Unmet challenges in high risk hematological malignancies: from benchside to clinical practice

Scientific Board:
Marco Ladetto (Alessandria)
Umberto Vitolo (Turin)

Turin, September 13-14, 2018
Torino Incontra Centro Congressi

High Risk Aggressive Lymphoma.

How I treat DLBCL in relapse.

Annalisa Chiappella

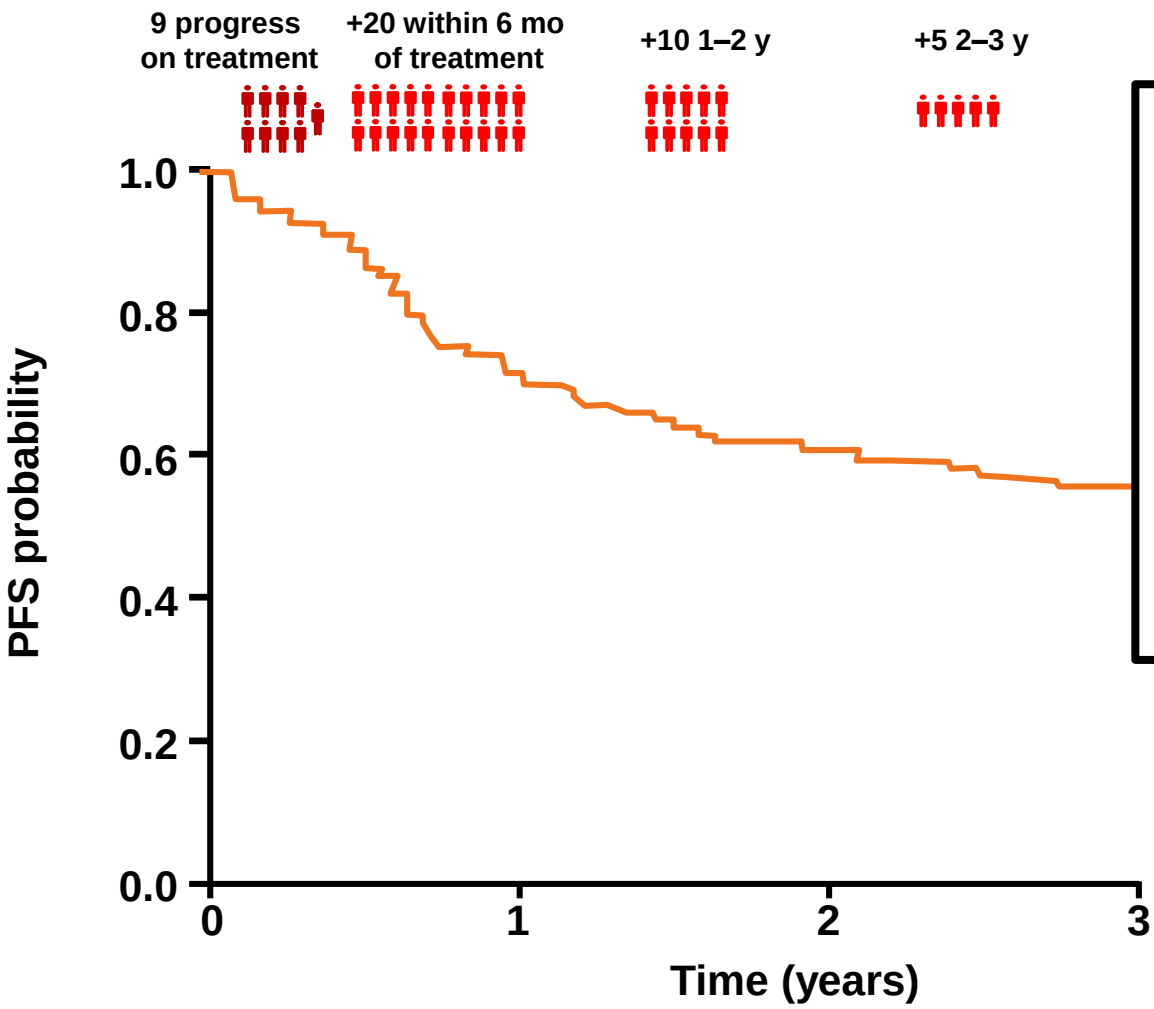
Hematology

AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

Disclosures: Annalisa Chiappella

Research Support/P.I.	N/A
Employee	N/A
Consultant	N/A
Major Stockholder	N/A
Conferences/Educational Activities	Amgen, Celgene, Janssen, Nanostring, Roche, Teva
Scientific Advisory Board	Celgene, Janssen

GELA LNH-98.5: 87% of all progression events occurred in the first 3 years



In GELA-LNH 98.5 – all patients

After 3 years:

56/100 patients were progression-free and may be cured

44/100 patients had progressed or died

Coiffier B, et al. Blood 2010; 116:2040–2045.

How I treat DLBCL in relapse?

clinical practice guidelines

Annals of Oncology 26 (Supplement 5): v116–v125, 2015
doi:10.1093/annonc/mdv304

Diffuse large B-cell lymphoma (DLBCL): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

H. Tilly[1], M. Gomes da Silva[2], U. Vitolo[3], A. Jack[4], M. Meignan[5], A. Lopez-Guillermo[6], J. Walewski[7], M. André[8], P. W. Johnson[9], M. Pfreundschuh[10] & M. Ladetto[11], on behalf of the ESMO Guidelines Committee*

Chemosensitive disease:

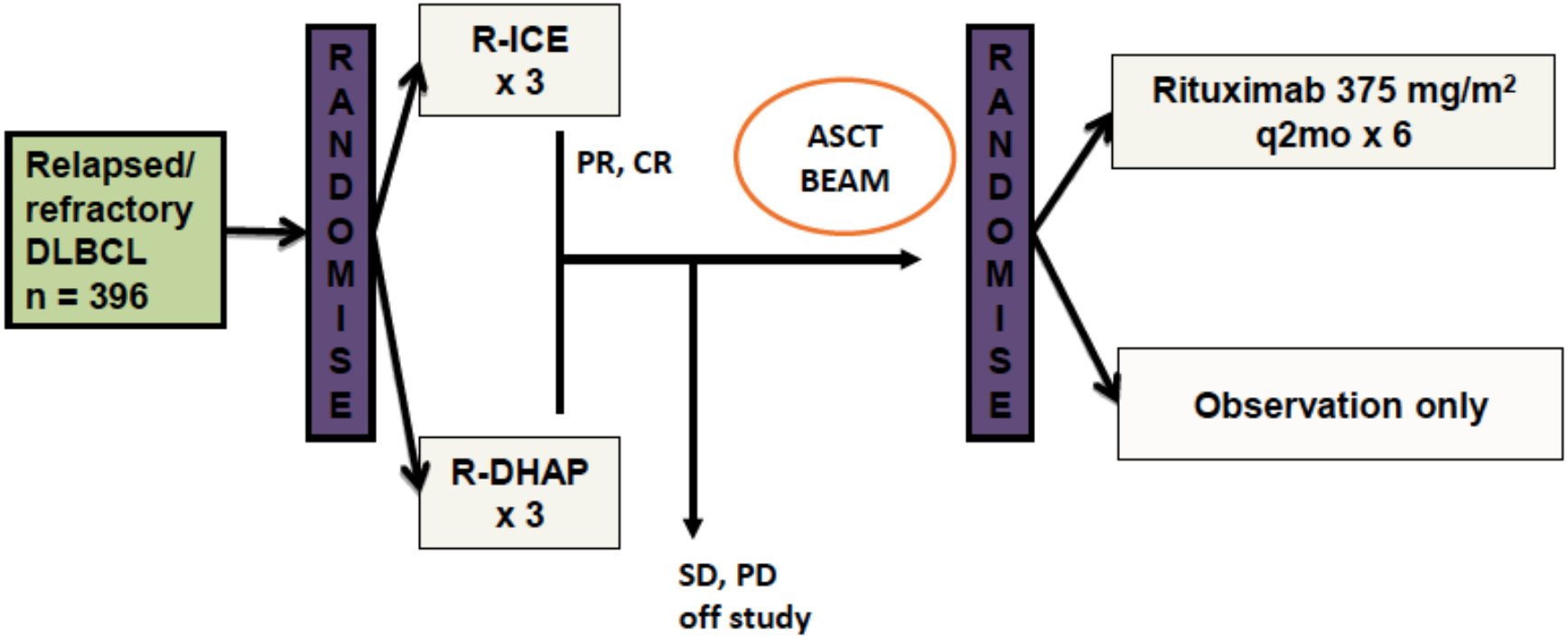
- ✓ **Autologous stem cell transplant**

«In patients aged <65–70 years with good PS and no major organ dysfunction, salvage regimens with rituximab and chemotherapy followed, ***in responsive patients****, by HDC and ASCT, are recommended [II, A]»*

High Dose Chemotherapy plus ASCT: CORAL trial experience

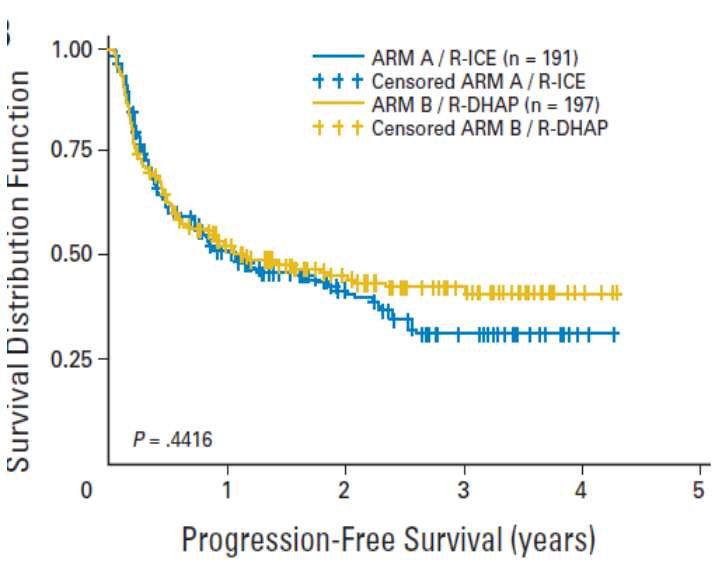
Rituximab Maintenance Therapy After Autologous Stem-Cell Transplantation in Patients With Relapsed CD20 Diffuse Large B-Cell Lymphoma: Final Analysis of the Collaborative Trial in Relapsed Aggressive Lymphoma

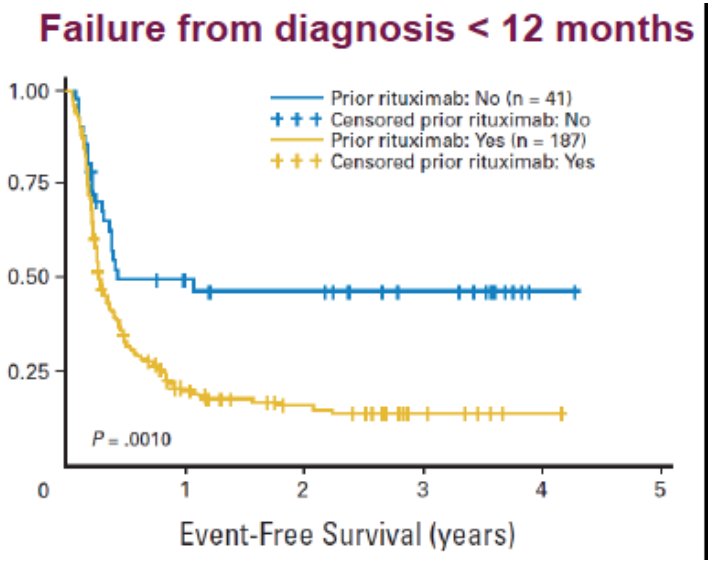
Christian Gisselbrecht, Norbert Schmitz, Nicolas Mounier, Devinder Singh Gill, David C. Linch, Marek Trneny, Andre Bosly, Noel J. Milpied, John Radford, Nicolas Ketterer, Ofer Shpilberg, Ulrich Dührsen, Hans Hagberg,David D. Ma, Andreas Viardot, Ray Lowenthal, Josette Brie`re, Gilles Salles, Craig H. Moskowitz and Bertram Glass



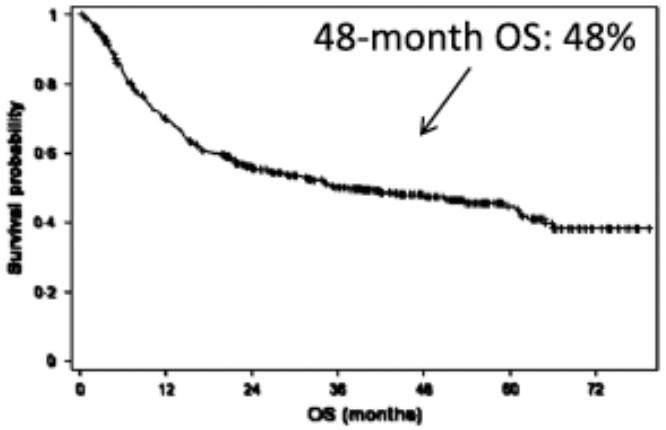
Gisselbrecht C et al, J Clin Oncol 2010

High Dose Chemotherapy plus ASCT: CORAL trial experience

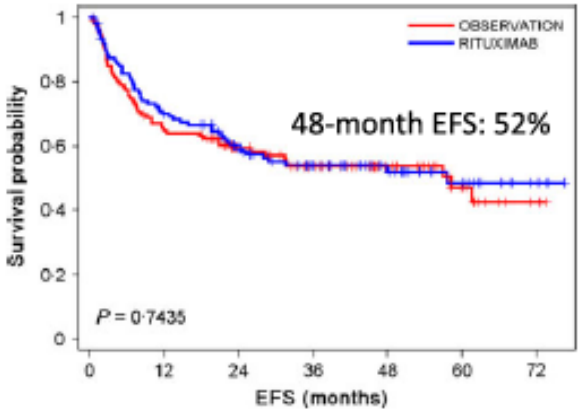




OS from **first** randomisation



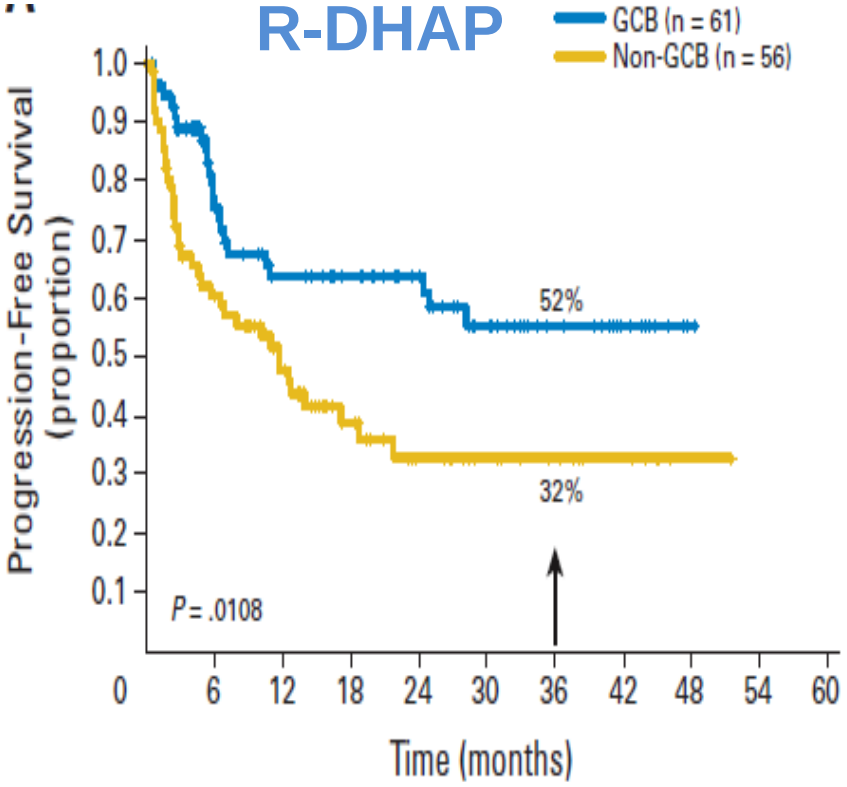
EFS from **second** randomisation

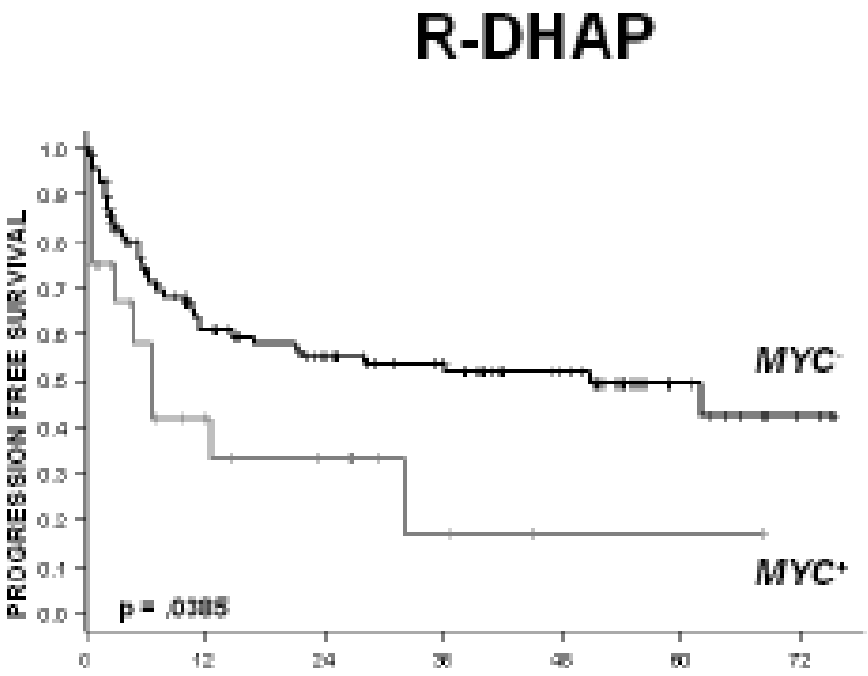


Gisselbrecht C et al, J Clin Oncol 2010; Gisselbrecht C and Van Den Este E, Br J Haematol 2018

Prognostic factors RR/DLBCL: Bio-CORAL trial experience

COO and MYC+ influence PFS at relapse according to second-line treatment for DLBCL





Thieblemont C et al, J Clin Oncol 2011

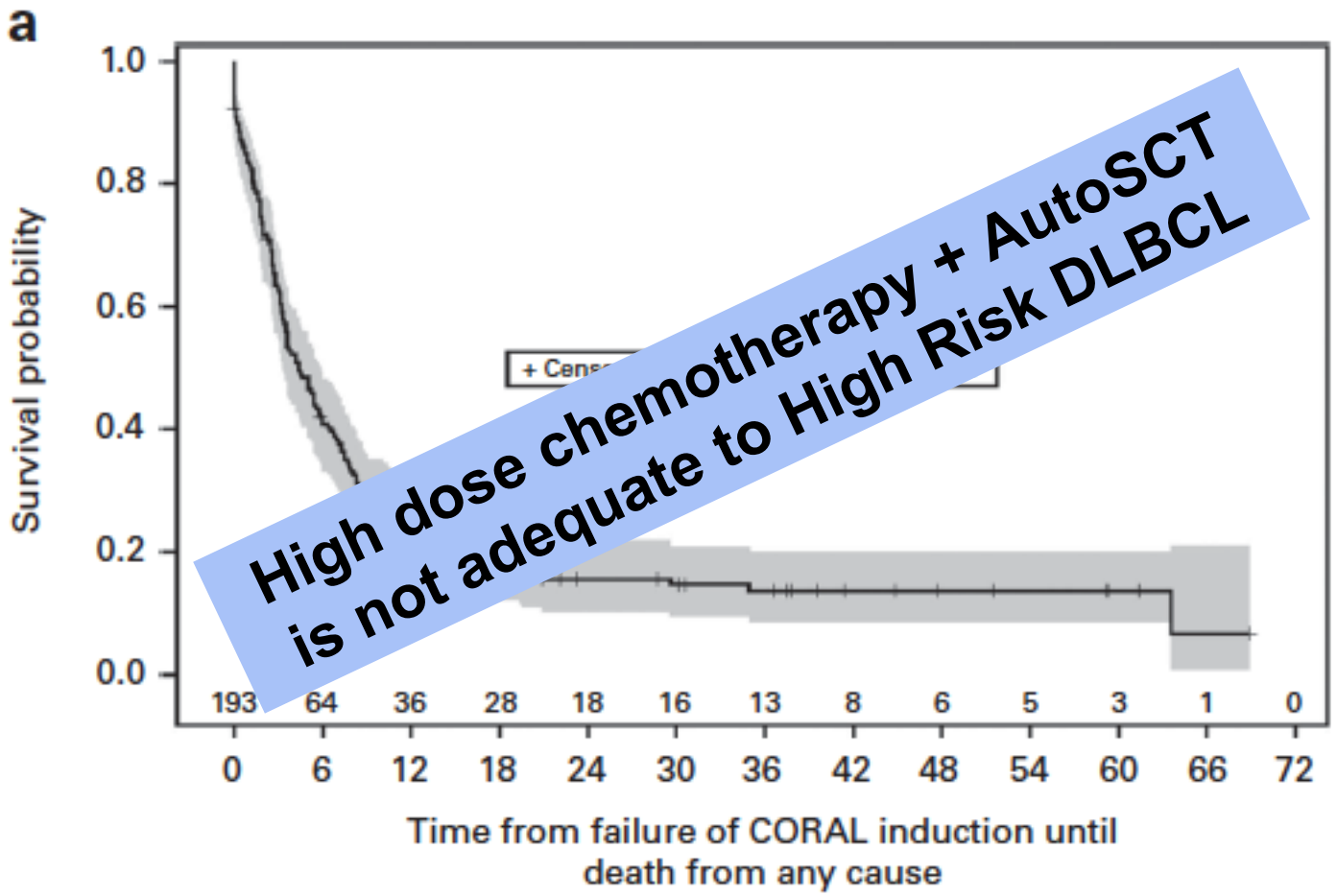
ORIGINAL ARTICLE

Outcome of patients with relapsed diffuse large B-cell lymphoma who fail second-line salvage regimens in the International CORAL study

E Van Den Neste[1], N Schmitz[2], N Mounier[3], D Gill[4], D Linch[5], M Trneny[6], N Milpied[7], J Radford[8], N Ketterer[9], O Shpilberg[10], U Dührsen[11], D Ma[12], J Brière[13], C Thieblemont[13], G Salles[14], CH Moskowitz[15], B Glass[2] and C Gisselbrecht[13]

Bone Marrow Transplantation (2016) **51**, 51–57

www.nature.com/bmt



CLINICAL TRIALS AND OBSERVATIONS

Outcomes in refractory diffuse large B-cell lymphoma: results from the international SCHOLAR-1 study

Michael Crump,[1] Sattva S. Neelapu,[2] Umar Farooq,[3] Eric Van Den Neste,[4] John Kuruvilla,[1] Jason Westin,[2] Brian K. Link,[3] Annette Hay,[1] James R. Cerhan,[5] Liting Zhu,[1] Sami Boussetta,[4] Lei Feng,[2] Matthew J. Maurer,[5] Lynn Navale,[6] Jeff Wiezorek,[6] William Y. Go,[6] and Christian Gisselbrecht[4]

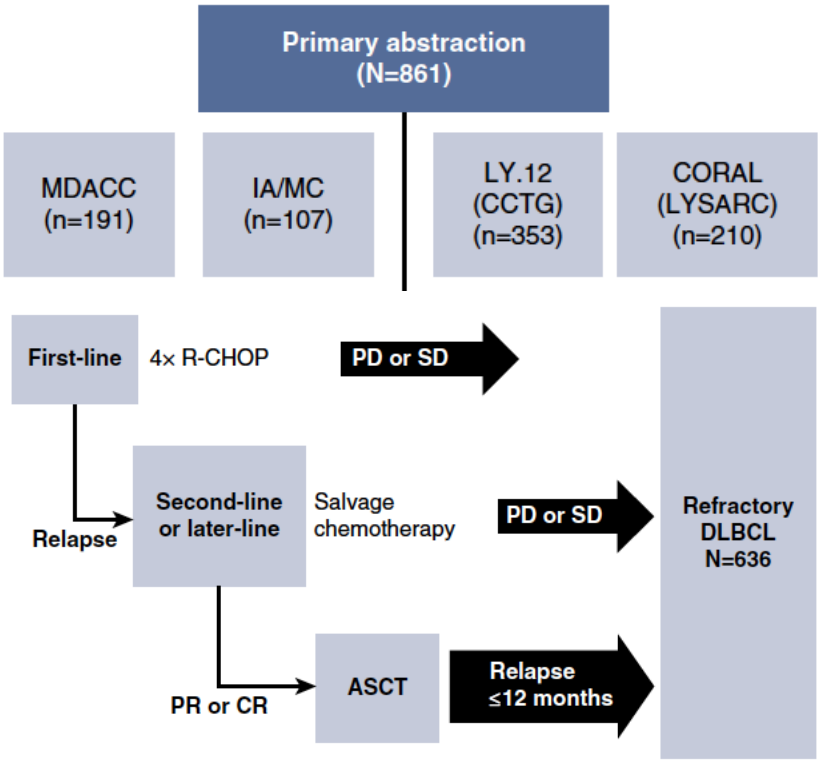
blood

BLOOD, 19 OCTOBER 2017 • VOLUME 130, NUMBER 16

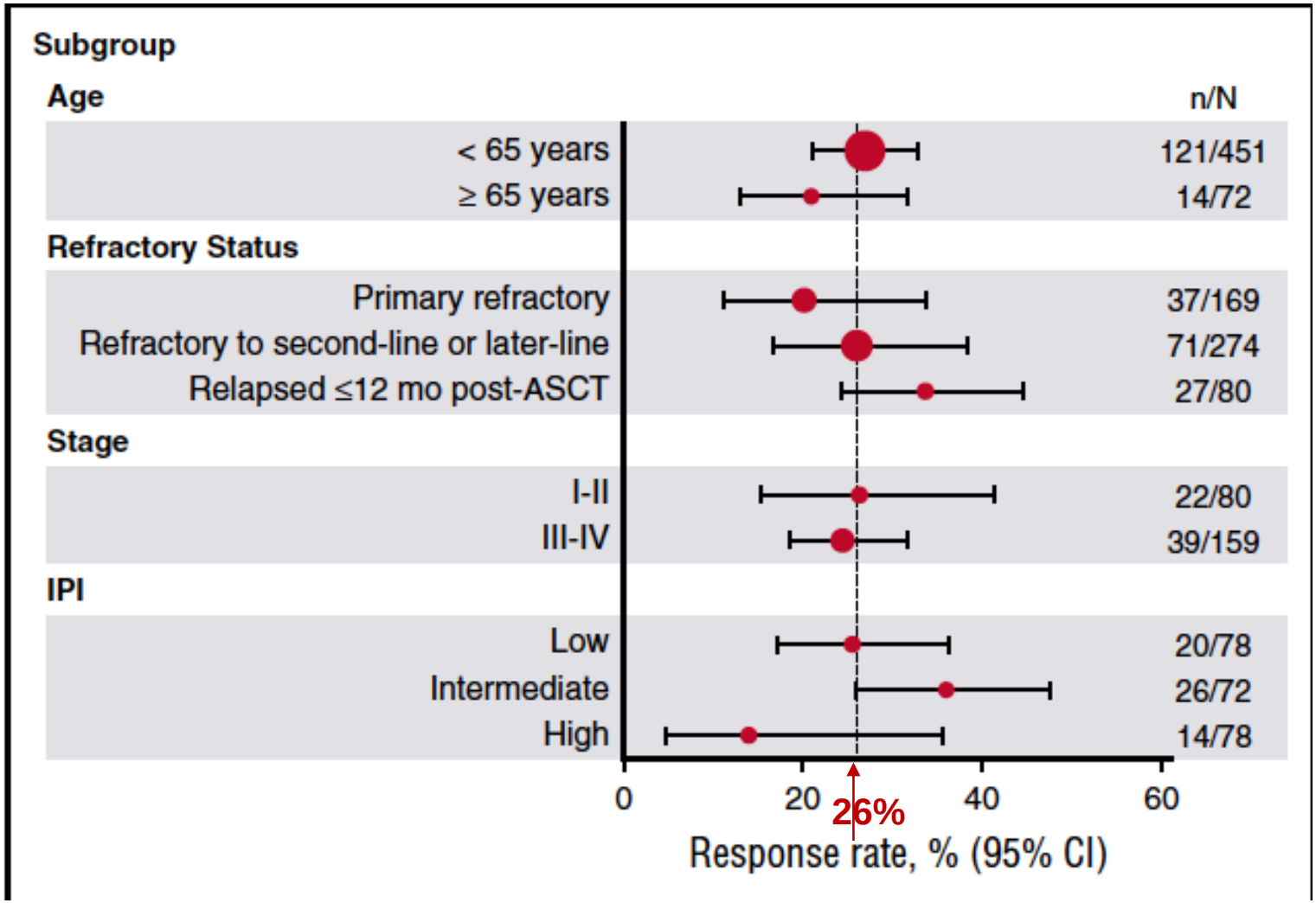
Large retrospective analysis of outcomes in 636 refractory DLBCL

How did these patients with refractory DLBCL respond to the next line of therapy?

- ✓ ORR 26% (CR 7%)
- ✓ Median OS 6.3 months

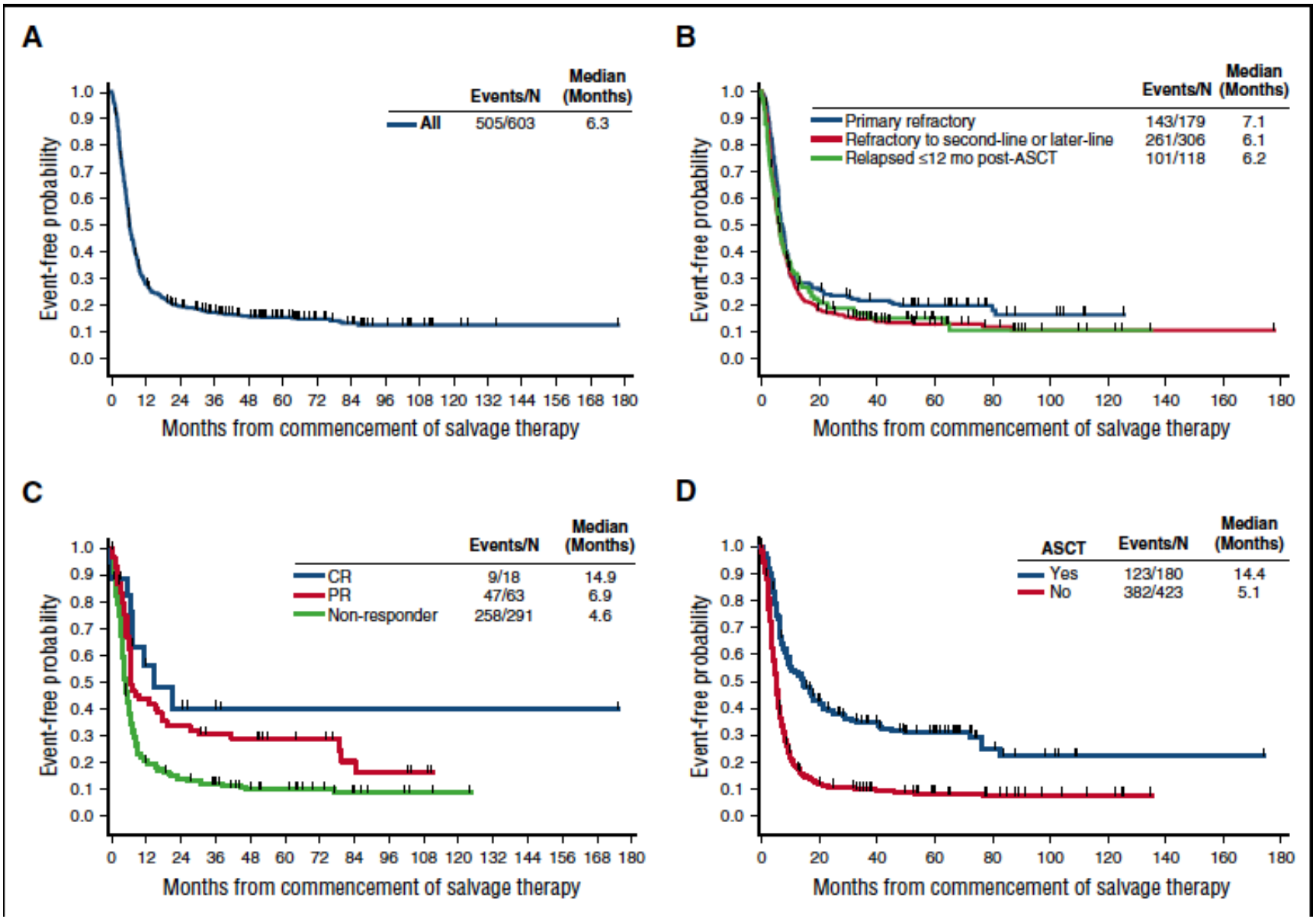


High Risk DLBCL



Crump M et al. Blood 2017; 130 (16): 1800–1808

High Risk DLBCL



Crump M et al. Blood 2017; 130 (16): 1800–1808

How I Treat «High Risk» DLBCL in Relapse?

Chemorefractory eligible to high dose chemotherapy:

- ✓ **Allogeneic stem cell transplant**

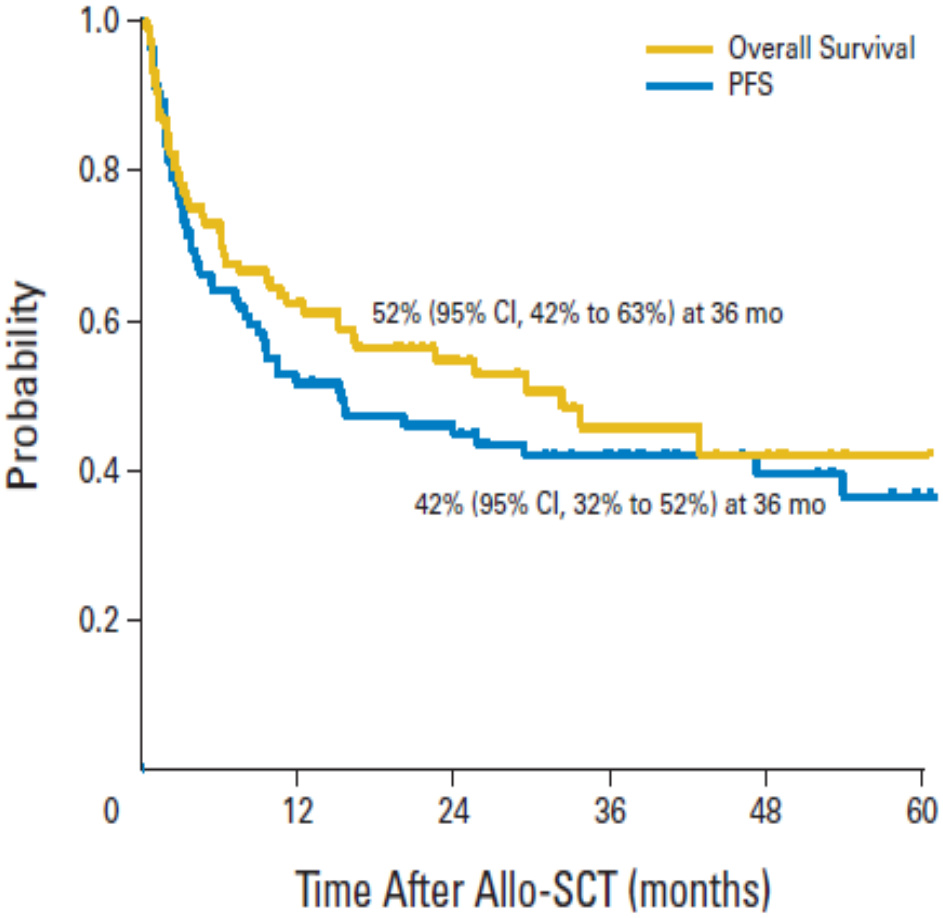
Not eligible to high dose chemotherapy:

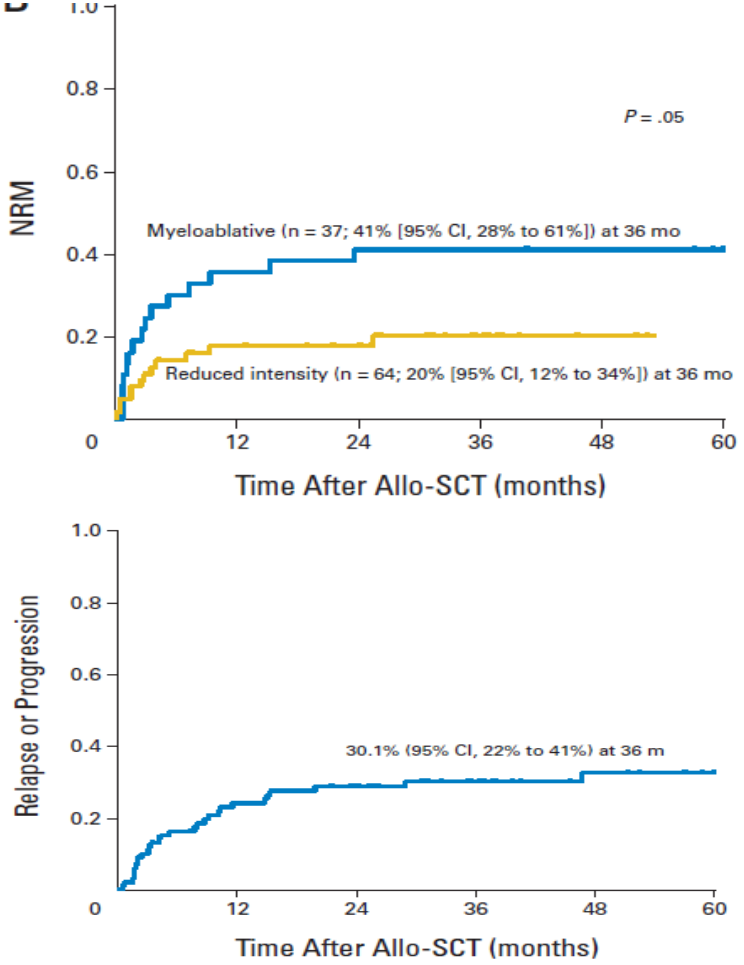
- ✓ Chemotherapy
- ✓ Novel drugs
  - monotherapy
  - combos

Allo-SCT in refractory/relapsed DLBCL: EBMT Registry

First allo-SCT in relapsed DLBCL after a previous ASCT between 1997 and 2006 and availability of an HLA-identical sibling or a matched unrelated donor.

101 patients; median age 46 (18-66); 75 chemosensitive, 26 chemorefractory



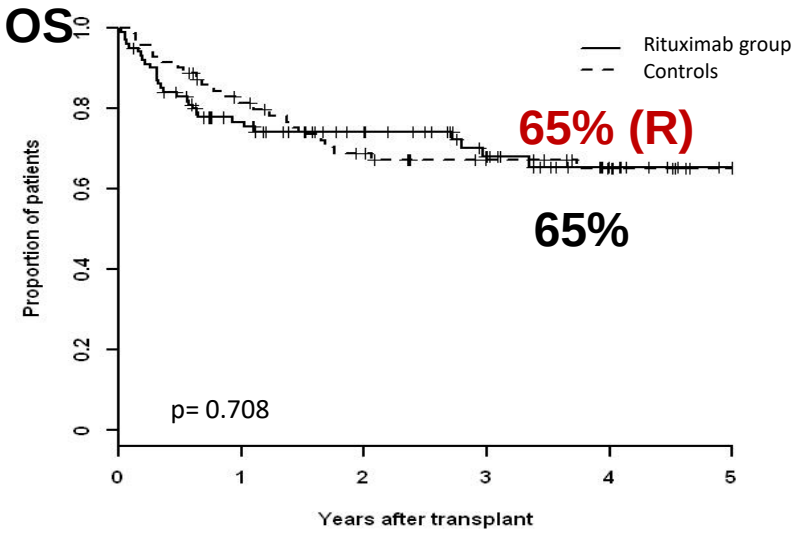


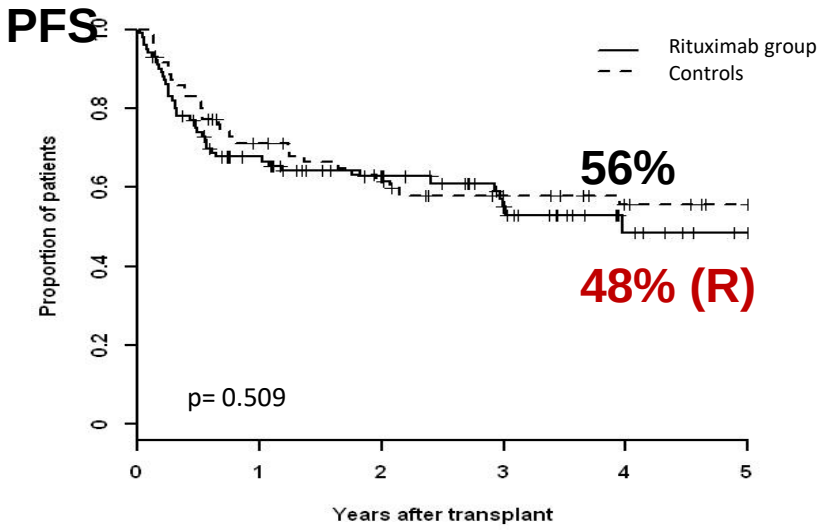
median follow-up for survivors 36 months

Van Kampen RJW et al, J Clin Oncol 2011

RIC with high-dose Rituximab followed by alloSCT in relapsed NHL
Rituximab-conditioning versus control group

	Study (Rituximab) N=110	Control (No Rituximab) N=71
Age (median)	52 years	51 years
Indolent/aggressive	57 (56%)/44 (44%)	32 (45%)/39 (55%)
CR at transplant	40 (39%)	31 (44%)
HLA related/unrel/mismatch	54 (54%)/47 (47%)/14 (13%)	39 (55%)/32 (45%)/14 (20%)
N°previous lines (median)	3	3
Prior autoSCT	62 (61%)	46 (65%)





Dodero A et al, BBMT 2017

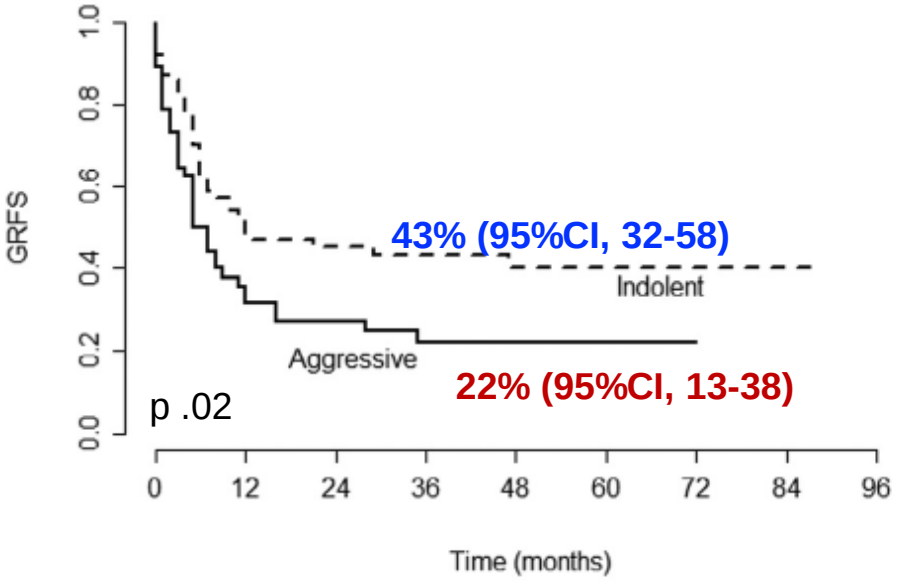
Allogeneic Stem Cell Transplantation for Relapsed/Refractory B Cell Lymphomas: Results of a Multicenter Phase II Prospective Trial including Rituximab in the Reduced-Intensity Conditioning Regimen

Biol Blood Marrow Transplant 23 (2017) 1102–1109

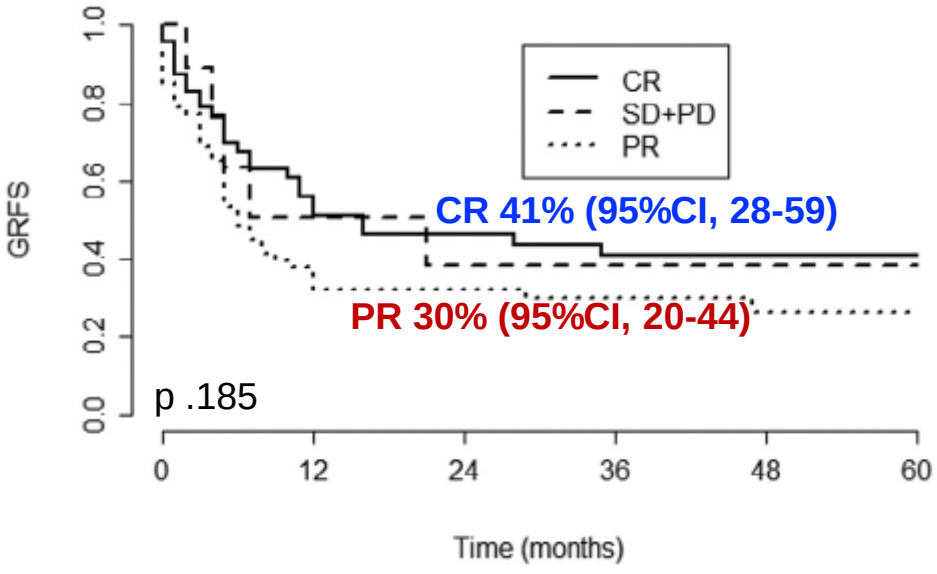
Anna Dodero [1,*], Francesca Patriarca [2], Giuseppe Milone [3], Barbara Sarina [4], Rosalba Miceli [5], Anna Iori [6], Francesco Barretta [5], Elisabetta Terruzzi [7], Alberto Mussetti [1], Massimo Pini [8], Alberto Bosi [9], Alida Dominietto [10], Nicola Cascavilla [11], Francesco Onida [12], Franco Narni [13], Lucia Farina [1], Alessandro Rambaldi [14], Paolo Corradini [1,15]

GVHD free and relapse free survival (GRFS) in B-cell lymphomas: a novel composite endpoint

3-yrs after alloSCT GRFS upon histotype



3-yrs after alloSCT GRFS upon pre-transplant disease status



Rituximab after lymphoma-directed conditioning and allogeneic stem-cell transplantation for relapsed and refractory aggressive non-Hodgkin lymphoma (DSHNHL R3): an open-label, randomised, phase 2 trial

Lancet Oncol 2014; 15:757–66

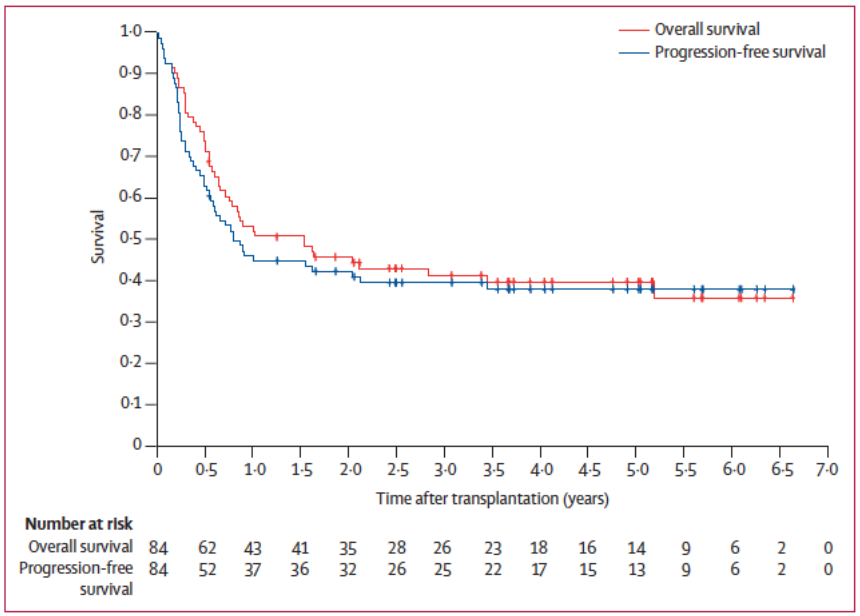
Bertram Glass*, Justin Hasenkamp*, Gerald Wulf, Peter Dreger, Michael Pfreundschuh, Martin Gramatzki, Gerda Silling, Christian Wilhelm, Matthias Zeis, Anke Görlitz, Sebastian Pfeiffer, Reinhard Hilgers, Lorenz Truemper, Norbert Schmitz, on behalf of the German High-Grade Lymphoma Study Group†

Aggressive B or T-cell lymphoma; primary refractory disease; early relapse (<12 months after first-line treatment) or relapse after autologous transplantation.

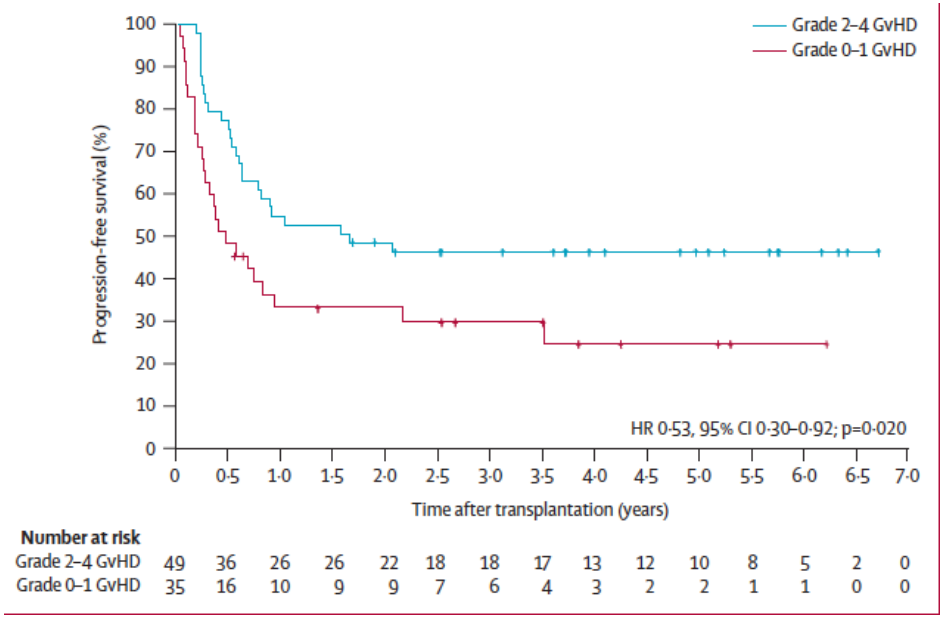
	Rituximab group (n=42)	Control group (n=42)
Patient age (years)		
Median (IQR)	47·0 (38·0–54·0)	49·5 (43·0–57·0)
≤40 years	14 (33%)	7 (17%)
>40 years	28 (67%)	35 (83%)
Duration of last remission		
<3 months (refractory)	22 (52%)	26 (62%)
<12 months (early relapse)	8 (19%)	4 (10%)
>12 months (late relapse)*	12 (29%)	12 (29%)
Previous high-dose treatment and stem-cell transplantation		
Yes	22 (52%)	23 (55%)
No	20 (48%)	19 (45%)
Median lines of treatment before allogeneic stem-cell transplantation (IQR)	4 (3–5)	4 (3–6)
Disease status at transplantation		
Refractory	23 (55%)	23 (55%)
Sensitive or untested	19 (45%)	19 (45%)
Median follow-up (IQR; years)	4·5 (3·3–5·9)	3·9 (2·4–5·2)

DSHNHL R3

OS and PFS



PFS according to severity of aGVHD



	Hazard ratio (95% CI)	p value
GvHD 0 or 1	2·24 (1·22–4·10)	0·0008
Mismatched donor	3·13 (1·61–6·10)	0·0008
Refractory*	2·03 (1·01–4·06)	0·046
≥4 lines of treatment	2·65 (1·39–5·05)	0·0031
No anti-thymocyte globulin	2·87 (1·38–5·99)	0·0049

GvHD=graft-versus-host-disease. *Never or short (<12 months) in remission.

Table 2: **Results of multivariate analysis for progression-free survival**

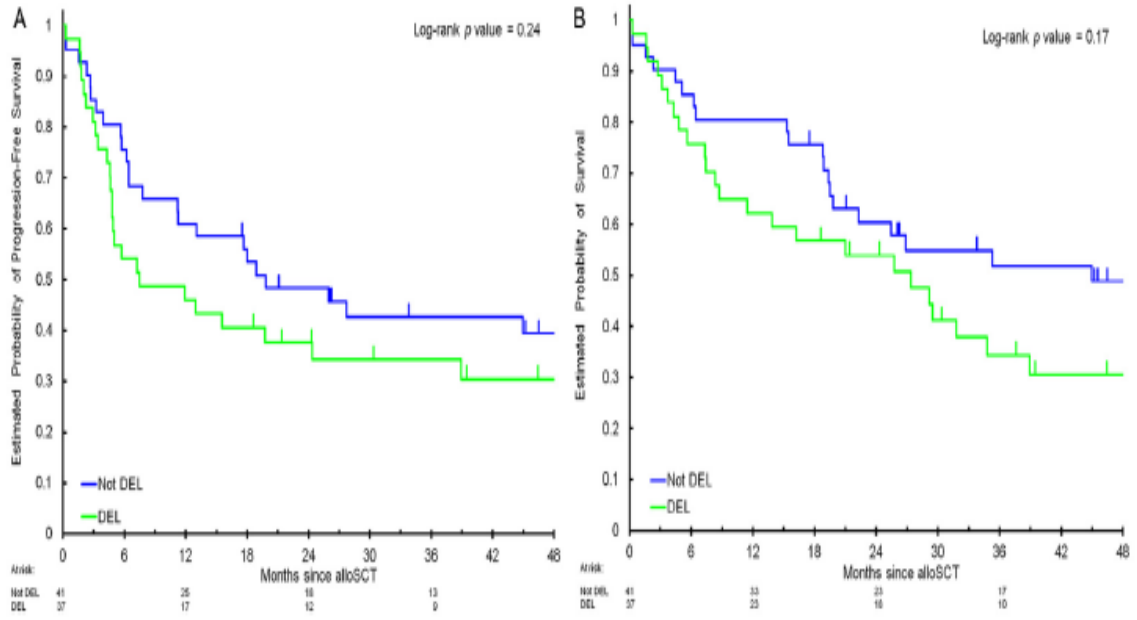
Glass B et al, Lancet Oncol 2014

Biology of Blood and Marrow Transplantation
journal homepage: www.bbmt.org
ASBMT American Society for Blood and Marrow Transplantation
Biol Blood Marrow Transplant 24 (2018) 514-520

Outcomes after Allogeneic Stem Cell Transplantation in Patients with Double-Hit and Double-Expressor Lymphoma

Alex F. Herrera [1,*], Scott J. Rodig [2], Joo Y. Song [3], Young Kim [3], Gabriel K. Griffin [2], Dongyun Yang [4], Liana Nikolaenko [1], Matthew Mei [1], Victoria Bedell [3], Paola Dal Cin [2], Christine Pak [2], Edwin P. Alyea [5], Lihua E. Budde [1], Robert Chen [1], Yi-Bin Chen [6], Wing C. Chan [3], Corey S. Cutler [5], Vincent T. Ho [5], John Koreth [5], Amrita Krishnan [1], Joyce L. Murata-Collins [3], Sarah Nikiforow [5], Joycelynne Palmer [4], German A. Pihan [7], Raju Pillai [3], Leslie Popplewell [1], Steven T. Rosen [1], Tanya Siddiqi [1], Aliyah R. Sohani [8], Jasmine Zain [1], Larry W. Kwak [1], Dennis D. Weisenburger [3], David M. Weinstock [5], Robert J. Soiffer [5], Joseph H. Antin [5], Stephen J. Forman [1], Auayporn P. Nademanee [1], Philippe Armand [5]

AlloSCT produced durable remissions in patients with rel/ref aggressive B-NHL irrespective of DEL and DHL status, justifying its consideration in the treatment of patients with rel/ref DEL/DHL.



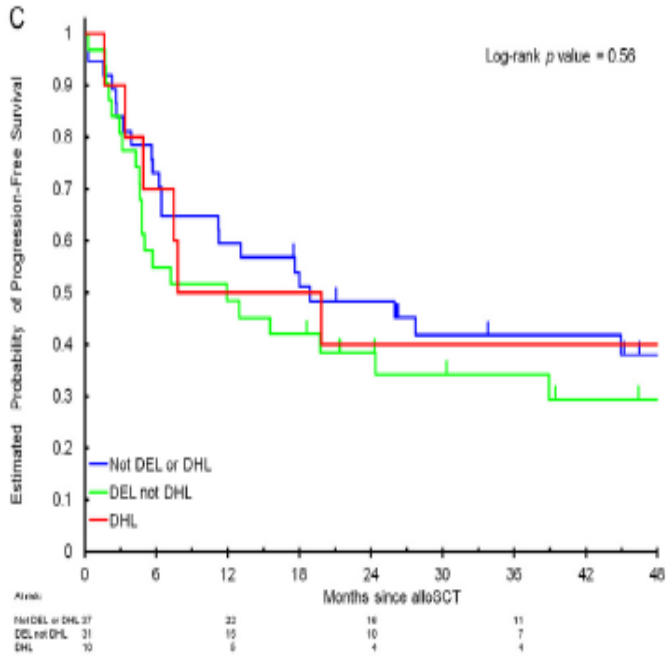


Figure 1. PFS (A) and OS (B) after alloSCT in patients with DEL compared with non-DEL patients.

How I Treat «High Risk» DLBCL in Relapse?

Chemorefractory eligible to high dose chemotherapy:

- ✓ Allogeneic stem cell transplant

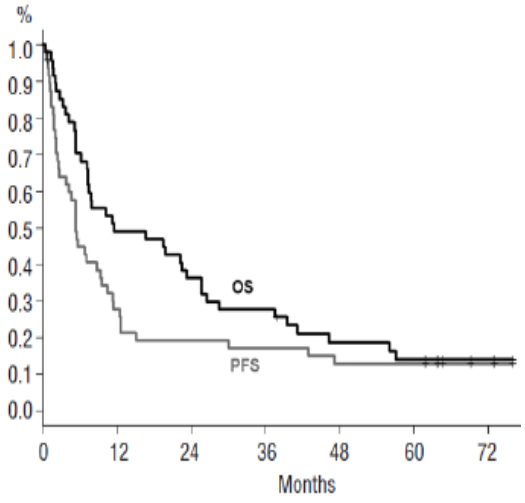
Not eligible to high dose chemotherapy:

- ✓ **Chemotherapy**
- ✓ Novel drugs
  - monotherapy
  - combos

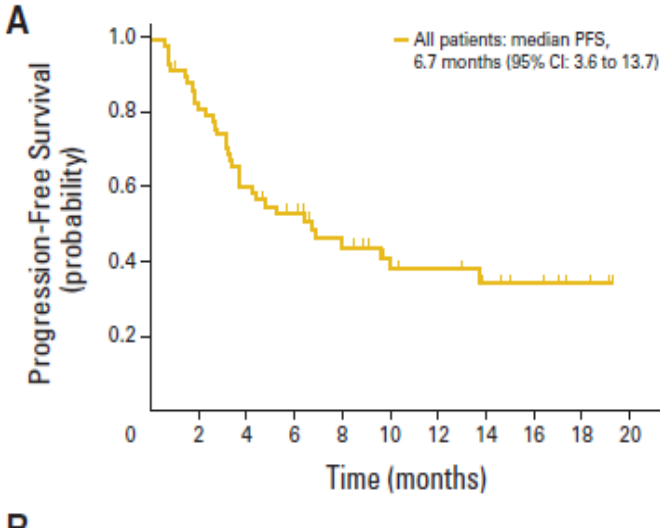
Chemotherapy

REGIMEN	N	Median age	ORR%	CR %	PFS	Reference
R-GEMOX	49	69	46	38	5-yrs 12.8%	Mounier N, Haematol 2013
R-Bendamustine	59	67	63	37	Median 6.7 mo	Ohmachi K, L Clin Oncol 2013
Pixantrone	70	60	37	20	Median 5.3 mo	Pettengel R, Lancet Oncol 2012

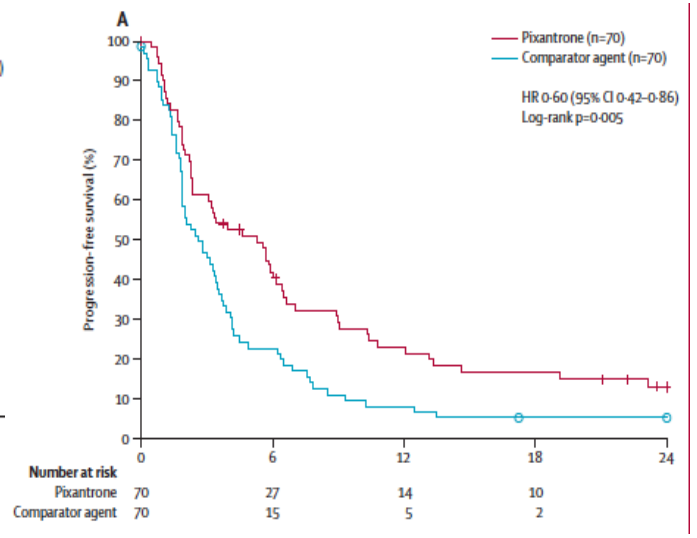
R-GEMOX



R-BENDAMUSTINE



PIXANTRONE



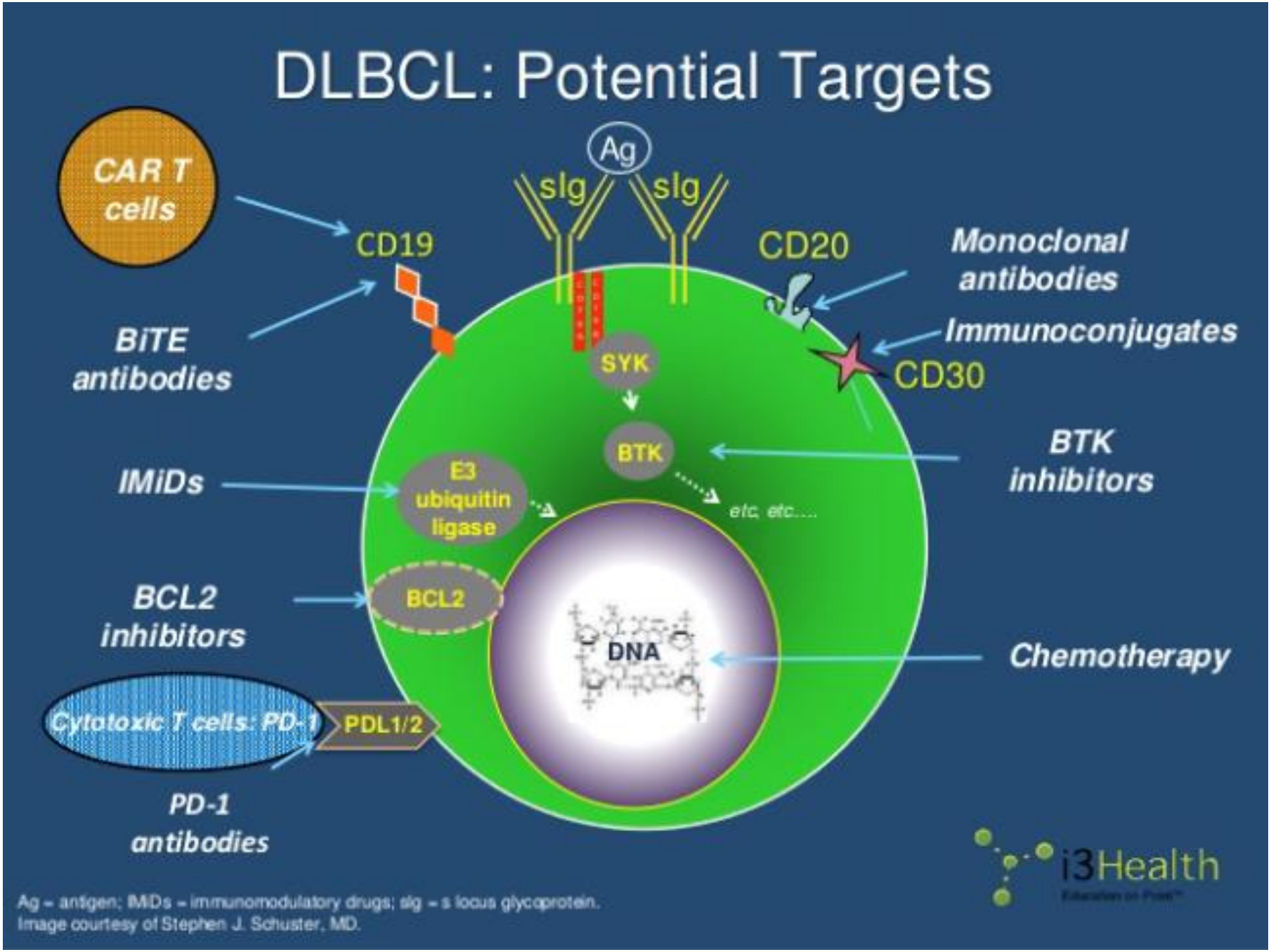
How I Treat «High Risk» DLBCL in Relapse?

Chemorefractory eligible to high dose chemotherapy:

- ✓ Allogeneic stem cell transplant

Not eligible to high dose chemotherapy:

- ✓ Chemotherapy
- ✓ **Novel drugs**
  - **monotherapy**
  - **combos**



Schuster SJ, educational; medscape.com

Novel agents: monotherapy

Table II. Overall response rate of new selected single agents in DLBCL patients.

Agent	Target	Status	ORR	DLBCL subtype	References
Ibrutinib	BTK	Phase I/ II	37%	ABC	Wilson *et al* (2015)
Fostamatinib	SYK	Phase II	3%	DLBCL	Flinn *et al* (2016)
			22%		Friedberg *et al* (2010)
Lenalidomide	Immunomodulator	Phase II	42%	DLBCL	Zinzani *et al* (2015)
			52%	ABC	Hernandez-Ilizaliturri *et al* (2011)
Bortezomid + chemotherapy	NF-κB	Phase II	83%	ABC	Dunleavy *et al* (2009)
Tazemetostat	EZH2	Phase II	60%	DLBCL	Italiano *et al* (2018)
Everolimus	mTOR	Phase II	30%	GCB	Witzig *et al* (2011)
Temsirolimus	mTOR	Phase II	28%	DLBCL	Smith *et al* (2010)
CUDC 907	PI3Kδ + HDAC	Phase II	37%	GCB/*MYC*	Oki *et al* (2017)
Bendamustine	Nitrogen mustard/ purine-like	Phase II	44%	DLBCL	Weidmann *et al* (2002)
Obinutuzumab	CD20	Phase II	32%	DLBCL	Morschhauser *et al* (2013)
MOR00208	CD19	Phase II	29%	DLBCL	Jurczak *et al* (2018)
Blinatumumab	B-specific CD19/CD3	Phase II	43%	DLBCL	Viardot *et al* (2016)
Polatuzumab vedotin	CD79b	Phase I	25%	DLBCL	Palanca-Wessels *et al* (2015)
Nivolumab	Anti-PD1	Phase I	36%	DLBCL	Lesokhin *et al* (2016)

ABC, activated B cell; DLBCL, diffuse large B cell lymphoma; GCB, germinal centre B cell; ORR, overall response rate.

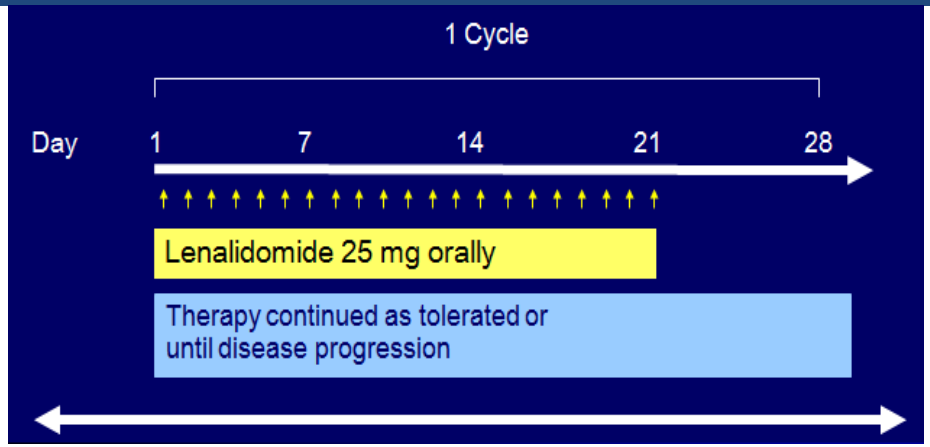
Gisselbrecht C and Van Den Este E, Br J Haematol 2018

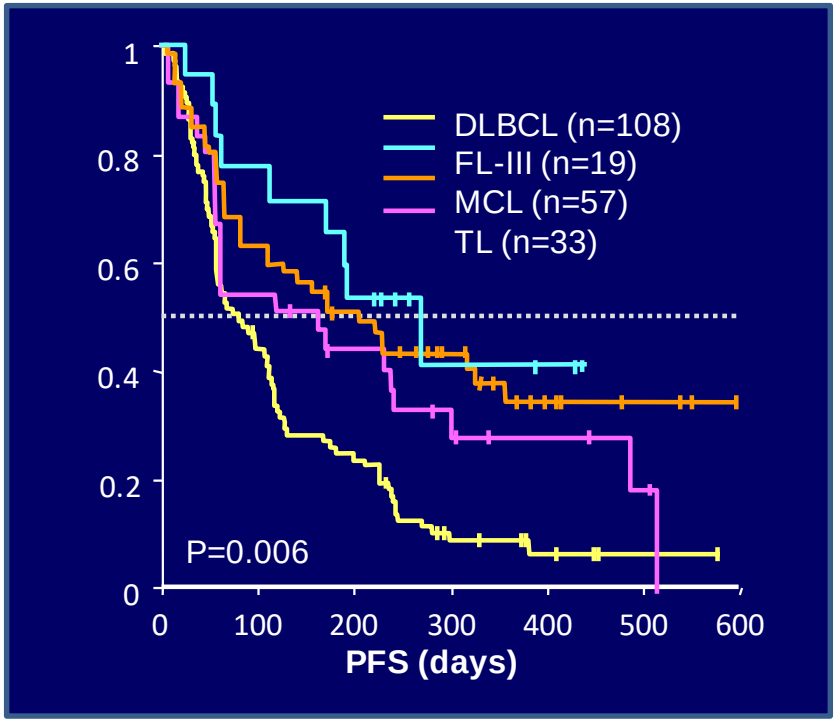
Activity of lenalidomide in R/R DLBCL

R/R DLBCL	n	ORR	CR/CRu	Median PFS, mo
All patients[1]	26	19%	12%	4.0*
All patients[2]	108	28%	7%	2.7
All patients[3]	40	28%	15%†	2.6
GCB by IHC	23	9%	4%	1.7
Non-GCB by IHC	17	53%	29%	6.2
All patients[4]	51	27%	N/A	3.1
GCB by IHC	23	26%	N/A	2.3
Non-GCB by IHC	28	29%	N/A	3.5
GCB by GEP	14	21%	N/A	3.0
ABC by GEP	11	46%	N/A	18.9

*Included all patients in mixed NHL population.

†CR only (not CRu)





Direct comparisons between trial designs should not be made due to differences between trial designs and patient characteristics.

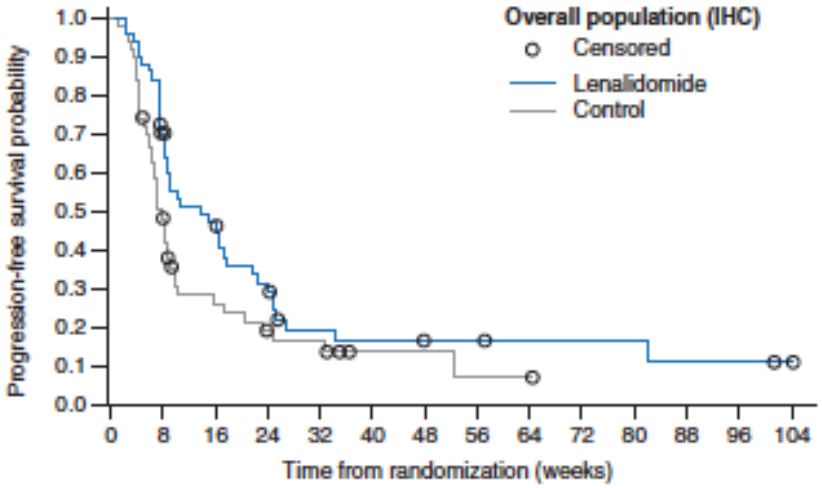
1. Wiernik PH, et al. J Clin Oncol. 2008;26:4952-7.
2. Witzig TE, et al. Ann Oncol. 2011;22:1622-7.
3. Hernandez-Ilizaliturri FJ, et al. Cancer. 2011;117:5058-66.
4. Czuczman MS, et al. ASH 2014. Abstract 628.

Clinical Cancer Research

A Phase 2/3 Multicenter, Randomized, Open-Label Study to Compare the Efficacy and Safety of Lenalidomide Versus Investigator's Choice in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma

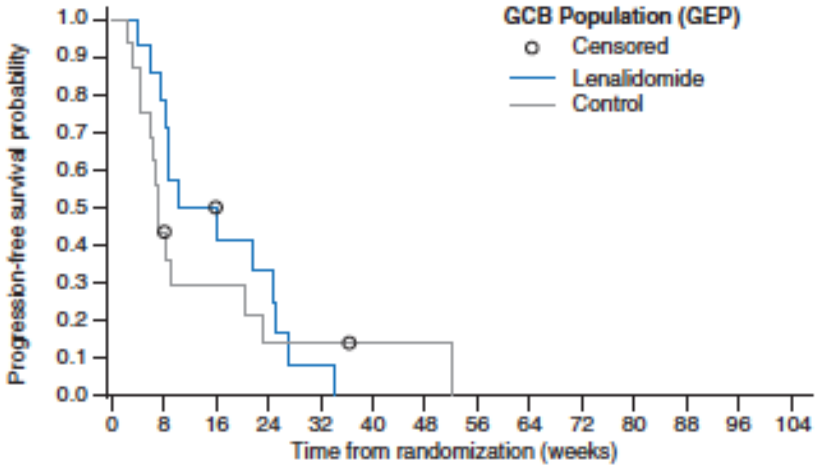
Myron S. Czuczman[1], Marek Trněný[2], Andrew Davies[3], Simon Rule[4], Kim M. Linton[5], Nina Wagner-Johnston[6], Randy D. Gascoyne[7], Graham W. Slack[7], Pierre Brousset[8], David A. Eberhard[9], Francisco J. Hernandez-Ilizaliturri[1], Gilles Salles[10], Thomas E. Witzig[11], Pier Luigi Zinzani[12], George W. Wright[13], Louis M. Staudt[14], Yandan Yang[14], P. Mickey Williams[15], Chih-Jian Lih[16], Jacqueline Russo[17], Anjan Thakurta[17], Patrick Hagner[17], Pierre Fustier[18], Dale Song[17], and Ian D. Lewis[19]

A



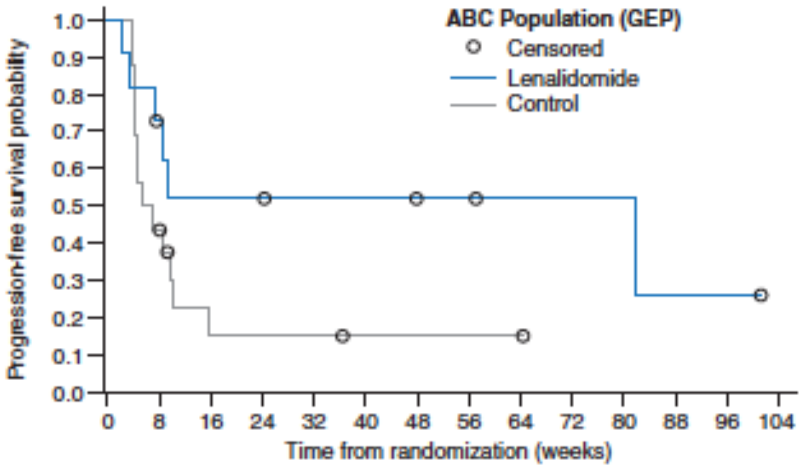
Group	n	Median (weeks) (range)	HR (95% CI)	*P* value
Lenalidomide overall	51	13.6 (8.6–17.7)	0.64 (0.41–0.99)	0.041
Control overall	51	7.9 (6.3–9.0)		

D



Group	n	Median (weeks) (range)	HR (95% CI)	*P* value
Lenalidomide GCB	14	13.2 (8.3–24.9)	0.77 (0.35–1.68)	0.506
Control GCB	16	7.1 (6.0–20.6)		

E



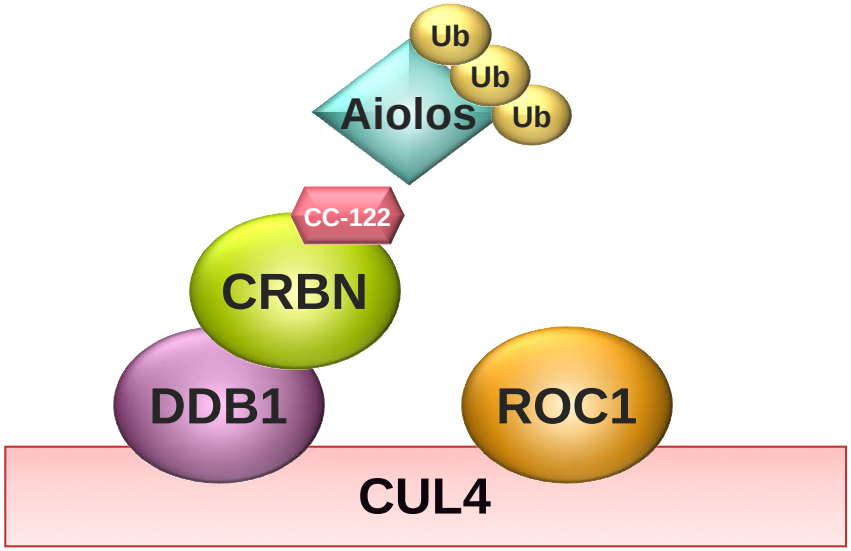
Group	n	Median (weeks) (range)	HR (95% CI)	*P* value
Lenalidomide ABC	11	82.0 (7.3–NA)	0.44 (0.15–1.23)	0.105
Control ABC	16	6.2 (4.3–10.1)		

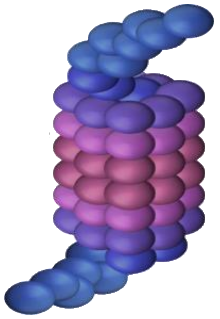
Czuczman M et al, Clin Canc Res 2017

CC-122, A NOVEL CEREBLON-MODULATING AGENT, IN COMBINATION WITH OBINUTUZUMAB IN PATIENTS WITH RELAPSED AND REFRACTORY B-CELL NON-HODGKIN LYMPHOMA

CC-122 Substrate Degradation Explains Duality of Effects

Aiolos: transcriptional repressor of ISGs in lymphoma cells and IL-2 in T cells





Proteasome

Tumoricidal effects

↑ISGs (IRF7, OAS)

T- and NK-cell activation

↑IL-2

IFN; interferon; IRF, interferon regulatory factor; ISG, interferon-stimulated gene; IL, interleukin; NK, natural killer; OAS, oligoadenylate synthetase; Ub, ubiquitin.

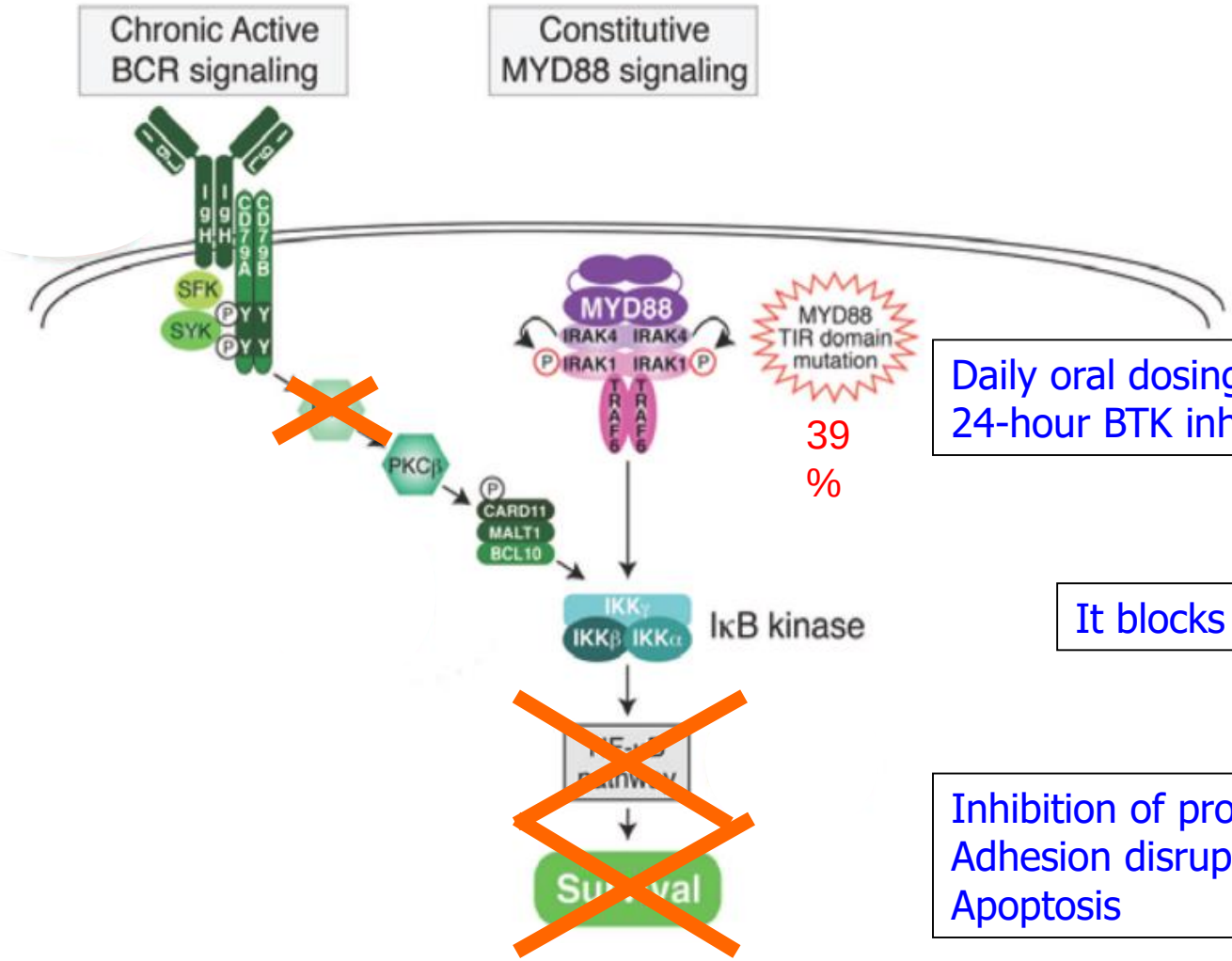
Michot JM et al, EHA 2018, oral presentation

CC-122, A NOVEL CEREBLON-MODULATING AGENT, IN COMBINATION WITH OBINUTUZUMAB IN PATIENTS WITH RELAPSED AND REFRACTORY B-CELL NON-HODGKIN LYMPHOMA

Best Overall Response by Histology	Treated Patients (n = 49)	DLBCL (n = 19)	FL + MZL[a] (n = 30)
ORR, n (%)	32 (65)	**9 (47)**	23 (77)[b]
CR	14 (29)	**2 (11)**	12 (40)
PR	18 (37)	**7 (37)**	11 (37)
SD, n (%)	5 (10)	**3 (16)**	2 (7)
PD, n (%)	7 (14)	**4 (21)**	3 (10)
Not evaluable/missing, n (%)	5 (10)	**3 (16)**	2 (7)
mPFS (95% CI),[b] mo	13.8 (3.8–21.2)	**4.7 (1.8–13.8)**	16.6 (5.4–NR)
6-mo PFS rate,[b] % (95% CI)	59.5 (42.7–72.8)	**40.0 (15.9–63.3)**	71.9 (49.5–85.7)
mDOR (95% CI),[b] mo	10.2 (8.4–NR)	**10.2 (1.8–10.2)**	19.4 (8.4–NR)

Michot JM et al, EHA 2018, oral presentation

Targeting B-cell receptor signaling through inhibition of Bruton tyrosine kinase (BTK)



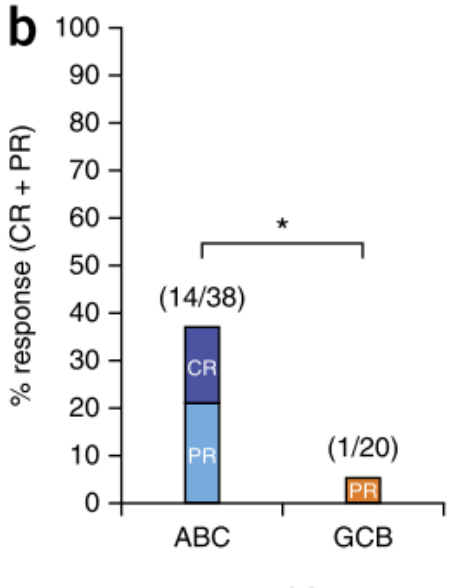
Daily oral dosing produces 24-hour BTK inhibiton

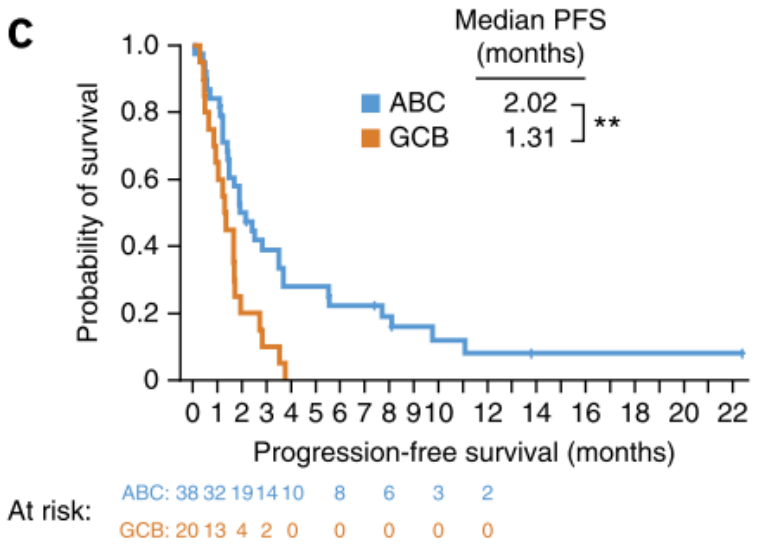
It blocks NF-κB

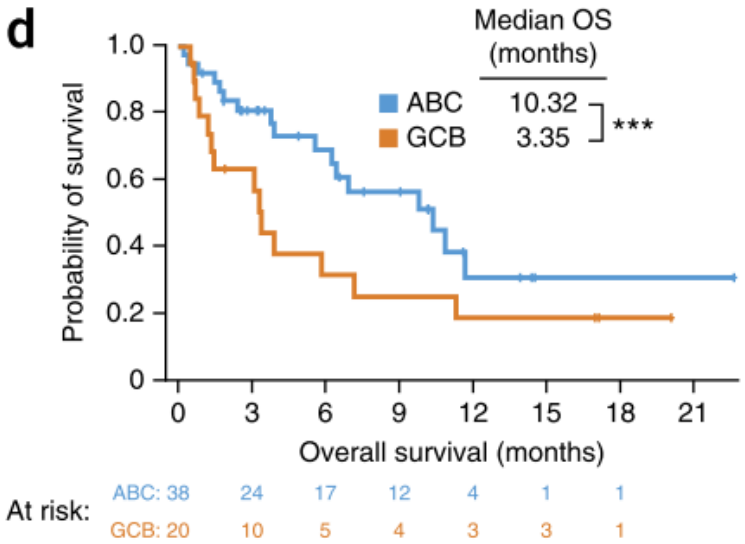
Inhibition of proliferation
Adhesion disruption
Apoptosis

Ibrutinib has a preferential activity in ABC DLBCL: phase II interim results

Characteristics	ABC (*N* = 38)	GCB (*N* = 20)	Unclassified (*N* = 17)	Unknown (*N* = 5)
Median age, years (range)	60 (34–89)	65 (28–92)	63 (44–85)	65 (58–78)
Sex (male)	66%	70%	82%	60%
ECOG performance score ≥ 2	5%	20%	24%	40%
RIPI (poor)	63%	59%	50%	60%
Median time from diagnosis, months (range)	19 (4–118)	17 (11–104)	21 (7–332)	19 (9–57)
Median number of prior regimens (range)	3 (1–7)	3.5 (1–7)	3 (1–4)	3 (1–3)
Prior ASCT	13%	30%	24%	40%
Chemotherapy-refractory disease	66%	65%	59%	50%







PR, partial response; SPD, sum of the products of the greatest perpendicular diameter.

Wilson WH, et al. Nat Med. 2015;21:922-6.

blood® 19 APRIL 2018 | VOLUME 131, NUMBER 16

A phase 1 study of ibrutinib in combination with R-ICE in patients with relapsed or primary refractory DLBCL

Craig S. Sauter,[1,2] Matthew J. Matasar,[1,2] Heiko Schoder,[3] Sean M. Devlin,[4] Pamela Drullinsky,[1,2] John Gerecitano,[1,2] Anita Kumar,[1,2] Ariela Noy,[1,2] Maria L. Palomba,[1,2] Carol S. Portlock,[1,2] David J. Straus,[1,2] Andrew D. Zelenetz,[1,2] Susan J. McCall,[1] Shoshana T. Miller,[1] Amanda I. Courtien,[1] Anas Younes,[1,2] and Craig H. Moskowitz[1,2]

Patient characteristics,* n = 21	No. (%) or median (range)
Age, y	59 (19-75)
Time from primary diagnosis	
Primary rel/ref <12 mo	17 (81)
Relapse >12 mo	4 (19)
Karnofsky performance status	
≥90	12 (57)
<90	9 (43)
Elevated LDH	8 (38)
Stage	
I/II	10 (48)
III/IV	11 (52)
Histology	
De novo DLBCL	12 (57)
GC	3 (14)
Non-GC	9 (43)
PMBL	4 (19)
Richter transformation	5 (24)
Secondary age-adjusted IPI	
Low/low-intermediate, 0-1	13 (62)
High-intermediate/high, 2-3	8 (38)

3 R-ICE + ibrutinib days 1 to 21.
3+3 design.
Ibrutinib dose level (DL) 1: 420 mg;
DL 2 560 mg; DL 3 840 mg daily.
No DLTs.

R-ICE + iBTK 840 mg days 1-21

95% of cycles with g3 haematological AEs.
60% of patients with g3 extra-haemat AEs.

14/15 collected HPCs
median CD34/kg > 5.5 x 10^6

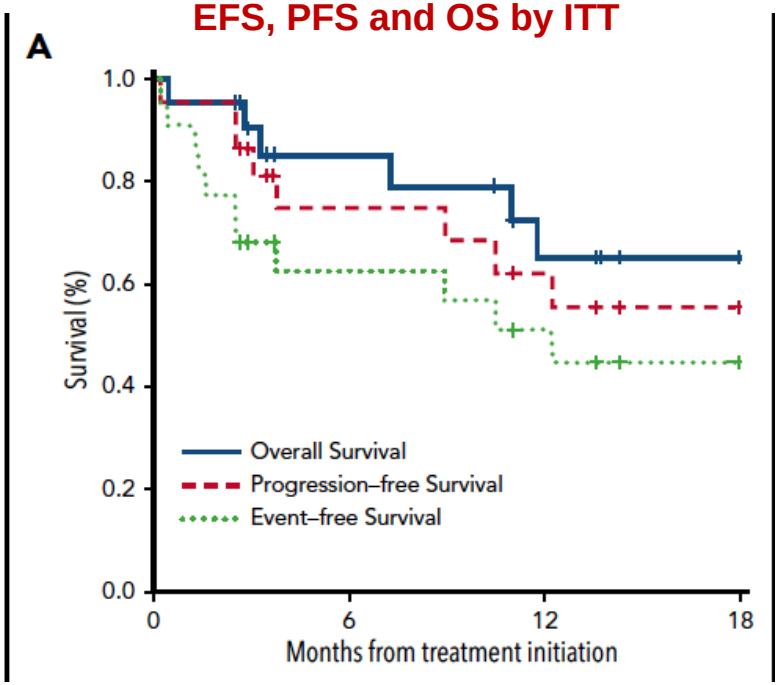
blood® 19 APRIL 2018 | VOLUME 131, NUMBER 16

A phase 1 study of ibrutinib in combination with R-ICE in patients with relapsed or primary refractory DLBCL

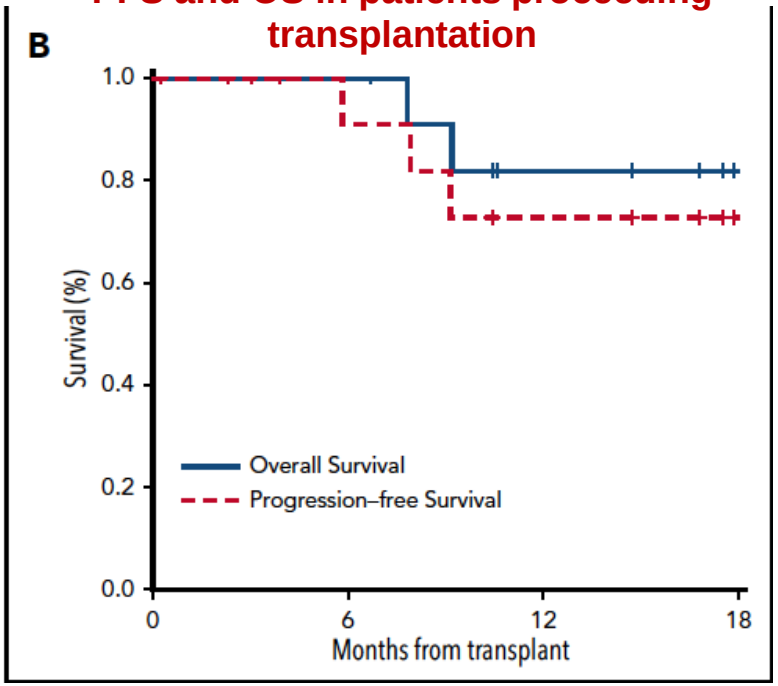
Table 2. FDG-PET response

FDG-PET response, n = 20 evaluable	CR (%)	PR (%)	ORR, %
COO/subtype			
GC, n = 3	1 (33)	0 (0)	33
Non-GC, n = 8	8 (100)*	0 (0)	100
PMBL, n = 4	0 (0)	4 (100)	100
Richter, n = 5	2 (40)	3 (60)	100
Overall, n = 20	11 (55)	7 (35)	90

EFS, PFS and OS by ITT

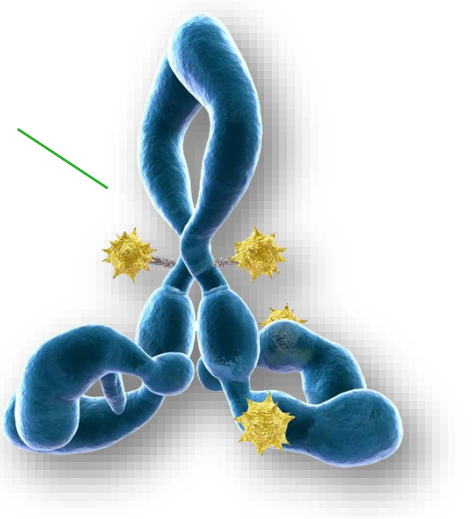


PFS and OS in patients proceeding transplantation

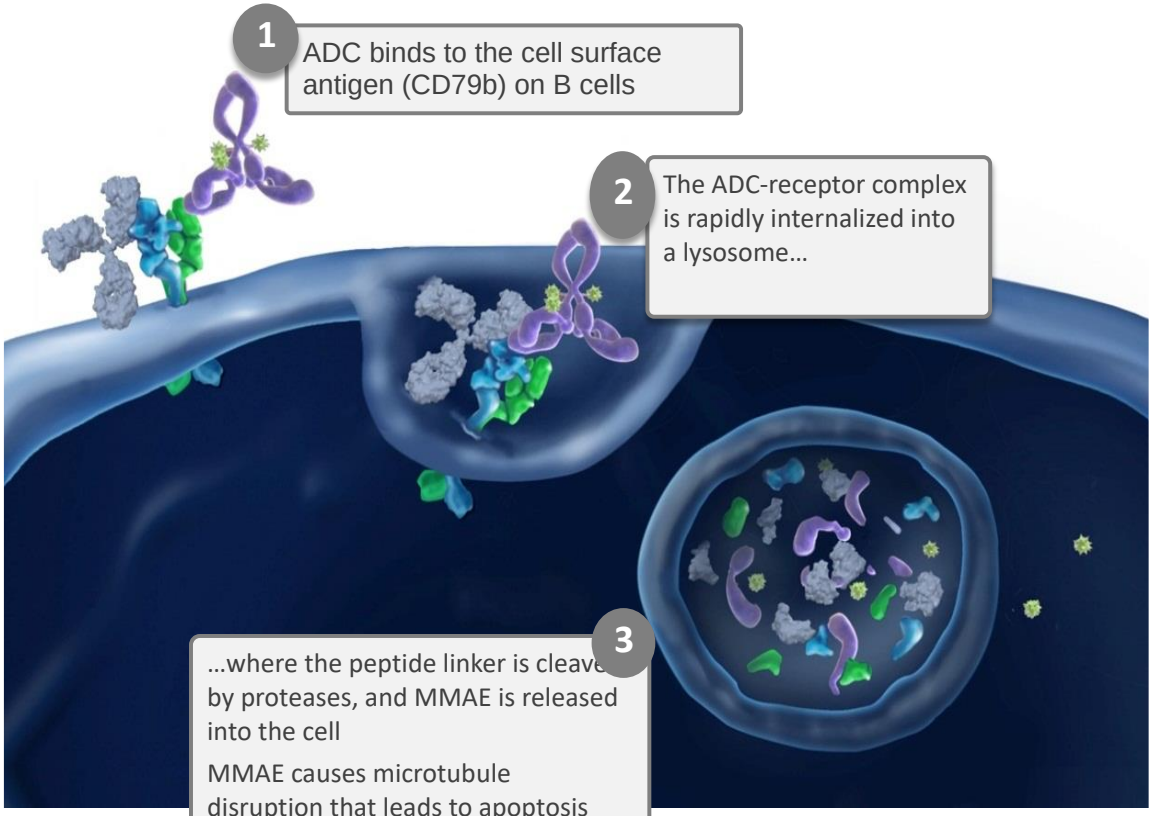


Polatuzumab vedotin

Compound	RG7596
Generic name	Polatuzumab vedotin
Other names	DCDS4501A
Molecule type	Antibody-drug conjugate (ADC)



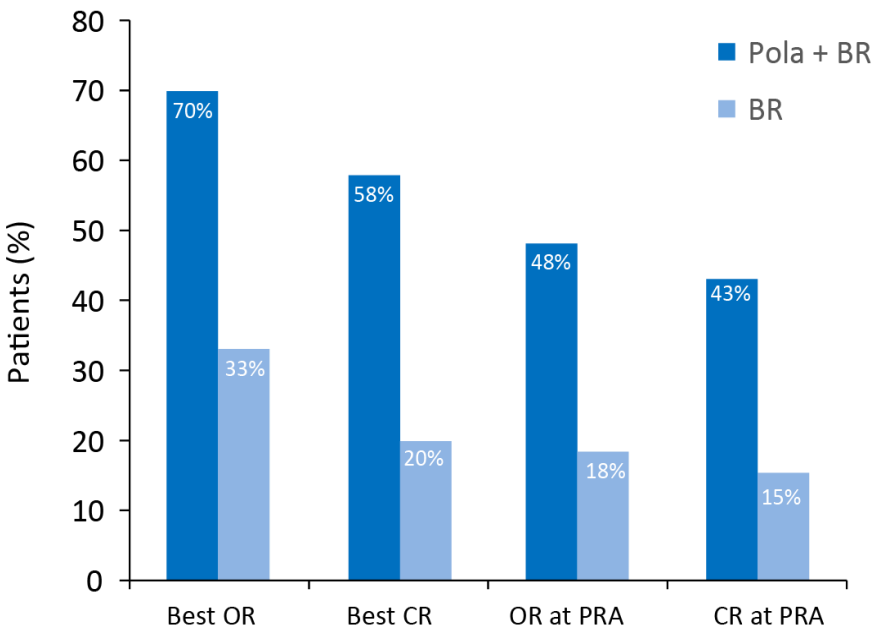
Binds CD79b and ADC-receptor complex internalized

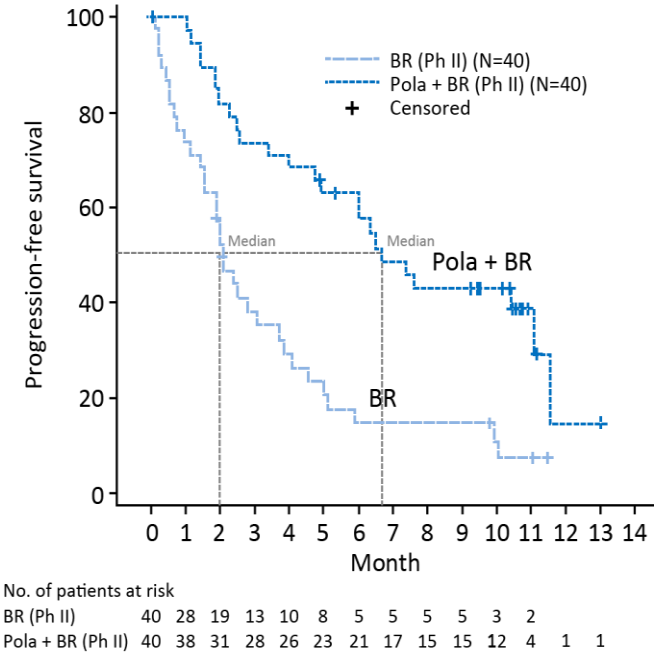


References: 1. Morschhauser et al. *ASH.* 2014 [abstract 4457]. **2.** Morschhauser F, et al. *EHA*. 2014 [abstract S1349]. **3.** Palanca-Wessels MC, et al. *Lancet Oncol*. 2015;16:704-715. **4.** Yu SF, et al. *Clin Cancer Res*. 2015;21:3298-3306; **5.** Pfeifer M, et al. *Leukemia*. 2015;29:1578-1586; **6.** http://www.biooncology.com/pipeline-molecules/polatuzumab-vedotin. Note: Polatuzumab vedotin is being developed in collaboration with Seattle Genetics.

Polatuzumab Vedotin + BR vs BR in R/R DLBCL.

Key eligibility criteria: 40 DLBCL with ≥1 prior therapy. Ineligible for SCT.



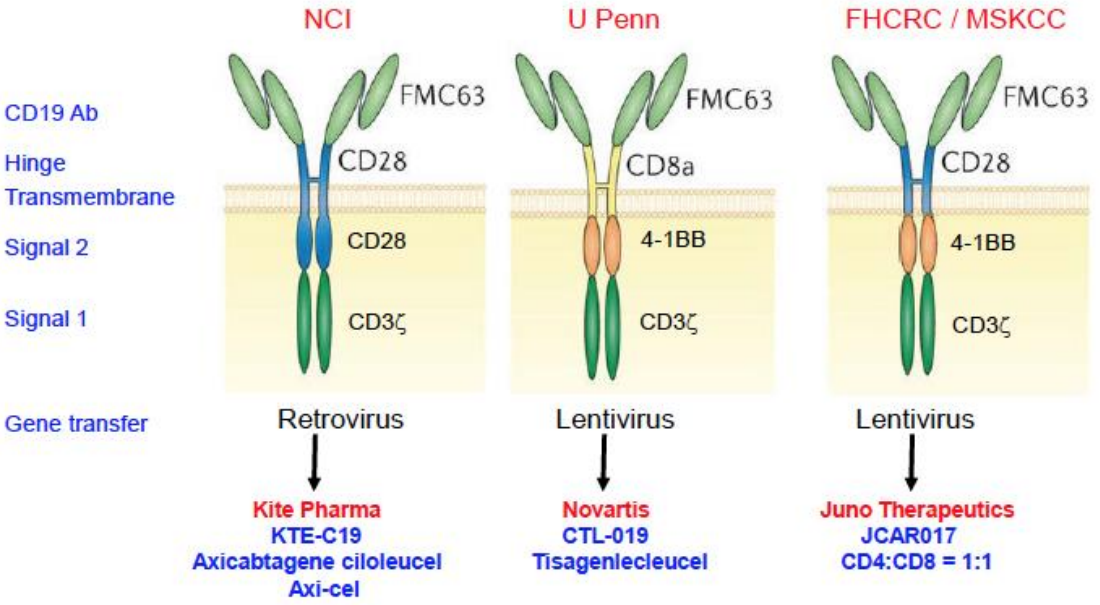


All	Pola + BR N=40	BR N=40
Median OS, mo (95% CI)	11.8 (9.5, NE)	4.7 (3.7, 8.3)
HR (95%CI)	0.35 (0.19, 0.67)	
p-value	0.0008	
1 year OS (%)	48	24

All	Pola + BR N=40	BR N=40
Median PFS, mo (95% CI)	6.7 (4.9, 11.1)	2.0 (1.5, 3.7)
HR (95%CI)	0.31 (0.18, 0.55)	
p-value	< 0.0001	

Sehn et al; Presented at the 59th ASH, Dec 2017, Abstract No.: 2821

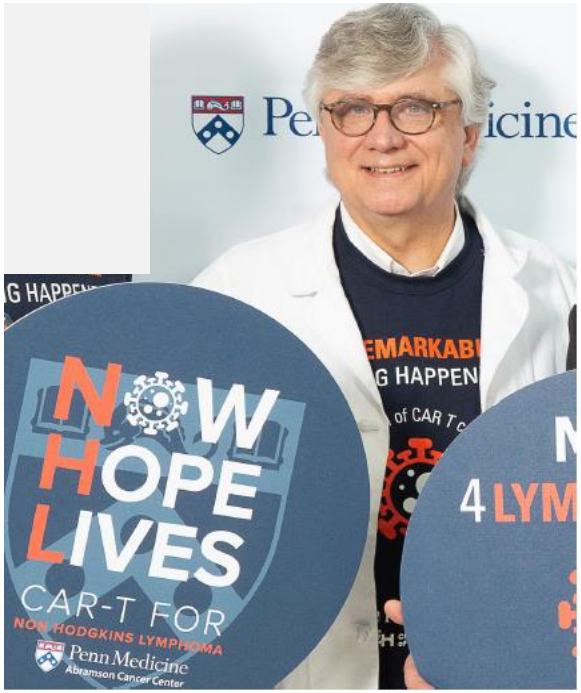
CART



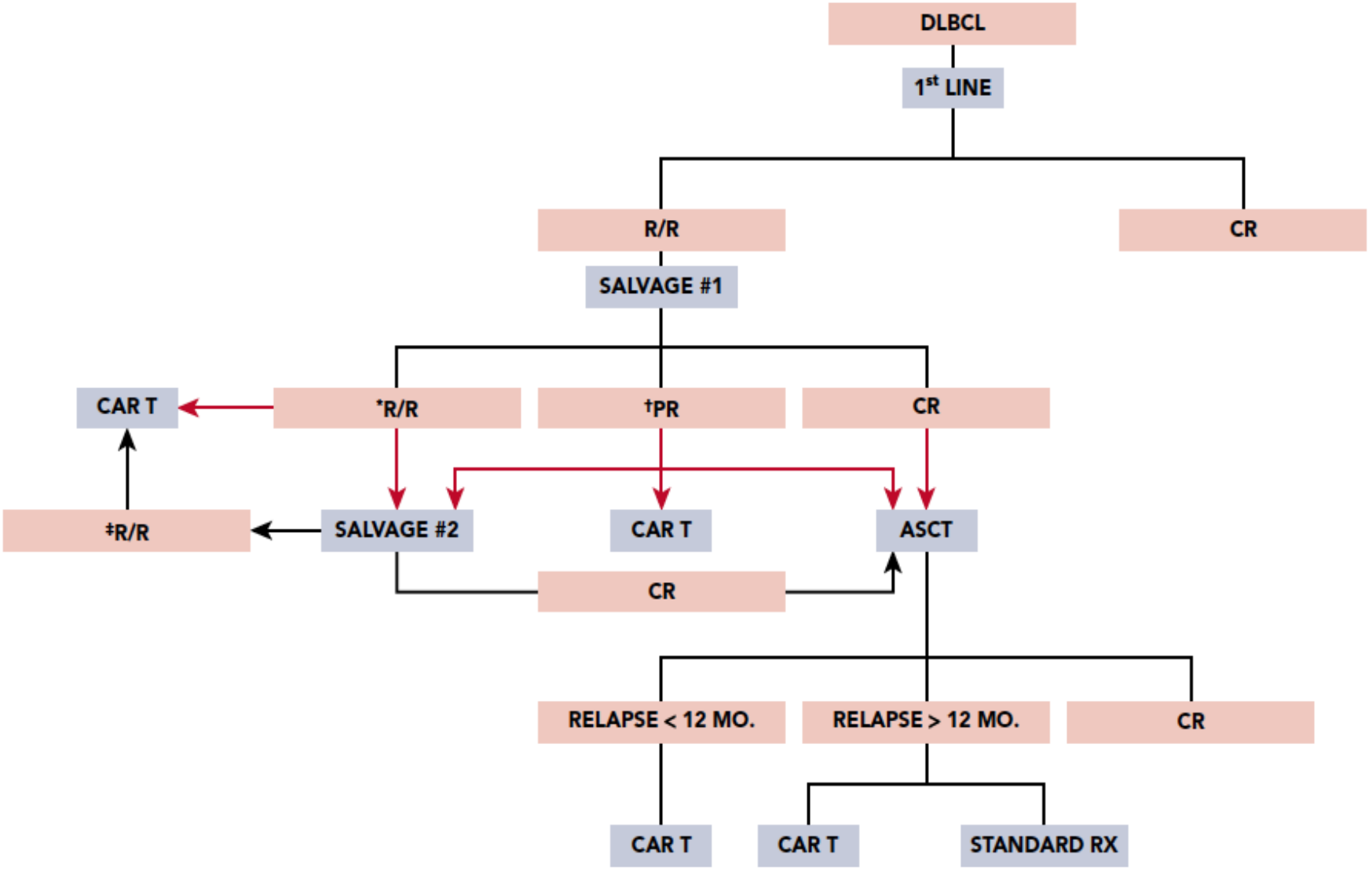
Adapted from van der Steegen et al. Nat Rev Drug Discov, 2015

"THIS IS AN EXCITING EVENT – SEEING THIS LIFESAVING THERAPY BECOME AVAILABLE WIDELY TO A LARGE PATIENT POPULATION"

STEPHEN J. SCHUSTER, MD



Future perspectives…



Chow VA, Shadman M and Gopal AK, Blood 2018; 132 (8): 777-781.

Acknowledgements

Lymphoma Team Hematology Torino

U. Vitolo

G. Benevolo

C. Boccomini

B. Botto

A. Castellino

A. Chiappella

M. Nicolosi

M. Novo

L. Orsucci

P. Pregno

E. Santambrogio

F. Vassallo

Pathological and Biological Team Torino

FONDAZIONE FIL ITALIANA LINFOMI