



IL PAZIENTE DLBCL ALLA RICADUTA: ANCORA UN UNMEET NEED?

DOTT. MUSURACA GERARDO

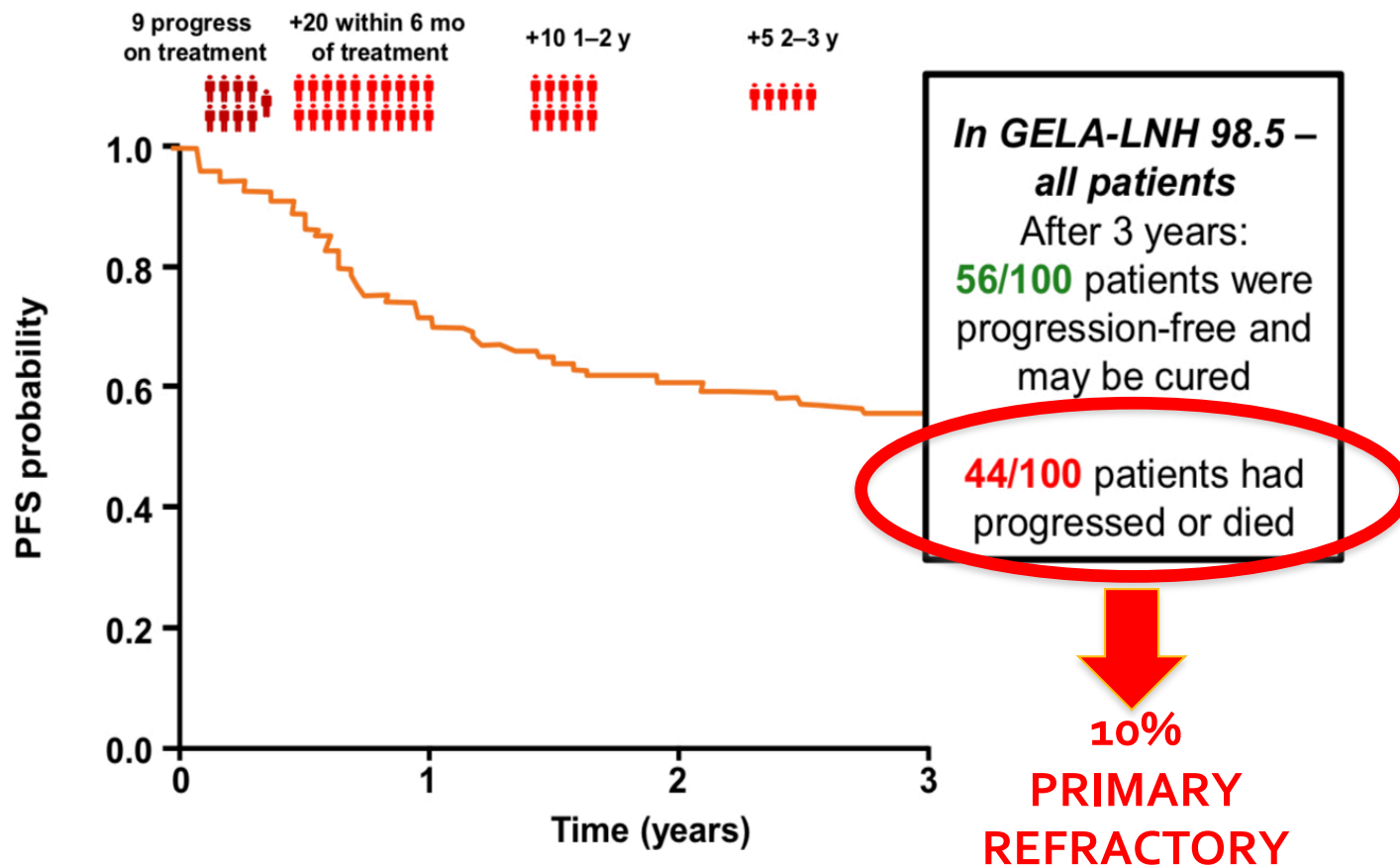
BOLOGNA 05/11/2018

NUOVI ORIZZONTI
TERAPEUTICI nel
MONDO dei
“LINFOMI”

ISTITUT
SCIENTIFIC
ROMAGNOL
PER LO STUDI E LA CURA
DEI TUMORI

DLBCL AFTER FIRST LINE R-CHOP

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



HOW I TREAT RELAPSE/REFRACTORY DLBCL

RETAGGING:

- CLINICAL RISK
- PET
- BIOPSY

CLINICAL RISK

sAAPII:

-LDH

-STAGE

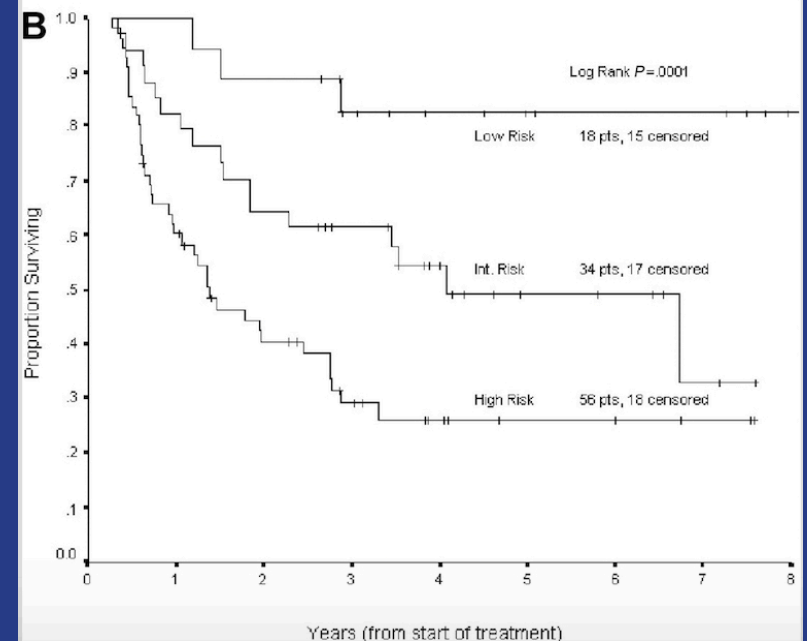
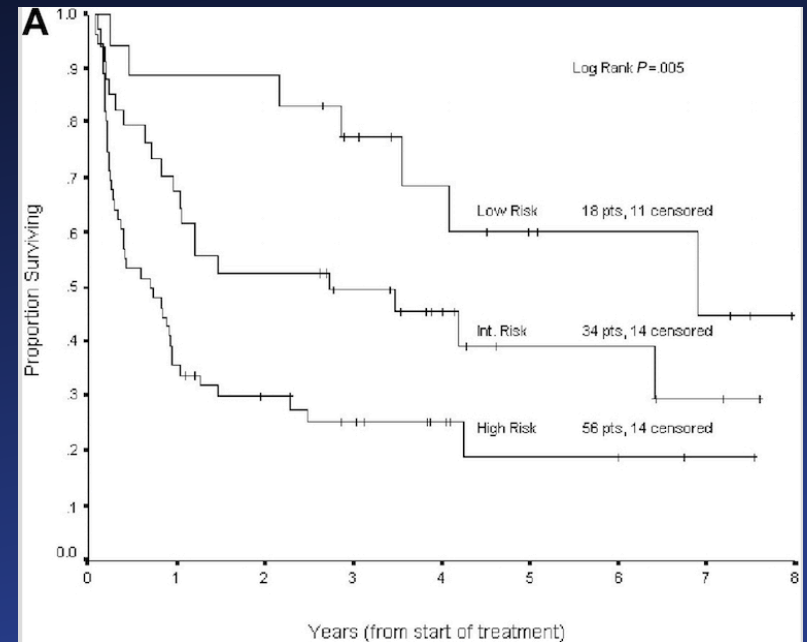
-PS 80 %



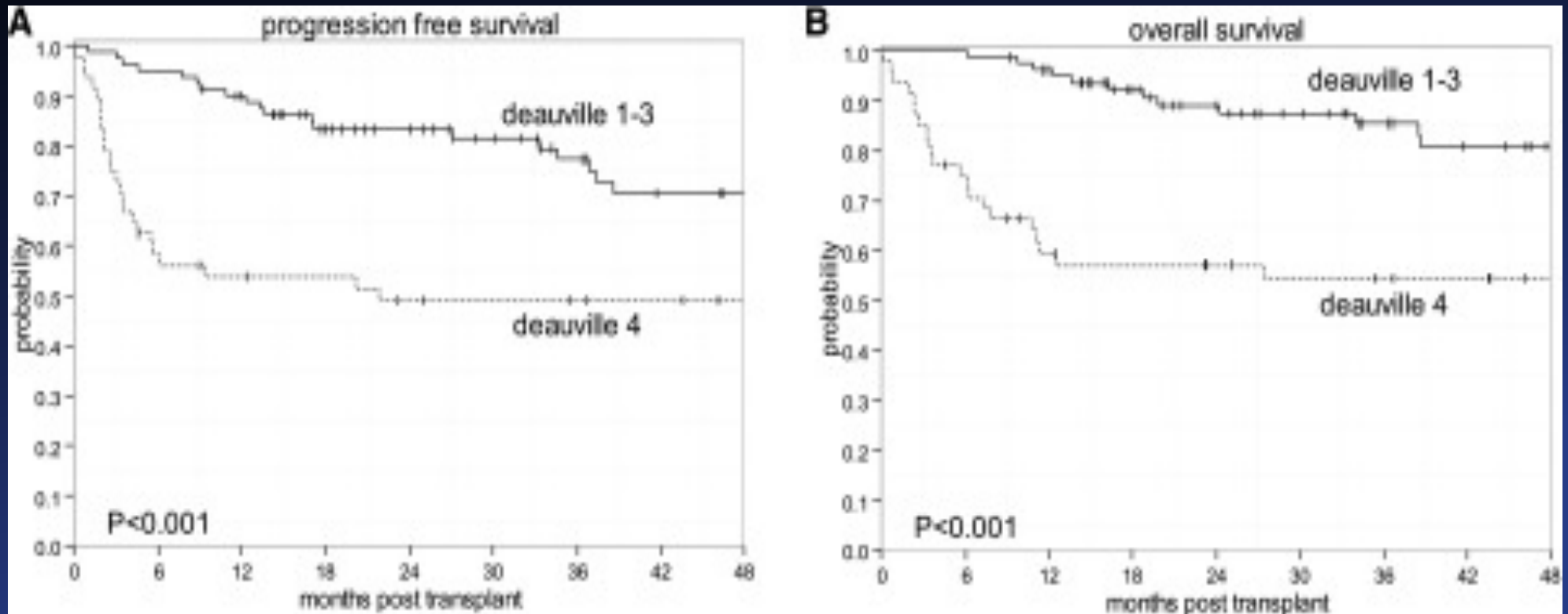
LOW RISK (0)
INTERMEDIATE (1)
HIGH RISK (2-3)

PFS

OS



PET RESTAGING



STRONGLY PREDICTIVE OF
SALVAGE RESPONSE
ACCORDING TO
Deauville score

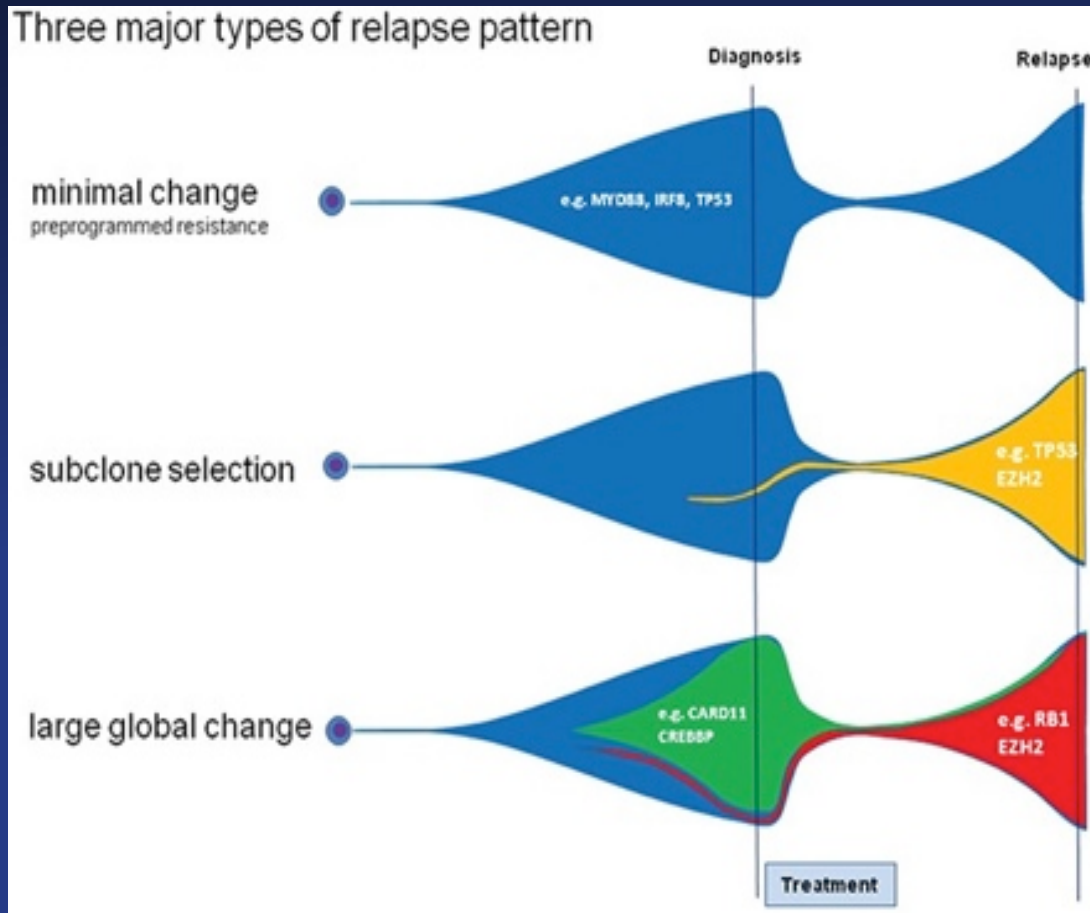
ABOUT 40-50%
CAN BE CURED !

PFS rate 77% vs 49%
OS rate 86% vs 54%

Sauter et al Blood 2015

NEW BIOPSY

ACQUIRED ONCOGENIC EVENTS UNDER CHEMOTHERAPY SELECTION PRESSURE



TO DETERMINE:

- MYC/BCL2/BCL6 STATUS
- GCB or ABC



TARGET THERAPIES

Melchardt et al Oncotarget 2016
Rizzo et al Am J Hematol 2017
Morin et al Clin Canc Res 2016

HOW I TREAT RELAPSE/REFRACTORY DLBCL

TREATMENTS:

- FIT PATIENTS FOR TRANSPLANT
- TRANSPLANT INELEGIBLE PATIENTS
- NOVEL APPROACHES

FIT PATIENTS FOR TRANSPLANT

STANDARD OF CARE: AUTOLOGOUS STEM CELL TRANSPLANTATION

WHICH IS:

- THE BEST SALVAGE REGIMEN?
- THE BEST CONDITIONING REGIMEN?
- MAINTENANCE AFTER AUTOLOGOUS?

FIT PATIENTS FOR TRANSPLANT

Table I. Salvage chemotherapy regimens in randomized studies for DLBCL [Gisselbrecht *et al*, 2010 (CORAL study); Crump *et al*, 2014 (LY.12 study); van Imhoff *et al*, 2017 (ORCHARRD study)].

Salvage induction	N	RR	Transplant rate	PFS
R-ICE	202	64%	51%	3-year: 31%
R-DHAP (CORAL)	194	63%	55%	3-year: 42%
(R)-DHAP (LY12)	304	45%	49%	3-year: 28%
(R)-GDP	306	44%	52%	3-year: 28%
R-DHAP (ORCHARRD)	223	42%	37%	2-year: 26%
O-DHAP (ORCHARRD)	222	38%	33%	2-year: 24%

(R)-GDP, (rituximab)-gemcitabine, dexamethasone, cisplatin; DLBCL, diffuse large B cell lymphoma; O-DHAP, Ofatumumab- dexamethasone, cytarabine, cisplatin; PFS, progression-free survival; R-DHAP, rituximab-dexamethasone, cytarabine, cisplatin; R-ICE, rituximab-ifosfamide, etoposide, carboplatin; RR, relative risk.

**R-DHAP vs R-ICE vs GDP:
NO SIGNIFICATIVE DIFFERENCES**

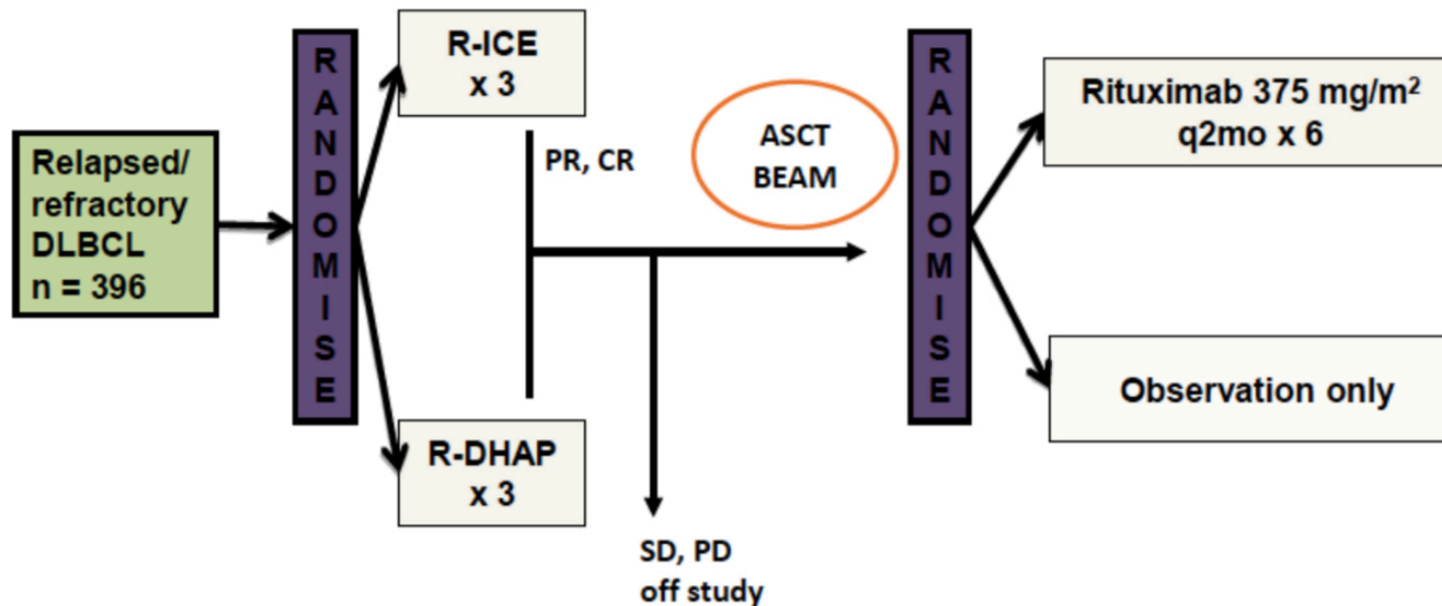
Gisselbrecht *et al* JCO 2010
Crump *et al* JCO 2014
Van Imhoff *et al* JCO 2017

FIT PATIENTS FOR TRANSPLANT

High Dose Chemotherapy plus ASCT: CORAL trial experience

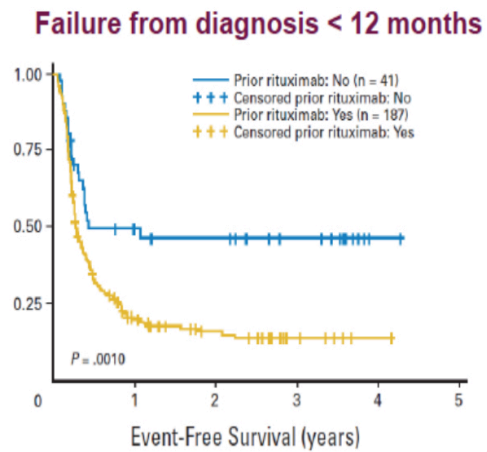
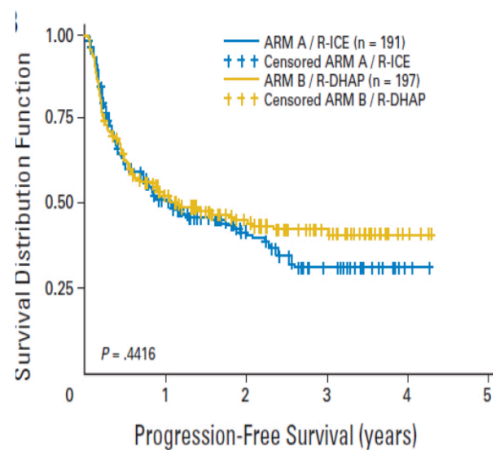
Rituximab Maintenance Therapy After Autologous Stem-Cell Transplantation in Patients With Relapsed CD20 Diffuse Large B-Cell Lymphoma: Final Analysis of the Collaborative Trial in Relapsed Aggressive Lymphoma

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

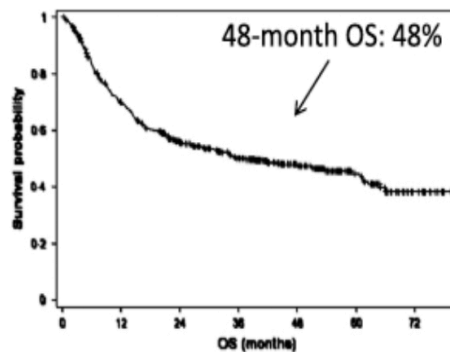


FIT PATIENTS FOR TRANSPLANT

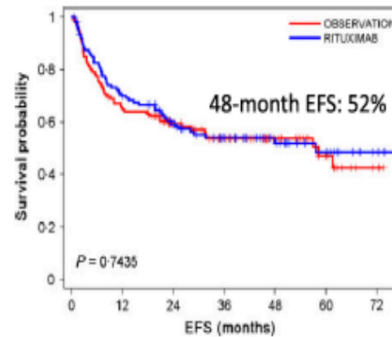
High Dose Chemotherapy plus ASCT: CORAL trial experience



OS from **first** randomisation



EFS from **second** randomisation



POOR FACTORS:

- PRIOR RITUXIMAB
- PRIMARY REFRACTORY
- HIGH sAA IPI

TRANSPLANTED PATIENTS

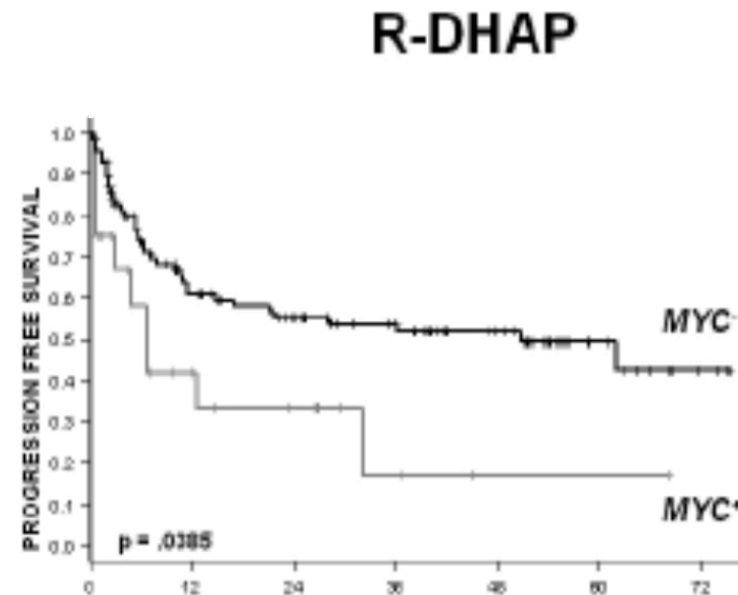
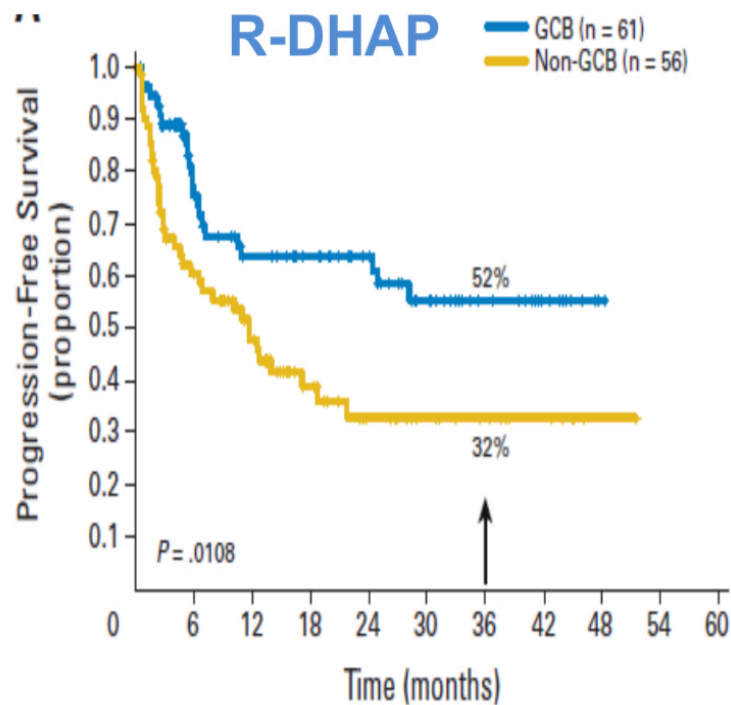
PFS: 53%

**NO ADVANTAGE
TO MAINTENANCE
AFTER ASCT**

FIT PATIENTS FOR TRANSPLANT

Prognostic factors RR/DLBCL: Bio-CORAL trial experience

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



FIT PATIENTS FOR TRANSPLANT

FAILURE OF FIRST SALVAGE (CORAL)



SECOND SALVAGE

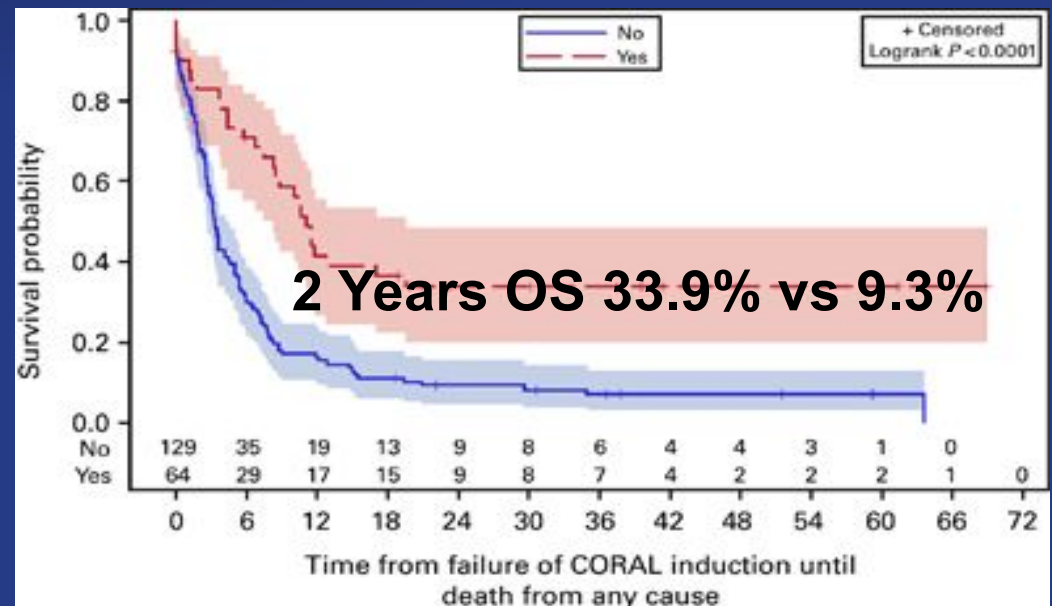
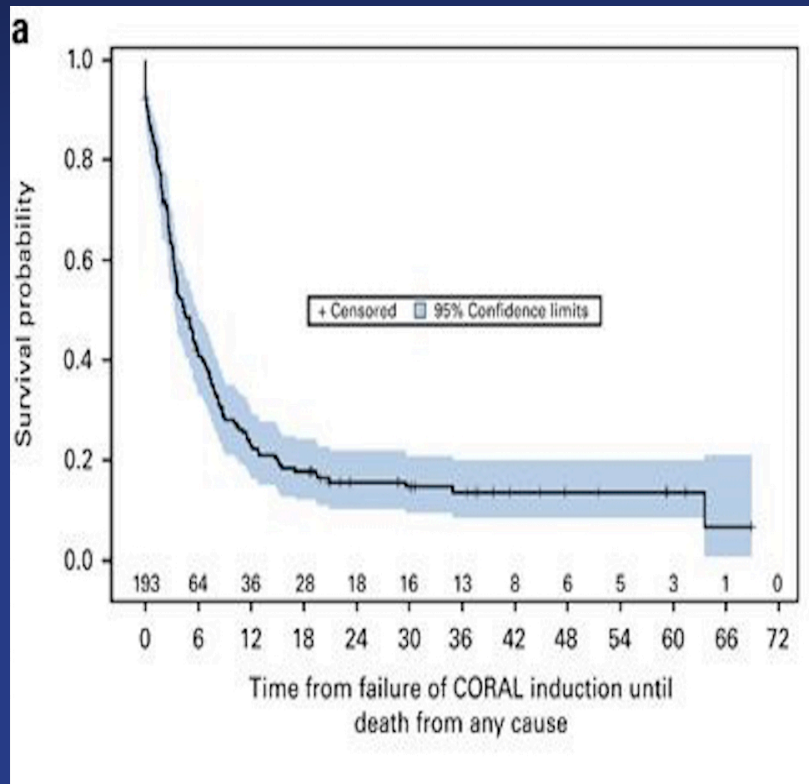
ORR:

ICE 43.5% (vs DHAP)

DHAP 42.3% (vs ICE)



31.5% TRANSPLANTED



FIT PATIENTS FOR TRANSPLANT

CONDITIONING REGIMEN

BEAM (CARMUSTINE, ETOPOSIDE, CYTARABINE, MELPHALAN)

IS THE STANDARD OF CARE

NO ADVANTAGE +Ibritumomab tiuxetan

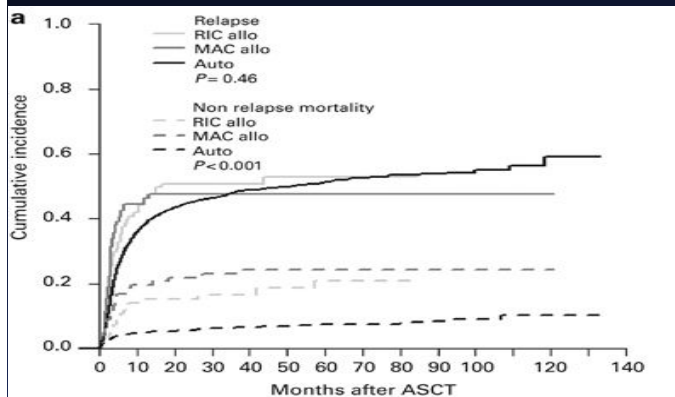
(Chahoud et al Clin Canc Research 2018)

NO ADVANTAGE +high dose Rituximab

(Srour et al Br J Haematol 2017)

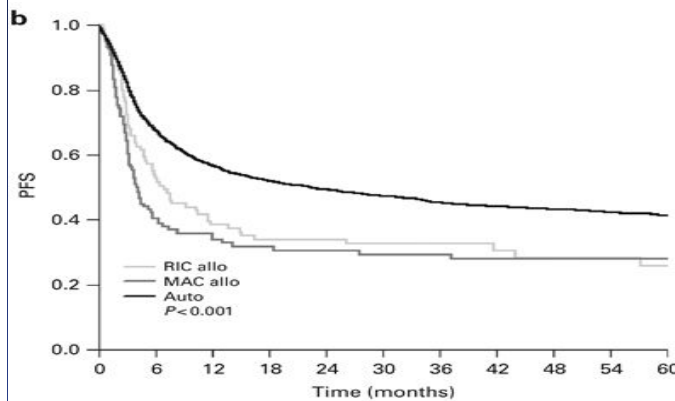
FIT PATIENTS FOR TRANSPLANT

ALLO TRANSPLANT



4 year NRM

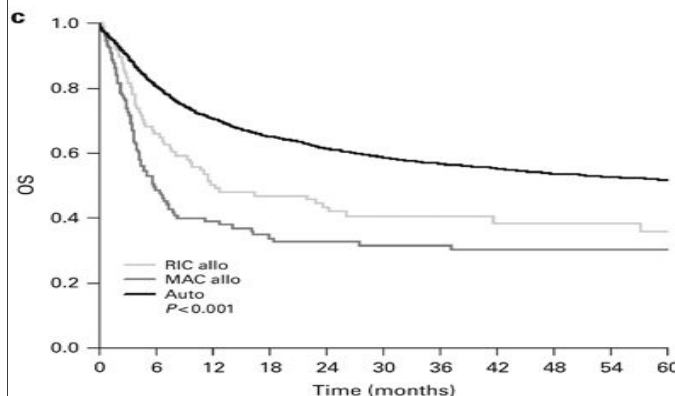
AUTO: 7% RIC: 20%, MAC: 27%



4210 PATIENTS R/R DLBCL

AUTO vs ALLO

AS FIRST TRANSPLANT PROCEDURE



4 year OS

AUTO: 60% RIC: 52%, MAC: 38%

FIT PATIENTS FOR TRANSPLANT

ALLOTRANSPLANT



Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org



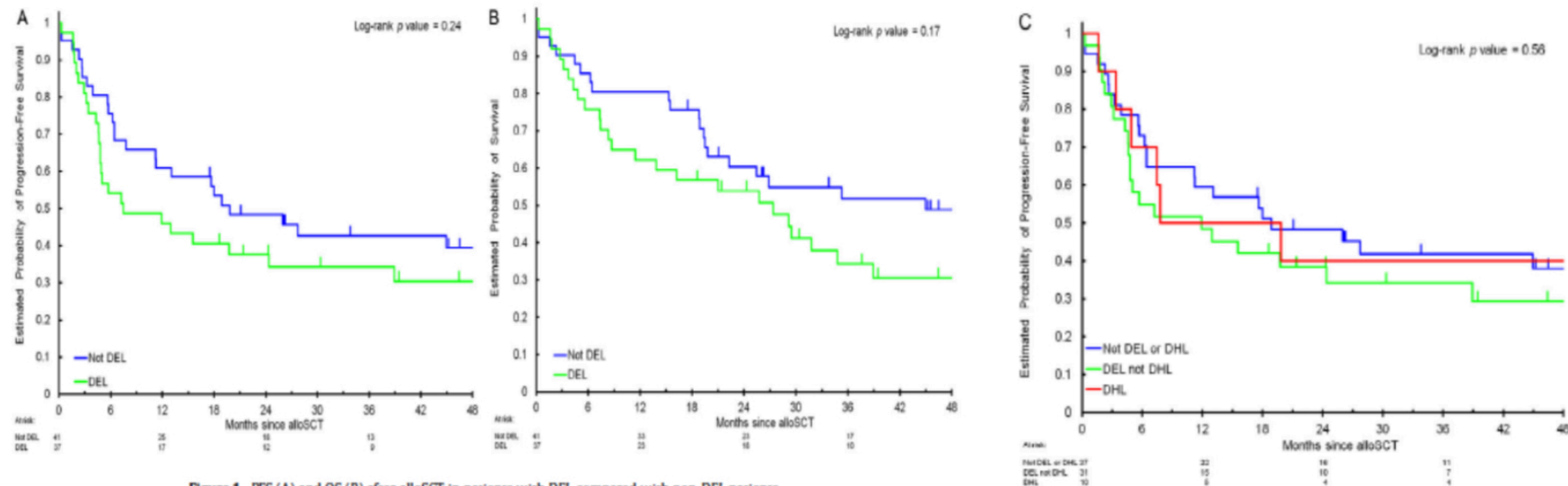
Biol Blood Marrow Transplant 24 (2018) 514–520

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, Auaporn P. Nademanee ¹, Philippe Armand ⁵

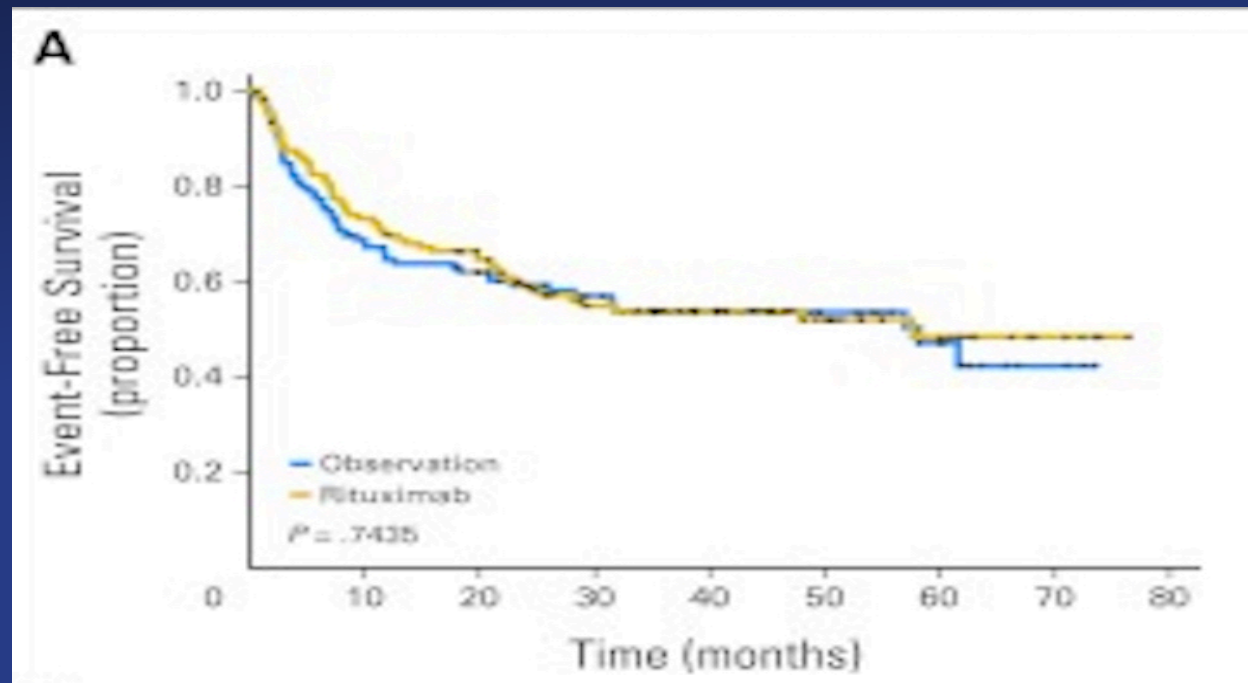
AlloSCT produced durable remissions in patients with rel/ref aggressive B-NHL irrespective of DEL and DHL status, justifying its consideration in the treatment of patients with rel/ref DEL/DHL.



FIT PATIENTS FOR TRANSPLANT

MAINTENANCE AFTER AUTO

NO INDICATION
TO MAINTENANCE WITH RITUXIMAB
AFTER AUTO



HOW I TREAT RELAPSE/REFRACTORY DLBCL TRANSPLANT INELEGIBLE PATIENTS

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 Gisselbrecht⁴

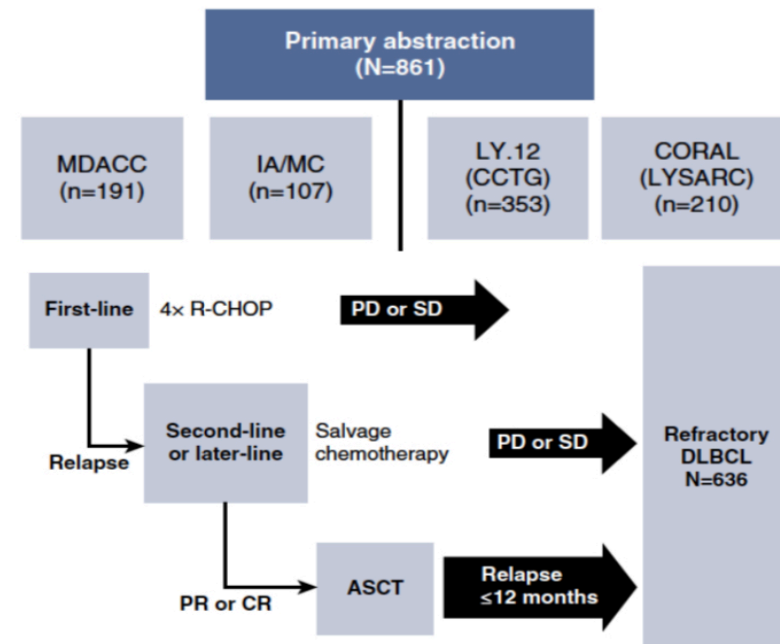


BLOOD, 19 OCTOBER 2017 · VOLUME 130, NUMBER 16

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



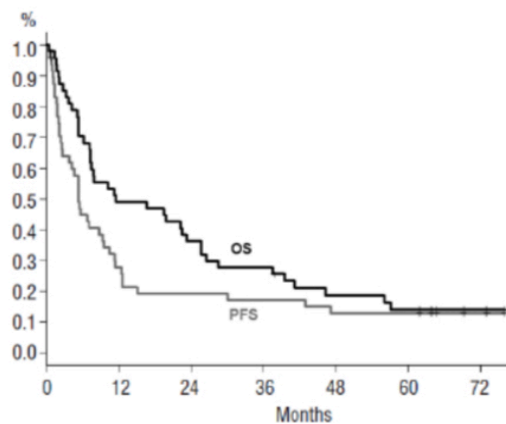
HOW I TREAT RELAPSE/REFRACTORY DLBCL

TRANSPLANT INELEGIBLE PATIENTS

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

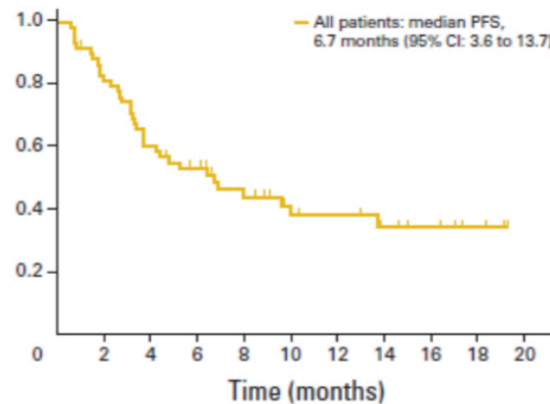


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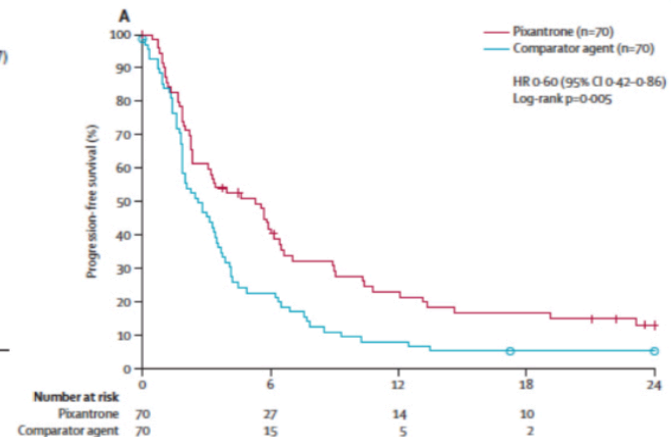
Progression-Free Survival (probability)

D

R-BENDAMUSTINE

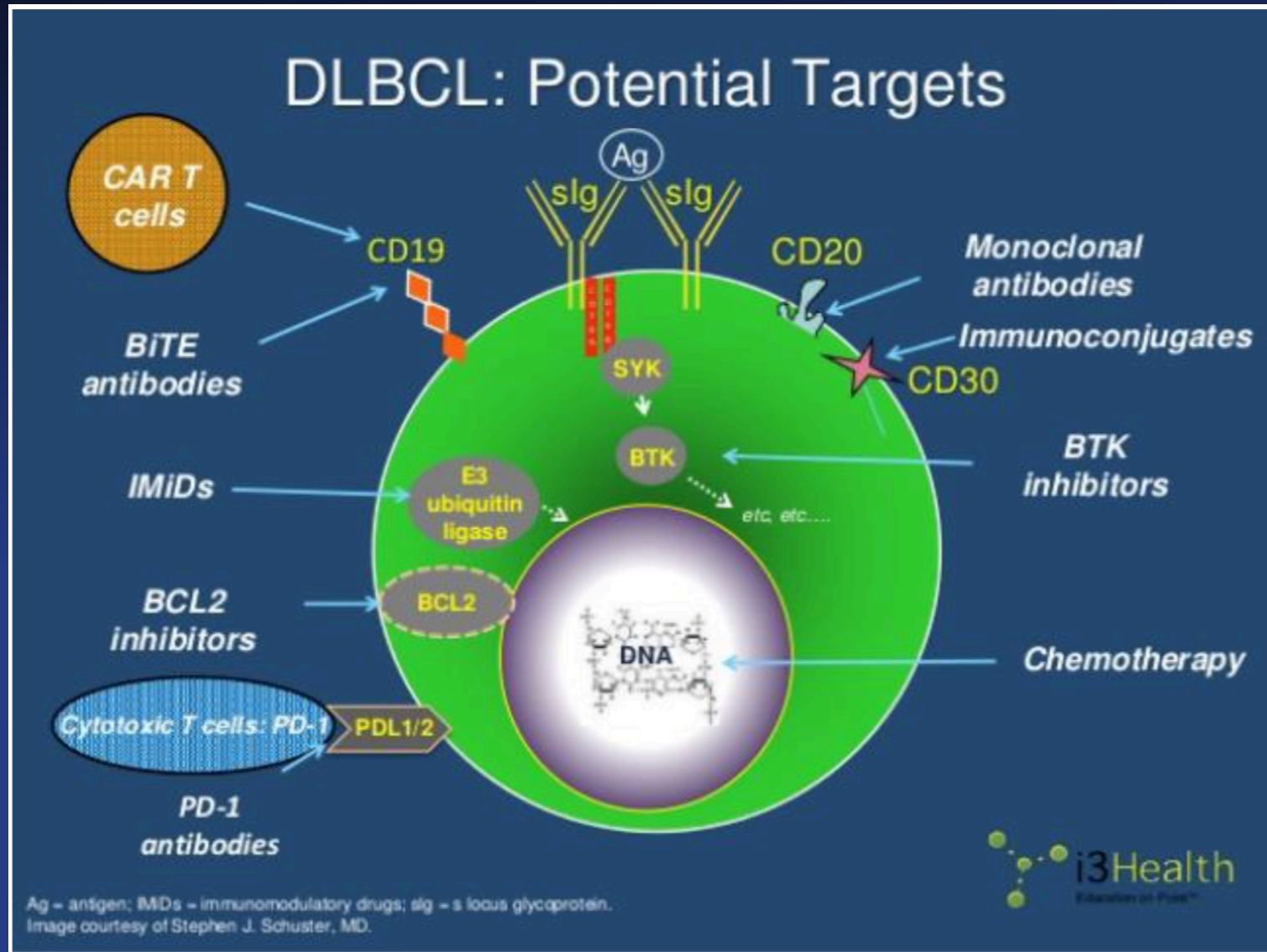


PIXANTRONE



HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES



HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

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

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

HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

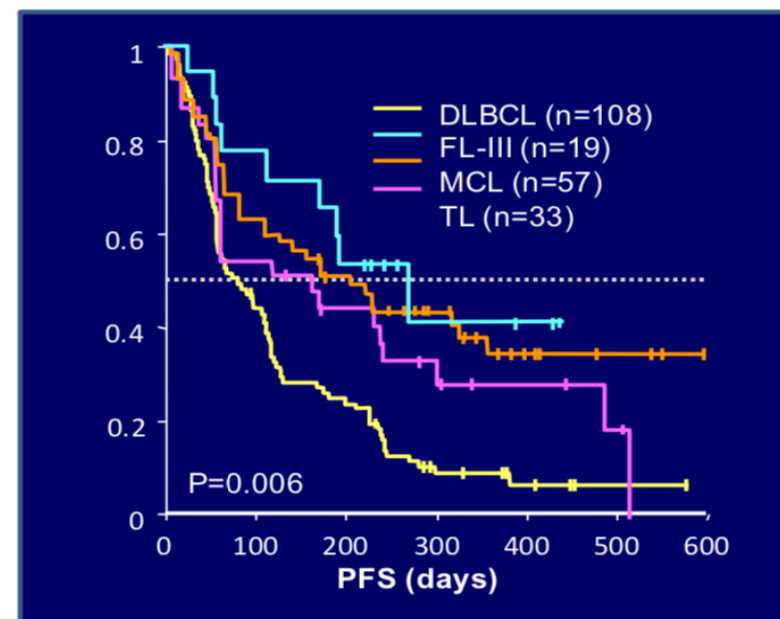
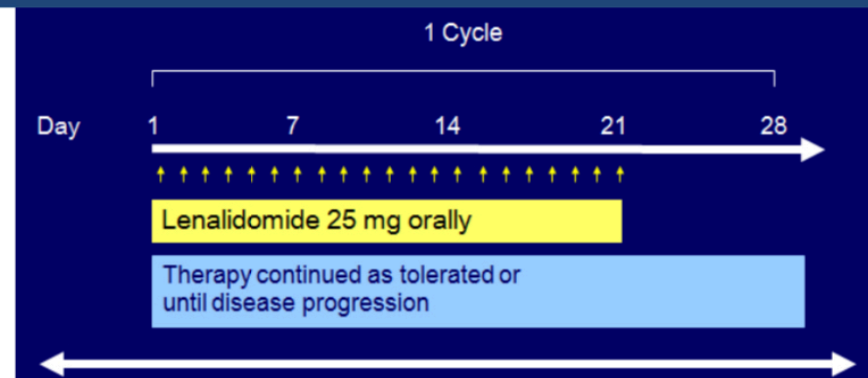
Activity of lenalidomide in R/R DLBCL

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	11	46%	N/A	18.9
ABC by GEP				

*Included all patients in mixed NHL population.

[†]CR only (not CRu)

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.



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

HOW I TREAT RELAPSE/REFRACTORY DLBCL

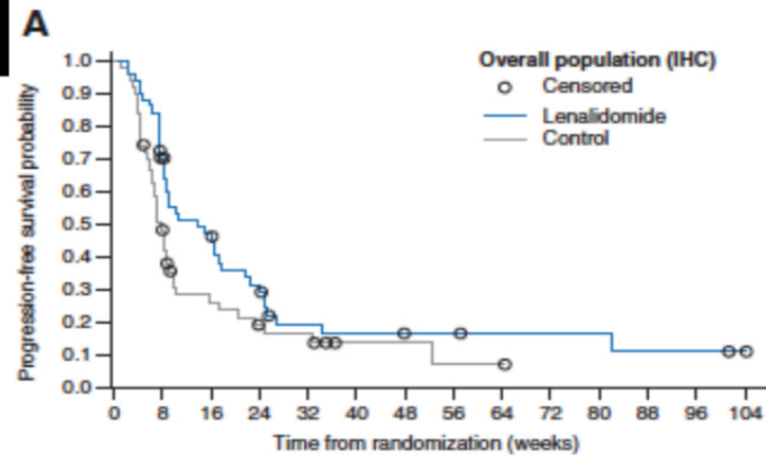
NOVEL APPROACHES

Cancer Therapy: Clinical

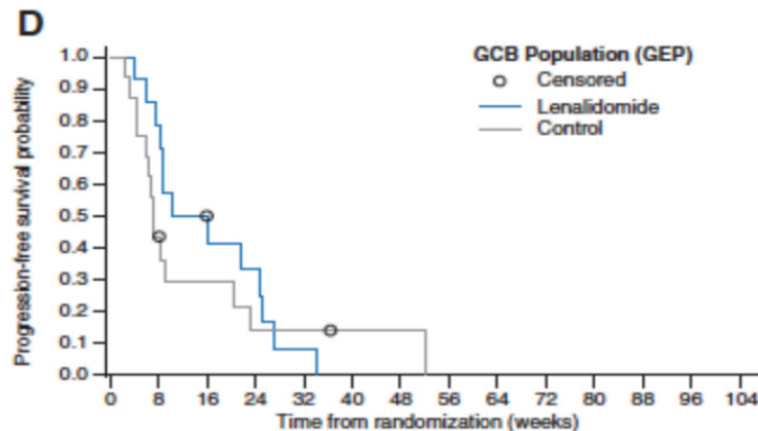
Clinical
Cancer
Research

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

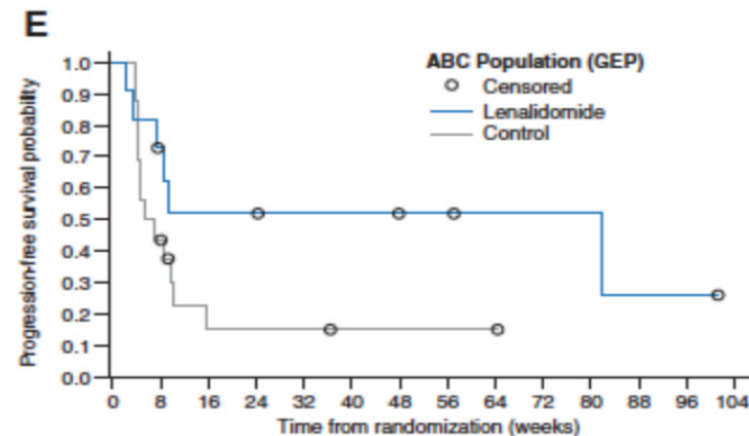
Myron S. Czuczman¹, Marek Trnėný², Andrew Davies³, Simon Rule⁴, Kim M. Linton⁵, Nina Wagner-Johnston⁶, Randy D. Gascoyne⁷, Graham W. Slack⁷, Pierre Brousset⁸, David A. Eberhard⁹, Francisco J. Hernandez-Ilizaliturri¹, Gilles Salles¹⁰, Thomas E. Witzig¹¹, Pier Luigi Zinzani¹², George W. Wright¹³, Louis M. Staudt¹⁴, Yandan Yang¹⁴, P. Mickey Williams¹⁵, Chih-Jian Lih¹⁶, Jacqueline Russo¹⁷, Anjan Thakurta¹⁷, Patrick Hagner¹⁷, Pierre Fustier¹⁸, Dale Song¹⁷, and Ian D. Lewis¹⁹



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)		



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)		

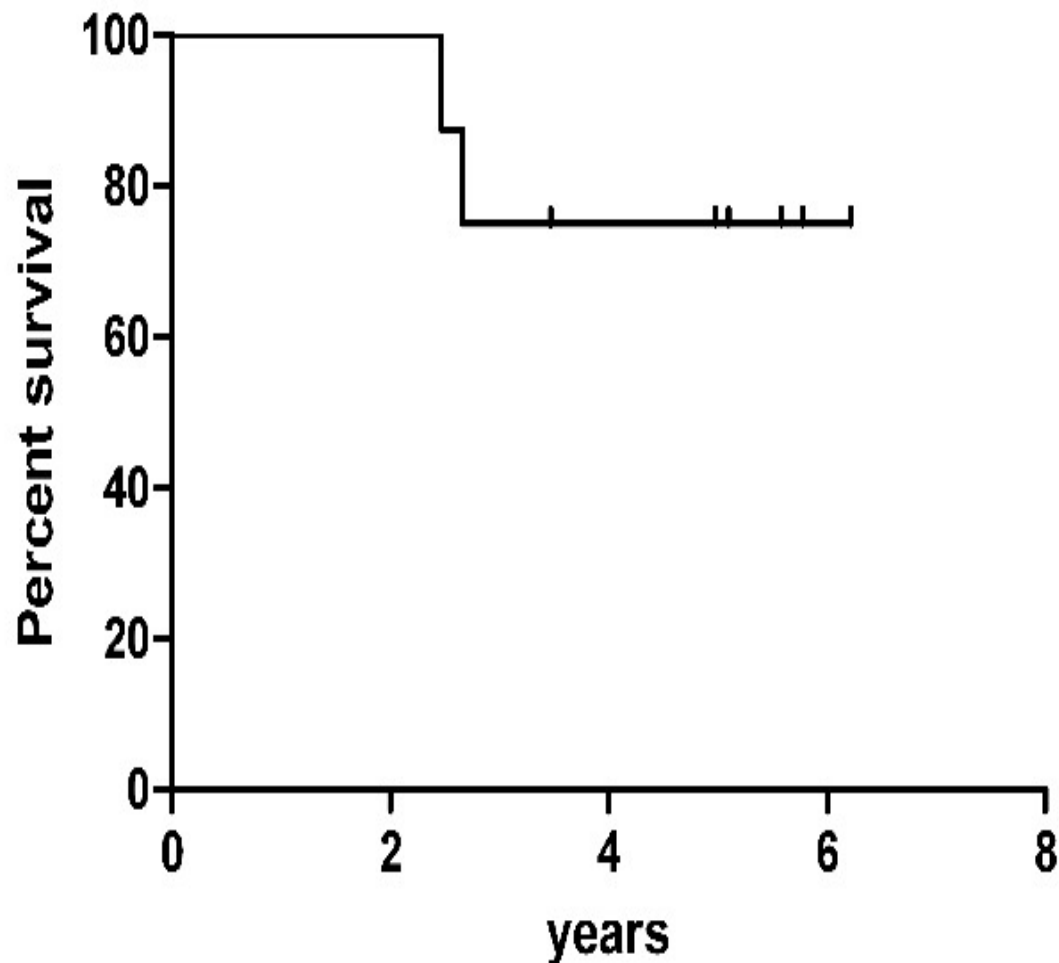


Group	n	Median (weeks) (range)	HR (95% CI)	P value
Lenalidomide ABC	11	82.0 (7.3–NA)	0.44 (0.15–1.23)	0.105
Control ABC	16	6.2 (4.3–10.1)		

HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

LENALIDOMIDE+ RITUXIMAB+ LENA MAINTENANCE



23 PATIENTS

35% ORR (8 PZ)

34.8% OS AT 6 YEARS

DFS 75% AT 6 YEARS

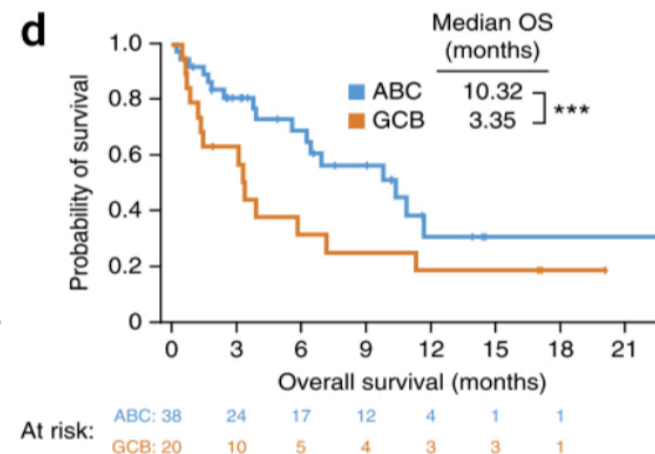
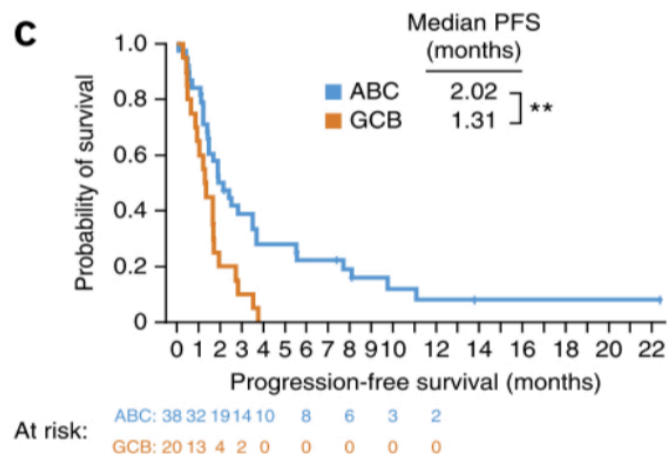
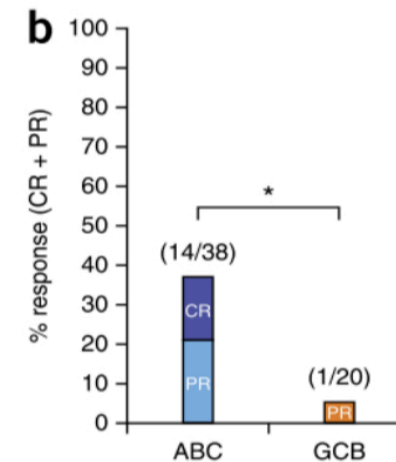
Zinzani et al Hematologica 2016

HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

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%
RIP1 (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.

HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

CLINICAL TRIALS AND OBSERVATIONS

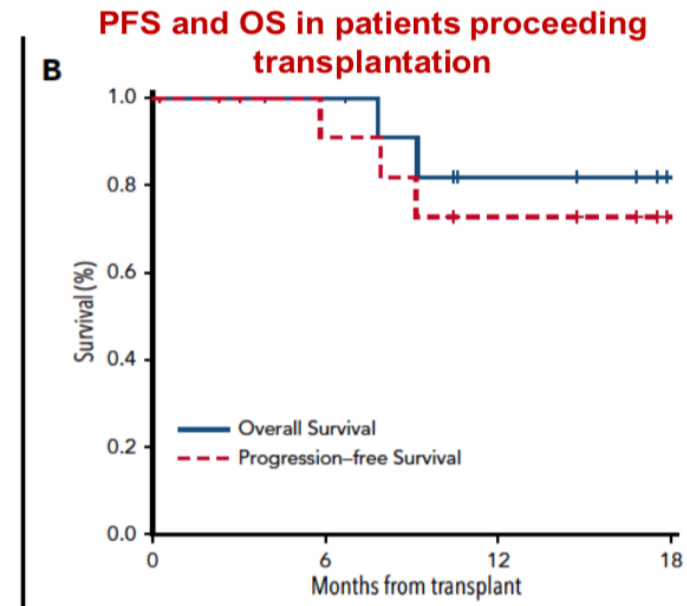
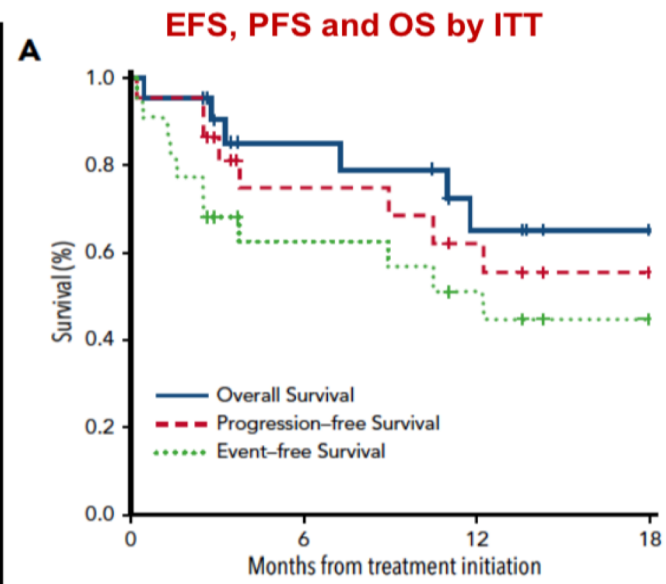
blood® 19 APRIL 2018 | VOLUME 131, NUMBER 16

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

Table 2. FDG-PET response

Sauter et al Blood 2018

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

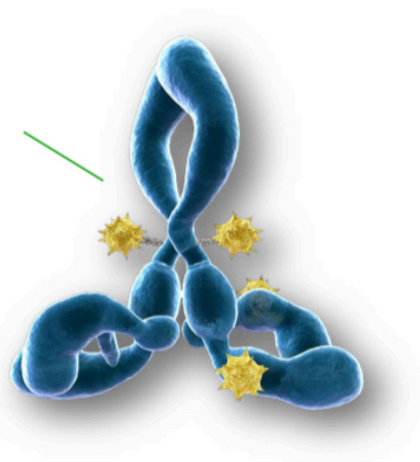


HOW I TREAT RELAPSE/REFRACTORY DLBCL

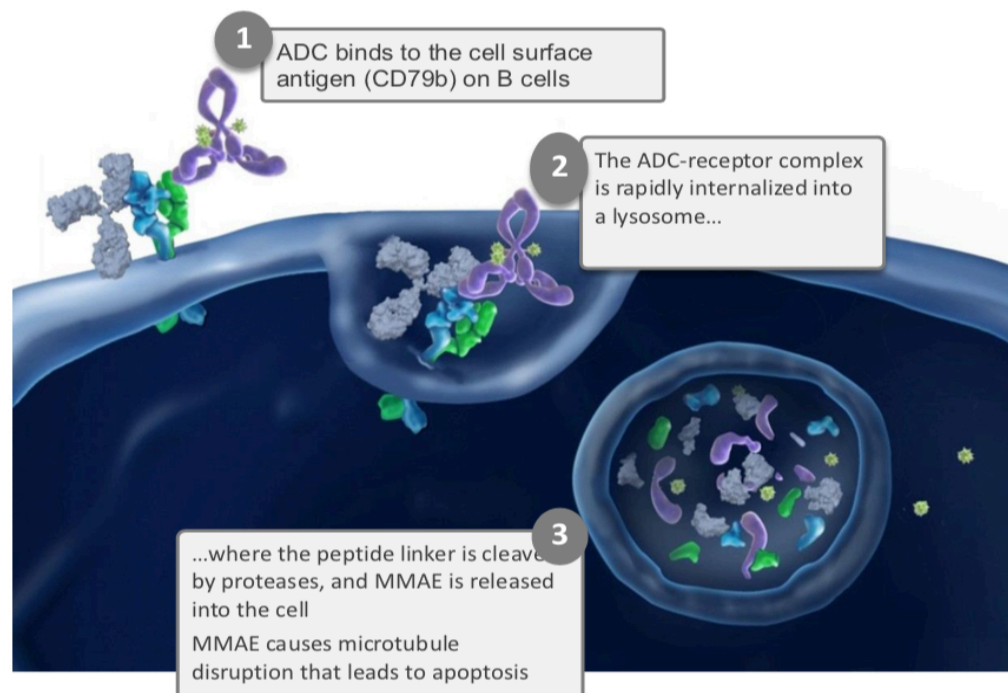
NOVEL APPROACHES

Polatuzumab vedotin

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



Binds CD79b and ADC-receptor complex internalized



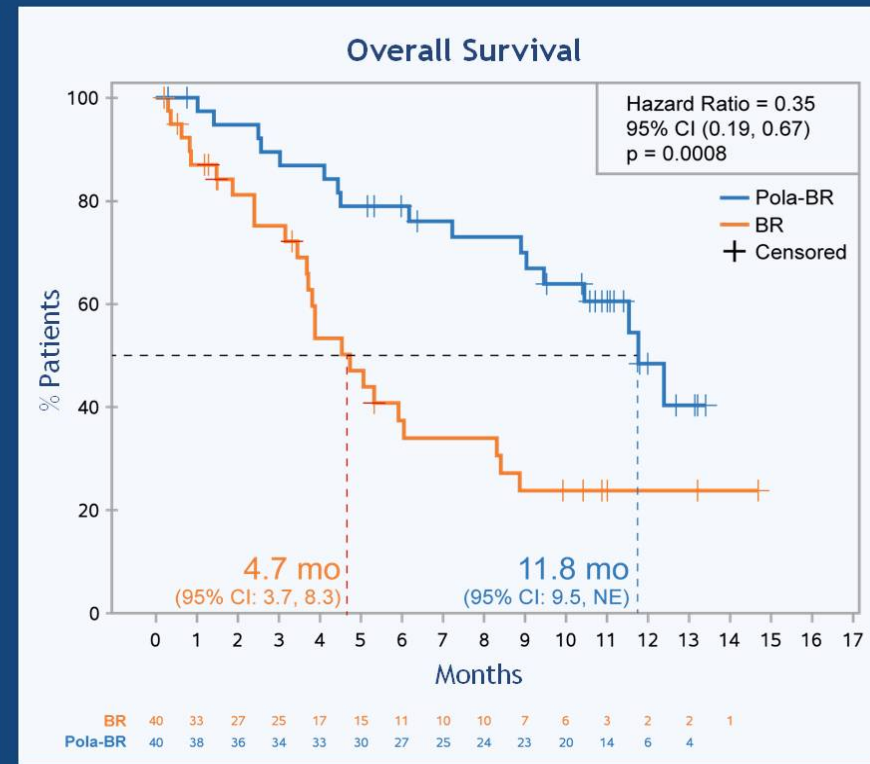
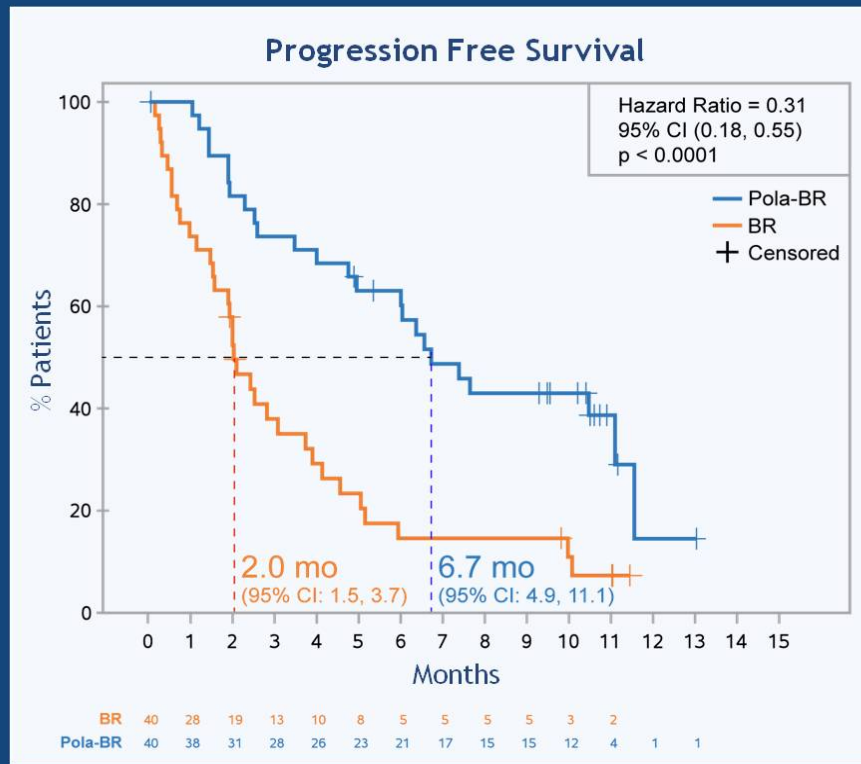
References: 1. Morschhauser et al. *ASH*. 2014 [abstract 4457]. 2. Morschhauser F, et al. *EHA*. 2014 [abstract S1349]. 3. Palanca-Wessels MC, et al. *Lancet Oncol*. 2015;16:704-715. 4. Yu SF, et al. *Clin Cancer Res*. 2015;21:3298-3306; 5. Pfeifer M, et al. *Leukemia*. 2015;29:1578-1586; 6. <http://www.biooncology.com/pipeline-molecules/polatuzumab-vedotin>.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

HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

POLATUZUMAB+ BR vs BR IN DLBCL

DLBCL: PFS and OS significantly longer with Pola-BR

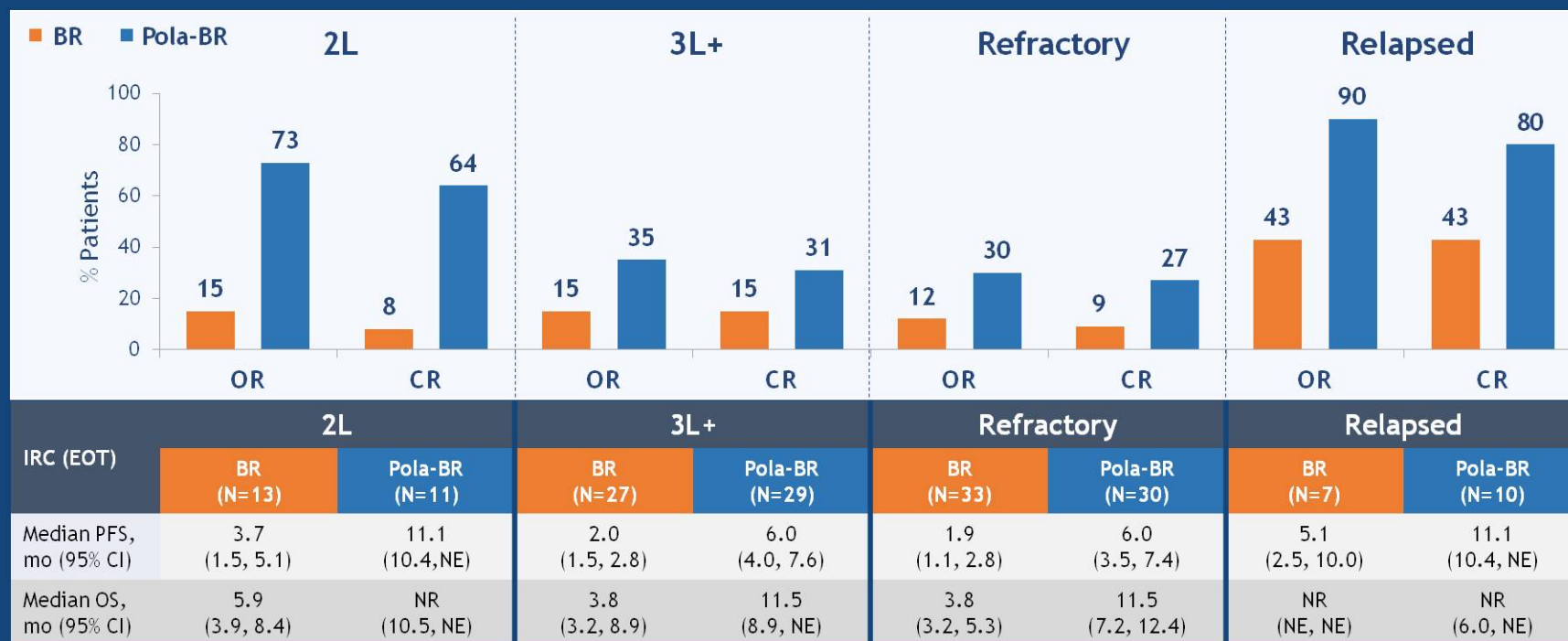


HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

POLATUZUMAB+ BR vs BR IN DLBCL

DLBCL: PET-CR Rates Higher with Pola-BR Regardless of Prior Lines of Therapy or Refractory Status



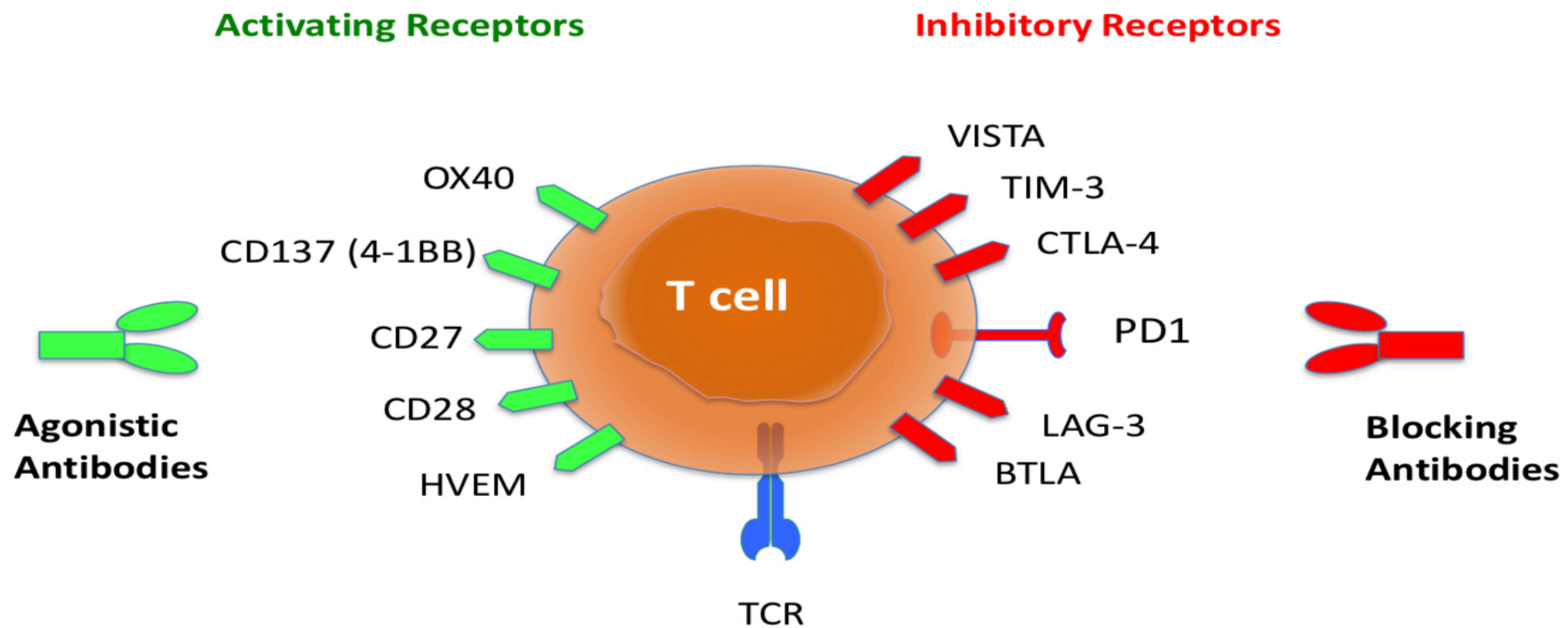
2L, second line therapy; 3L+ third-line-plus; CR, complete response; OR, objective response; PFS, progression-free survival; OS, overall survival

HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

Therapeutic Activation of Autologous T Cells

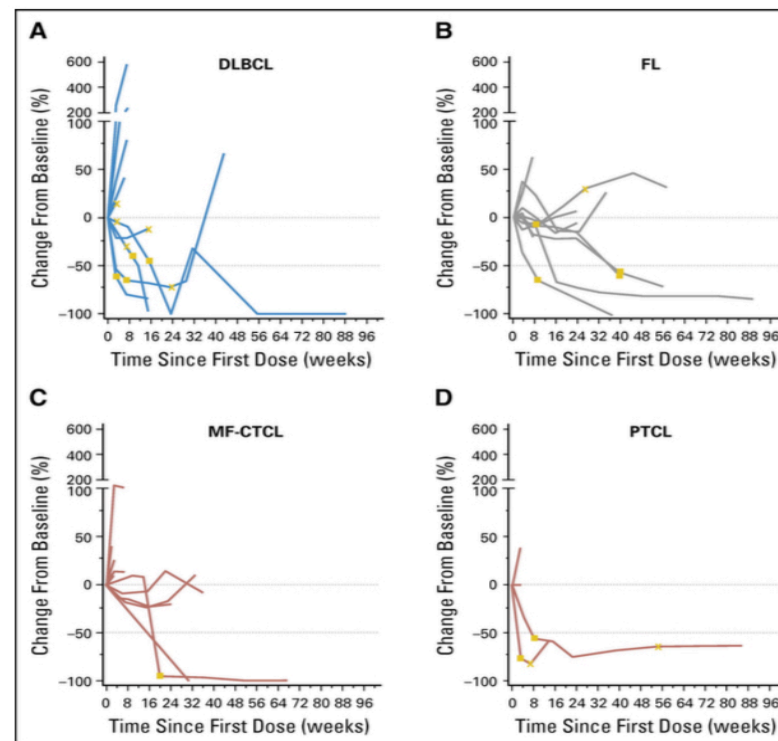
Immune checkpoint inhibitors



HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

Nivolumab in Patients With Relapsed or Refractory Hematologic Malignancy: Preliminary Results of a Phase Ib Study



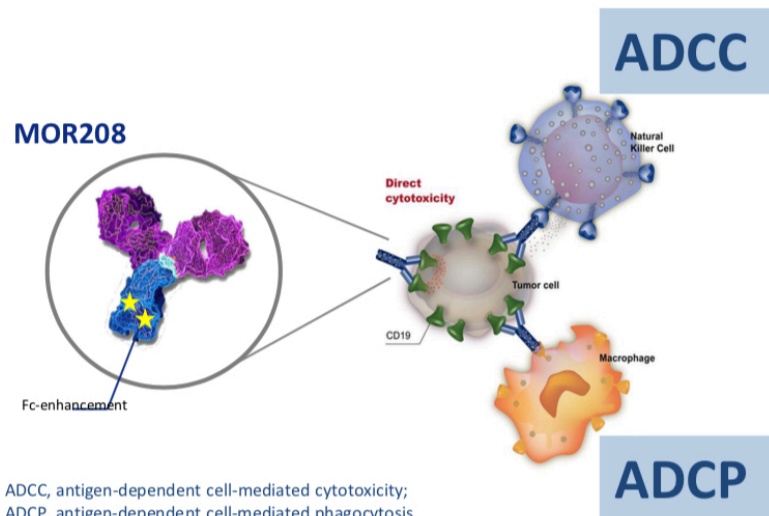
ORR: 36%
Median DR: 22 wks

HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

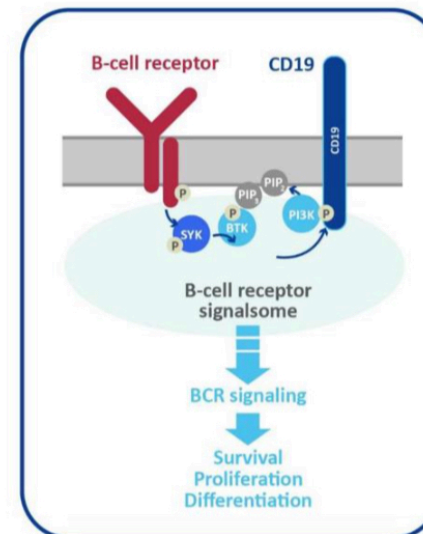
MOR208: An Enhanced CD19 Antibody

- **MOR208** is an Fc-enhanced monoclonal antibody that targets CD19
- Fc-enhancement of MOR208 leads to a potentiation of **ADCC** and **ADCP**
- MOR208 induces **direct cytotoxicity**



Horton HM et al. Cancer Res 2008; 68:8049-57

Direct cytotoxicity



Katz B-Z et al Leukemia & Lymphoma 2014
Fujimoto M, et al. Immunity 2000
Poe JC, et al. J Immunol;2012

Polish
Lymphoma
Research
Group



Prof. Wojciech Jurczak MD, PhD

HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

MOR208 Single Agent in R/R NHL

MOR208

Showed encouraging single-agent activity in R-R DLBCL and R-R iNHL for further development:

- **ORR: 26% in DLBCL and 29% in iNHL**
- **Target lesion shrinkage also observed in patients with stable disease** (5/6 DLBCL and 14/17 iNHL)
- Efficacious in patients with **rituximab-refractory disease**

MOR208

Is able to induce **long-lasting responses** in DLBCL and iNHL

- **12 month PFS rate: 39%** in DLBCL and iNHL
- Longest responses: five iNHL and one DLBCL patient are on treatment for more than 4 years

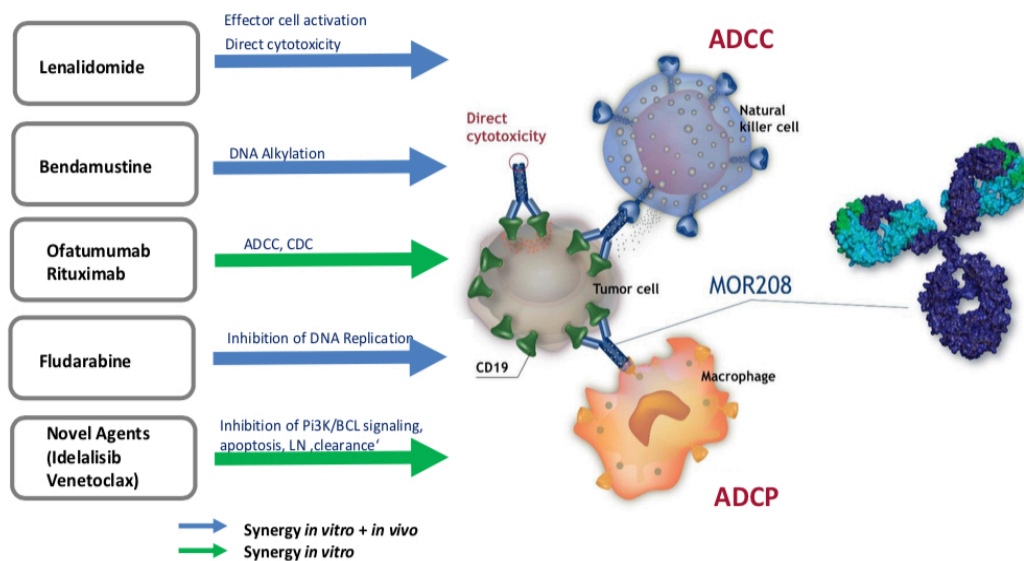
MOR208

- **Well tolerated**, also in long-term treatment

HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

MOR 208 - Synergy with all tested B cell therapies



L-MIND II phase trial in R/R DLBCL

B-MIND III phase trial in R/R DLBCL

COSMOS phase II study in R/R CLL

HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

MOR 208 + LEN Promising PFS Compared to Existing and Upcoming Therapies in NTE-R/R DLBCL

	L-MIND Cut-Off Dec.12, 2018	Dang et al., BJH 2017*	Sehn et al., ASH 2017	Pettengel et al., The Lancet, 2012	SCHOLAR-1 Crump et al., Blood, 2017**	ZUMA-1 Locke And Neelapu et al.,ASH, 2017
Regimen	MOR208 + LEN	R + bendamustine	polatuzumab + R + bendamustine	pixantrone	Salvage chemotherapies and radiation	axi-cel
Phase	2	3	2	3	Retrospective study	2
Evaluable patient population	R/R DLBCL n=68	R/R DLBCL n=137	R/R DLBCL n=40	R/R DLBCL n=104	Refractory DLBCL n=635	Refractory DLBCL n=108
Best ORR	49%	49%	70%	37%	26%	82%
Best CR	31%	18%	58%	11.4%	8%	58%
Median PFS, months	Not reached 12 mo PFS rate 50.4%	3.7	6.7	5	n/a	5.9
Median overall survival, months	NR*** at med FU	9.5	11.8	7.5	6.6	NR

HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

CD19 CAR T NHL Trial Data

	ZUMA-1 (Kite)	JULIET (Novartis)	Transcend (Juno)
Source	Phase 2 Primary Analysis ASH 2017	Phase 2 Interim Analysis ASH 2017	Phase 1 Interim Analysis ASH 2017
Enrollment	111 enrolled; 101 dosed	160 enrolled; 99 dosed (81 evaluable for response)	140 enrolled; 108 dosed (4 pending)
Population	<ul style="list-style-type: none"> • 78% refractory; 0% relapsed • 22% post ASCT • 16% TFL; 8% PMCBCL 	<ul style="list-style-type: none"> • 41% refractory; 59% relapsed • 47% post ASCT • 19% TFL; 0% PMBCL 	<ul style="list-style-type: none"> • 67% refractory; 24% relapsed • 40% post ASCT • 21% TFL; 0% PMBCL
Efficacy	<ul style="list-style-type: none"> • ORR: 82%; 54% CR • ITT ORR: 75%; 50% CR • Ongoing: 42%; 40% CR • Median follow-up 15.4 m 	<ul style="list-style-type: none"> • ORR: 53%; 40% CR • ITT ORR: 27%; 20% CR • Ongoing: 37%; 30% CR • Median follow-up 6 m 	<ul style="list-style-type: none"> • ORR: 74%; 52% CR • ITT ORR: 55%; 38% CR • Ongoing: 47%; 42% CR • Median follow-up 6 m
Safety*	<ul style="list-style-type: none"> • G3+ CRS 13% • G3+ NE 28% • G5 AE 3% 	<ul style="list-style-type: none"> • G3+ CRS 23% • G3+ NE 12% • G5 AE X% 	<ul style="list-style-type: none"> • G3+ CRS 1% • G3+ NE 15% • G5 AE 4%

* Different grading scales are used to assess CRS, neurotoxicity across trials.

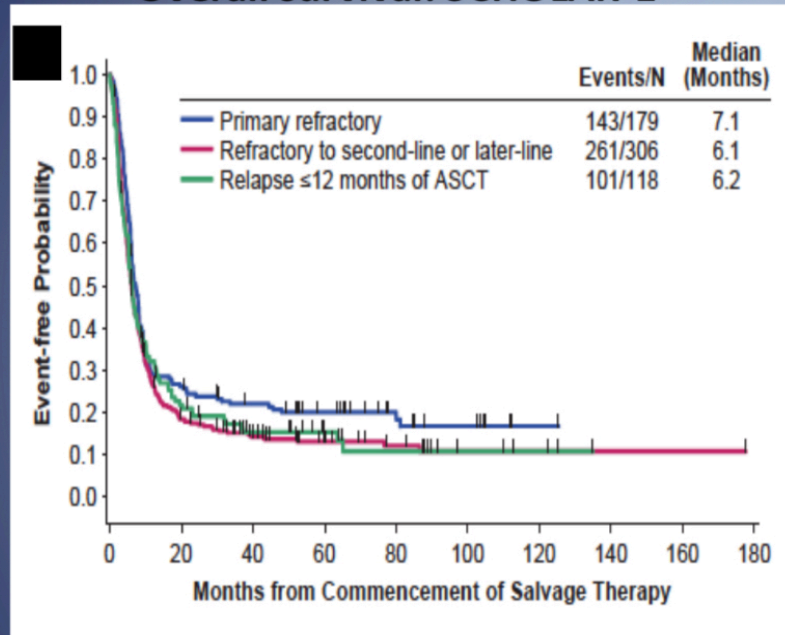
HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

CART

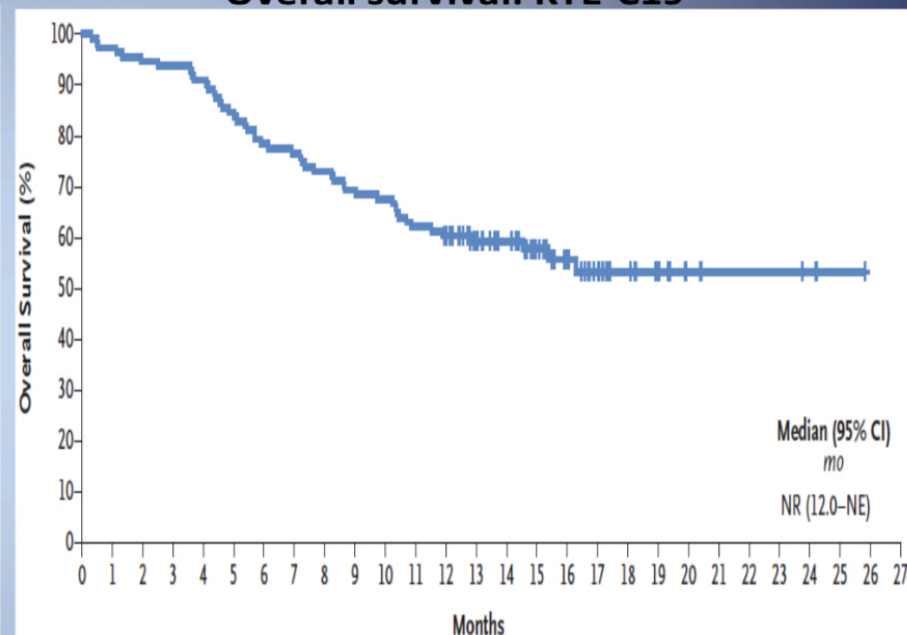
Outcomes in refractory DLBCL: Historical vs. KTE-C19

Overall survival: SCHOLAR-1



- N = 636
- ORR = 26%; CR rate = 7%
- Median OS = 6.3 months

Overall survival: KTE-C19



- N = 108
- ORR = 82%; CR rate = 58%
- Median OS = >18 months

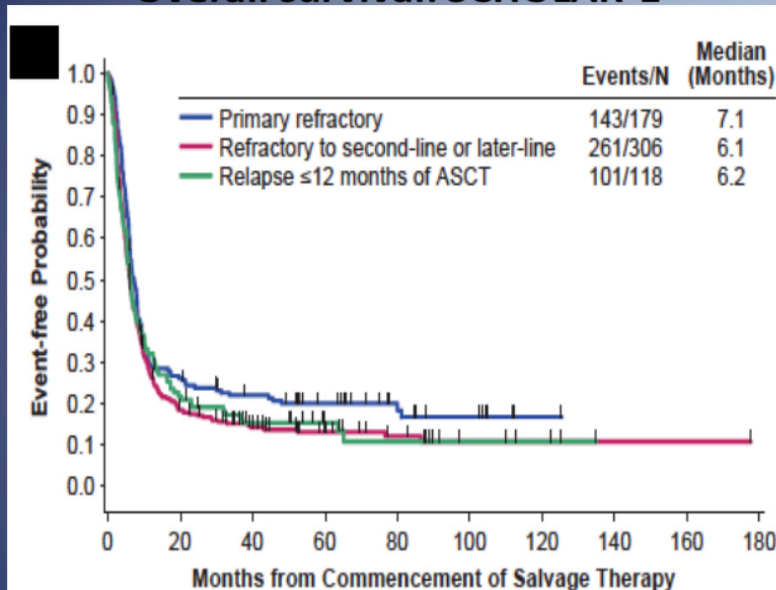
HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

CART

Outcomes in refractory DLBCL: Historical vs. CTL019

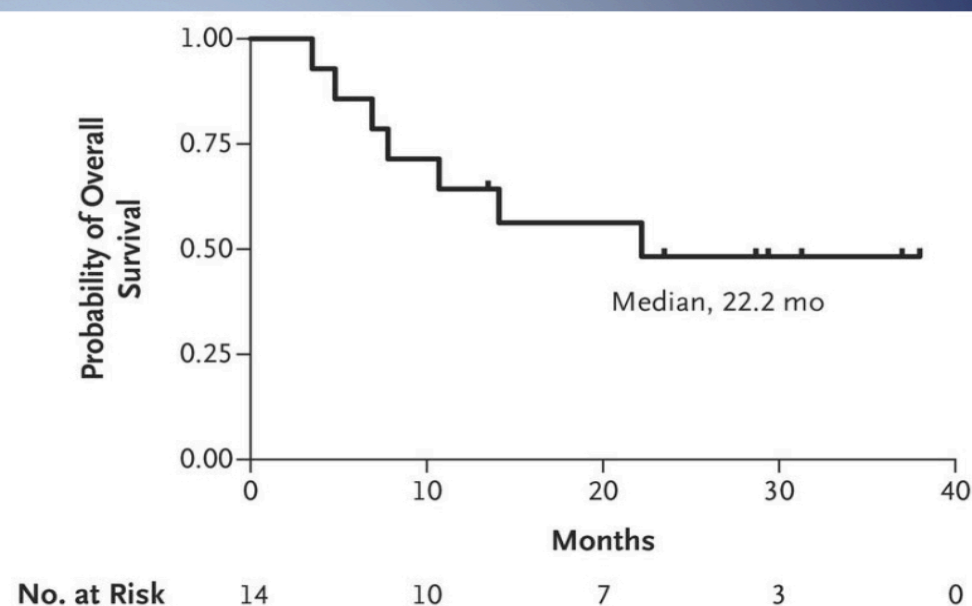
Overall survival: SCHOLAR-1



- N = 636
- ORR = 26%; CR rate = 7%
- Median OS = 6.3 months

Crump et al. Blood 2017

Overall survival: CTL019



- N = 28
- ORR = 53%; CR rate = 40%
- Median OS = 22.2 months

Schuster et al, N Eng J Med 2017

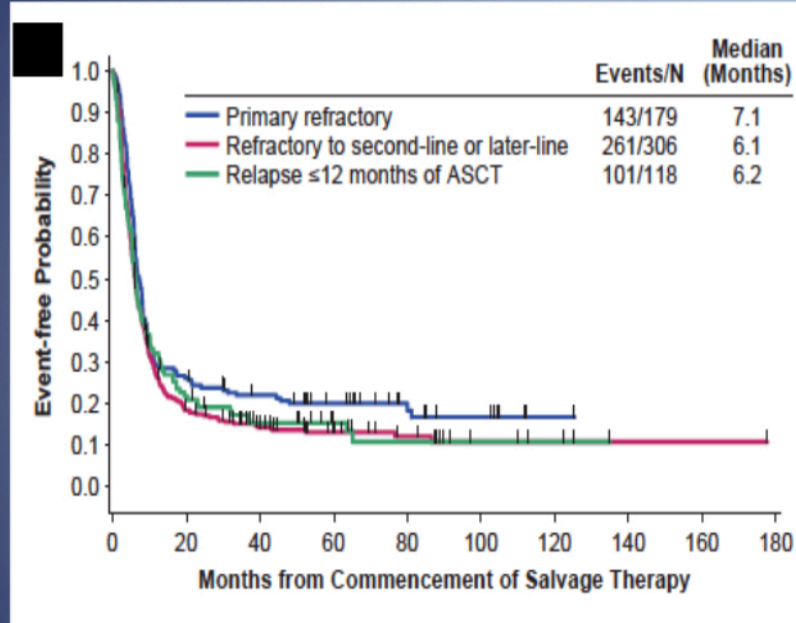
HOW I TREAT RELAPSE/REFRACTORY DLBCL

NOVEL APPROACHES

CART

Outcomes in refractory DLBCL: Historical vs. JCAR017

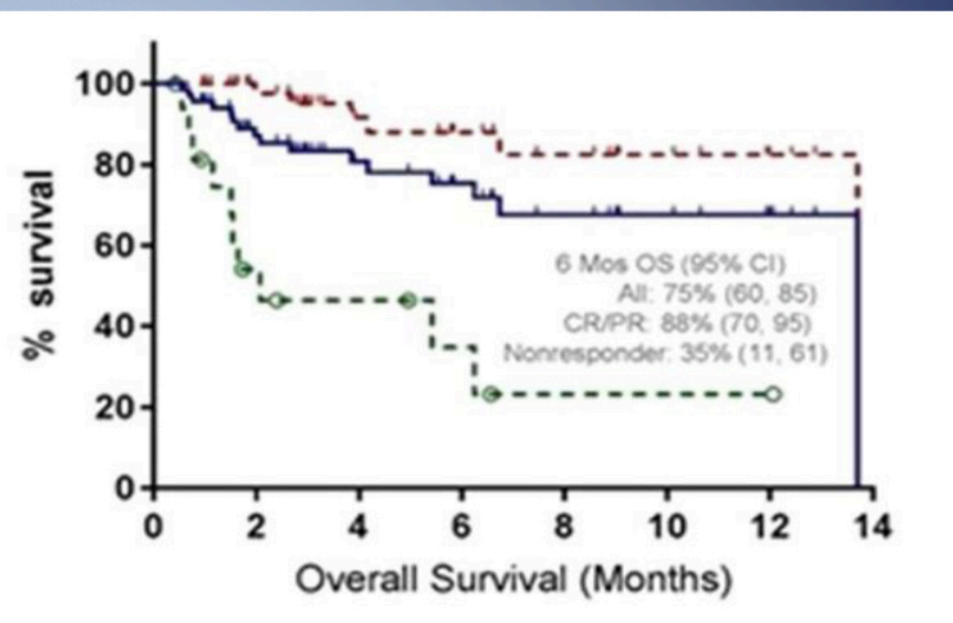
Overall survival: SCHOLAR-1



- N = 636
- ORR = 26%; CR rate = 7%
- Median OS = 6.3 months

Crump et al. Blood 2017

Overall survival: JCAR017

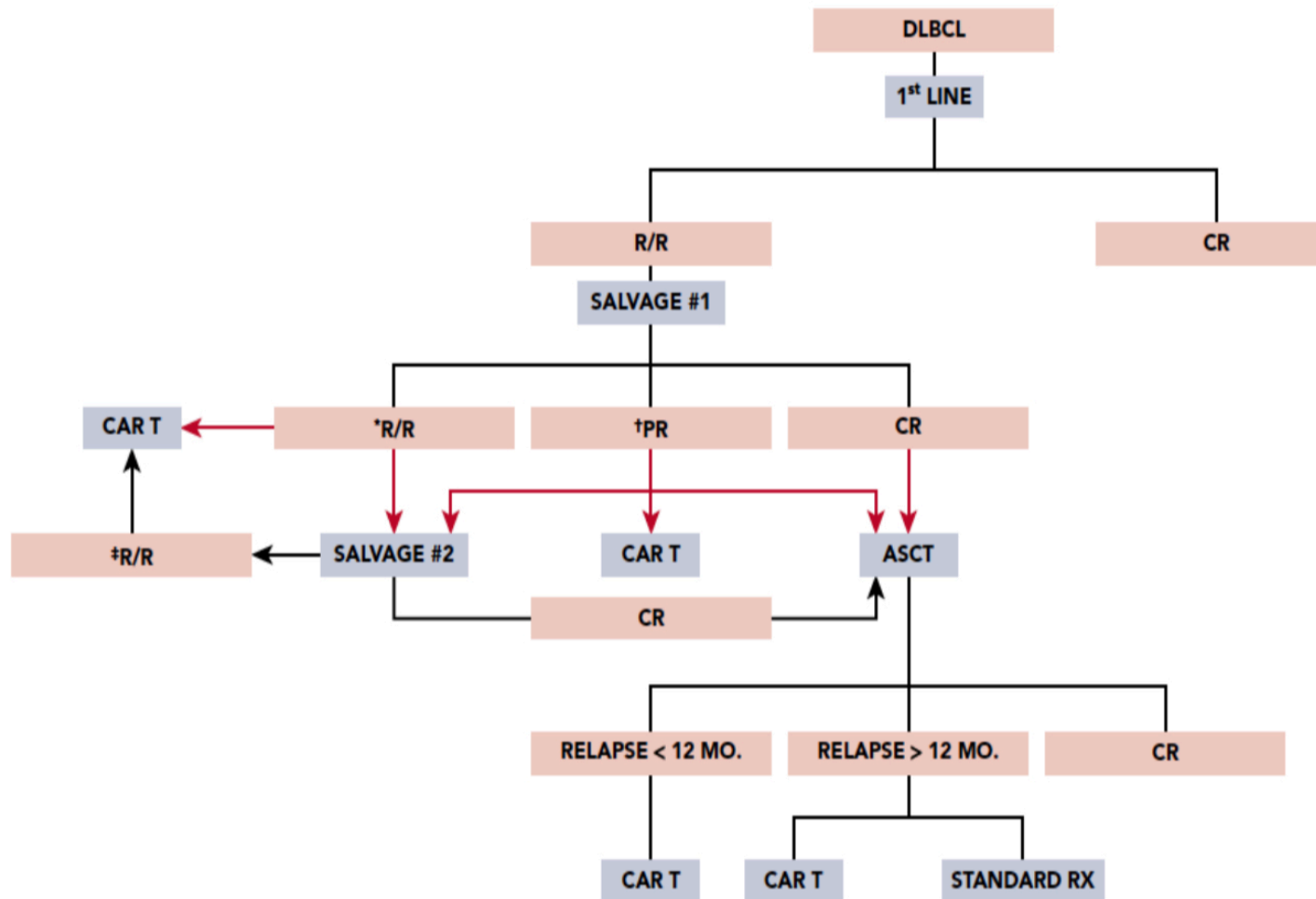


- N = 68
- ORR = 75%; CR rate = 53%
- Median OS = 13.7 months

Abramson et al, ASH 2017

HOW I TREAT RELAPSE/REFRACTORY DLBCL

Future perspectives...



THANKS

