Società Italiana di Ematologia

FORMAZIONE SIE

I linfomi: un nome con almeno 40 sfaccettature!

25 giugno 2026

Bologna
Royal Hotel Carlton

Sessione 1: LINFOMI NON HODGKIN AGGRESSIVI

Moderatori: P. Corradini (Milano), P.L. Zinzani (Bologna)

Linfomi Primitivi del Mediastino (PMBCL)

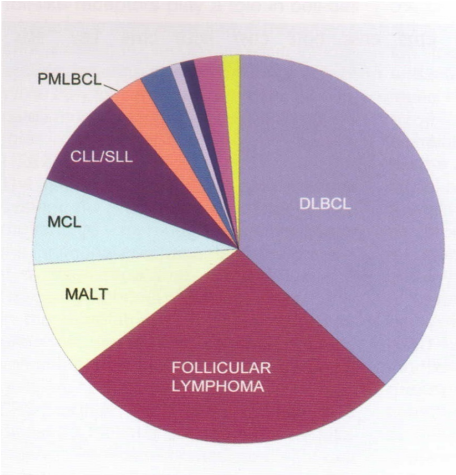
Maurizio Martelli

Ematologia Azienda Policlinico Umberto 1
Univ. Sapienza Roma

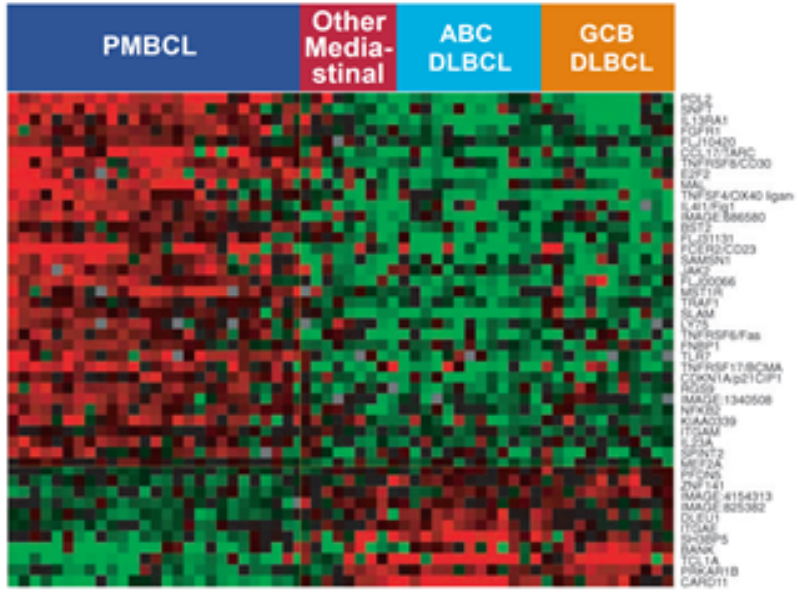
Disclosures of Maurizio Martelli

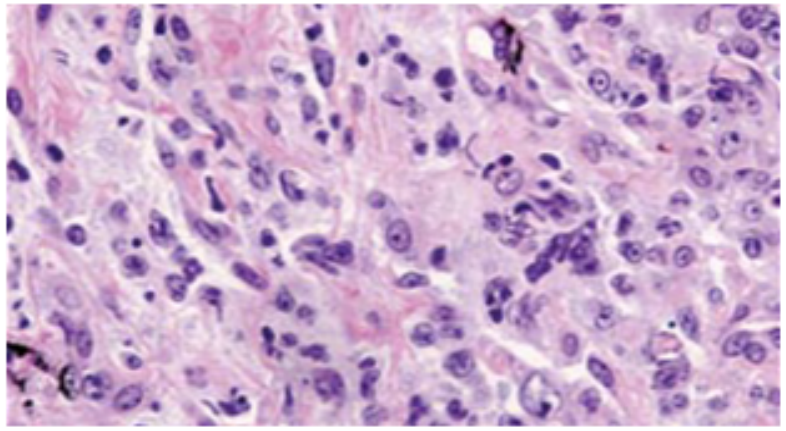
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Abbvie			X		X	x	
Beigene						x	
Eli Lilly					X	x	
Recodati Rare disease					X	x	
Incyte			X			X	
Kite Gilead			X		X	x	
Novartis						X	
Janssen							
Roche			X		X	X	
SOBI						X	
Takeda						X	
BMS						x	

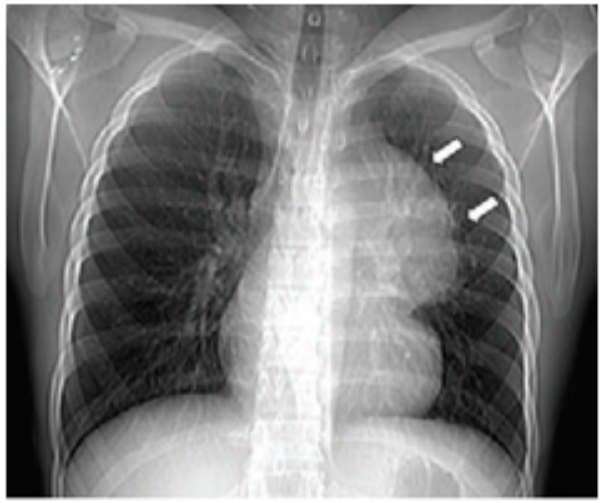
Distinctive features of PMBCL

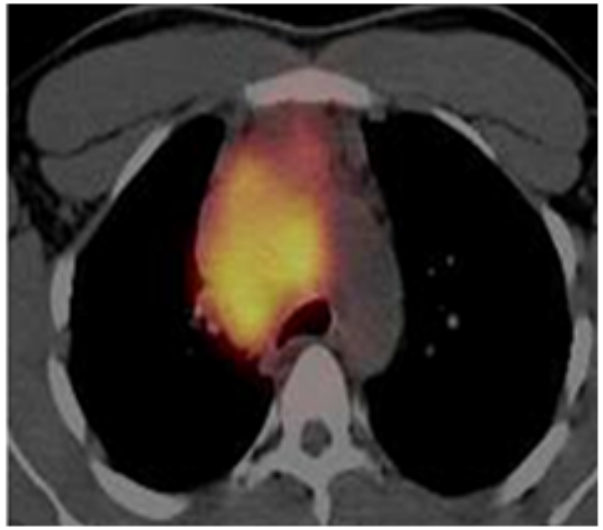


CD20	100%
CD30	87%
CD23	70%
CD15	---
Bcl-6	80%
IRF4	75%
Bcl-2	80%
BOB.1/Oct-2	80%
MAL protein	70%



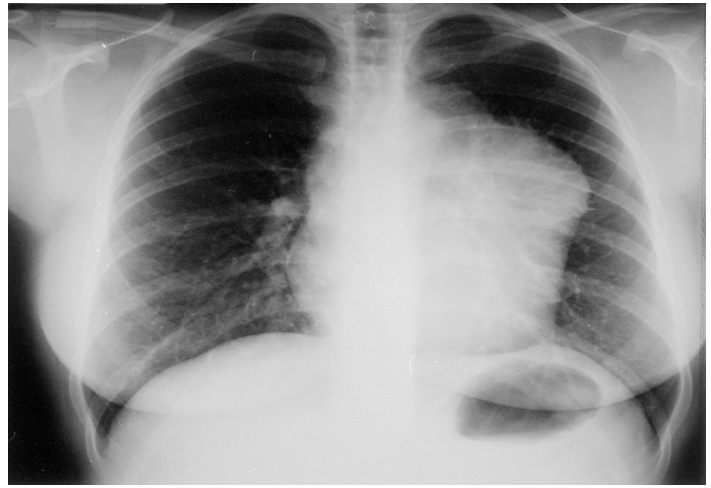






Distinctive Clinical features

- Bulky anterior mediastinal mass
- Usually stage I/II (bulky mass)
- Local typically extension
  - Pleuro-pericardial effusions
  - Vena Cava Syndrome (VCS)
  - Dyspnoea, cough
  - Dysphagia



- No infradiaphragmatic lymph node
- No marrow involvement
- Tipical extranodal sites (kidney, ovary, pancreas) more common at relapse

VCS (50%) may be a clinical emergency

Borderland between PMBCL, MGZL and cHL

MGZL

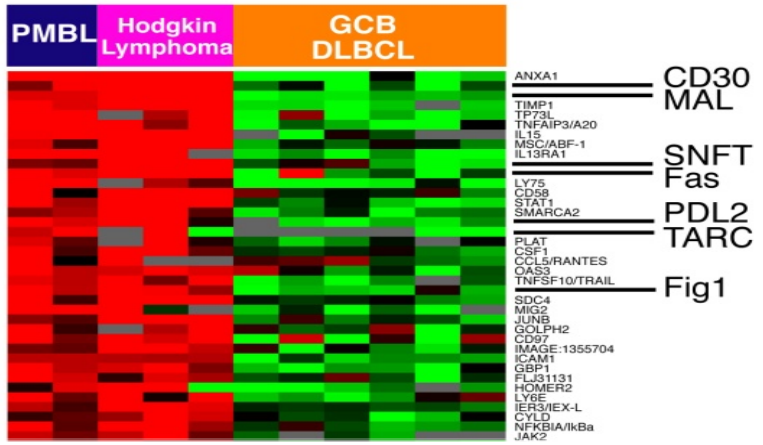
HL, morphology

CD20+,CD15-

CD30+

OCT2+,BOB 1 +

Extensive Gene Expression Overlap Between Hodgkin Lymphoma and Primary Mediastinal Large B Cell Lymphoma



MGZL

PMBCL morphology

CD20-,CD15+

CD30+,

OCT2+,BOB 1 +

ORIGINAL ARTICLE

(*Am J Surg Pathol* 2005;29:1411–1421)

Mediastinal Gray Zone Lymphoma

The Missing Link Between Classic Hodgkin's Lymphoma and Mediastinal Large B-Cell Lymphoma

Alexandra Traverse-Glehen, MD, Stefania Pittaluga, MD, PhD,* Philippe Gaulard, MD,† Lynn Sorbara, PhD,* Miguel A. Alonso, PhD,‡ Mark Raffeld, MD,* and Elaine S. Jaffe, MD*

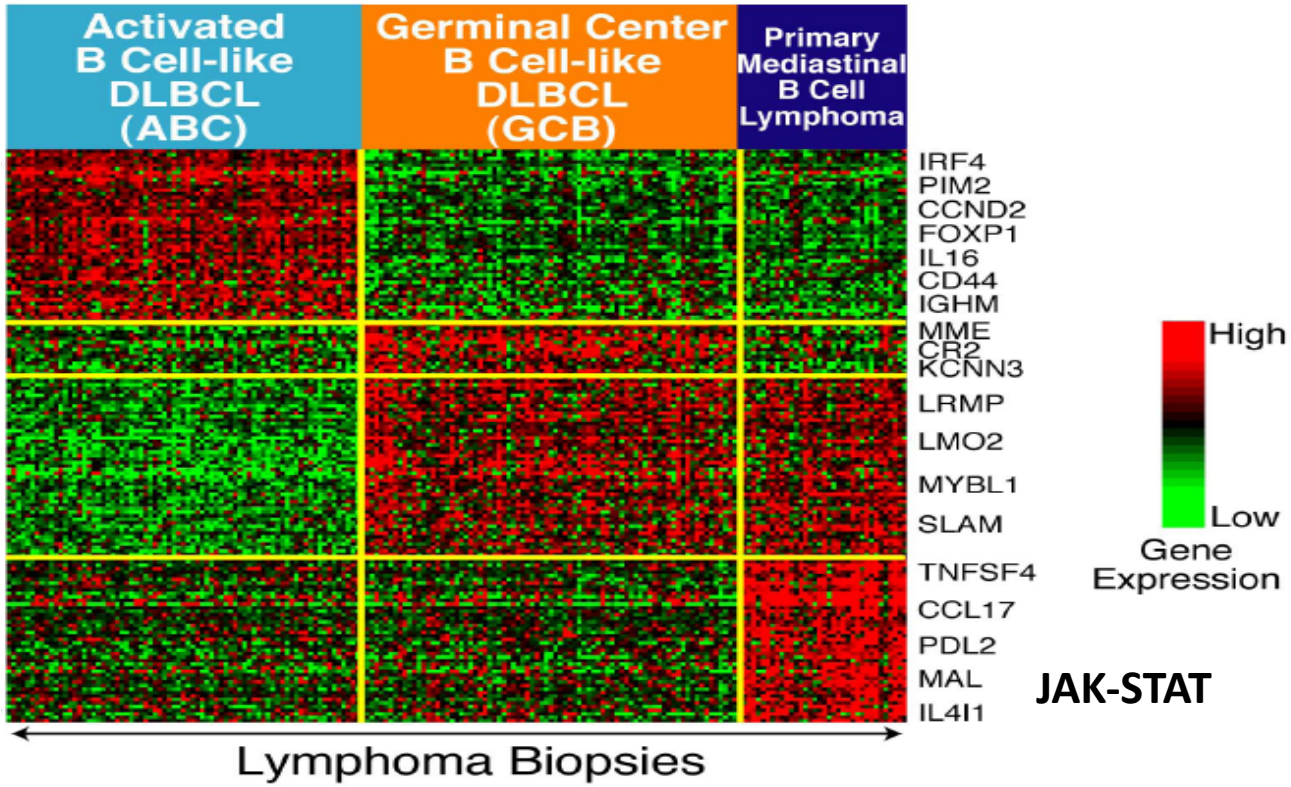
HL

CD15+; OCT2-

Jaffe E . Educational ASH 2010

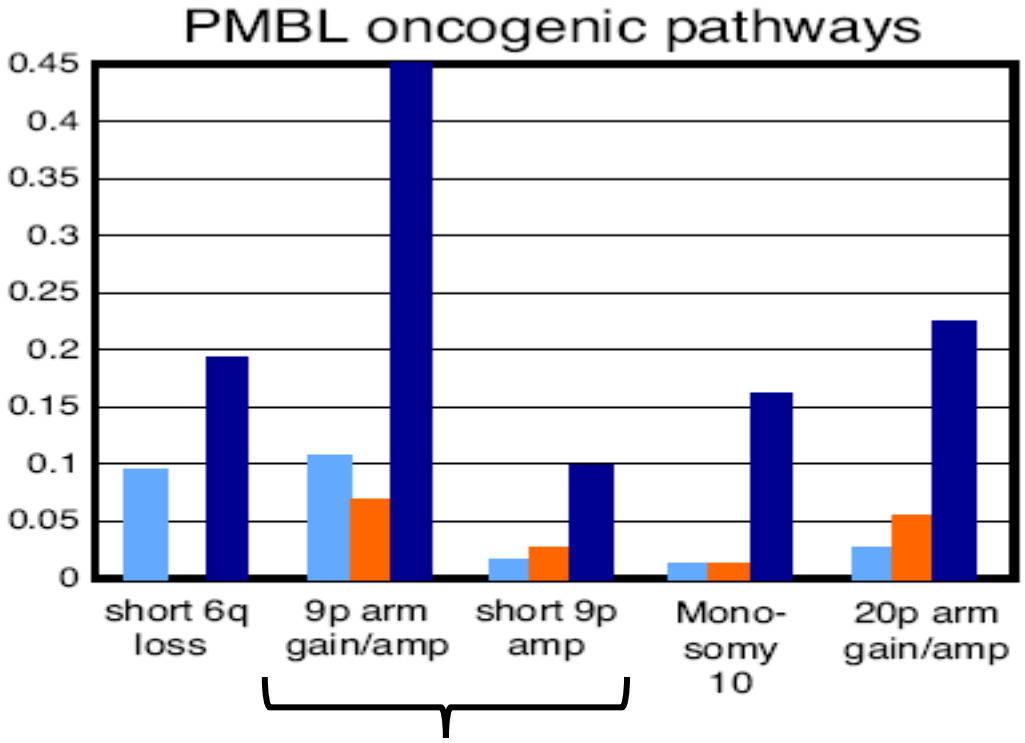
Genomic hybridization: amplification of JAK2, PDL1, PDL2

PMBL transcriptional signature: constitutively activated JAK2



JAK-STAT

Recurrent amplification involving *JAK2* is the underlying genetic basis



JAK2, PDL1,PDL2

Rosenwald et al. JEM, 2003, Lenz et al, PNAS 2008

Outline of discussion

- Front-line chemoimmunotherapy regimen
  (*R-CHOP 21, R-CHOP 14, R-V/MACOP-B or more intensive DA-EPOCH-R)*

- Role of EOT PET-CT scan to evaluate the clinical response and if it can drive mediastinal RT

- Salvage therapy for Relapsed/ Refractory patients

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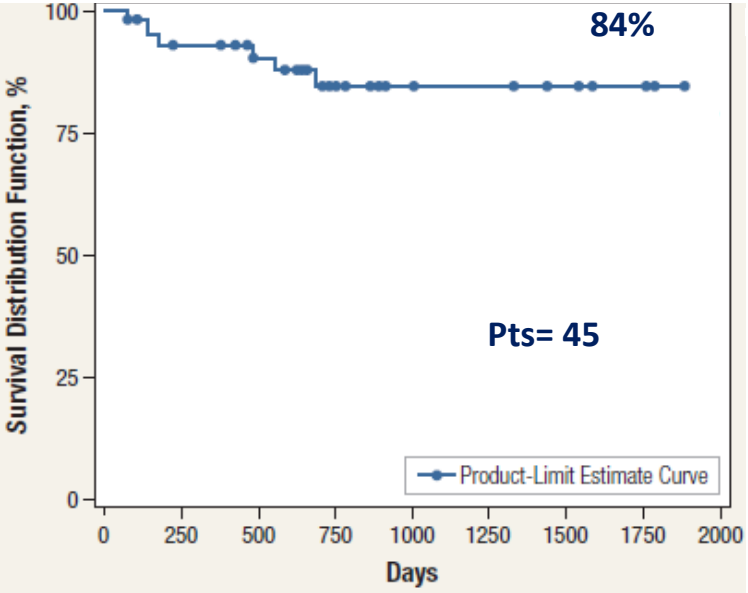
R-V/MACOP-B + mediastinal RT in PMBCL
(Italian experience)

Rituximab Combined With MACOP-B or VACOP-B and Radiation Therapy in Primary Mediastinal Large B-Cell Lymphoma: A Retrospective Study

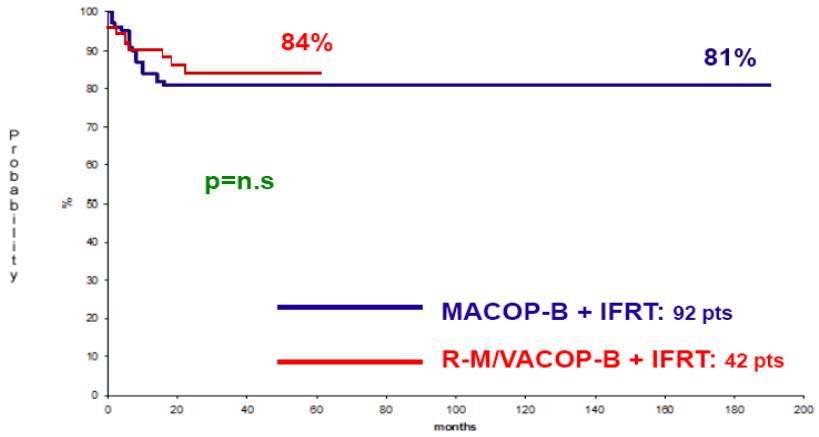
PFS



Zinzani et al Clin.Lymphoma Myeloma 2009

M-VACOP-B+/-Rituximab in Primary Mediastinal Lymphoma: Retrospective study in 134 pts

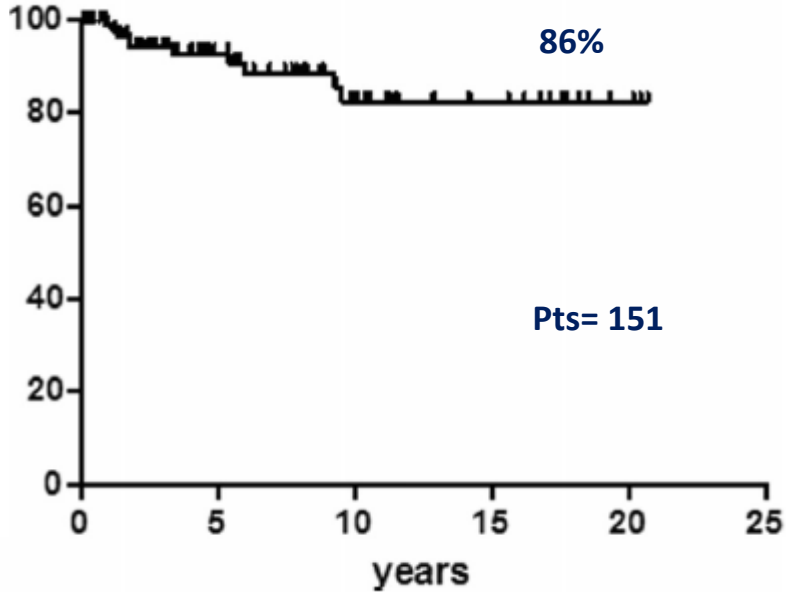
PFS



Martelli et al ICML 2011

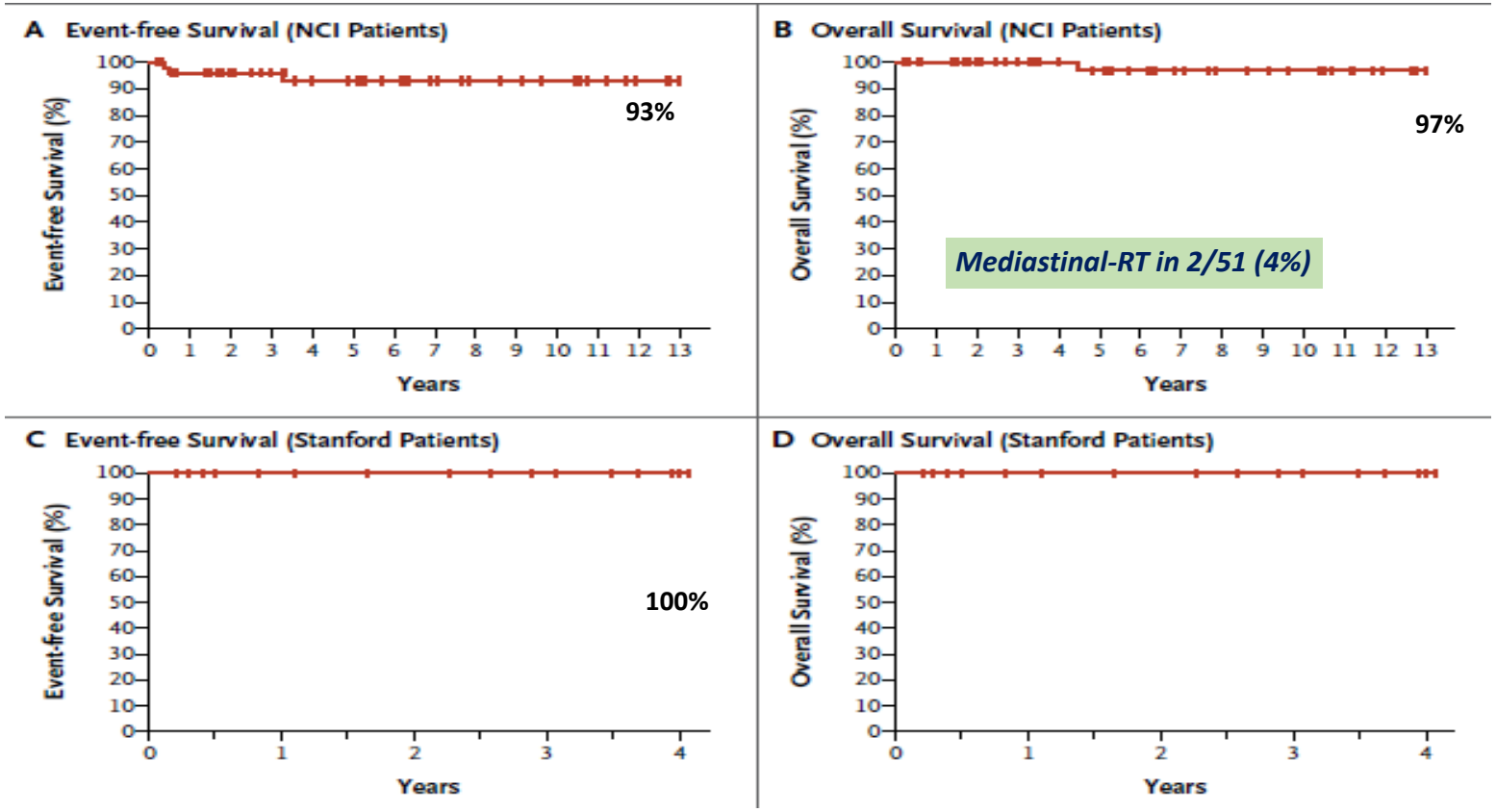
Treatment and outcome of PMBCL : a three decade monocentric experience with 151 patients

DFS



Casadei et al Ann. of Hematology 2021

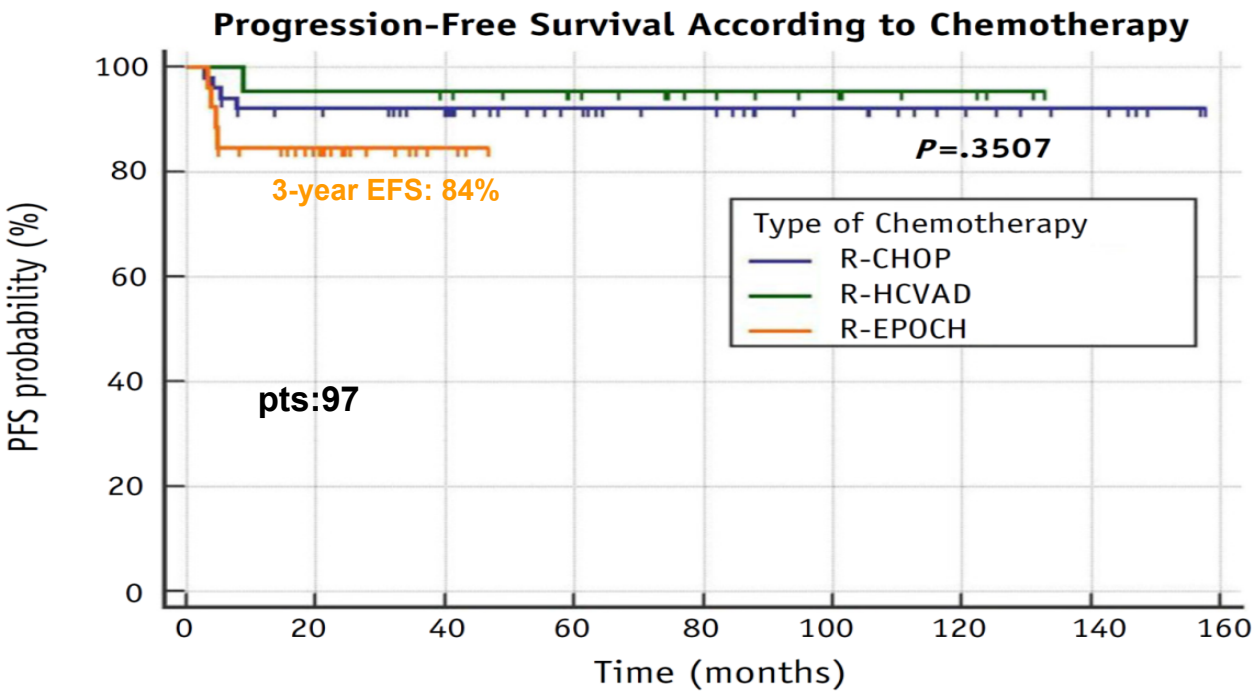
DA-EPOCH+R: NCI results (phase 2 study, 52 patients with an accrual over 8 years)

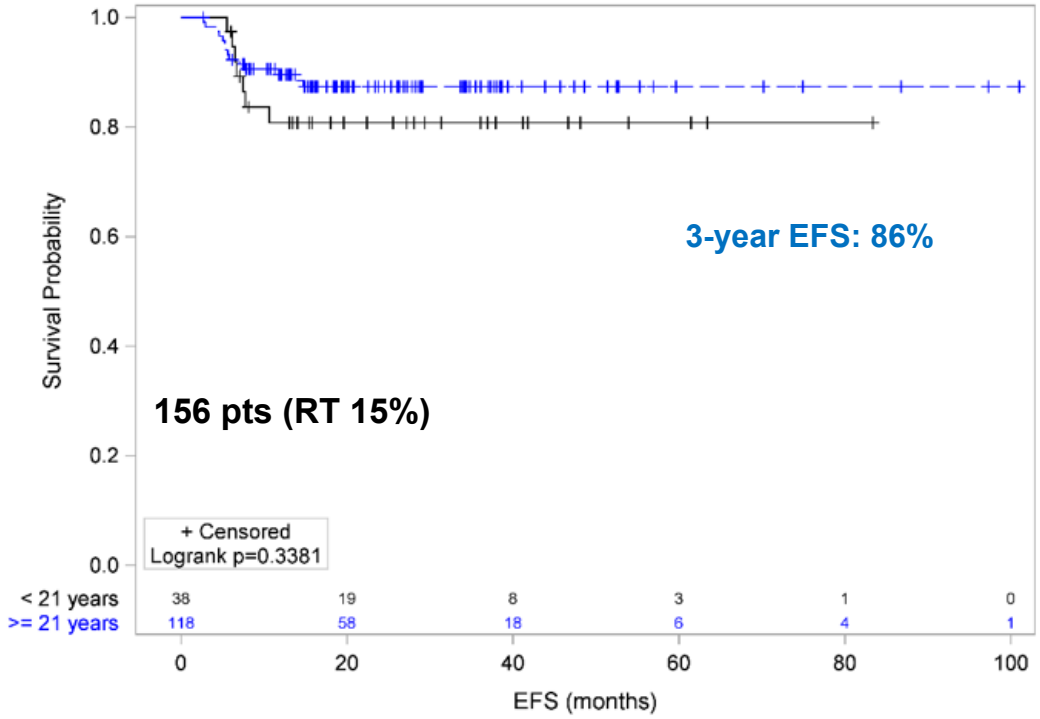


DA-EPOCH-R gives an high cure rate without the need of a mediastinal radiotherapy and should be considered the new standard therapy

Dunleavy K et al N.Engl. J. Med 2013

First-line treatment : DA-EPOCH-R retrospective studies





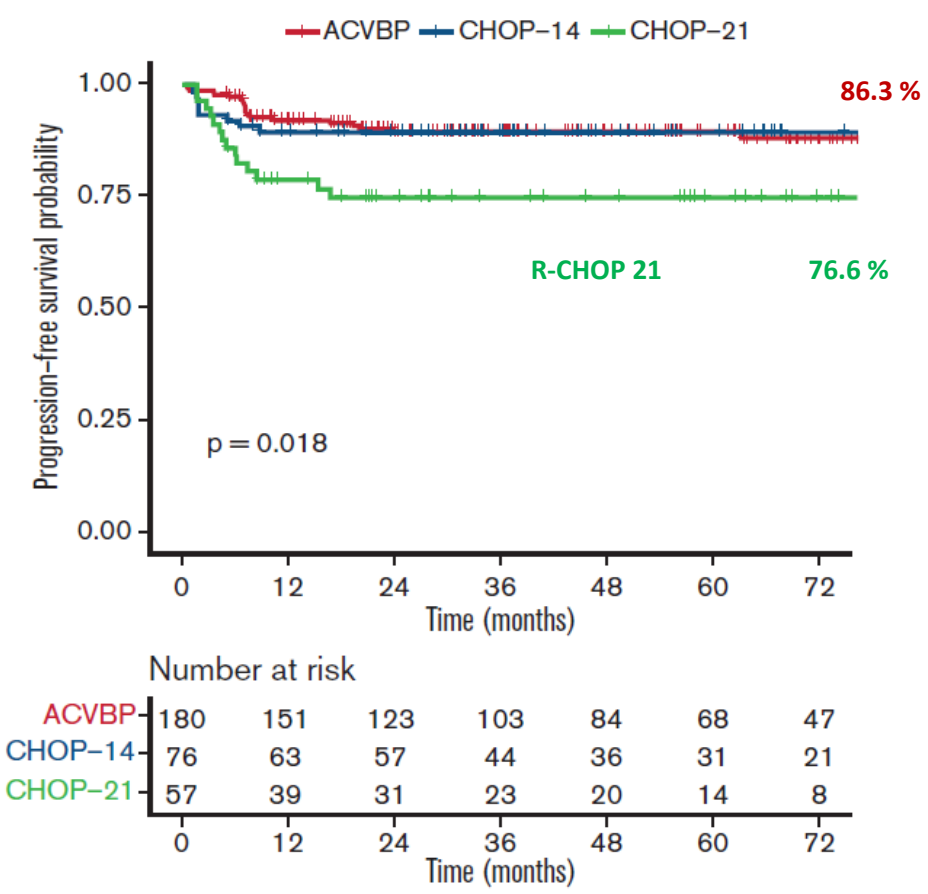
Pinnix CC et al. Int J Radiat Oncol Biol Phys. 2015; 92:113-121

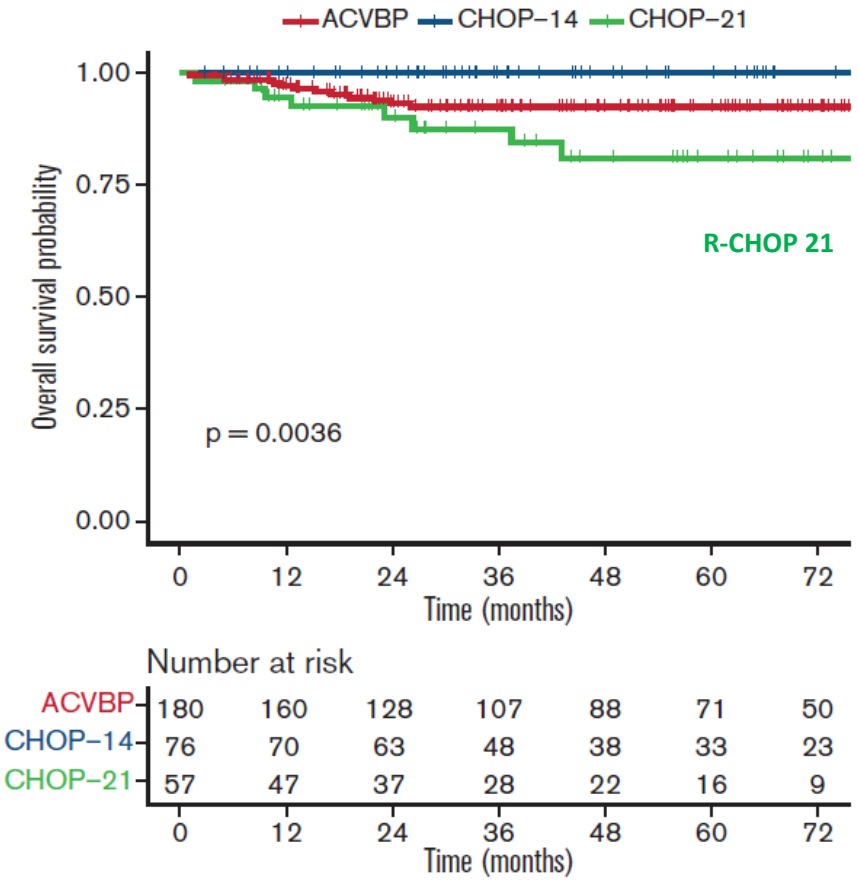
Giulino-Roth L. Br J Haematol, 2017; 179: 739-747

REGULAR ARTICLE

blood advances

Outcomes after first-line immunochemotherapy for primary mediastinal B-cell lymphoma: a LYSA study

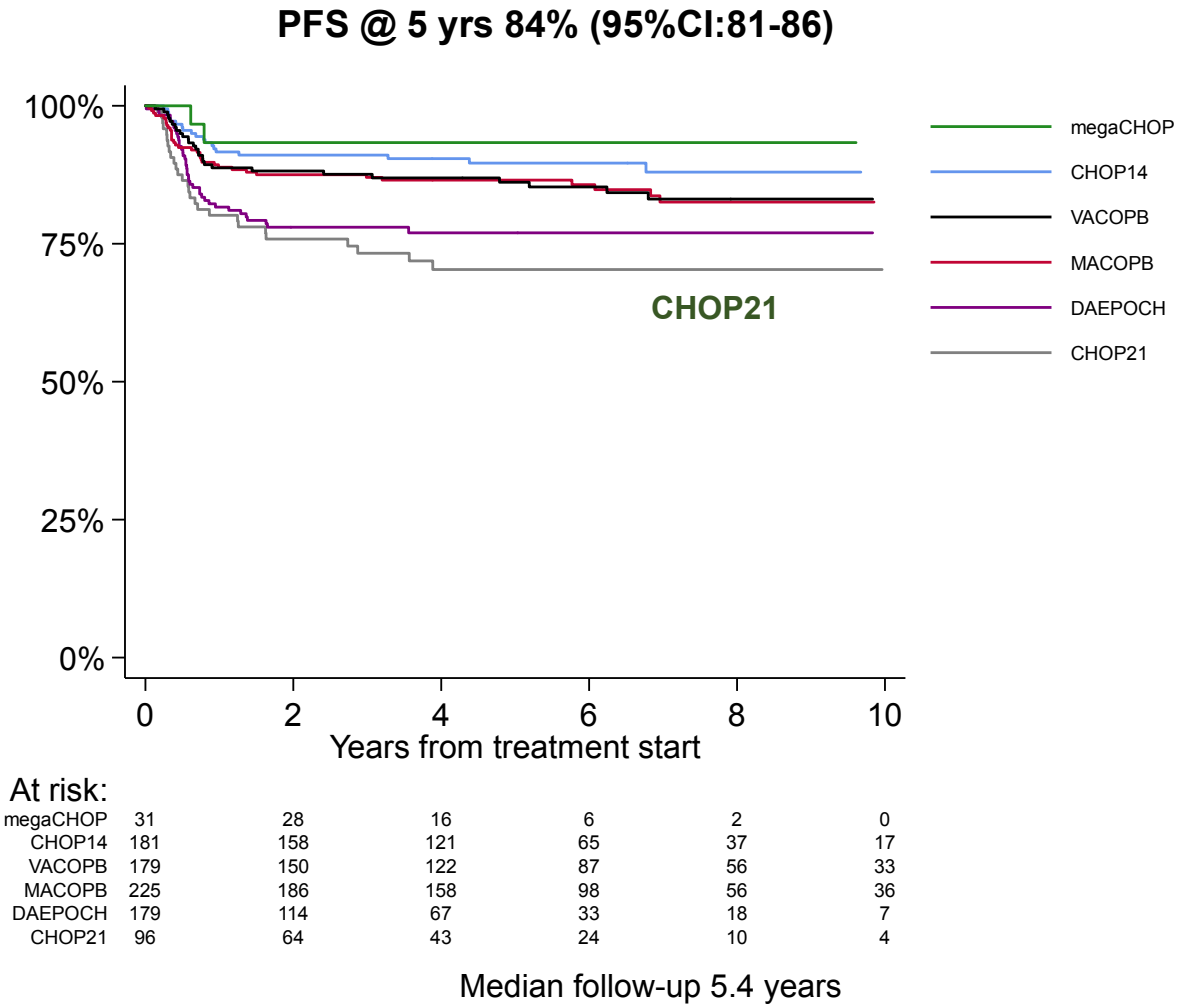




Camus V. *Blood Adv*, 2021; 5: 3862-3872

Italian Retrospective Study on PMBCL

- Retrospective, multicenter analysis of adult patients with newly diagnosed PMBCL in **37 Italian hematological centers** from Jan 2007 to Dec 2019 in **931 patients with PMBCL**



Balzarotti M. et al ASH 2023

blood®

Available online 15 September 2025

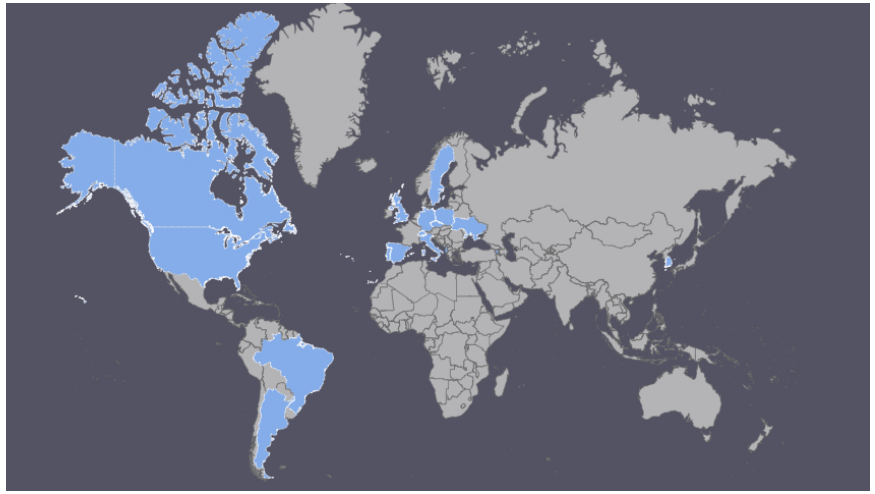
Impact of immunochemotherapy regimens on outcomes of patients with primary mediastinal B-cell lymphoma in the IELSG37 trial

Emanuele Zucca [*,1,2,3], Luca Ceriani [*,2,3,4], Giovannino Ciccone [*,5], Alice Di Rocco [6], Maria Cristina Pirosa [1,2], Iryna Kriachok [7], Barbara Botto [8], Monica Balzarotti [9], Alessandra Tucci [10], Sara Veronica Usai [11], Vittorio Ruggero Zilioli [12], Elsa Pennese [13], Luca Arcaini [14,15], Anna Dabrowska-Iwanicka [16], Andrés JM Ferreri [17,18], Francesco Merli [19], Weili Zhao [20], Luigi Rigacci [**,21], Claudia Cellini [22], David Hodgson [23]... Maurizio Martelli [*,6]

IELSG-37 prospective randomized International study

545 patients with PMBCL enrolled from **74 centres in 13 countries**

- **Italy 380**
- UK 44
- Ukraine 25
- Switzerland 17
- Poland 15
- Czech Republic 14
- China 12
- Norway 11
- Canada 10
- Sweden 7
- Germany 5
- USA 3
- Portugal 2



Accrual
September 2012
August 2019

Front-line chemotherapy regimens

Regimen	N	Percent
R-CHOP21	**98**	**18.0**
R-CHOP14	**146**	**26.8**
R-V/MACOP-B	**169**	**31.0**
DA-EPOCH-R	**88**	**16.1**
R-megaCHOP	19	3.5
R-CHOEP	13	2.4
GMALL-BALL/NHL2002	12	2.2
All	***545***	***100.00***

→ **N = 501**

Zucca, Martelli et al. Blood 2025

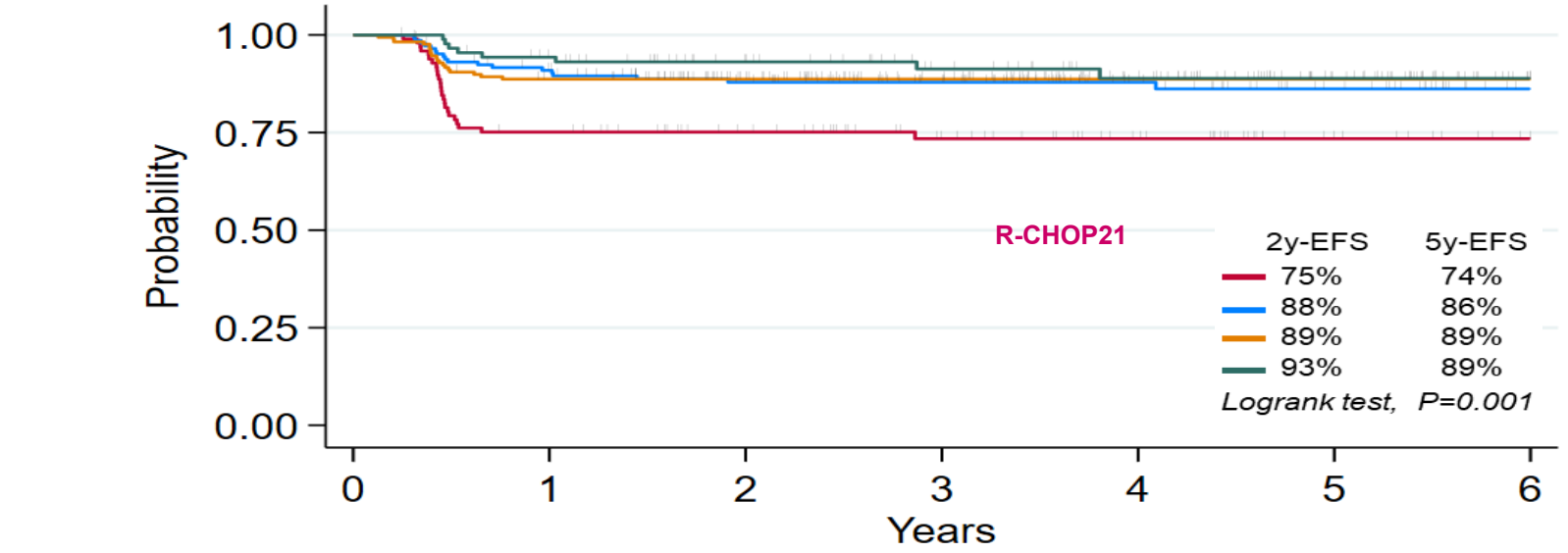
EOT-PET- metabolic response after front line therapy

Regimen	Deauville score (5-point scale), N (%)				
	1	2	3	4	5
R-CHOP21	3 (3)	25 (27)	23 (25)	20 (22)	21 (23)*
R-CHOP14	2 (2)	36 (26)	40 (28)	52 (37)	11 (8)
R-V/MACOP-B	4 (3)	33 (20)	53 (32)	61 (37)	15 (9)
DA-EPOCH-R	1 (1)	35 (41)	20 (23)	25 (29)	5 (6)

**P-value = 0.001*

Zucca, Martelli et al. Blood 2025

Event-free survival by regimens

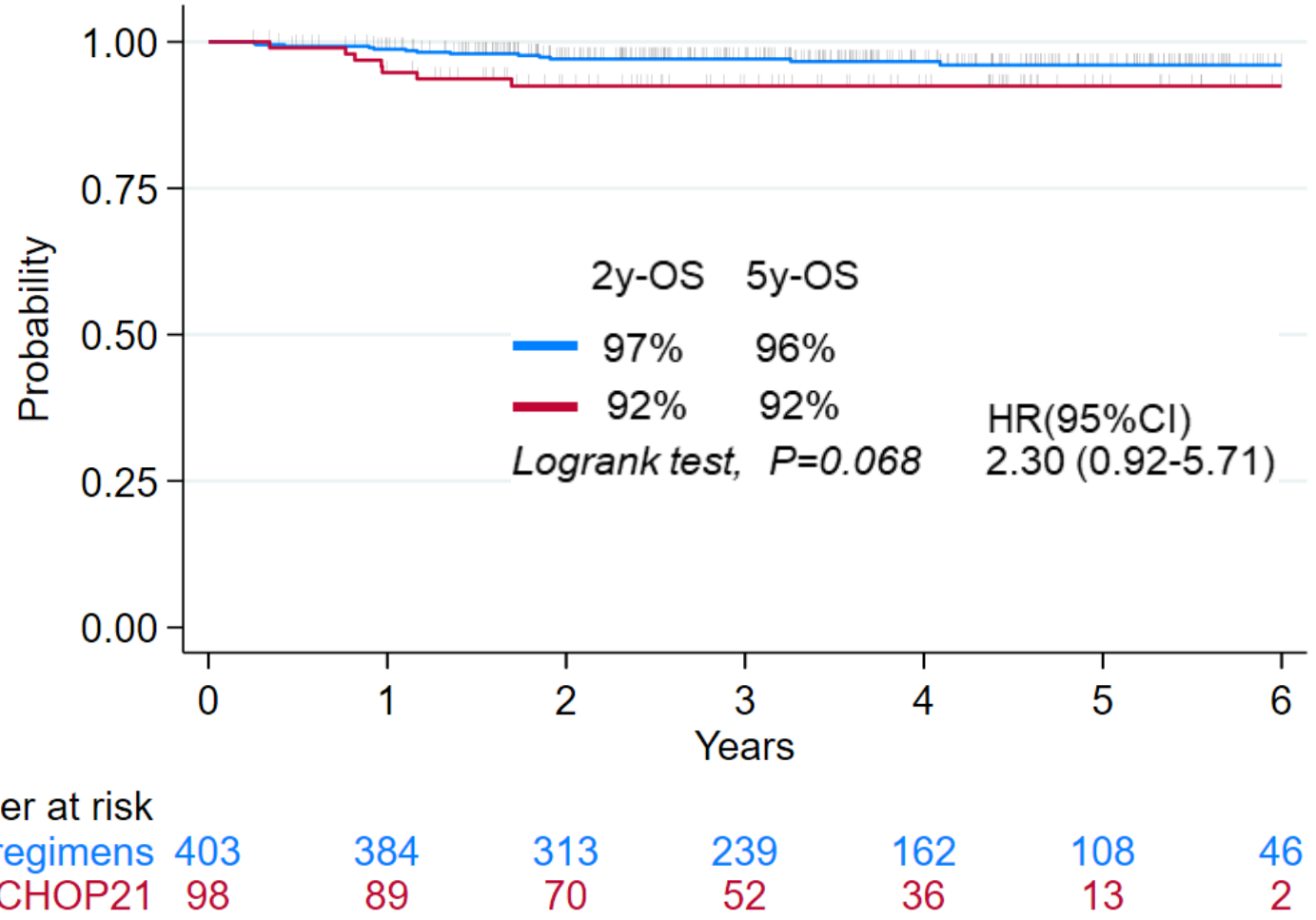


Number at risk

R-CHOP21	98	71	58	41	26	9	1
R-CHOP14	146	126	103	81	53	36	15
R-V/MACOP-B	169	146	123	95	66	44	15
DA-EPOCH-R	88	79	61	48	35	22	15

Zucca, Martelli et al. Blood 2025

OS, R-CHOP21 compared to other regimens



Zucca, Martelli et al. Blood 2025

Outline of discussion

- Front-line chemoimmunotherapy regimen
  (*R-CHOP 21, R-CHOP 14, R-V/MACOP-B or more intensive DA-EPOCH-R)*

- **Role of EOT PET-CT scan to evaluate the clinical response and if it can drive mediastinal RT**

- Salvage therapy for Relapsed/ Refractory patients

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

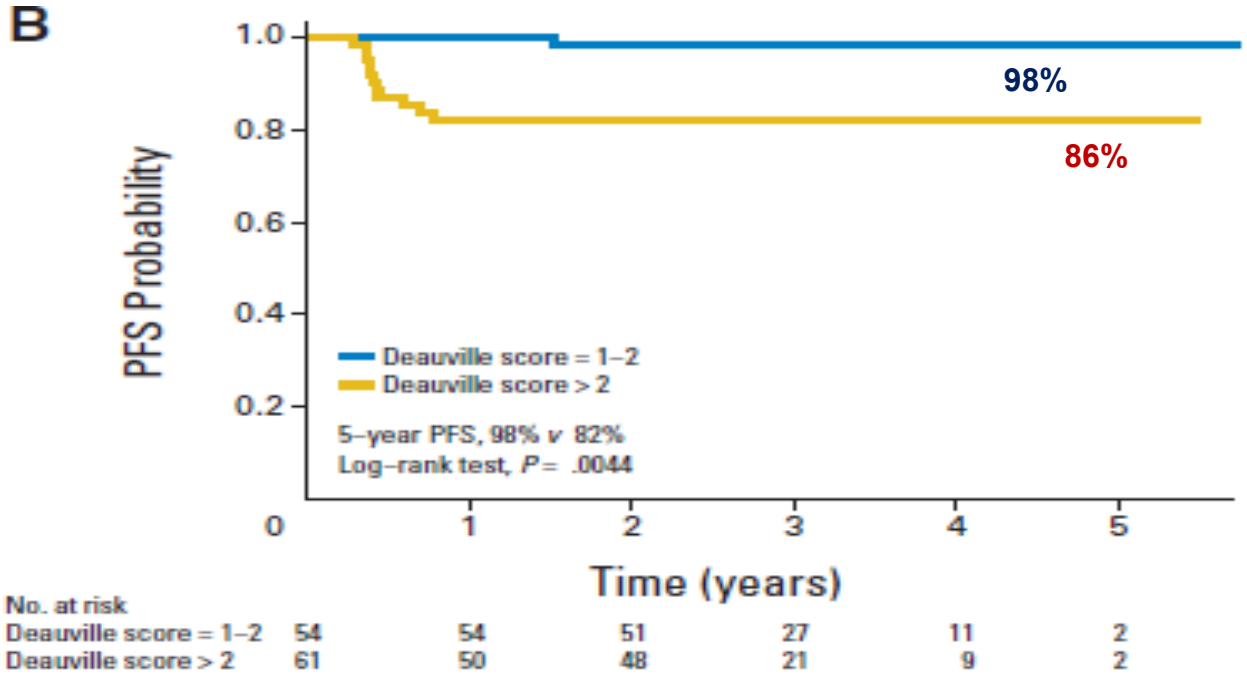
[^{18}F]Fluorodeoxyglucose Positron Emission Tomography Predicts Survival After Chemoimmunotherapy for Primary Mediastinal Large B-Cell Lymphoma: Results of the International Extranodal Lymphoma Study Group IELSG-26 Study

Maurizio Martelli, Luca Ceriani, Emanuele Zucca, Pier Luigi Zinzani, Andrés J.M. Ferreri, Umberto Vitolo, Caterina Stelitano, Ercole Brusamolino, Maria Giuseppina Cabras, Luigi Rigacci, Monica Balzarotti, Flavia Salvi, Silvia Montoto, Armando Lopez-Guillermo, Erica Finolezzi, Stefano A. Pileri, Andrew Davies, Franco Cavalli, Luca Giovanella, and Peter W.M. Johnson

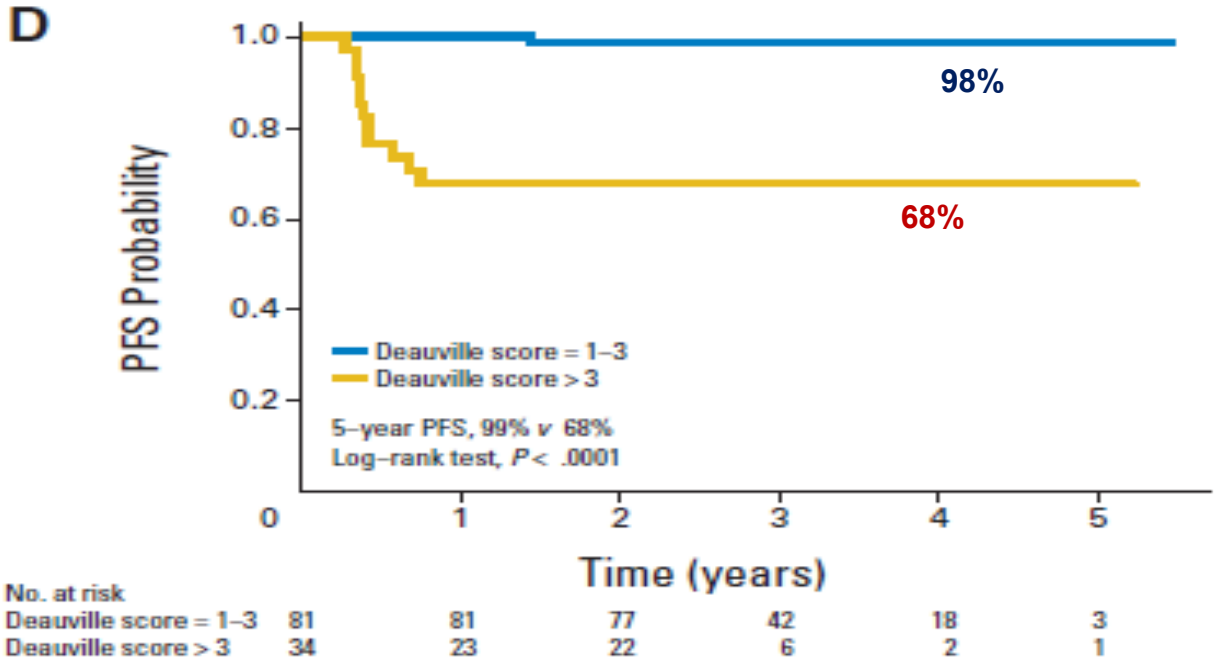
Martelli M et al. J.Clin.Oncol. May 5, 2014

PFS according to PET response defined by the MBP and Liver cut-point

MBP



Liver



- ***Negative post-therapy PET/CT scan*** after R-CHT is significantly ***associated with a longer PFS.***
- ***Liver uptake*** represents ***a more appropriate cut-point*** **than** ***MBP*** to identify those patients with *a significant increased risk of relapse or progressive disease.*

Martelli M et al. J.Clin.Oncol. May 5, 2014

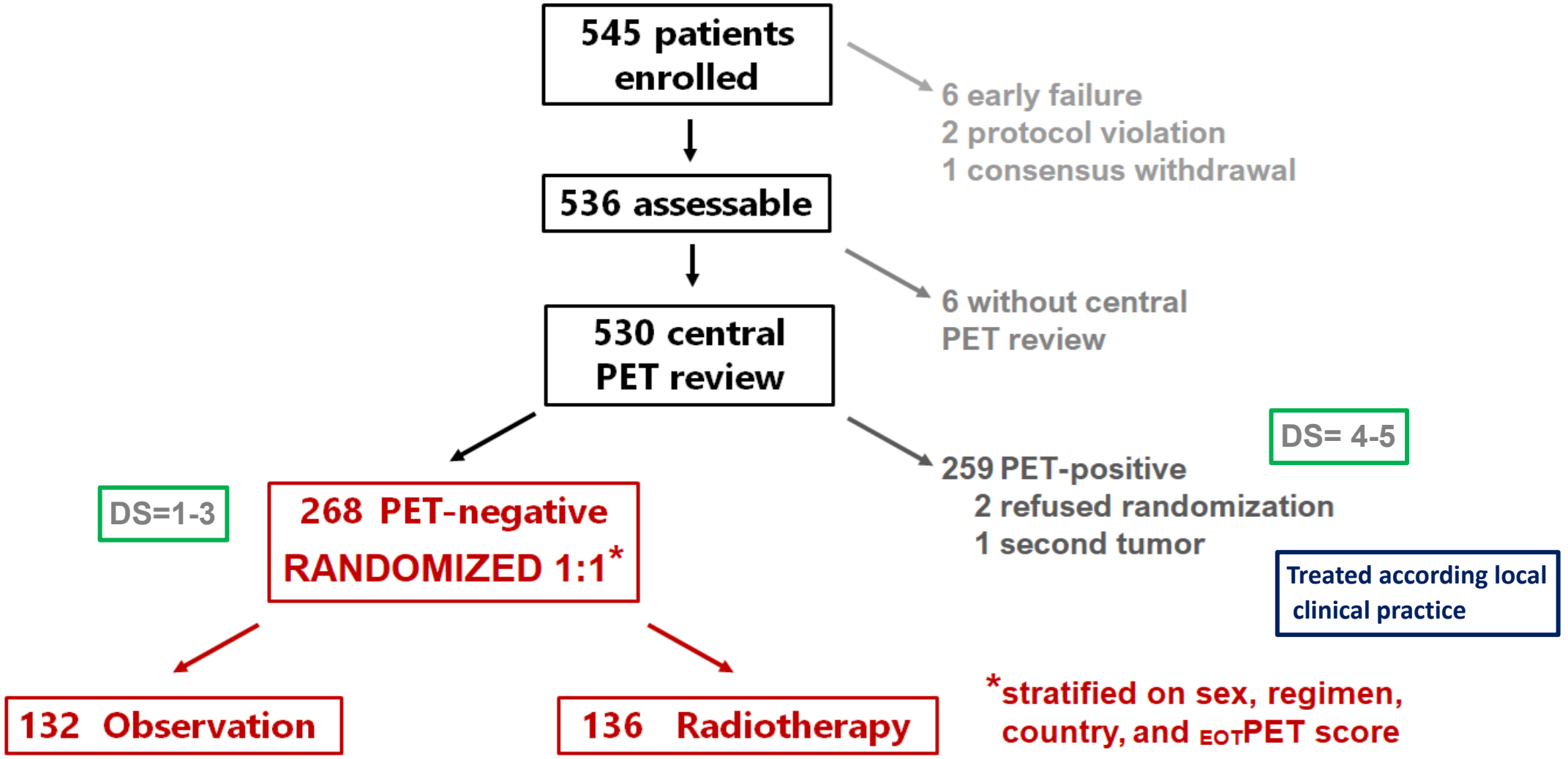
Original Reports | Hematologic Malignancy

Omission of Radiotherapy in Primary Mediastinal B-Cell Lymphoma: IELSG37 Trial Results

Maurizio Martelli, MD[1]; Luca Ceriani, MD[2,3,4]; Giovannino Ciccone, MD, PhD[5]; Umberto Ricardi, MD[6]; Iryna Kriachok, MD[7]; Barbara Botto, MD, PhD[8]; Monica Balzarotti, MD[9]; Alessandra Tucci, MD[10]; Sara Veronica Usai, MD[11]; Vittorio Ruggero Zilioli, MD[12]; Elsa Pennese, MD[13]; Luca Arcaini, MD[14,15]; Anna Dabrowska-Iwanicka, MD[16]; Andrés J.M. Ferreri, MD[17,18]; Francesco Merli, MD[19]; Weili Zhao, MD[20]; Luigi Rigacci, MD[21]; Claudia Cellini, MD[22]; David Hodgson, MD[23]; Codruta Ionescu, MD[24]; Carla Minoia, MD, PhD[25]; Elisa Lucchini, MD[26,27]; Michele Spina, MD[28]; Alexander Fosså, MD[29,30]; Andrea Janikova, MD[31]; Kate Cwynarski, MD[32]; George Mikhaeel, MD[33]; Mats Jerkeman, MD[34]; Alice Di Rocco, MD[1]; Yana Stepanishyna, MD[7]; Umberto Vitolo, MD[8,35]; Armando Santoro, MD[9,36]; Alessandro Re, MD[10]; Benedetta Puccini, MD[21]; Jacopo Olivieri, MD[26]; Luigi Petrucci, MD[1]; Sally F. Barrington, MD[37]; Bogdan Malkowski, MD[38]; Ur Metser, MD[39]; Annibale Versari, MD[40]; Stephane Chauvie, PhD[41]; Jan Walewski, MD[16]; Marek Trneny, MD[42]; Franco Cavalli, MD[2]; Mary Gospodarowicz, MD[23]; Peter W.M. Johnson, MD[43]; Andrew Davies, MD[43]; and Emanuele Zucca, MD[2,4,44]; on behalf of the International Extranodal Lymphoma Study Group (IELSG)

J Clin Oncol. 2024 Dec;42(34):4071-4083.

IELSG-37 prospective randomized International study



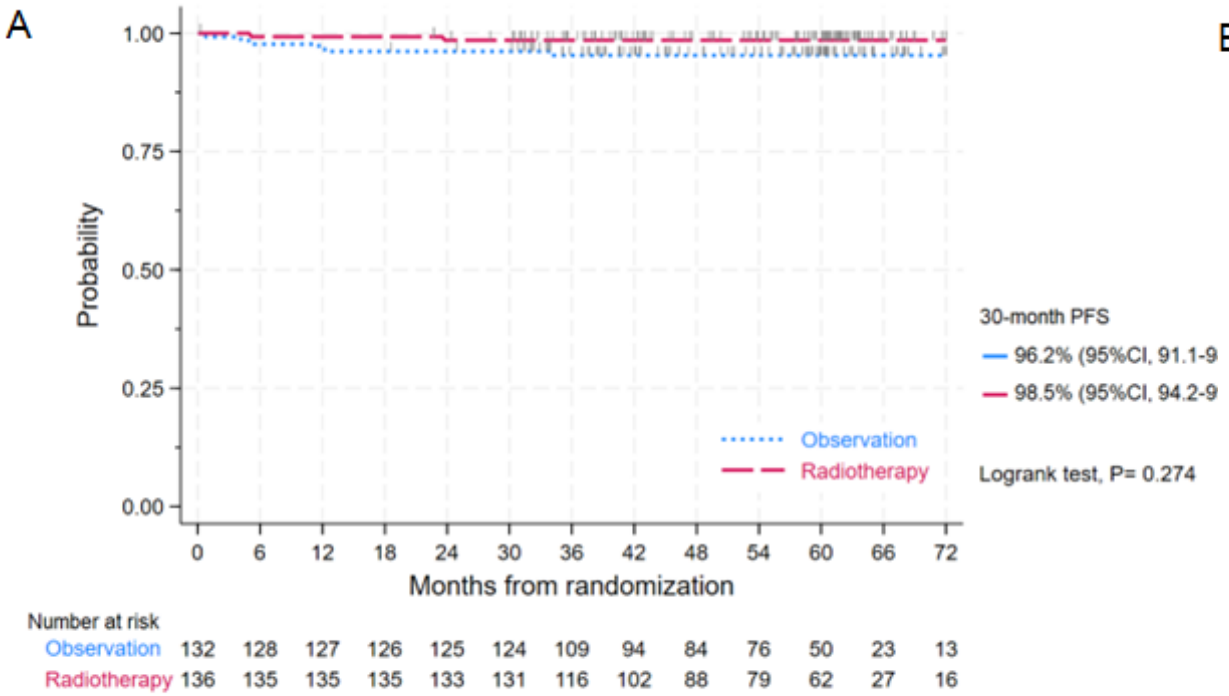
Baseline demographic and clinical features

Feature		Radiotherapy	Observation
Number of patients		**136**	**132**
Median age, years (IQR)		35.5 (29-46.5)	35.5 (29-46.5)
Sex, N (%)	Female	88 (65)	83 (63)
	Male	48 (35)	49 (37)
EGOG PS, N (%)	0	74 (54)	69 (52)
	1	50 (37)	54 (41)
	≥2	12 (9)	9 (7)
Bulky disease, N (%)	>10 cm	89 (65)	79 (60)
Elevated LDH, N (%)	>UNL	91 (67)	88 (67)
R-IPI score, N (%)	Low risk	30 (22)	31 (23)
	Intermediate risk	98 (72)	96 (73)
	High risk	8 (6)	5 (4)

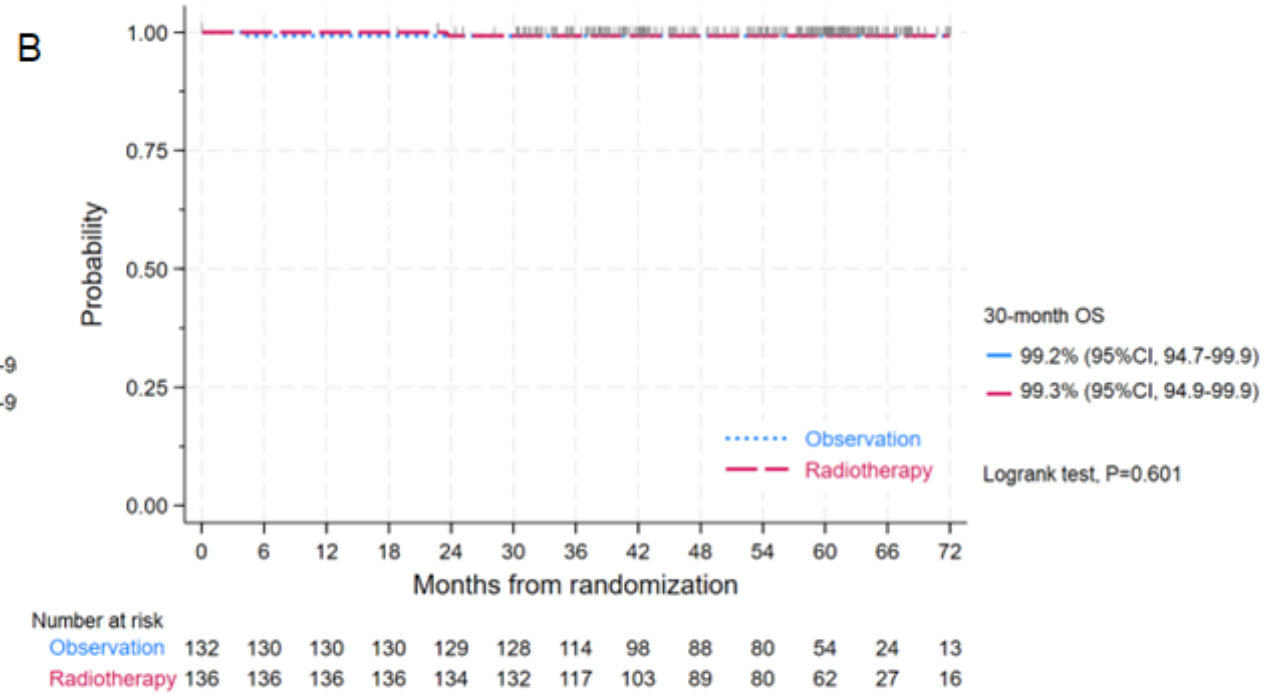
Martelli M et al. J.Clin. Oncol. 2024.

Final results

PFS primary endpoint



OS secondary endpoint



Mediastinal RT may be safely omitted **in patients with CMR (DS=1-3) after front-line immunochemotherapy**

Martelli et al.J.Clin.Oncol 2024

EOT-PET no CMR (DS= 4-5) after front line therapy

EOT- PET DS 4-5 (259 pts out of study) and treated according to local clinical practice

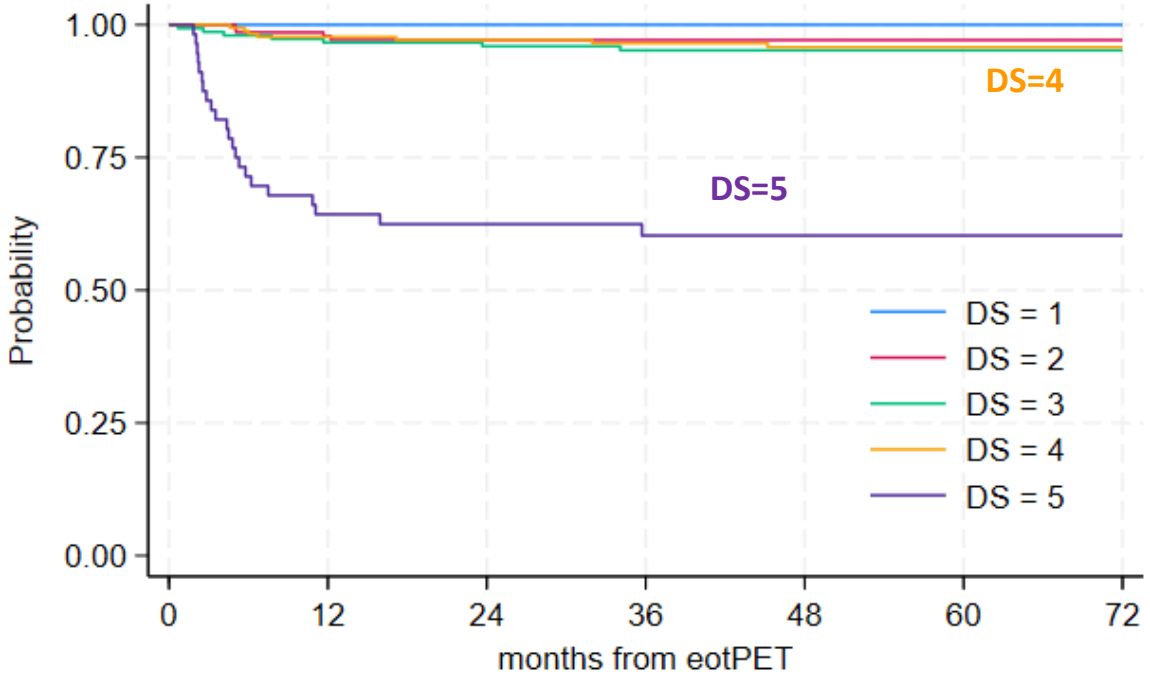
Regimen	Deauville score (5-point scale), N (%)				
	1	2	3	4	5
R-CHOP21	3 (3)	25 (27)	23 (25)	20 (22)	21 (23)*
R-CHOP14	2 (2)	36 (26)	40 (28)	52 (37)	11 (8)
R-V/MACOP-B	4 (3)	33 (20)	53 (32)	61 (37)	15 (9)
DA-EPOCH-R	1 (1)	35 (41)	20 (23)	25 (29)	5 (6)

**P-value = 0.001*

Martelli et al.J.Clin.Oncol 2024

PFS according to DS=4 EOT- PET scan

A



Number at risk

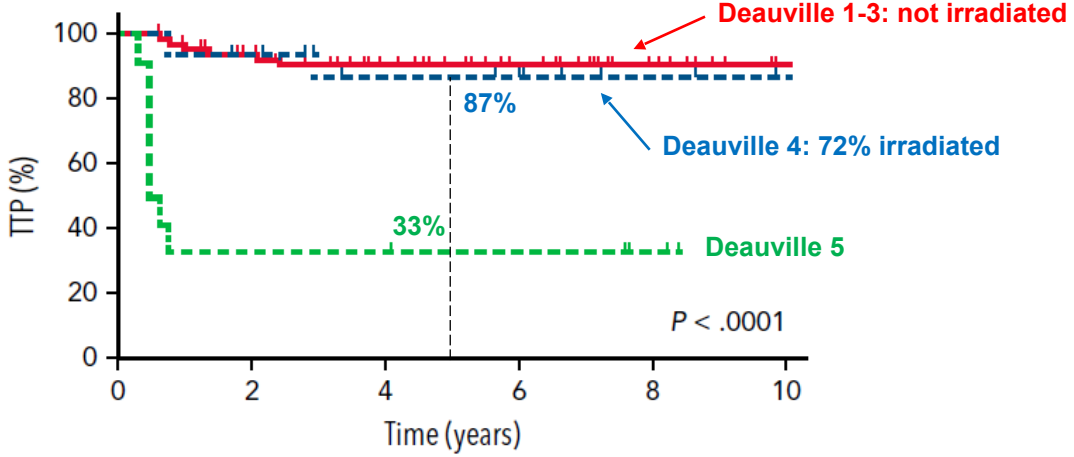
DS1	10	10	10	10	7	4	2
DS2	139	136	134	121	95	64	24
DS3	151	144	140	119	95	62	12
DS4	174	170	169	150	121	69	24
DS5	56	36	34	28	24	10	2

- DS-4 pts outcomes similar to those of pts achieving a CMR (DS 1-3)
- **Consolidation RT DS-4 140/174 (80%)**
- ASCT in 12 of 148 pts with RT
- ASCT in 4 of 15 DS4 pts with no RT

Martelli et al.J.Clin.Oncol 2024

Good outcome of EOT-PET with DS= 4

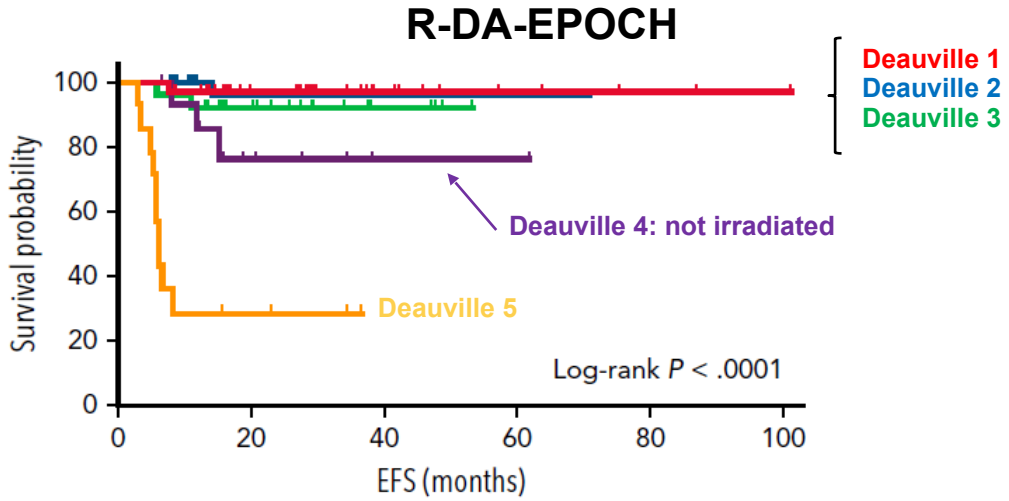
R-CHOP

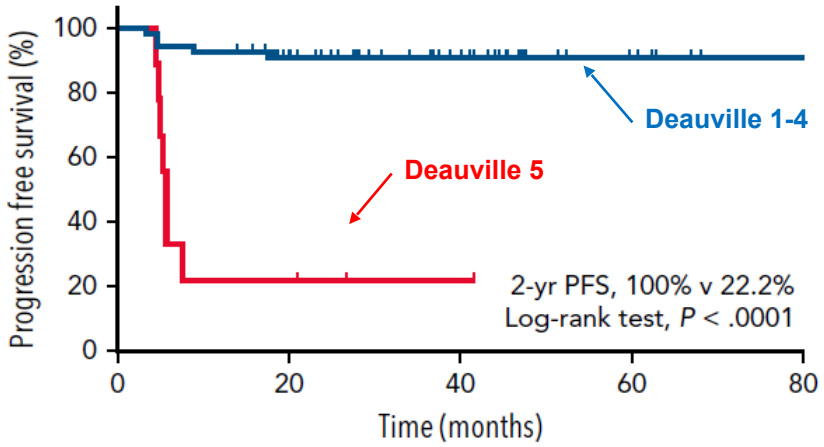


Number at risk = 103						
D1-3, DX	73	63	48	37	24	15
D4	18	17	12	10	7	5
D5	12	5	5	4	3	1

Hayden AR. *Blood*, 2020; 136: 2803-2811

R-DA-EPOCH



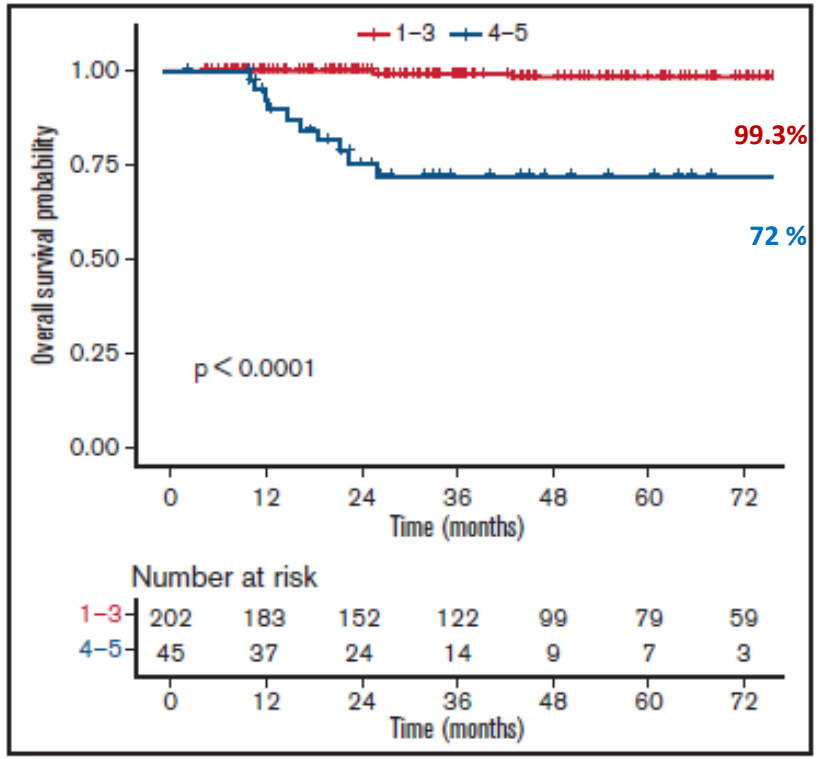


Pinnix CC. *Blood Adv*, 2018; 2: 1334-1343
Giulino-Roth L. Br J Haematol, 2017; 179: 739-747

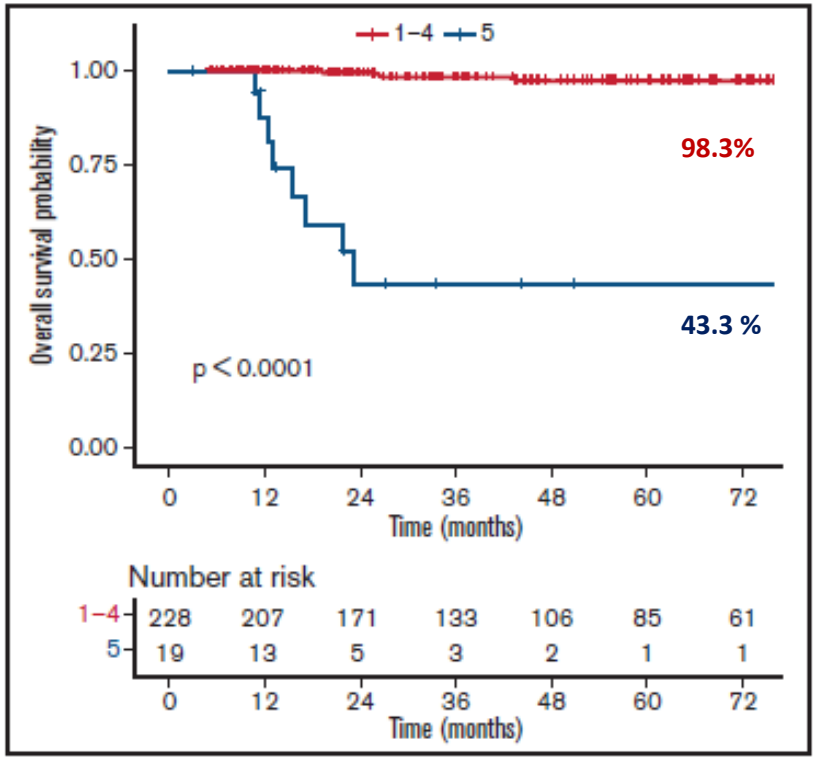
REGULAR ARTICLE
blood advances

Outcomes after first-line immunochemotherapy for primary mediastinal B-cell lymphoma: a LYSA study

OS according EOT–PET DS=1-3 vs DS= 4-5



OS according EOT–PET DS=1-4 vs DS =5



EOT-DS=4 good response **ΔSUVmax EOT-PET>70%)**

EOT-DS=4 insufficient response **ΔSUVmax EOT-PET≤70%).**

Only 17 (5,4%) patients received consolidation radiotherapy

Camus V. *Blood Adv*, 2021; 5: 3862-3872

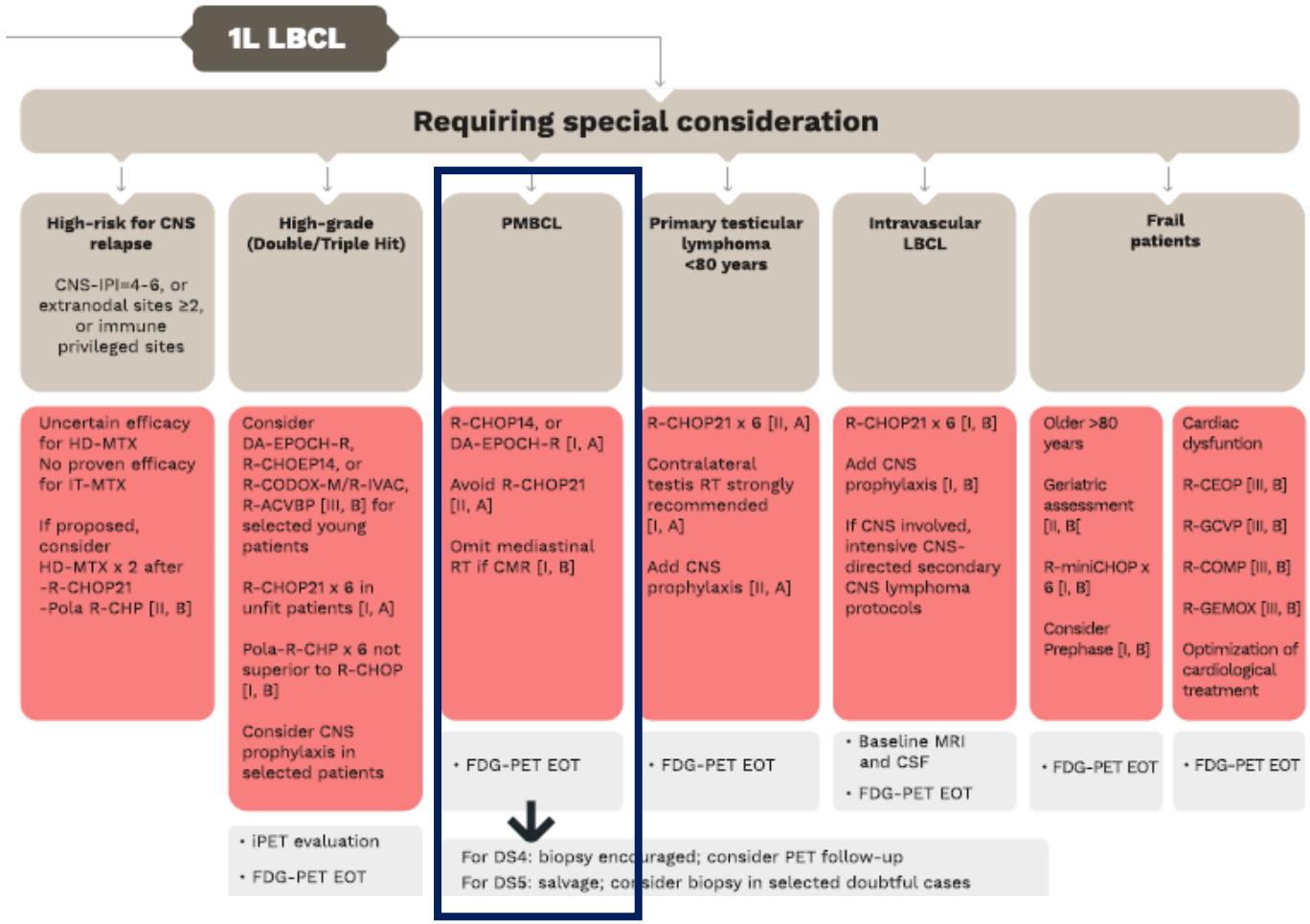
GUIDELINES - EXPERT OPINION

HemaSphere eha

Large B-cell lymphoma (LBCL): EHA Clinical Practice Guidelines for diagnosis, treatment, and follow-up

Received: 13 March 2025 | Accepted: 6 August 2025

DOI: 10.1002/hem3.70207



Recommendation for PMBCL ≤80

- Treat with R-CHOP14 or more intensified regimens including R-M/VACOP-B, R-ACVBP, and DA-EPOCH-R for patients <80 **[I, A]**.
- Omit mediastinal RT in patients achieving CMR after chemoimmunotherapy **[I, A]**.
- Avoid R-CHOP21 in favor of regimens with better outcomes **[II, A]**.
- For DS4 cases, biopsy should be encouraged; consider follow-up with FDG-PET, namely, after DA-EPOCH-R. Consider RT evaluating long-term complications **[II, B]**.
- DS5 cases require salvage treatment **[I, B]**. Consider biopsy in selected doubtful cases.

Outline of discussion

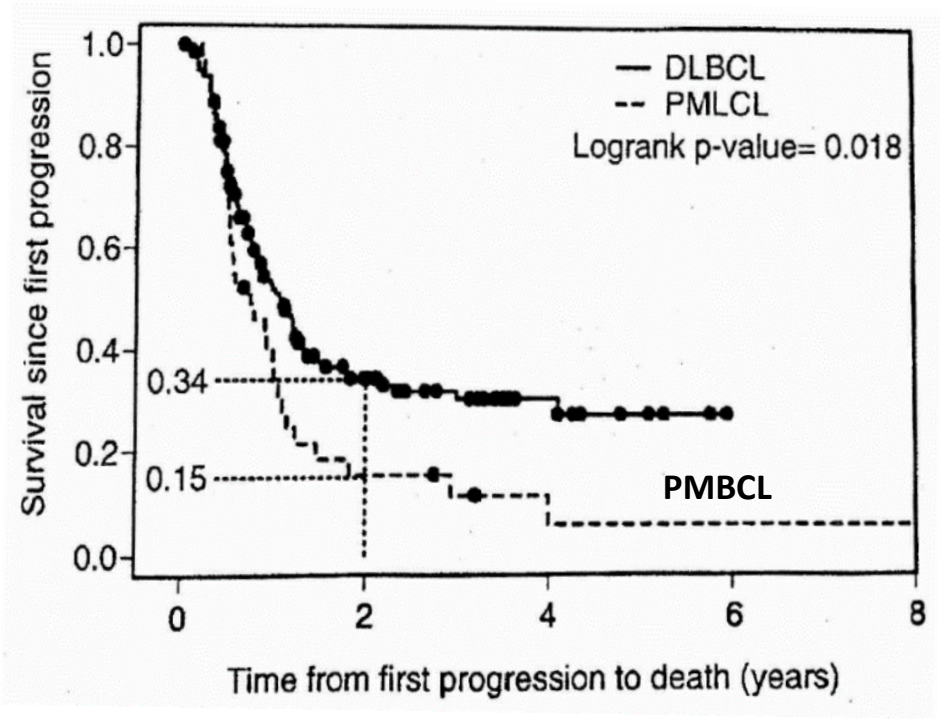
- Front-line chemoimmunotherapy regimen
  (*R-CHOP 21, R-CHOP 14, R-V/MACOP-B or more intensive DA-EPOCH-R)*

- Role of EOT PET-CT scan to evaluate the clinical response and if can drive mediastinal RT

- **Salvage therapy for Relapsed/ Refractory patients**

Salvage therapy in RR / PMBCL

- **Relatively low incidence of relapse (15-20%) occur *within the first 18 months***
- The approach to “salvage” should be similar to that used in DLBCL (HDT/ASCT):
  - Chemosensitive disease after salvage chemotherapy is the most important prognostic factor ;
  - ***Inferior outcomes* if compared to DLBCL: CR (25% *vs* 48%); 2yrs OS after relapse/progression (15% *vs* 34%).**



Sehn LH. Blood, 1998; 91: 717-723

Kuruvilla J. Leuk Lymphoma, 2008; 49: 1329-1336

Anti-PD-1 immunotherapy in PMBCL: rationale

- PMBCL frequently shows amplification or rearrangements of the 9p24.1 *locus* (*programmed death ligand*, *PDL*).

Green MR. *Blood*, 2010; 116: 3268-3277 — Shi M. *Am J Surg Pathol*, 2014; 38: 1715-1723
Twa DDW. *Blood*, 2014; 123: 2062-2065

- This implies an **enhanced expression of the genes *PD-L1*, *PD-L2*** and *JAK2*, which confer an immune-escape capability to the neoplasm.

- The blockade of the PD-1/PD-L1/PD-L2 interaction by means of monoclonal (and not-cytotoxic) **anti-PD-1 antibodies (check-point inhibitor) has a sound rationale in relapsed and refractory disease**.

Green MR. *Blood*, 2010; 116: 3268-3277 — Shi M. *Am J Surg Pathol*, 2014; 38: 1715-1723

Pembrolizumab in Patients With Relapsed or Refractory PMBCL
Data from the KEYNOTE-013 and KEYNOTE-170 Studies

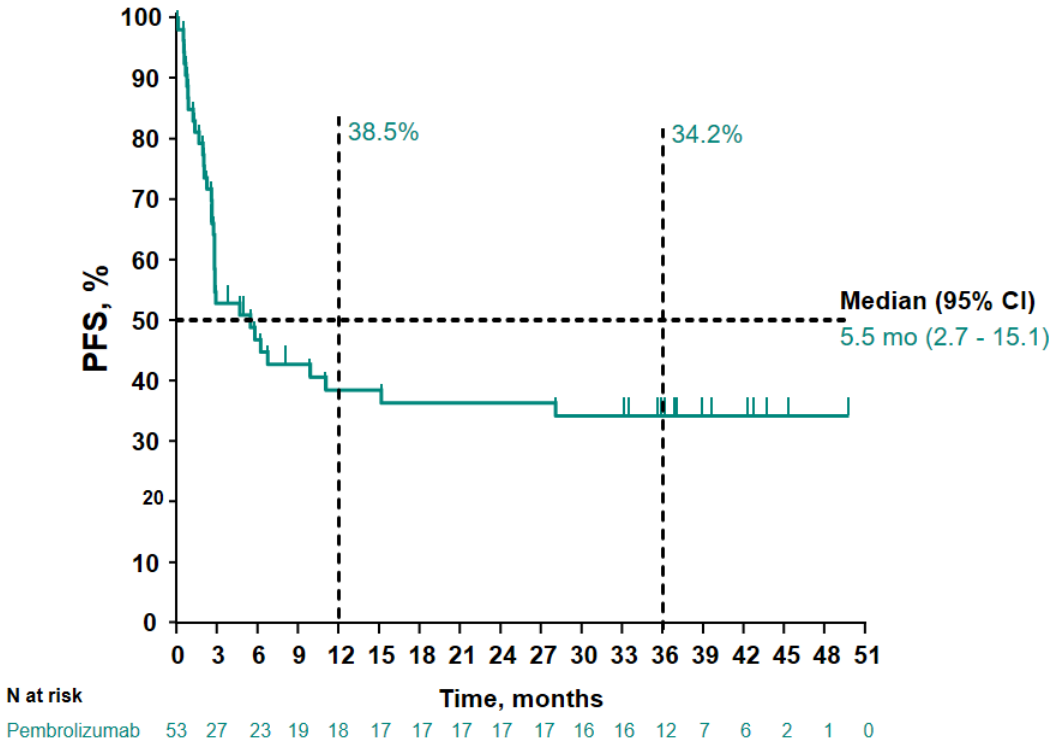
Response, n (%)	KEYNOTE-013 N = 21	KEYNOTE-170 N = 53
Overall response	**10 (48)**	**24 (45)**
Complete response	7 (33)	7 (13)
Partial response	3 (14)	17 (32)
Stable disease	5 (24)	5 (9)
Progressive disease	4 (19)	12 (23)
Non-evaluable/No assessment*	**2 (10)**	**12 (23)**

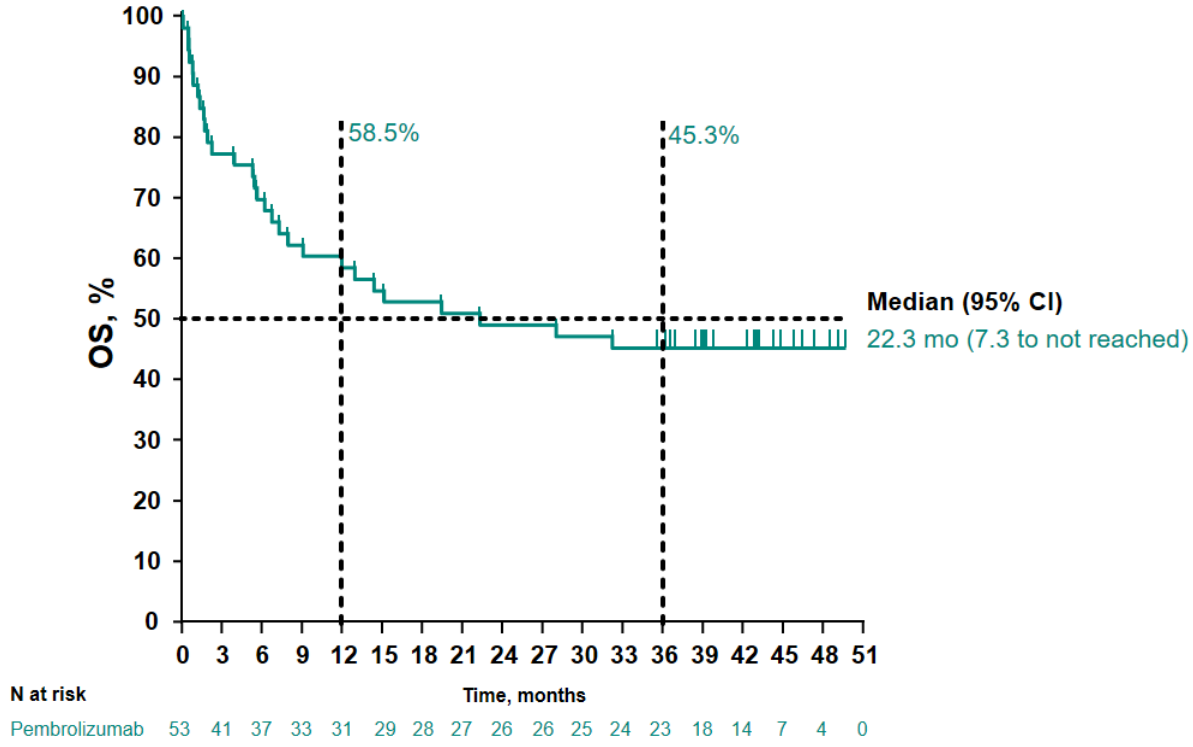
Data cutoff: April 4, 2018 (KN013); April 13, 2018 (KN170).
BICR, blinded independent central review; *Patients with insufficient data for assessment of response.

Zinzani PL. Blood 2017; 130: 267-270 Armand P. J Clin Oncol 2019; 37: 3291-3299

36 months update
KEYNOTE-170

Pembrolizumab in Relapsed or Refractory Primary Mediastinal Large B-Cell Lymphoma





Zinzani PL. *Blood*, 2023; 142: 141-145

Nivolumab Combined With Brentuximab Vedotin for Relapsed/Refractory Primary Mediastinal Large B-Cell Lymphoma: Efficacy and Safety From the Phase II CheckMate 436 Study

Pier Luigi Zinzani, MD, PhD[1]; Armando Santoro, MD[2]; Giuseppe Gritti, MD, PhD[3]; Pauline Brice, MD[4]; Paul M. Barr, MD[5]; John Kuruvilla, MD[6]; David Cunningham, MD[7]; Justin Kline, MD[8]; Nathalie A. Johnson, MD[9]; Neha Mehta-Shah, MD[10]; Thomas Manley, MD[11]; Stephen Francis, MS[12]; Manish Sharma, MD[12]; and Alison J. Moskowitz, MD[13]

Zinzani PL. *J Clin Oncol*, 2019; 37: 3081-3089

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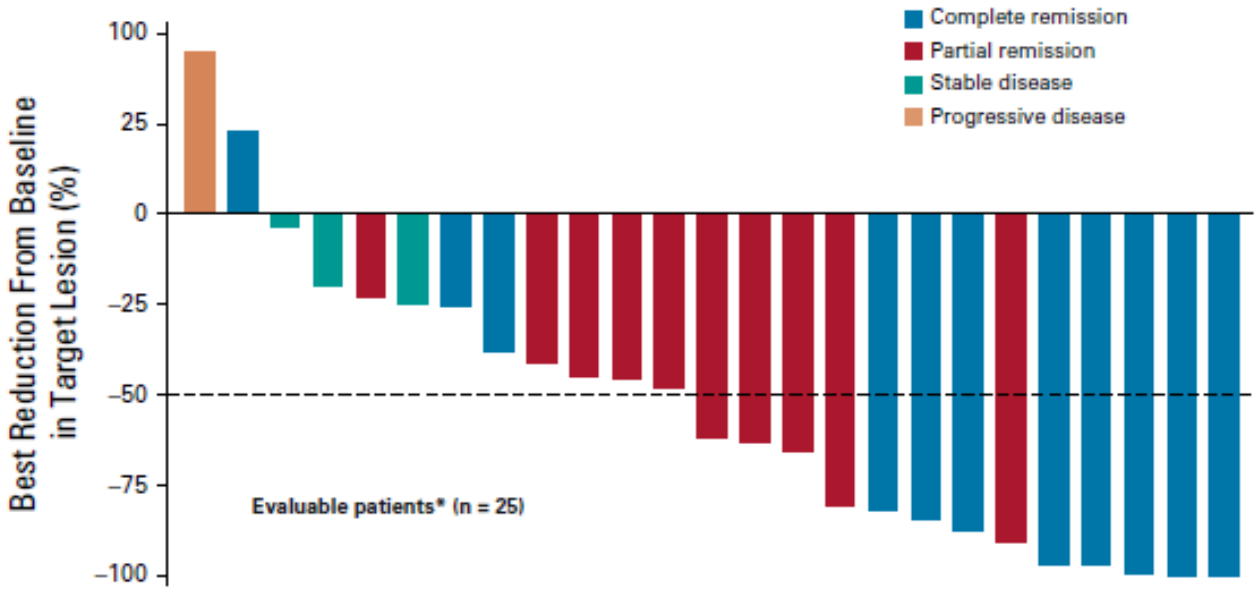
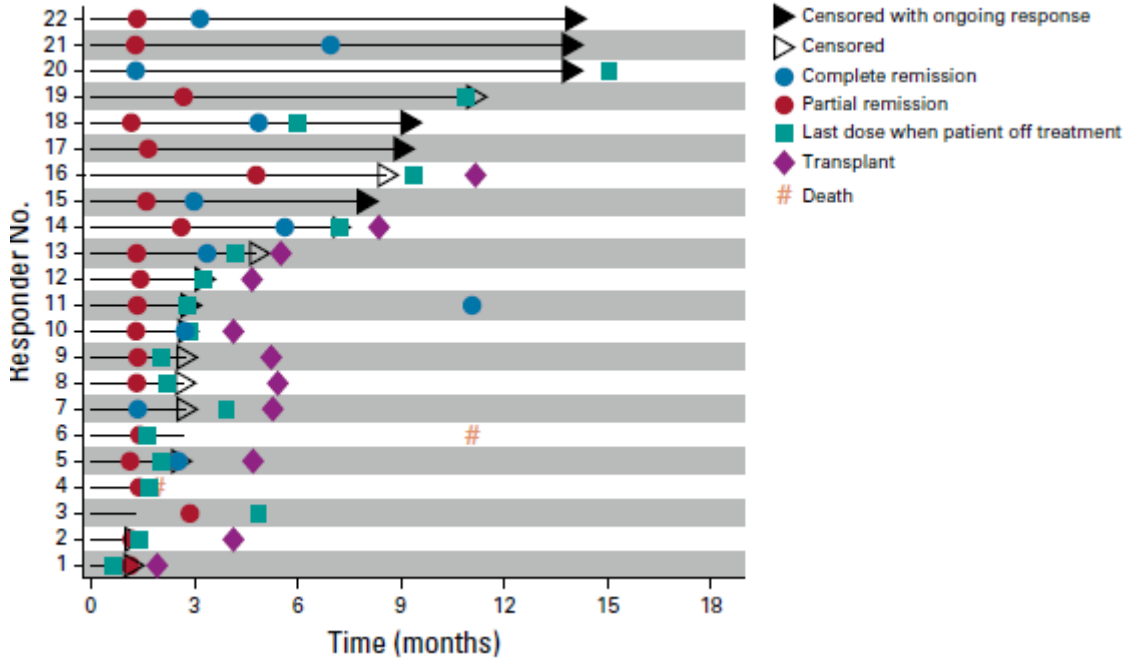
- *30 patients with R/R PMBCL(refractory 67%)*
- *median follow up 11 months*
- *ORR = 22/30 (73%) , CR =11 (37%), PR= 11(37%)*
- *Transplant 11pts (5 ASCT , 6 Allo)*

A

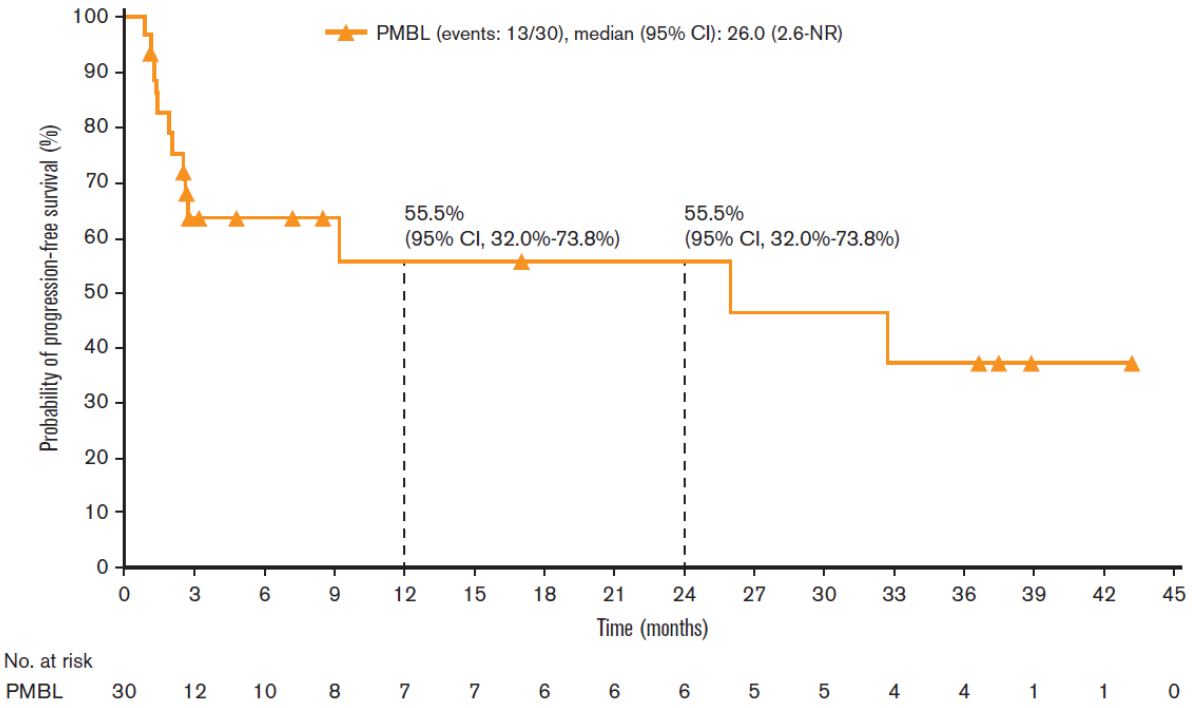


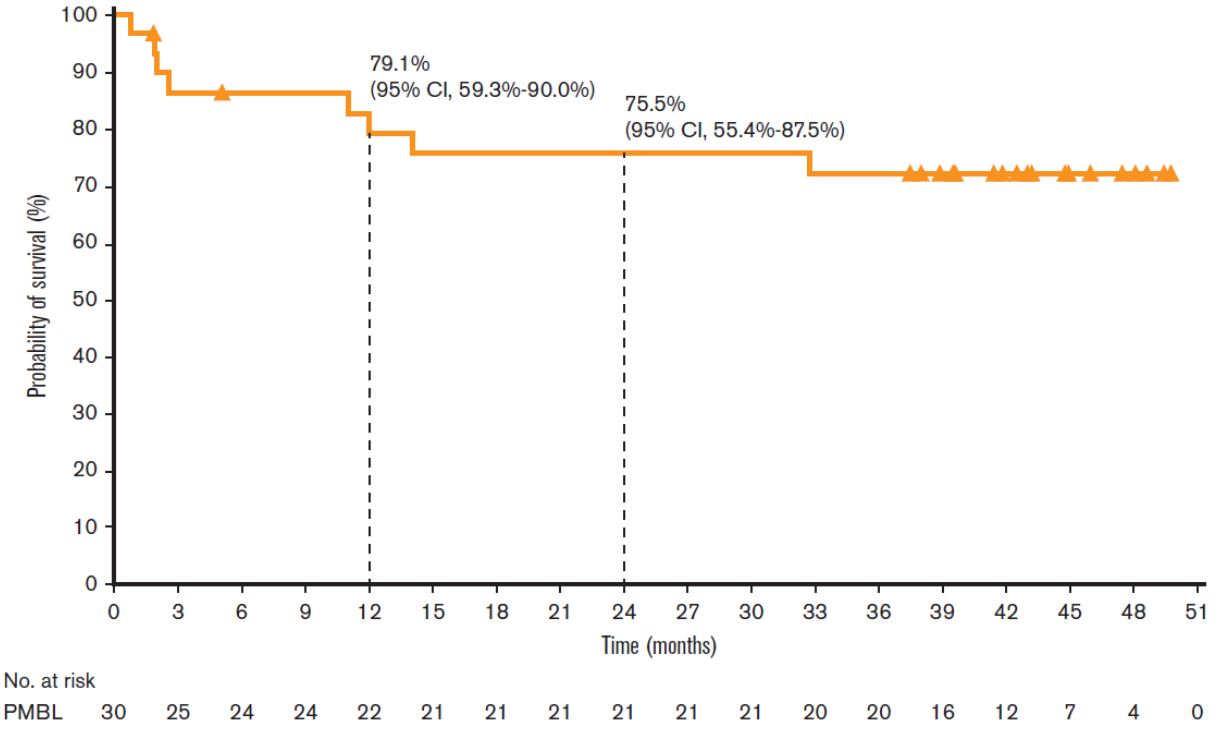


Zinzani PL et al. J. Clin Oncol 2019

Nivolumab Combined With Brentuximab Vedotin for Relapsed/Refractory Primary Mediastinal Large B-Cell Lymphoma: Efficacy and Safety From the Phase II CheckMate 436 Study

Pier Luigi Zinzani, MD, PhD[1]; Armando Santoro, MD[2]; Giuseppe Gritti, MD, PhD[3]; Pauline Brice, MD[4]; Paul M. Barr, MD[5]; John Kuruvilla, MD[6]; David Cunningham, MD[7]; Justin Kline, MD[8]; Nathalie A. Johnson, MD[9]; Neha Mehta-Shah, MD[10]; Thomas Manley, MD[11]; Stephen Francis, MS[12]; Manish Sharma, MD[12]; and Alison J. Moskowitz, MD[13]





12/22 (55%) responders proceeded to transplantation
50% of them were transplanted in CR

Zinzani PL. *Blood Adv*, 2023; 7: 5272-5280

RESEARCH LETTER

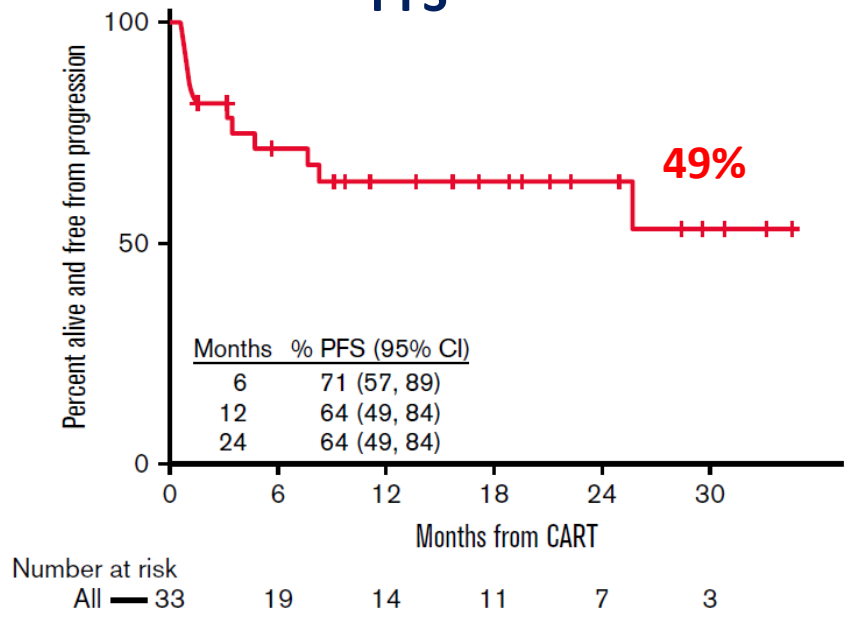
blood advances

Check for updates

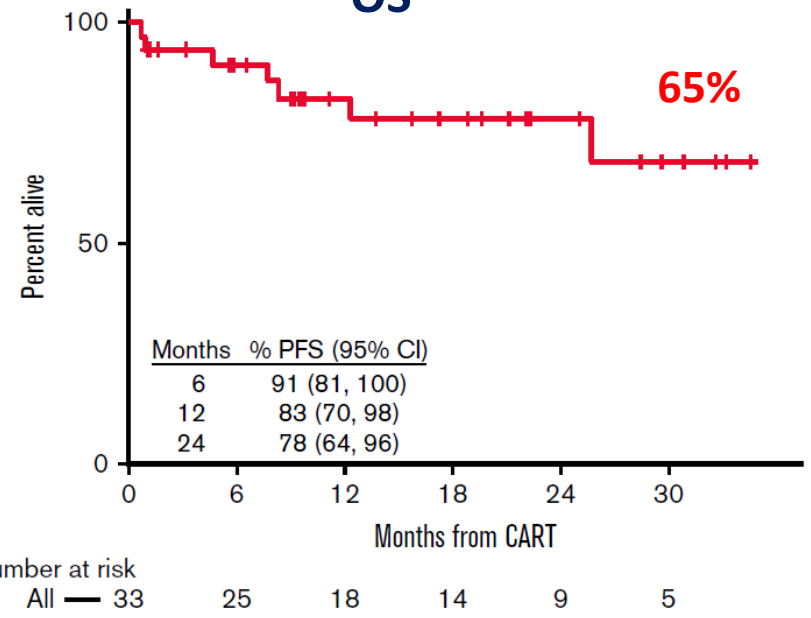
TO THE EDITOR:

Real-world outcomes of axicabtagene ciloleucel in adult patients with primary mediastinal B-cell lymphoma

PFS



OS



- **33 patients**
- **42% with bulky disease**
- **67% previously irradiated**
- **30% with prior autologous transplant**
- **Median 3 (1-9) lines of therapy**
- **ORR = 25 (76%) CRR= 22(67%)**

Crombie JL. Blood Adv, 2021; 5: 3563-3567

CART-SIE study

A multicenter prospective observational study on Chimeric Antigen Receptor (CAR) T-cell therapy for lymphoma: monitoring feasibility, efficacy, toxicity and biomarkers in a real life setting.

PI: Paolo Corradini (Milano)

659 patients enrolled and leukapheresed

97 not infused
- Rapidly progressive disease
- Severe infection
- Persistent complete response
- Manufacturing failure
- Manufacturing ongoing

562 patients infused

556 evaluable*

* Data entry complete in e-crf for response at day +30

Axi-cel
n = 250

- **PMBCL** n = 70
- **DLBCL** n = 190

Tisa-cel
n = 229

Brexu-cel
n = 67

Patient flow: March 2019 – July 2023

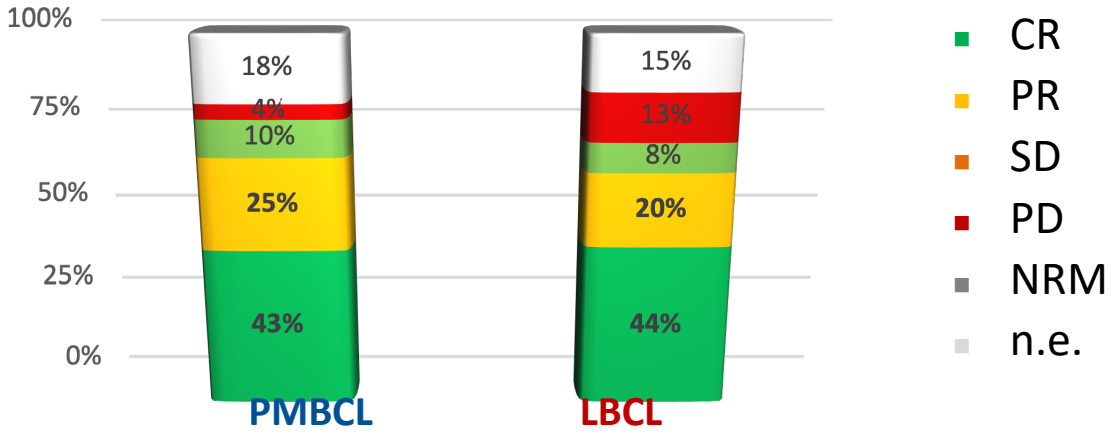
Chiappella A, et al Leukemia 2024

Response (day +30 and + 90), PFS and OS after CAR-T infusion

median follow up 12.01 months

Day + 30: ORR 68% vs. 64%

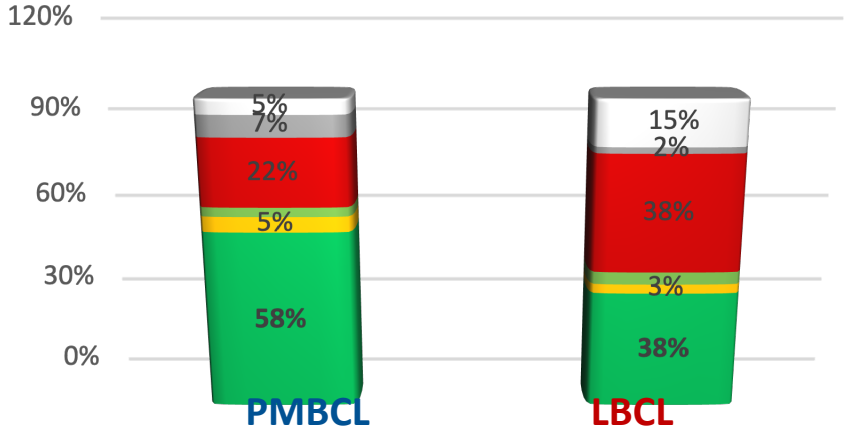
p 0.2018



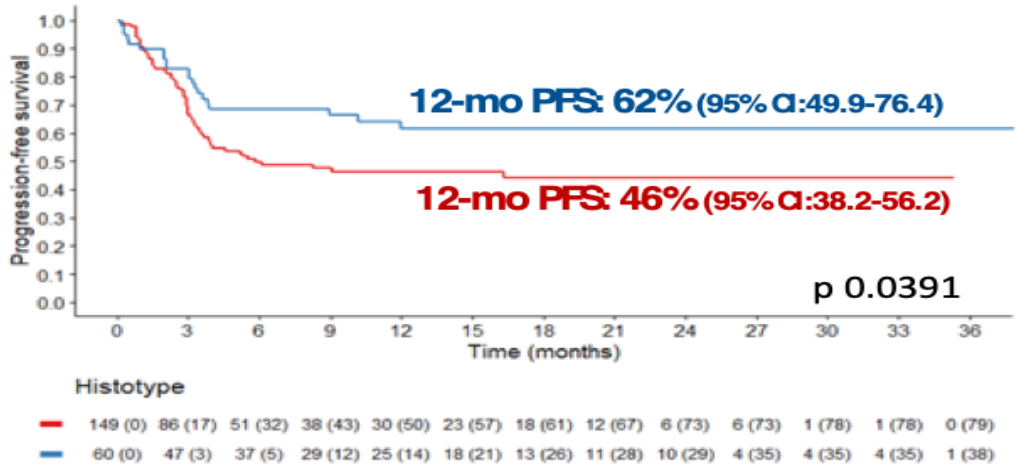
CR
PR
SD
PD
NRM
n.e.

Day + 90: ORR 63% vs. 41%

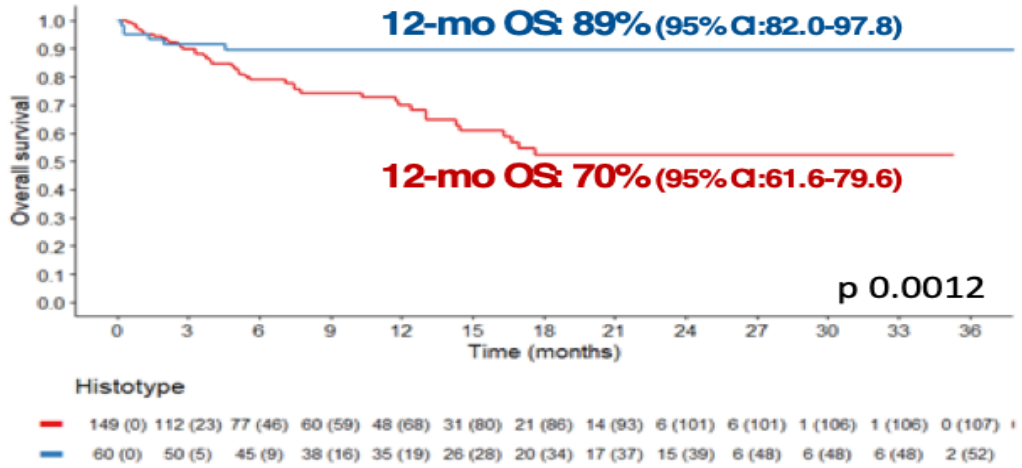
p 0.0183



PFS
PMBCL vs. LBCL

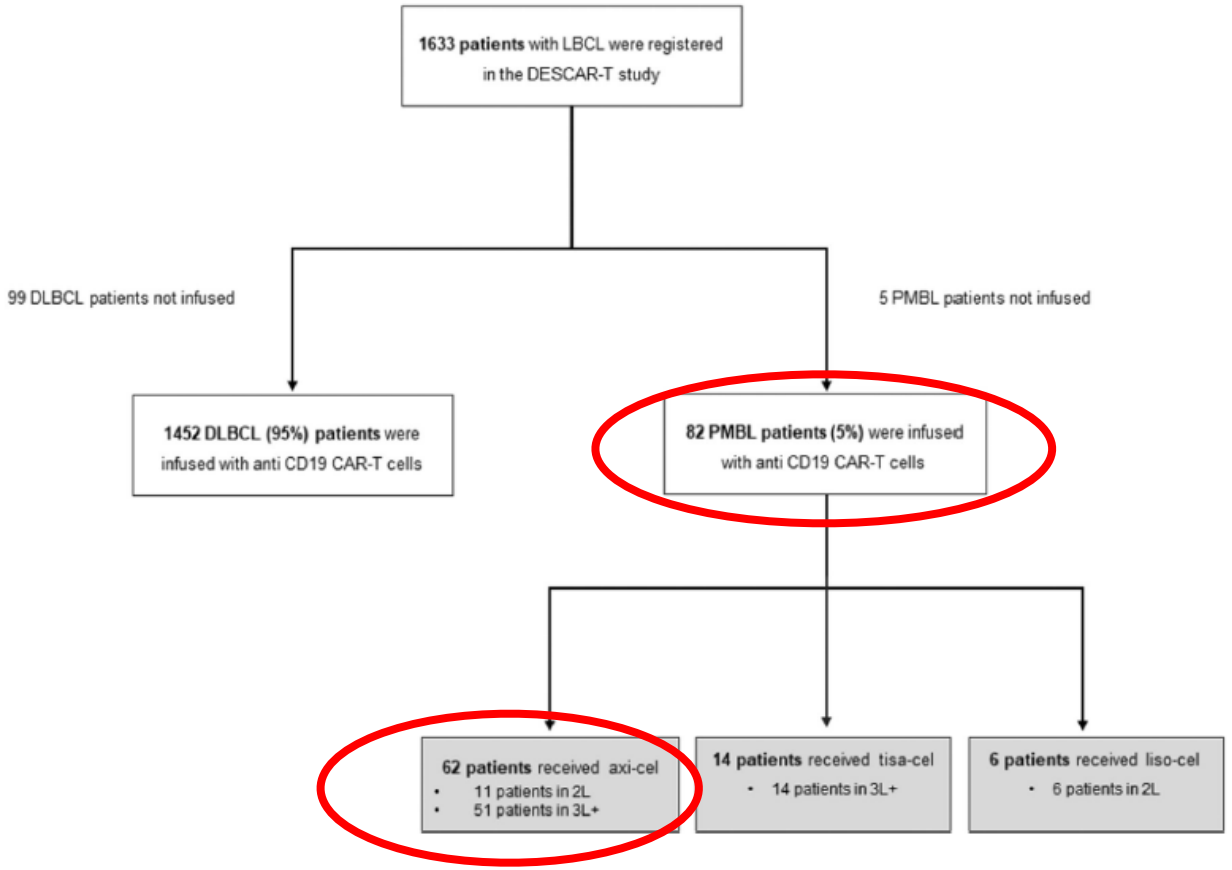


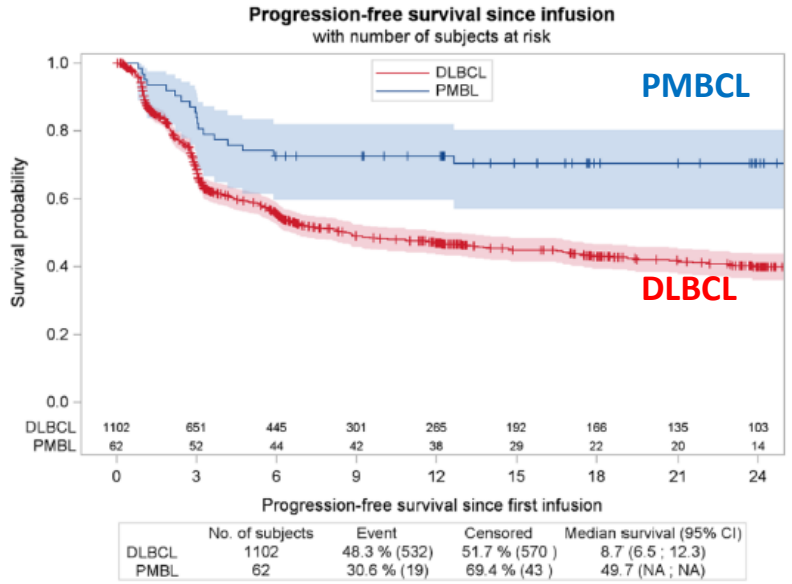
OS
PMBCL vs. LBCL

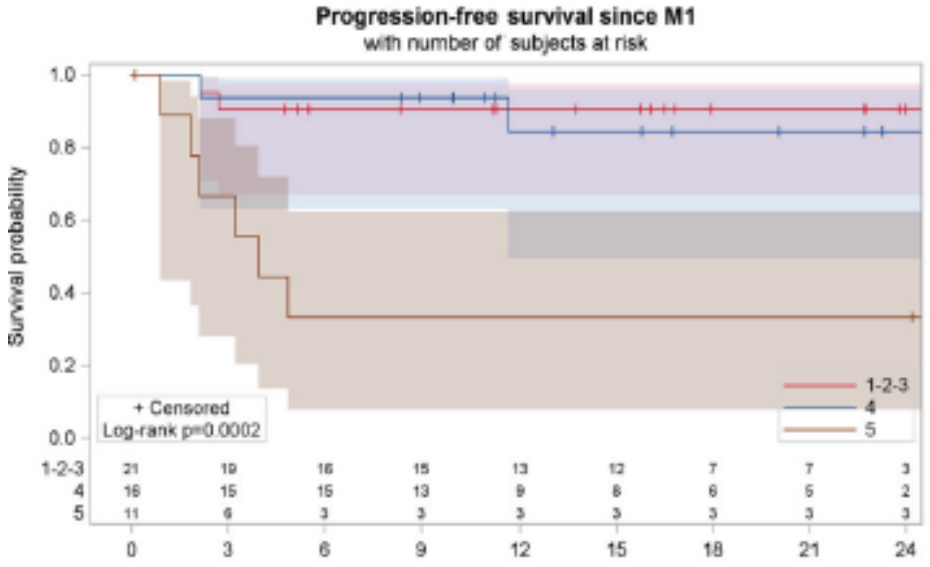


Chiappella A, et al Leukemia 2024

Outcomes of patients with relapsed or refractory primary mediastinal B-cell lymphoma treated with anti-CD19 CAR-T cells: CARTHYM, a study from the French national DESCAR-T registry





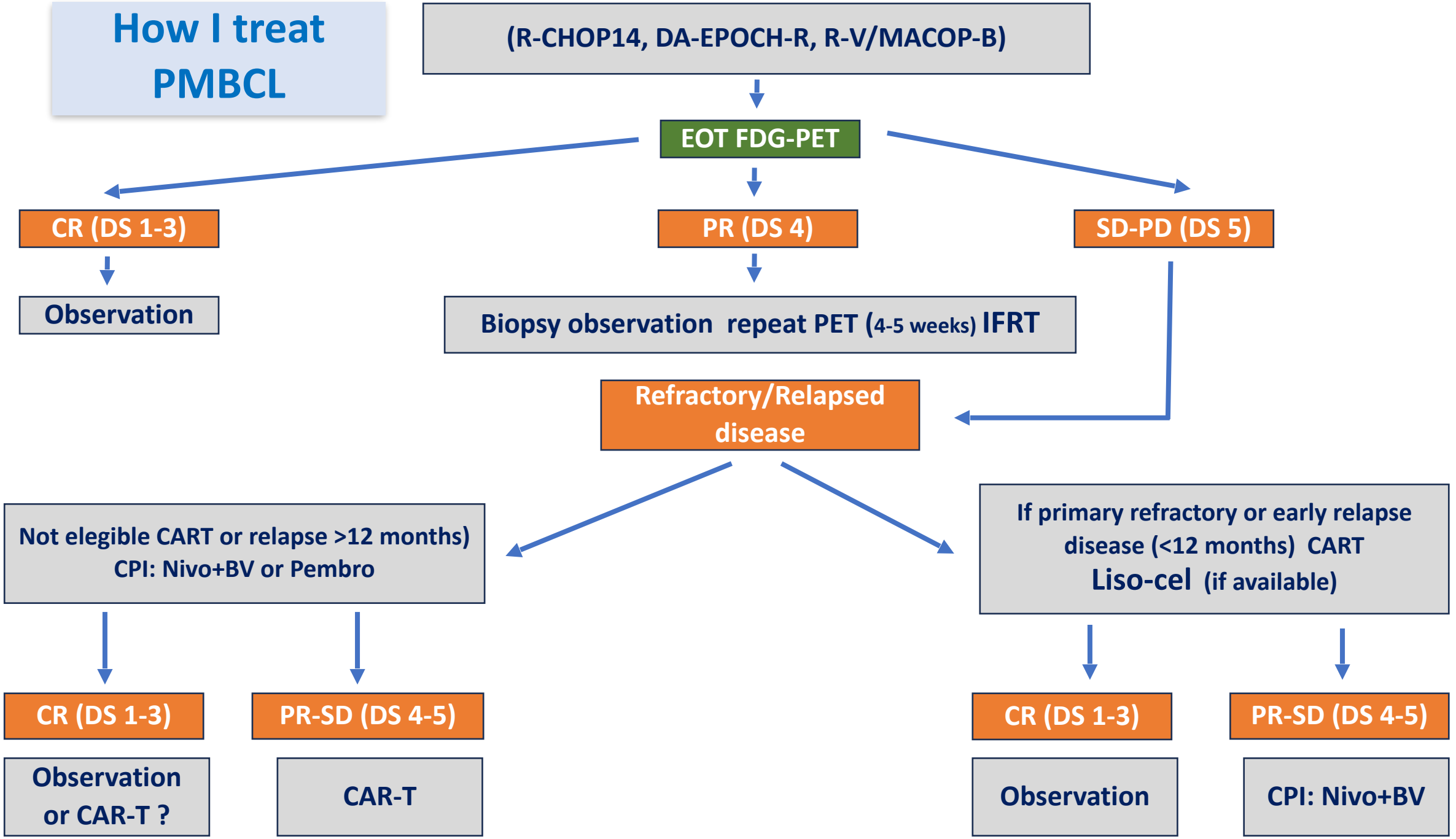


Galtier J. et al. Hemasphere 2024

Take home messages

- **PMBCL** is a curable disease in nearly 80% of cases. Anthracycline and rituximab-containing regimens are the mainstay of first-line approaches.
- **R-CHOP21** is a suboptimal regimen and **should not be recommended** as front-line therapy .
- **Dose-dense R-CHOP14, R-V/MACOP-B** or **DA-EPOCH-R** regimens have similar outcome.
- **Consolidation RT** in patients with an **EOT-PET scan (DS=1-3**) should be **definitively be omitted** (IELSG-37)
- **The outcome** and the **role of consolidative RT** in patients with **EOT-DS=4** is still debated. A personalized approach to balance the risk vs benefit of surveillance PET or consolidation RT should be discussed for each patient. Future studies should be planned considering **EOT-CT-DNA** and **ΔSUVmax EOT-PET >70%**
- The poor prognosis of **RR-PMBCL** and **EOT-DS=5** is nowadays improved by **CART** or **check-point inhibitor (CPI)**
- **CART** (Lisocel), if available, should be considered the best option as second line for early RR-PMBCL (<12 months)
- **Pembro or Nivo+ BV (CPI)** should be considered for patients **not eligible** or as **bridge therapy** to CART

How I treat PMBCL



Grazie per l'attenzione …..

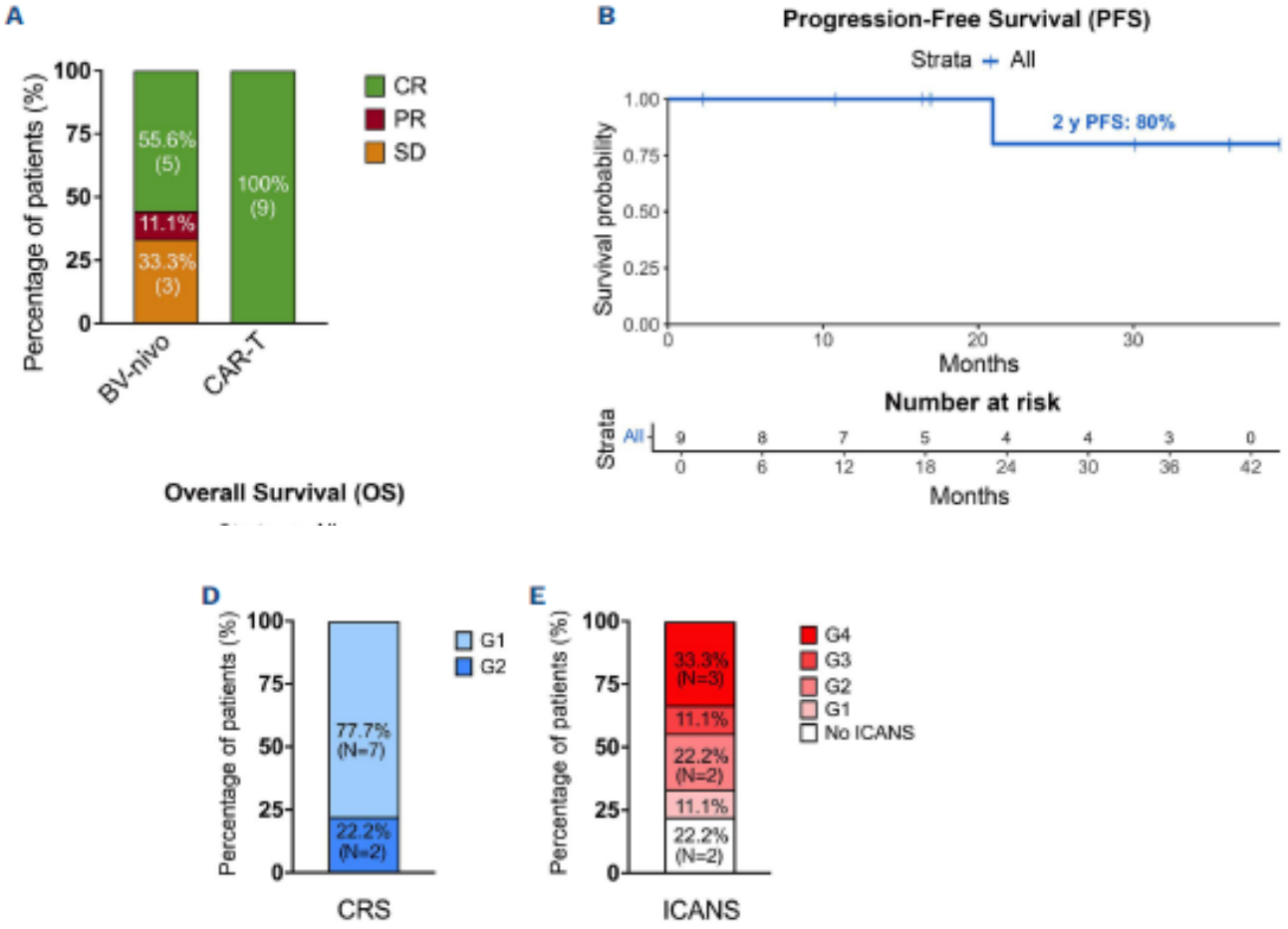
SAPIENZA UNIVERSITÀ DI ROMA

FONDAZIONE ITALIANA LINFOMI

SISTEMA SANITARIO REGIONALE
AZIENDA OSPEDALIERA UNIVERSITARIA POLICLINICO UMBERTO I

Brentuximab vedotin plus nivolumab as bridging therapy to CAR T-cells in relapsed/refractory primary mediastinal B-cell lymphoma

Characteristics	Values
N of patients	9
Male sex, N (%)	5 (55.6)
Age at BV-nivolumab start, years, median (range)	37 (21-75)
Stage at BV-nivolumab start, N (%) I II III IV	 1 (11.1) 2 (22.2) 0 (0) 6 (66.7)
Refractory to last line, N (%)	9 (100)
Time to relapse/progression after 1st line, months, median (range)	9 (3-15)
N of previous lines, median (range)	2 (2-4)
Prior ASCT, N (%)	2 (22.2)
Prior radiotherapy, N (%)	1 (11.1)
CAR-HEMATOTOX score, median (range)	1 (0-4)
N of BV-nivolumab cycles, median (range)	2 (1-3)
Time from diagnosis to CAR-T, months, median (range)	13 (7-35)
Time from leukapheresis to CAR-T infusion (vein-to-vein time), days, median (range)	45 (29-83)

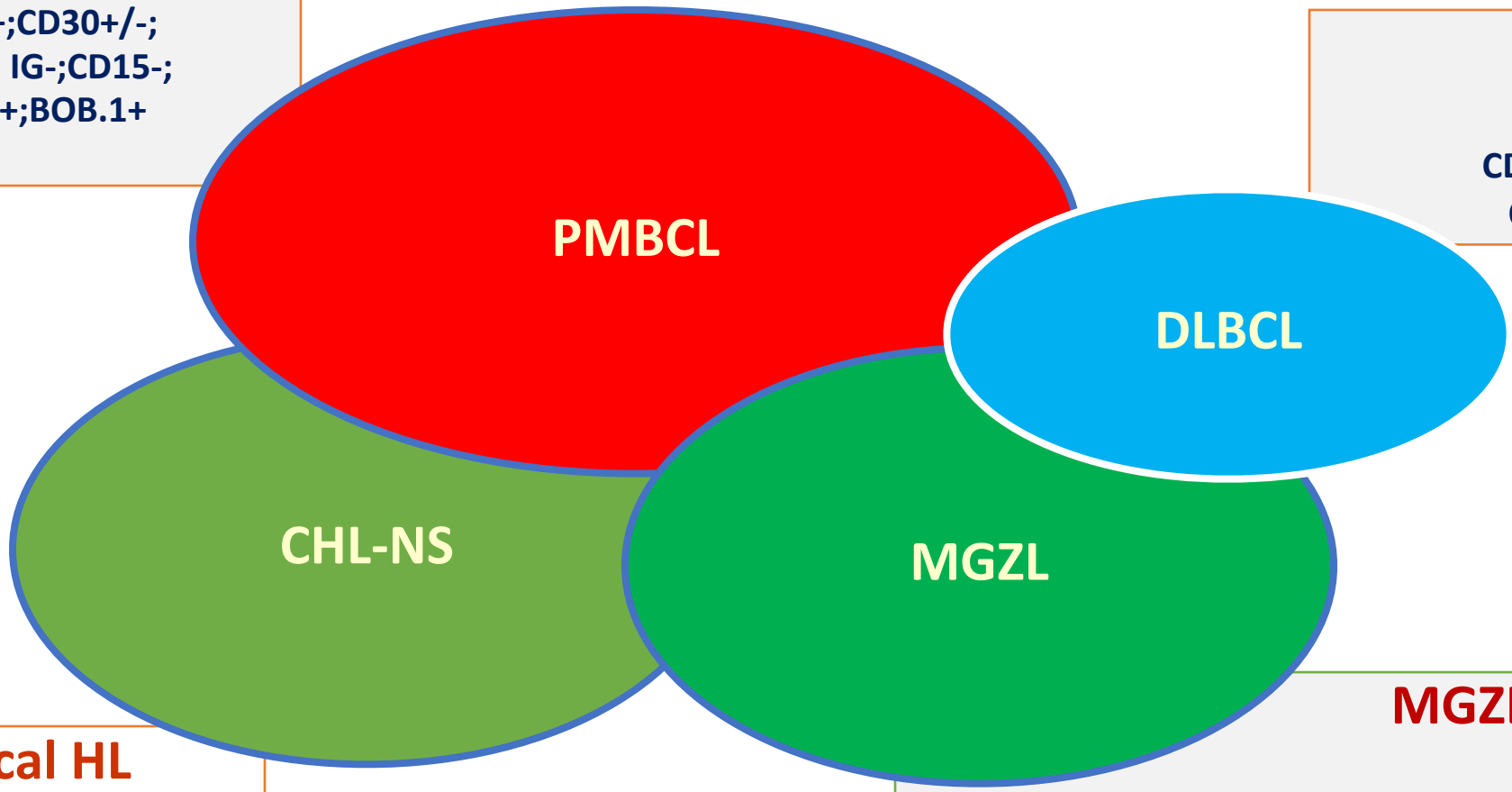


Santoro A et al Haematologica letter 2026

Mediastinal Lymphoma: diagnosis

PMBCL

CD20+;CD30+/-;
CD23+; IG-;CD15-;
OCT2+;BOB.1+



DLBCL

CD20+;CD30-;
CD23-; IG+; CD15-;
OCT2 +;BOB.1+

Classical HL

CD20-/+ weak; CD30+;
CD15+; OCT2- BOB.1-

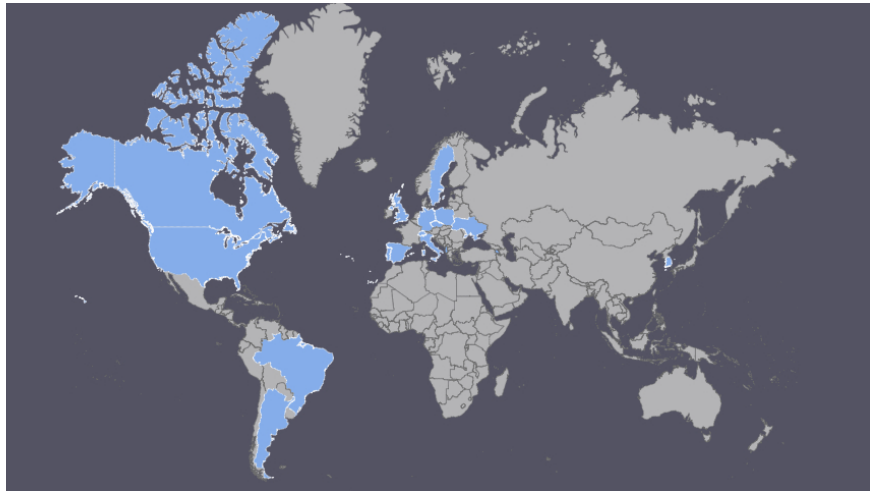
MGZL

HL morphology	*PMBCL morphology*
CD20+,CD15-	CD20-,CD15+
CD30+	CD30+,
OCT2+,BOB 1 +	OCT2+,BOB 1 +

IELSG-37 prospective randomized International study

545 patients with PMBCL enrolled from **74 centres in 13 countries**

- **Italy 380**
- UK 44
- Ukraine 25
- Switzerland 17
- Poland 15
- Czech Republic 14
- China 12
- Norway 11
- Canada 10
- Sweden 7
- Germany 5
- USA 3
- Portugal 2



Accrual
September 2012
August 2019