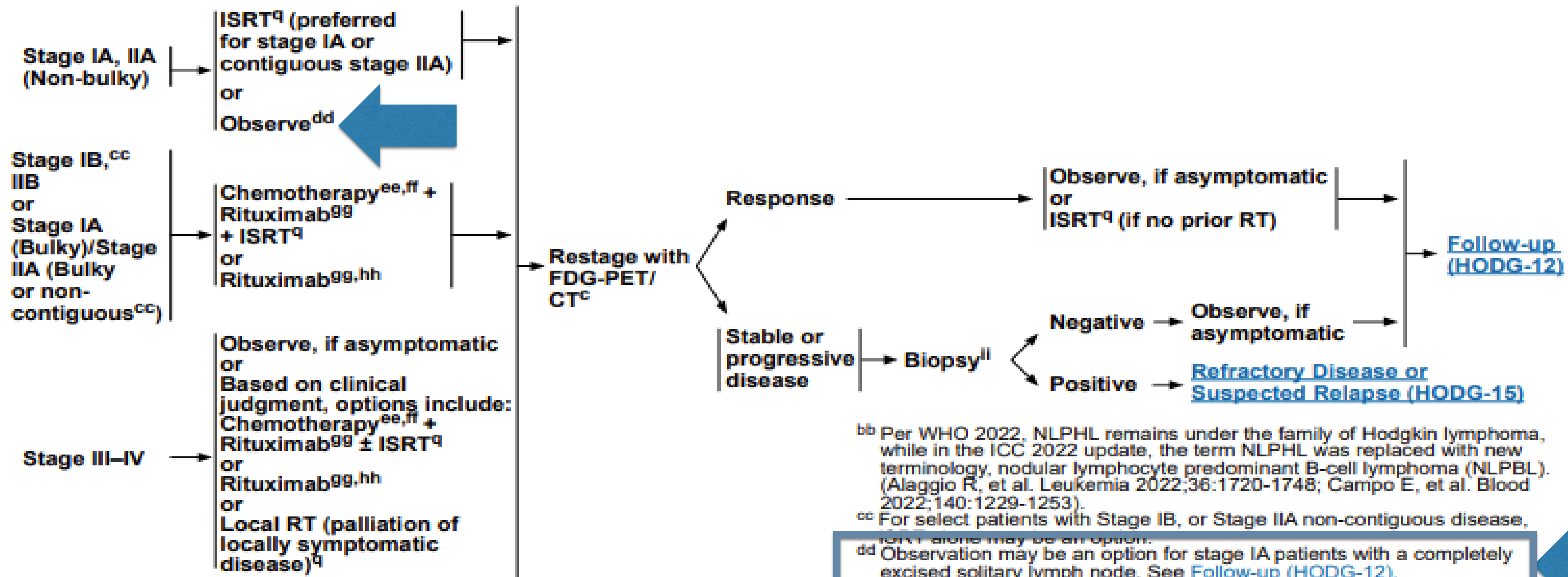
NCCN Guidelines Version 3.2024 Hodgkin Lymphoma (Age ≥18 years)

[NCCN Guidelines Index](#)
[Table of Contents](#)
[Discussion](#)

CLINICAL PRESENTATION:

Nodular Lymphocyte Predominant Hodgkin Lymphoma^{aa,bb}

PRIMARY TREATMENT



^c [Principles of FDG-PET/CT \(HODG-A\)](#).

^q [Principles of Radiation Therapy \(HODG-C\)](#).

^{aa} NLPBL has a different natural history and response to therapy than CHL, especially stages I–II. For that reason, separate guidelines are presented for NLPBL. Patients who present with bulky disease, subdiaphragmatic disease, or splenic involvement have a high risk for initial or later transformation to large cell lymphoma. Data suggest outcomes differ for typical immunohistochemical patterns (A/B) versus variant patterns (C/D/E/F). (Swerdlow SH, Campo E, Harris NL, et al. WHO classification of tumours of haematopoietic and lymphoid tissues. Lyon, France: IARC; 2017).

^{bb} Per WHO 2022, NLPBL remains under the family of Hodgkin lymphoma, while in the ICC 2022 update, the term NLPBL was replaced with new terminology, nodular lymphocyte predominant B-cell lymphoma (NLPBL). (Alaggio R, et al. Leukemia 2022;36:1720-1748; Campo E, et al. Blood 2022;140:1229-1253).

^{cc} For select patients with Stage IB, or Stage IIA non-contiguous disease, ISRT alone may be an option.

^{dd} Observation may be an option for stage IA patients with a completely excised solitary lymph node. See [Follow-up \(HODG-12\)](#).

^{ee} [Principles of Systemic Therapy \(HODG-B, 2-15\)](#).

^{ff} Generally, a brief course of chemotherapy (2–4 mo) would be given with RT.

^{gg} An FDA-approved biosimilar is an acceptable substitute for rituximab. Rituximab and hyaluronidase human injection for subcutaneous use may be substituted for rituximab after patients have received the first full dose of rituximab by intravenous infusion.

^{hh} Rituximab monotherapy can be used for palliation in select cases.

ⁱⁱ Biopsy is recommended for sites of progressive disease, especially subdiaphragmatic sites, to rule out transformation.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Surgical resection + Observation

Option for children

- 2 studies:

	EuroNET	COG
No of pts	57	52
	Stage 1A	Stage 1A, no bulk
Complete resection	86%	100%
Median FU	43m	26m
Relapse	27%	17%
Time to relapse	All within 26m	Median 10m
PFS	FFP 67%	2y EFS 80%

COG update (Appel JCO 2016):

- 75% PFS for observation vs > 90% PFS with chemo
- 100% OS.



RADIOFUNDAMENTALISM

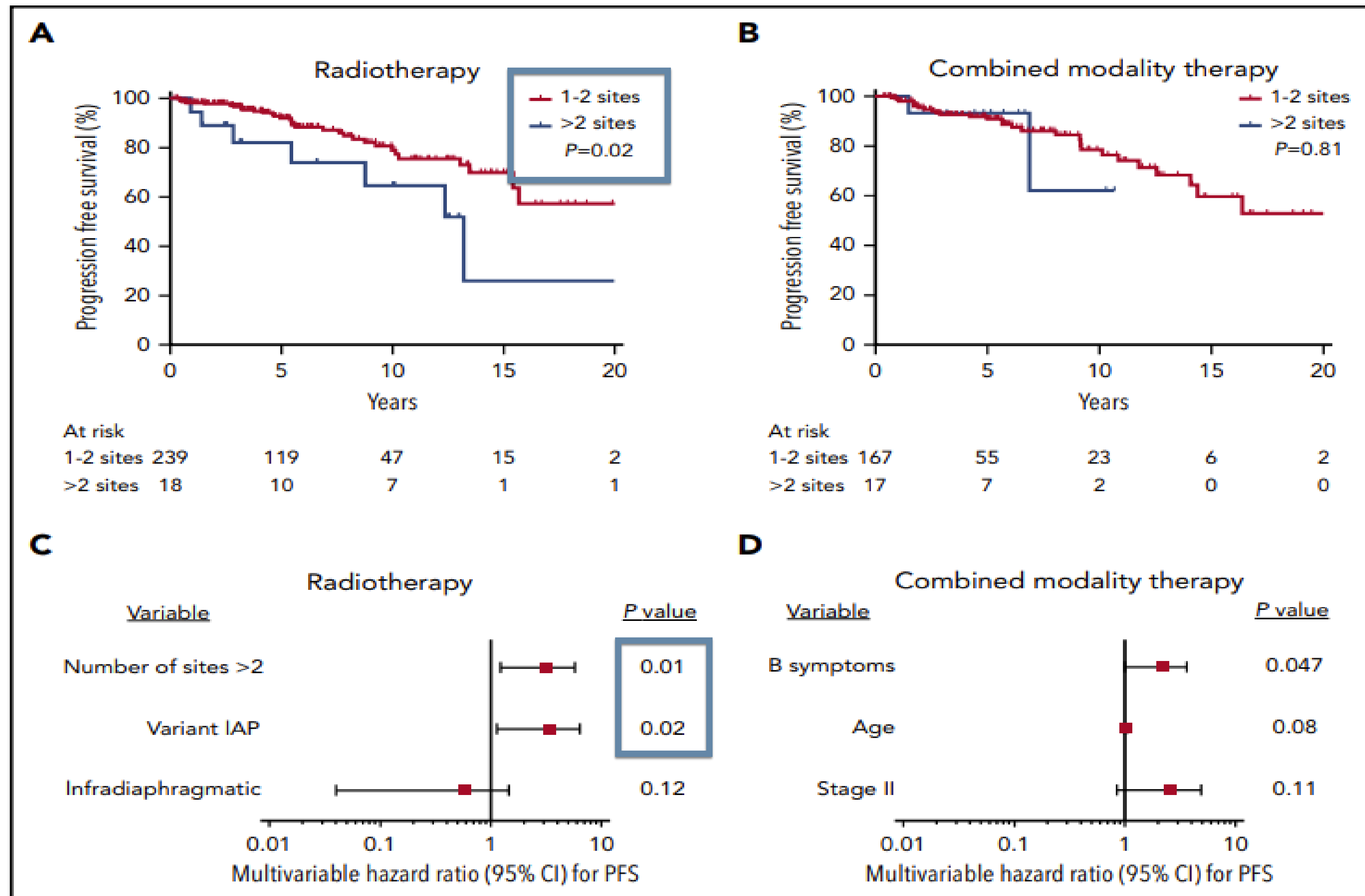
Milano, 14-15 aprile 2023

The young side of LYMPHOMA

gli under 40 a confronto

Stage I-II nodular lymphocyte-predominant Hodgkin lymphoma: a multi-institutional study of adult patients by ILROG

Michael S. Binkley,^{1,2} M. Shahzad Rauf,³ Sarah A. Milgrom,⁴ Chelsea C. Pinnix,⁴ Richard Tsang,⁵ Michael Dickinson,⁶ Andrea K. Ng,^{7,8} Kenneth B. Roberts,⁹ Sarah Gao,⁹ Alex Balogh,¹⁰ Umberto Ricardi,¹¹ Mario Levis,¹¹ Carla Casulo,¹² Michael Stolten,¹³ Lena Specht,¹⁴ John P. Plastaras,¹⁵ Christopher Wright,¹⁵ Christopher R. Kelsey,¹⁶ Jessica L. Brady,¹⁷ N. George Mikhael,¹⁷ Bradford S. Hoppe,^{18,19} Stephanie A. Terezakis,²⁰ Marco Picardi,²¹ Roberta Della Pepa,²¹ Youlia Kirova,²² Saad Akhtar,³ Irfan Maghfoor,³ Julie L. Koenig,^{1,2} Christopher Jackson,⁹ Erin Song,¹⁶ Shuchi Sehgal,²⁰ Ranjana H. Advani,²³ Yasodha Natkunam,²⁴ Louis S. Constine,¹³ Hans T. Eich,²⁵ Andrew Wirth,²⁶ and Richard T. Hoppe^{1,2}



The young side of LYMPHOMA

gli under 40 a confronto

International Prognostic Score for Nodular Lymphocyte-Predominant Hodgkin Lymphoma

Michael Sargent Binkley, MD, MS¹; Jamie E. Flerlage, MD, MS²; Kerry J. Savage, MD, MSc, BSc, FRCPC³; Saad Akhtar, MD⁴; Raphael Steiner, MD⁵; Xiao-Yin Zhang, BMBCh, MA, PhD⁶; Michael Dickinson, MBBS (Hons), DMedSci, FRACP, FRCPA⁷; Anca Prisca, MD⁸; Ajay Major, MD, MBA⁹; Peter G. Hendrickson, MD, PhD¹⁰; David Hopkins, MBChB, MRCP¹¹; Andrea Ng, MD, MPH¹²; Carla Casulo, MD¹³; Jonathan Baron, MD¹⁴; Kenneth B. Roberts, MD¹⁵; Jalila Al Kendi, MD¹⁶; Alex Balogh, MD¹⁷; Umberto Ricardi, MD¹⁸; Pallawi Torka, MD¹⁹; Lena Specht, MD, DMSc²⁰; Ravindu De Silva, MBBS²¹; Keir Pickard, MD, FRCPath²²; Lindsay J Blazin, MD, MPH²³; Michael Henry, MD²⁴; Christine M. Smith, MD²⁵; Daniel Halperin, MD²⁶; Jessica Brady, MBChB, FRCR²⁷; Bernadette Brennan, MD, BSc, MBChB, FRCPC²⁸; Maria Anatolevna Senchenko, MD²⁹; Marie Reeves, MSc, BSc³⁰; Bradford S. Hoppe, MD, MPH^{31,32}; Stephanie Terezakis, MD³³; Dipti Talaulikar, MD, PhD, DM (Haem) FRACP, FRCPA SFHEA^{34,35}; Marco Picardi, MD, PhD³⁶; Youlia Kirova, MD³⁷; Paige Fergusson³⁸; Eliza A. Hawkes, MBBS (Hons), FRACP, DMedSci^{39,40}; Denise Lee, MBBS, FRACP, FRCPA⁴¹; Nicole Wong Doo, MBBS, PhD, FRACP, FRCPA^{42,43}; Allison Barraclough, MBBS, BSc, FRACP, FRCPA⁴⁴; Chan Y. Cheah, MBBS(Hons), DMSc^{44,45}; Matthew Ku, MBBS, PhD, FRACP, FRCPA^{46,47}; Nada Hamad, MSc Forensic(Hons), MBBS(Hons), FRACP, FRCPA SpeCet(ClinRes)(Onc), FRCP^{48,49,50}; Howard Mutsando, MBChB, FRACP, FRCPA^{51,52}; Michael Gilbertson, MBBS(Hons), FRCPA, FRACP⁵³; Tamara Marconi, MBBS, FRACP, FRCPA⁵⁴; Nicholas Viiala, MBBS, FRCPA, FRACP^{55,56}; Matthew J Maurer, MS, DMSc⁵⁷; Dennis A Eichenauer, MD⁵⁸; and Richard T. Hoppe, MD⁵⁹; on behalf of the GLOW Consortium

Parameter	Total (N = 2,243), No. (%)	CT (n = 727), No. (%)	CMT (n = 684), No. (%)	RT (n = 538), No. (%)	Observation (n = 104), No. (%)	Rituximab Alone (n = 90), No. (%)	Active Surveillance (n = 76), No. (%)	Rituximab and RT (n = 24), No. (%)
Age at diagnosis, years								
Median	37	34	36	40	20	44	57	35
IQR	23-51	19-47	24-48	28-53	14-52	31-60	42-71	24-43
Range	2-89	2-88	3-82	11-89	4-80	16-85	12-84	18-65
Sex								
Male	1,681 (74.9)	575 (79.1)	508 (74.3)	398 (74.0)	71 (68.3)	64 (71.1)	47 (61.8)	18 (75.0)
Female	562 (25.1)	152 (20.9)	176 (25.7)	140 (26.0)	33 (31.7)	26 (28.9)	29 (38.2)	6 (25.0)
ECOG PS								
0-1	2,198 (98.0)	704 (96.8)	676 (98.8)	531 (98.7)	103 (99.0)	89 (98.9)	72 (94.7)	23 (95.8)
>1	45 (2.0)	23 (3.2)	8 (1.2)	7 (1.3)	1 (1.0)	1 (1.1)	4 (5.3)	1 (4.2)
Stage								
I	852 (38.0)	98 (13.5)	190 (27.8)	395 (73.4)	104 (100.0)	54 (60.0)	0 (0.0)	11 (45.8)
Extranodal	23 (1.0)	3 (0.4)	6 (0.9)	10 (1.9)	3 (2.9)	1 (1.1)	0 (0.0)	0 (0.0)
B symptoms	35 (1.6)	7 (1.0)	10 (1.5)	13 (2.4)	4 (3.9)	1 (1.1)	0 (0.0)	0 (0.0)
Spleen	2 (0.1)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.2)
II	784 (34.9)	164 (22.6)	427 (62.4)	136 (25.3)	0 (0.0)	15 (16.7)	31 (40.8)	11 (45.8)
Extranodal	40 (1.8)	5 (0.7)	21 (3.1)	9 (1.7)	0 (0.0)	2 (2.2)	3 (3.9)	0 (0.0)
B symptoms	53 (2.4)	11 (1.5)	32 (4.7)	7 (1.3)	0 (0.0)	1 (1.1)	1 (1.3)	1 (4.2)
Spleen	7 (0.3)	2 (0.3)	3 (0.4)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.3)	0 (0.0)
III	460 (20.5)	345 (47.5)	47 (6.9)	7 (1.3)	0 (0.0)	19 (21.1)	40 (52.6)	2 (8.3)
Extranodal	31 (1.4)	22 (3.0)	6 (0.9)	0 (0.0)	0 (0.0)	3 (3.3)	0 (0.0)	0 (0.0)
B symptoms	80 (3.6)	63 (8.7)	9 (1.3)	0 (0.0)	0 (0.0)	3 (3.3)	4 (5.3)	1 (4.2)
Spleen	60 (2.7)	40 (5.5)	10 (1.5)	0 (0.0)	0 (0.0)	7 (7.8)	3 (3.9)	0 (0.0)
IV	147 (6.6)	120 (16.5)	20 (2.9)	0 (0.0)	0 (0.0)	2 (2.2)	5 (6.6)	0 (0.0)
Extranodal	110 (4.9)	90 (12.4)	13 (1.9)	0 (0.0)	0 (0.0)	2 (2.2)	5 (6.6)	0 (0.0)
B symptoms	52 (2.3)	43 (5.9)	9 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Spleen	51 (2.3)	44 (6.1)	5 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.6)	0 (0.0)
Immunoarchitecture								
A/B typical	676 (30.1)	152 (20.9)	262 (38.3)	187 (34.8)	31 (29.8)	31 (35.6)	9 (12.2)	4 (16.7)
C	78 (3.5)	26 (3.6)	25 (3.7)	19 (3.5)	4 (3.8)	3 (3.4)	1 (1.4)	0 (0.0)
D	82 (3.6)	42 (5.8)	25 (3.7)	8 (1.5)	3 (2.9)	4 (4.6)	0 (0.0)	0 (0.0)
E	67 (3.0)	33 (4.5)	26 (3.8)	2 (0.4)	2 (1.9)	2 (2.3)	2 (2.7)	0 (0.0)
F	13 (0.6)	2 (0.3)	5 (0.7)	5 (0.9)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
Unknown	1,327 (59.2)	472 (64.9)	341 (49.9)	317 (58.9)	64 (61.5)	56 (64.4)	62 (87.8)	20 (83.3)
Follow-up, years								
Median	6.3	5.8	7.6	6.4	3.9	6.5	4.4	3.5
IQR	3.4-10.8	3.3-9.8	4.5-12.3	3.2-11.6	1.6-6.1	3.2-8.2	2.5-6.6	1.9-12.4

JOURNAL OF CLINICAL ONCOLOGY

2024

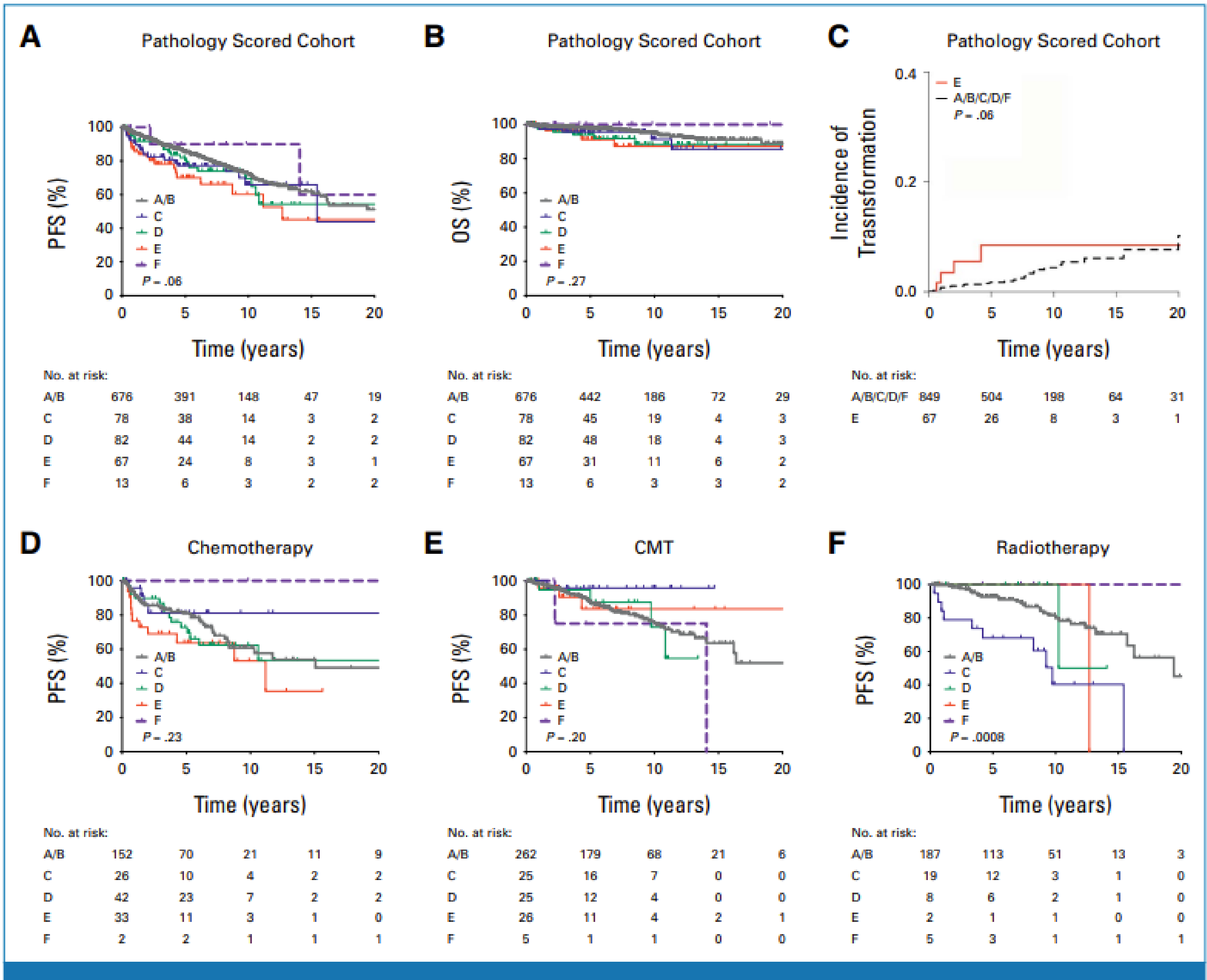
Pescara, 11-12 ottobre 2024

International Prognostic Score for Nodular Lymphocyte-Predominant Hodgkin Lymphoma

Michael Sargent Binkley, MD, MS¹; Jamie E. Flerlage, MD, MS²; Kerry J. Savage, MD, MSc, BSc, FRCPC³; Saad Akhtar, MD⁴; Raphael Steiner, MD⁵; Xiao-Yin Zhang, BMBCh, MA, PhD⁶; Michael Dickinson, MBBS (Hons), DMedSci, FRACP, FRCPA⁷; Anca Prisca, MD⁸; Ajay Major, MD, MBA⁹; Peter G. Hendrickson, MD, PhD¹⁰; David Hopkins, MBChB, MRCP¹¹; Andrea Ng, MD, MPH¹²; Carla Casulo, MD¹³; Jonathan Baron, MD¹⁴; Kenneth B. Roberts, MD¹⁵; Jalila Al Kendi, MD¹⁶; Alex Balogh, MD¹⁷; Umberto Ricardi, MD¹⁸; Pallawi Torka, MD¹⁹; Lena Specht, MD, DMSc²⁰; Ravindu De Silva, MBBS²¹; Keir Pickard, MD, FRCPath²²; Lindsay J Blazin, MD, MPH²³; Michael Henry, MD²⁴; Christine M. Smith, MD²⁵; Daniel Halperin, MD²⁶; Jessica Brady, MBBCh, FRCR²⁷; Bernadette Brennan, MD, BSc, MBChB, FRCPC²⁸; Maria Anatolevna Senchenko, MD²⁹; Marie Reeves, MSc, BSc³⁰; Bradford S. Hoppe, MD, MPH^{31,32}; Stephanie Terezakis, MD³³; Dipti Talaulikar, MD, PhD, DM (Haem) FRACP, FRCPA SFHEA^{34,35}; Marco Picardi, MD, PhD³⁶; Youlia Kirova, MD³⁷; Paige Fergusson³⁸; Eliza A. Hawkes, MBBS (Hons), FRACP, DMedSc^{39,40}; Denise Lee, MBBS, FRACP, FRCPA⁴¹; Nicole Wong Doo, MBBS, PhD, FRACP, FRCPA^{42,43}; Allison Barraclough, MBBS, BSc, FRACP, FRCPA⁴⁴; Chan Y. Cheah, MBBS(Hons), DMSc^{44,45}; Matthew Ku, MBBS, PhD, FRACP, FRCPA^{46,47}; Nada Hamad, MSc Forensic(Hons), MBBS(Hons), FRACP, FRCPA SpeCetClinRes(Onc), FRCP^{48,49,50}; Howard Mutsaers, MBChB, FRACP, FRCPA^{51,52}; Michael Gilbertson, MBBS(Hons), FRCPA, FRCPath⁵³; Tamara Marconi, MBBS, FRACP, FRCPA⁵⁴; Nicholas Viiala, MBBS, FRCPA, FRCPath^{55,56}; Matthew J Maurer, MS, DMSc⁵⁷; Dennis A Eichenauer, MD⁵⁸; and Richard T. Hoppe, MD⁵⁹; on behalf of the GLOW Consortium

IAPs were not associated with PFS or OS, but IAP E had higher risk of transformation (hazard ratio [HR], 1.81; P < .05).

There was a significant difference (P=.0008) in PFS for patients receiving radiotherapy alone, which was primarily driven by the poor outcomes of patients with IAP C



Radiotherapy

ILROG guidelines: GTV, CTV, PTV

- PET/planning-CT image registration is ideal to outline GTV (as no prior chemo).

Volume:

- No chemo. RT needs to control local microscopic disease
- No benefit to EF over IF-RT (Nogova 2005, Eichenaeur 2015)

Dose:

- No conclusive evidence of benefit >30Gy
- 4Gy: inferior outcome (local relapse 5/8 pts)
- NCCN: 30-36 Gy, ESMO: 30 Gy
- Standard: 30 Gy.....36Gy for bulky disease? (uncommon)

**Modern Radiation Therapy for Hodgkin
Lymphoma: Field and Dose Guidelines From the
International Lymphoma Radiation Oncology Group (ILROG)**



Lena Specht, MD, PhD,^{*} Joachim Yahalom, MD,[†] Tim Illidge, MD, PhD,[‡]
Anne Kiil Berthelsen, MD,[§] Louis S. Constine, MD,^{||} Hans Theodor Eich, MD, PhD,[¶]
Theodore Girinsky, MD,[#] Richard T. Hoppe, MD,^{**} Peter Mauch, MD,^{††}
N. George Mikhaeel, MD,^{‡‡} and Andrea Ng, MD, MPH^{††}, on behalf of ILROG

Grazie dell'attenzione



@MatroneFabio



fabio.matrone@cro.it