Diffuse Large B-cell Lymphoma: Treatment and Support

Owen A. O'Connor, MD, PhD

Professor of Medicine and Experimental Therapeutics

Director, Center of Lymphoid Malignancies

Herbert Irving Comprehensive Cancer Center at Columbia University Medical Center

Vinita Khanna, LCSW, ACHP-SW, OSW-C

MPH Candidate
Licensed Clinical Social Worker
Hematology/Bone Marrow Transplantation
University of Southern California
Keck Hospital of USC/Norris Comprehensive Cancer Center

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Disclosures

The planners and speakers have the following financial disclosures.

Name	Role	Disclosure
Owen A. O'Connor, MD, PhD	Speaker	Celgene research support; Data Safety Monitoring Committee (DSMC) participation Spectrum research support MundiEDL research support ADCT pharmaceuticals research support Trillium research support Merck research support TG Therapeutics research support
Vinita Khanna, LCSW, ACHP-SW, OSW-C	Speaker	None
Lauren Berger, MPH	Planner	None
Jackie Foster, MPH, RN, OCN	Planner	Stock ownership - Pfizer
Nicole Heino	Planner	None
Valarie Leishman, RN, BSN, MBA	Planner	None
Stacy Stickney Ferguson, MSW, LICSW	Planner	None

Continuing Education

- **Social Workers**: The Leukemia & Lymphoma Society (LLS), provider number 1105, is approved as a provider for social work continuing education by the Association of Social Work Boards (ASWB) www.aswb.org Approved Continuing Education Program (ACE). Approval Period: 12/10/2017 to 12/10/2020. LLS maintains responsibility for the program. Social workers should contact their regulatory board to determine course approval. Social workers will receive 1.25 CE clinical contact hours.
- The Leukemia & Lymphoma Society (LLS) is recognized by the New York State Education Department's State Board for Social Work as an approved provider of continuing education for licensed social workers #SW-0117. LLS maintains responsibility for this program. Social workers will receive 1.25 CE clinical contact hours for this activity.

Continuing Education cont.

- **Nurses**: The National Marrow Donor Program is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation (COA).

  Up to 1.25 contact hours may be claimed for this educational activity.

- **Insurance case managers:** This program has been pre-approved by The Commission for Case Manager Certification to provide continuing education credit to CCM® board certified case managers. The course is approved for 1.25 CE contact hour(s).

  Activity code: I00032893 Approval Number: 180002575

Continuing Education cont.

- **Medical technologists**: The NMDP is approved as a provider of continuing education in the clinical laboratory sciences through the ASCLS PACE Program. ASCLS PACE® 1861 International Drive, Suite 200, McLean, VA 22102.

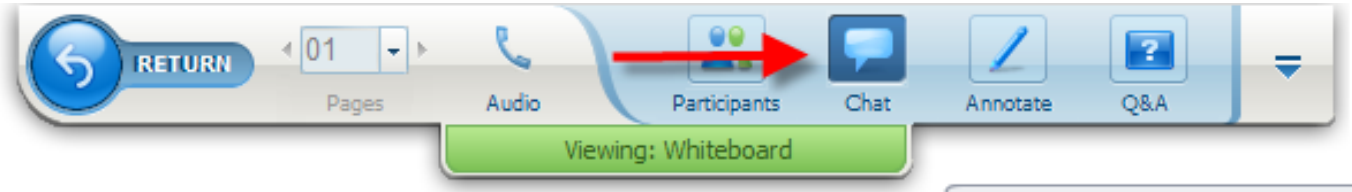
  Up to 1.0 contact hours may be claimed for program #115-032-18.

- All other health professionals will be issued a certificate of completion.

Webinar Evaluation

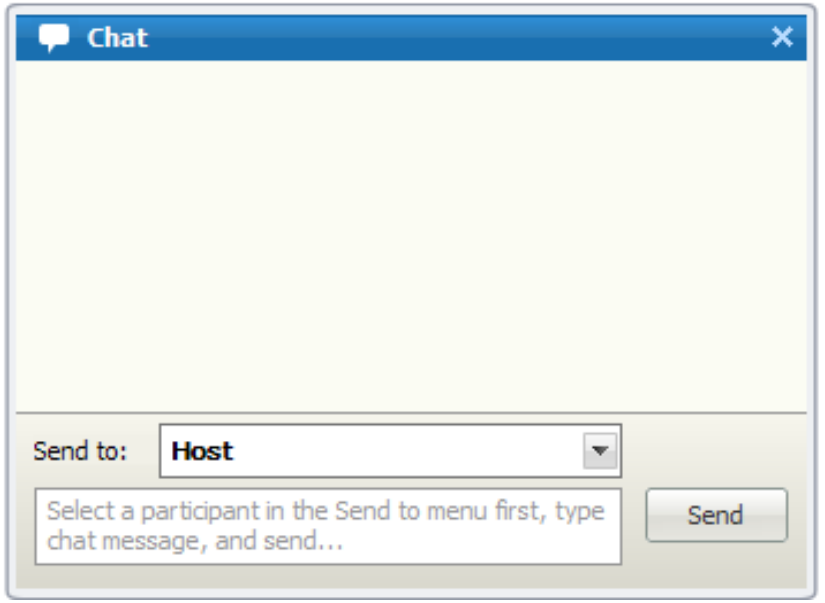
- Attendees will receive an email following the webinar with a link to the evaluation.
- All attendees completing the online program evaluation will receive a statement of continuing education or a certificate of attendance within 30 days.

Attendance and Questions



Utilize the chat feature to:

- Let us know the number of additional attendees listening as a group at your location.
- Ask a question.
  - Access the toolbar at the top of your screen. Click on the  icon.



For questions, support or concerns during the webinar, please email: nmdpeducation@nmdp.org

Learning Objectives

After attending this webinar, participants will be able to:

1. Summarize diagnosis criteria for diffuse large B cell lymphoma **(DLBCL)**.
2. Identify current and emerging therapies for **DLBCL**.
3. Explain the health care professional's role in monitoring for and managing short and long-term psychosocial effects of treatment for DLBCL.
4. Review the psychosocial impact of the treatment sequelae for patients.
5. Describe resources for support and education for patients.

Diffuse Large B-Cell Lymphoma: Treatment and Support

Owen A. O'Connor, M.D., Ph.D.

American Cancer Society Research Professor

Professor of Medicine and Experimental Therapeutics

Founding Director, Center for Lymphoid Malignancies

Department of Medicine

Columbia University Medical Center –

College of Physicians and Surgeons

The New York Presbyterian Hospital

New York, N.Y.

National Marrow Donor Program/Be The Match

The Leukemia & Lymphoma Society

Columbia University Medical Center

NCI CCC
A Comprehensive Cancer Center Designated by the National Cancer Institute

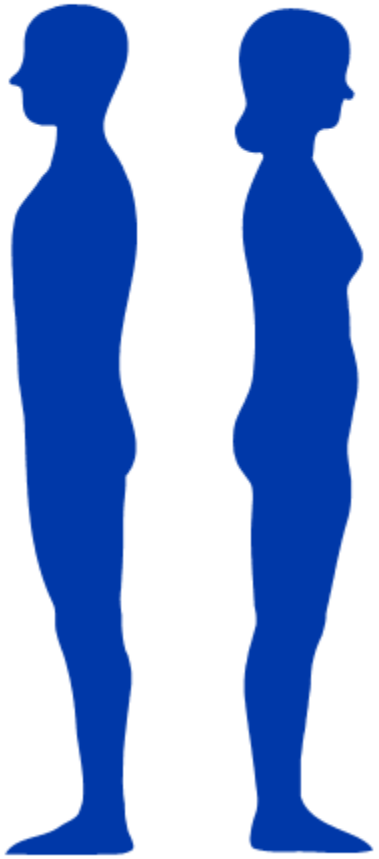
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

Estimated New Cancer Cases* in the US in 2016

Prostate = 176K / Breast = 244K / Lung = 226K / Colon = 134K / Uter/Blad = 109K

Nearly 900,000 cases per year of the Top 5

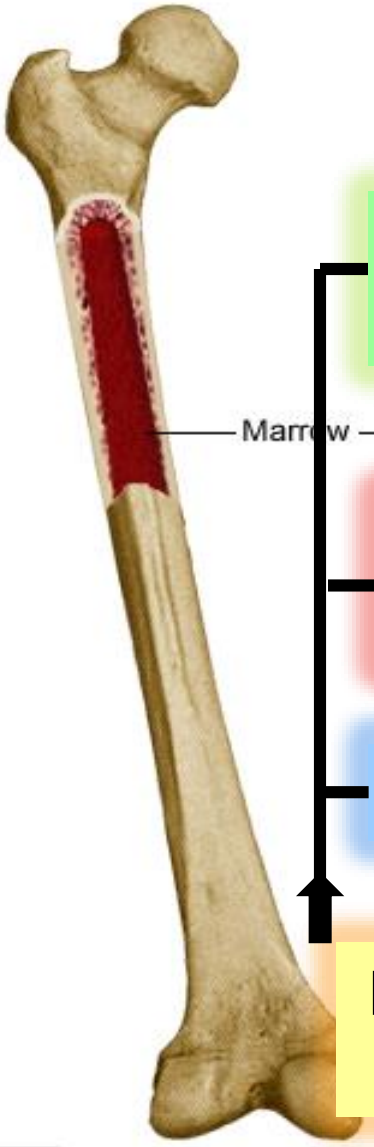
Males 841,390		Females 843,820	
Prostate	21%	29%	Breast
Lung & bronchus	14%	13%	Lung & bronchus
Colon & rectum	8%	8%	Colon & rectum
Urinary bladder	7%	7%	Uterine corpus
Melanoma of skin	6%	6%	Thyroid
Non-Hodgkin lymphoma	5%	4%	Non-Hodgkin lymphoma
Kidney & renal pelvis	5%	3%	Melanoma of skin
Oral cavity & pharynx	4%	3%	Leukemia
Leukemia	4%	3%	Pancreas
Liver & intrahepatic bile duct	3%	3%	Kidney & renal pelvis
All other sites	22%	21%	All other sites



~78,000 cases NHL / year in US

*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

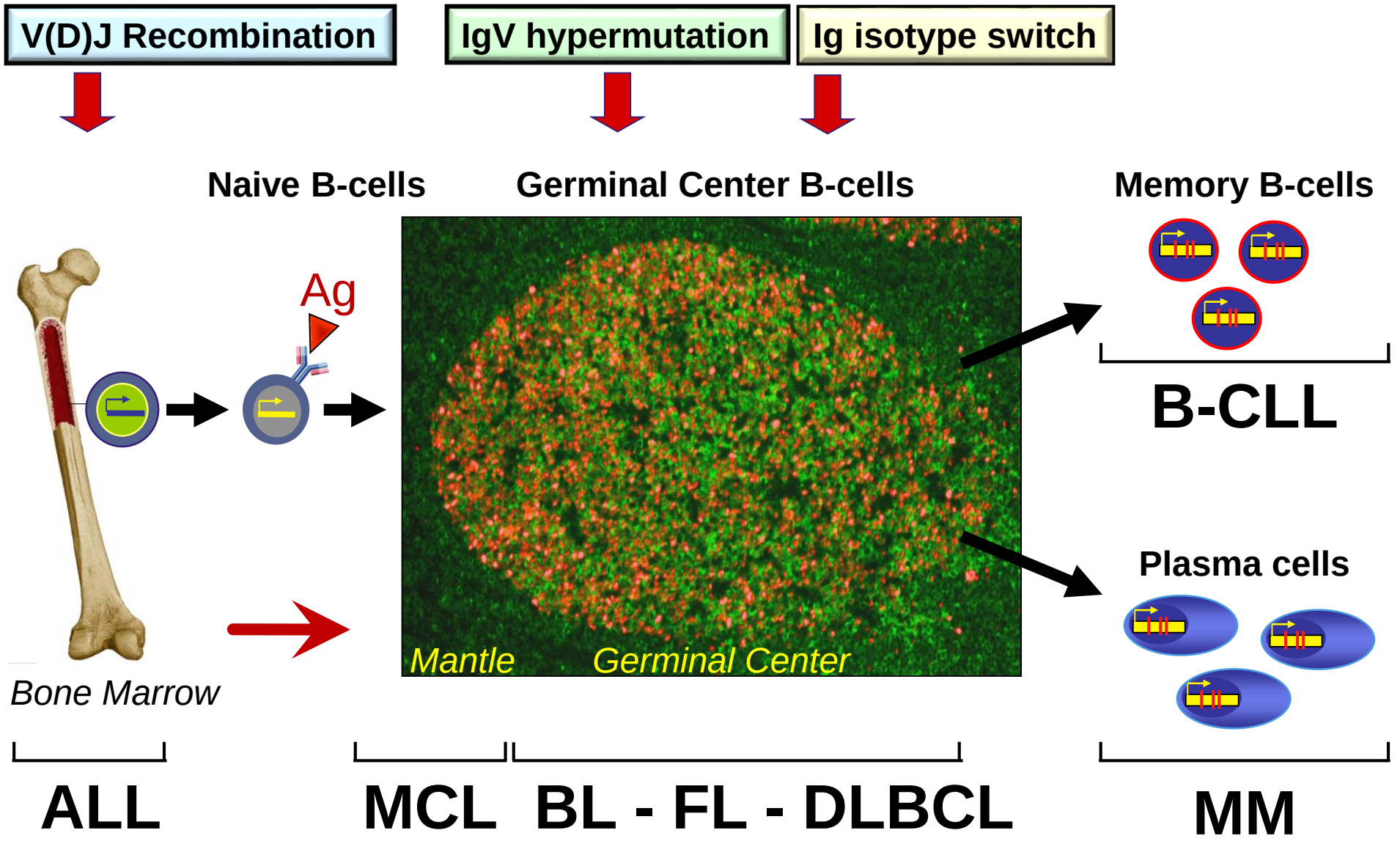
Defining the Spectrum of Origins of The Lymphoproliferative Malignancies



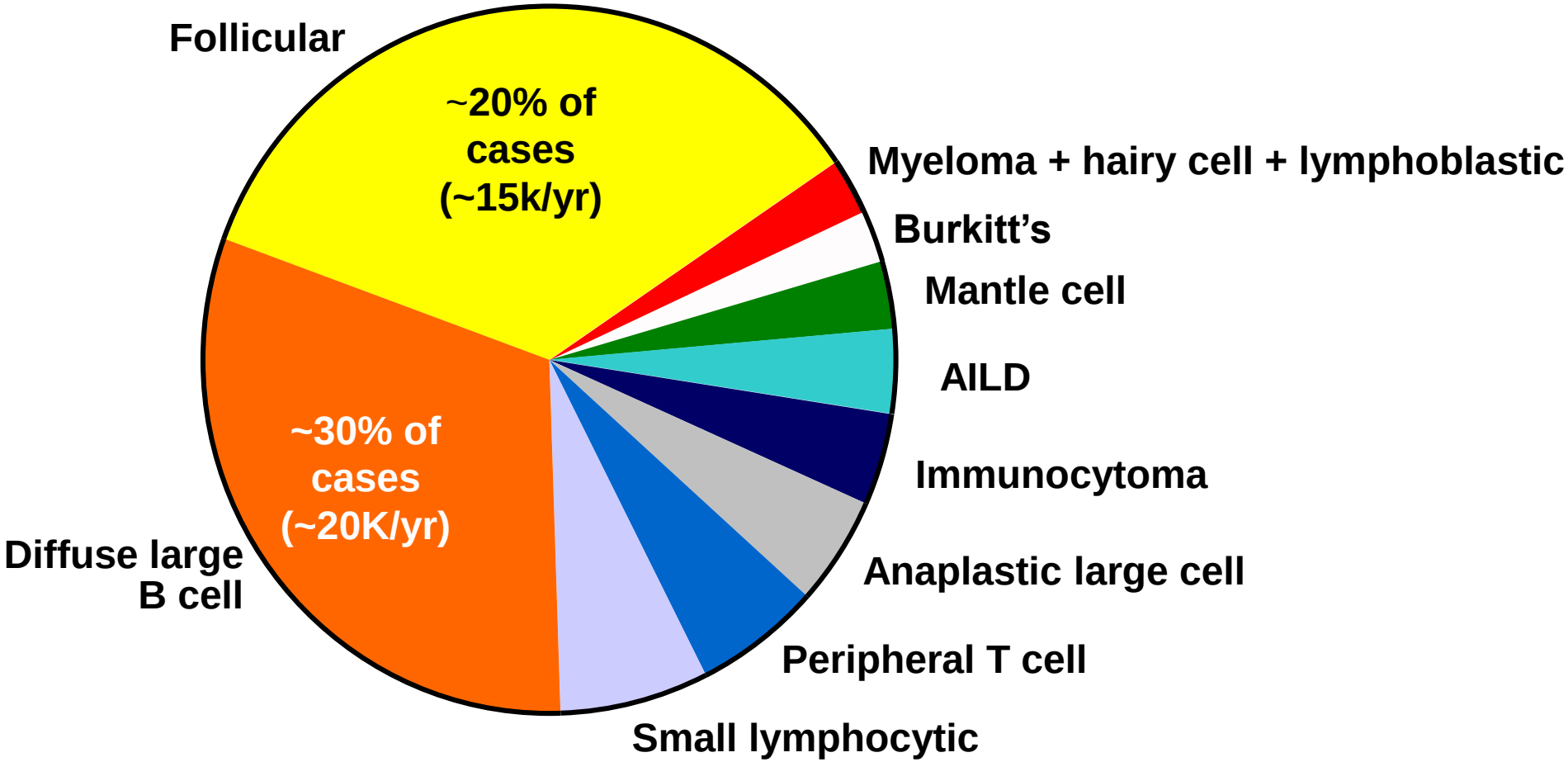
- **White Blood Cells**
  - Myeloid → Eosinophils, Basophils, Neutrophils
  - Lymphoid → B-Lymphocytes, T-Lymphocytes, NK Cells
- **Red Blood Cells**
- **Platelets**
- **Hematopoietic Stem Cell**

79 Types of Lymphoma (2016 WHO)

The Development of Lymphoid Neoplasm's is Complex and Heterogeneous



Frequency of T- and B- Cell Neoplasms in Lymph Node Biopsies



447 cases

Organizing 79 Types of Lymphoma

Aggressive Diseases

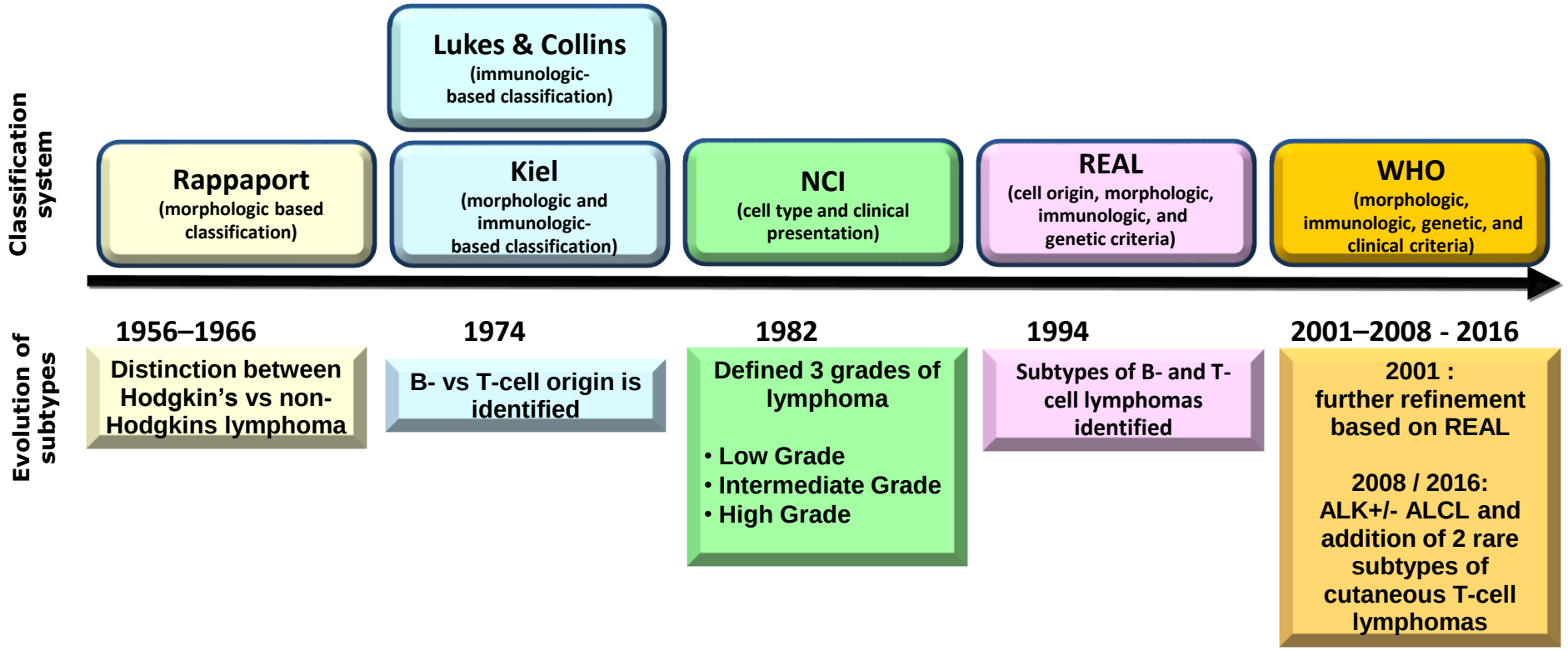
Pros	Cons
Potentially curable	Requires some form of chemotherapy
Relapsed disease can potentially be cured	Side effects of chemotherapy
Responds quick to treatment	Fast growing can produce symptoms quickly
4 to 6 months of treatment if cured	Relapse can be hard to manage

Indolent Diseases

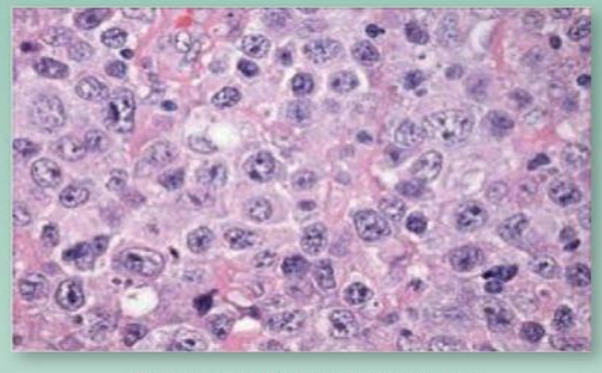
Pros	Cons
Very slow growing	Not curable – rare exceptions
Watching could be option	May require some form of lifelong therapy
Treatments less and less rely on chemotherapy	Can transform to aggressive disease
Can be relatively asymptomatic even with disease	Treatment side effects

History of NHL Classification

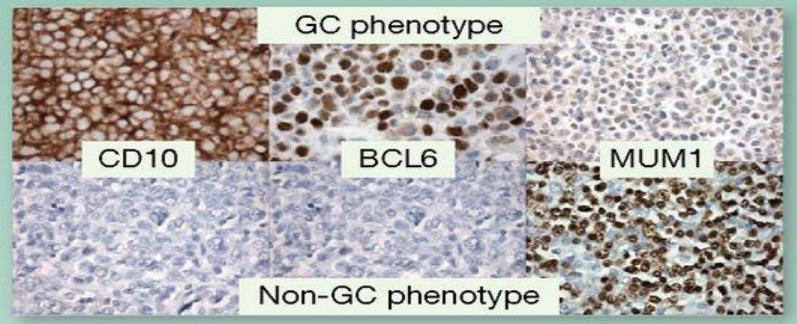
- **NHL classification schemes have evolved based on growing understanding of cancer cell characteristics[1]**
- **Subclassifications are driving more specific clinical trials and therapeutic approaches[2]**



1. National Cancer Institute. SEER training module for lymphoma. Available at http://training.seer.cancer.gov/lymphoma/abstract-code-stage/morphology/.
2. Armitage J, et al. *J Clin Oncol*. 2008;26:4124–4130.

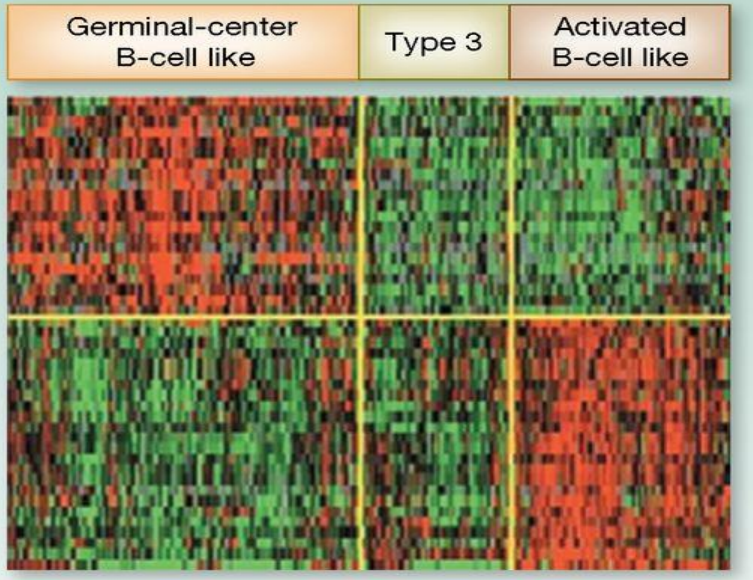


Tissue cytomorphology



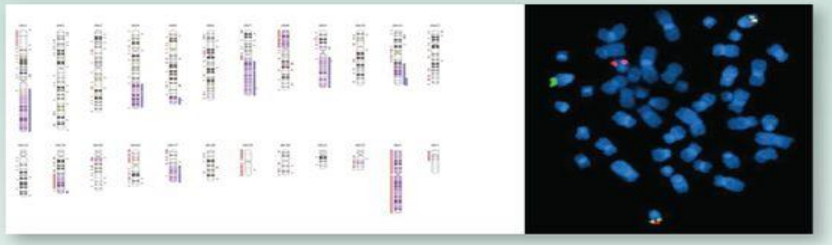
Immunohistochemistry

Large vs small cells / diffuse vs follicular



Gene expression profiling

Current chromosome and genetic analysis techniques



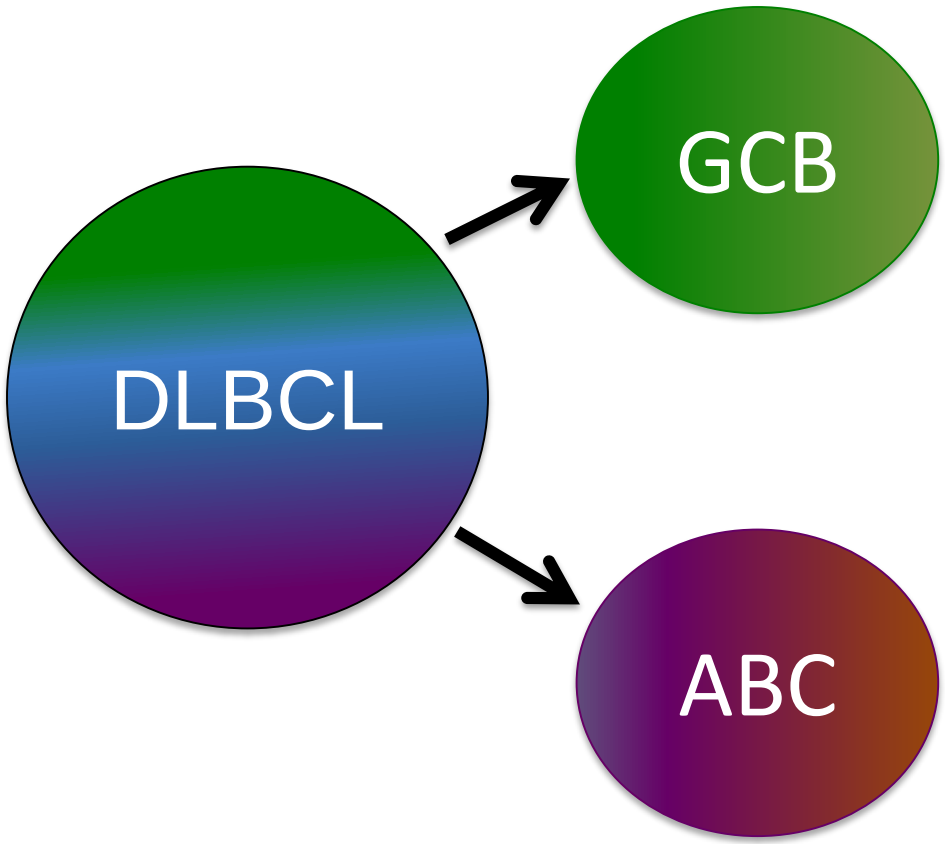
CGH FISH

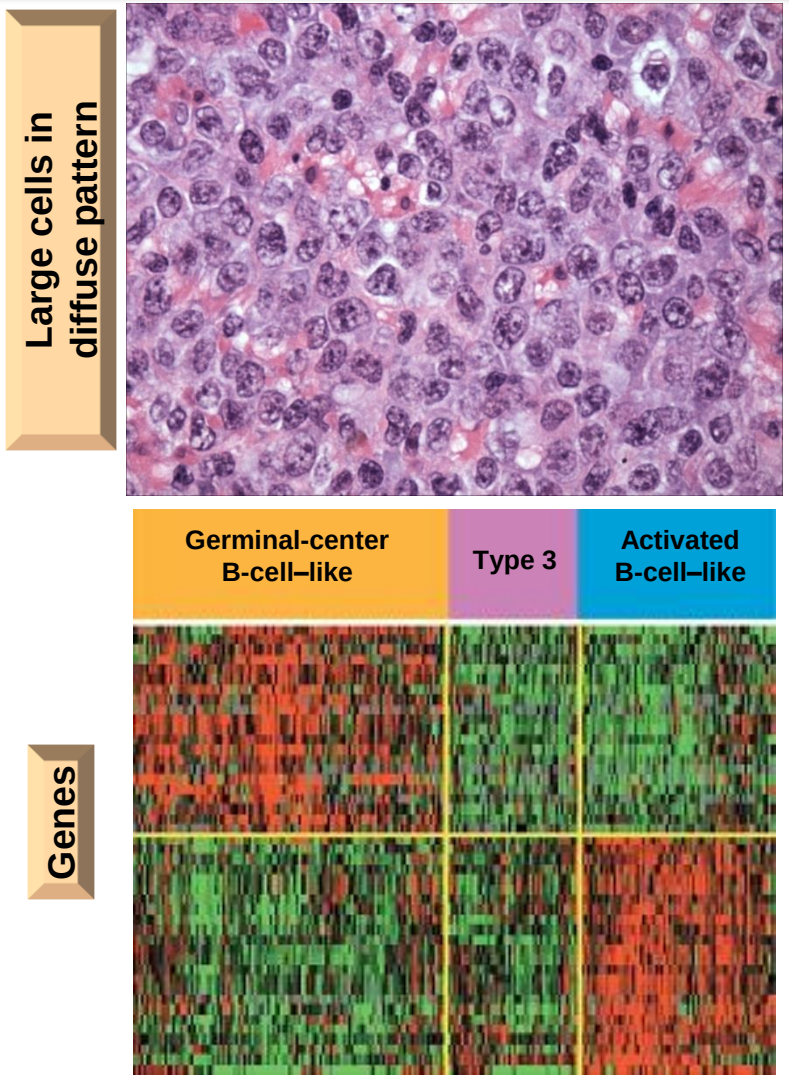
Detailed genetic analysis will be the key to discriminating patient populations

The future:
Next-generation sequencing
Single-nucleotide polymorphisms

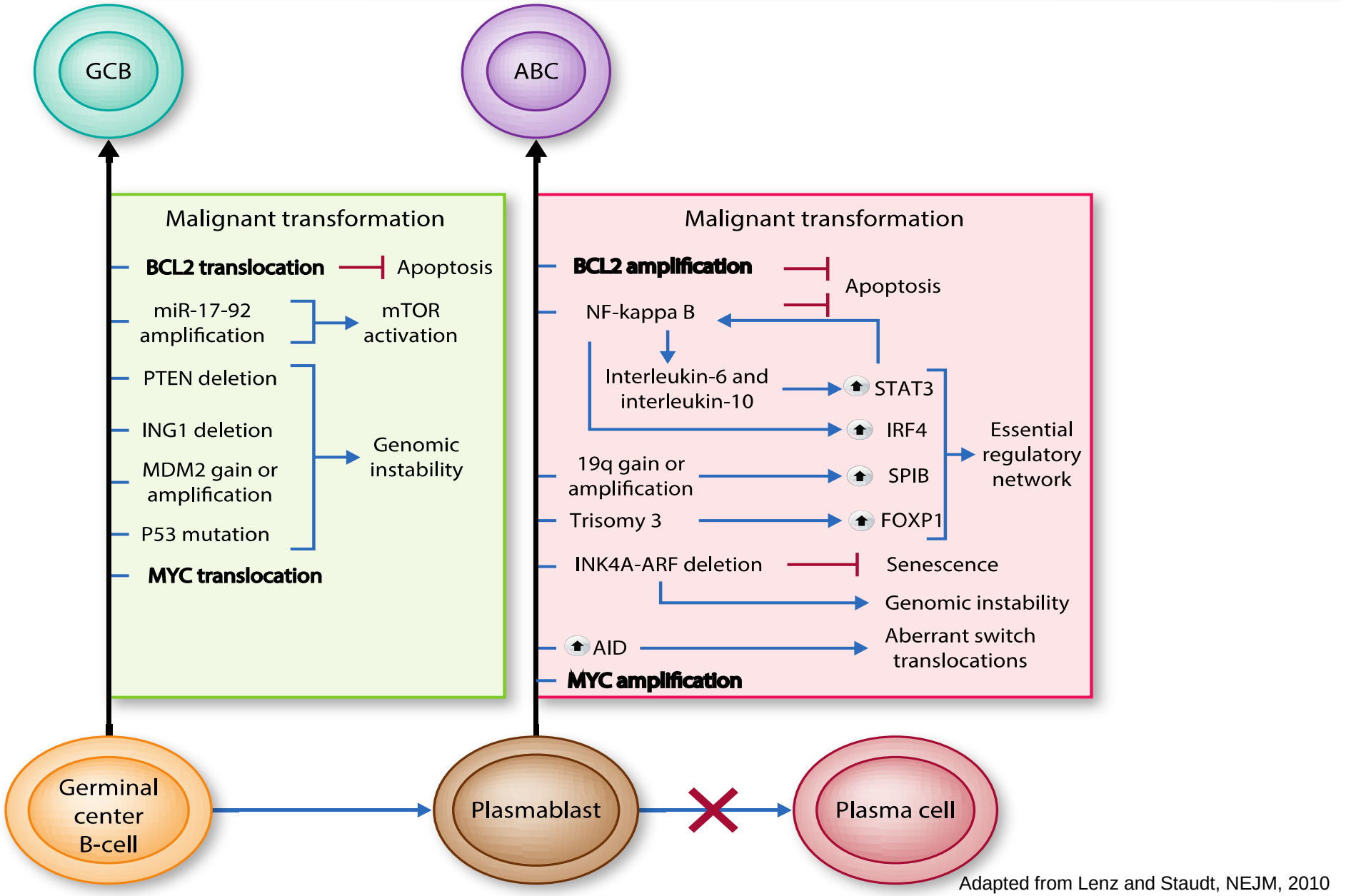
Owen A. O'Connor, and Kensei Tobinai Clin Cancer Res 2014;20:5173-5181

At a Molecular Level, DLBCL is Very Heterogeneous



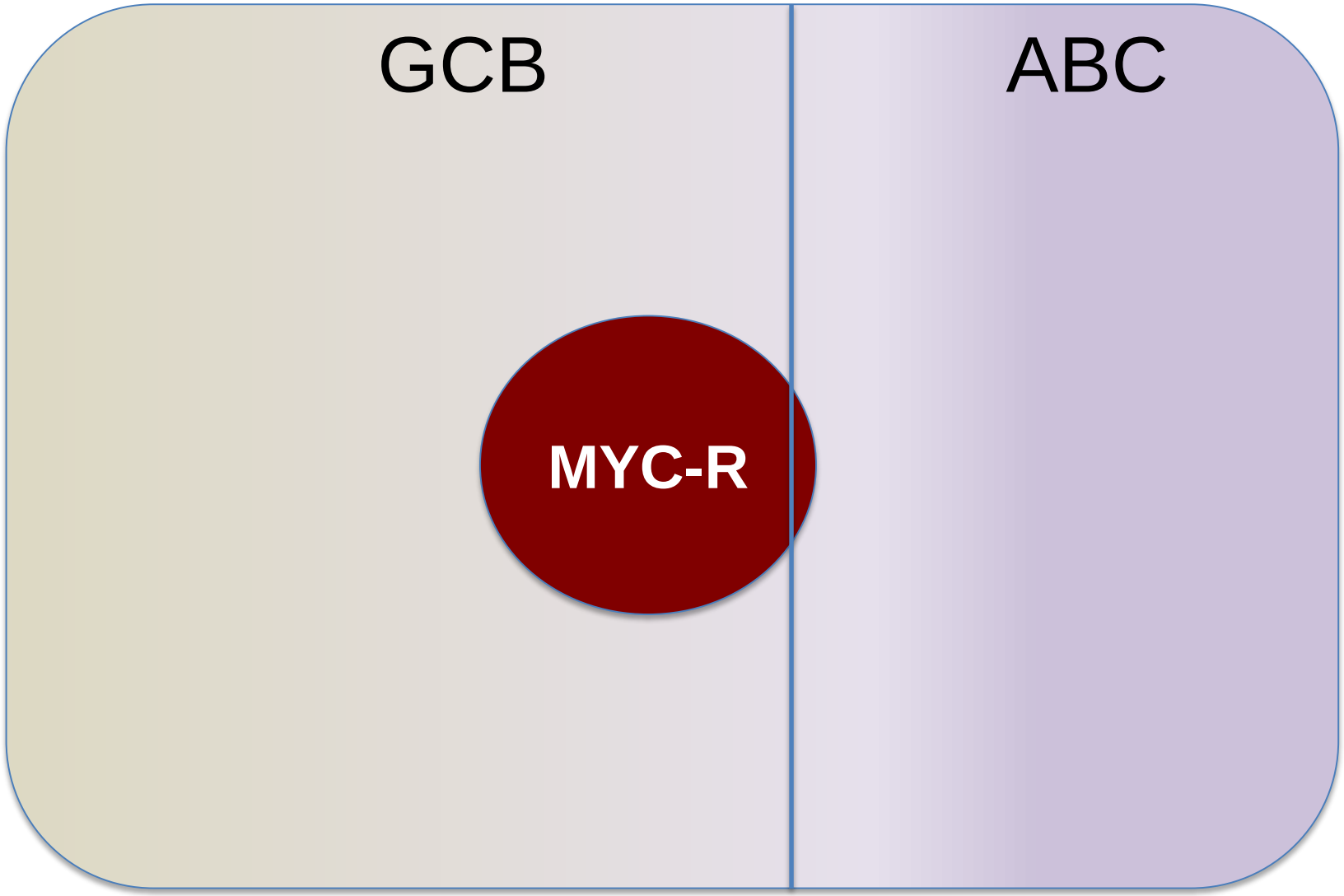


DISTINCT MOLECULAR DERANGEMENTS CLUSTER BY COO

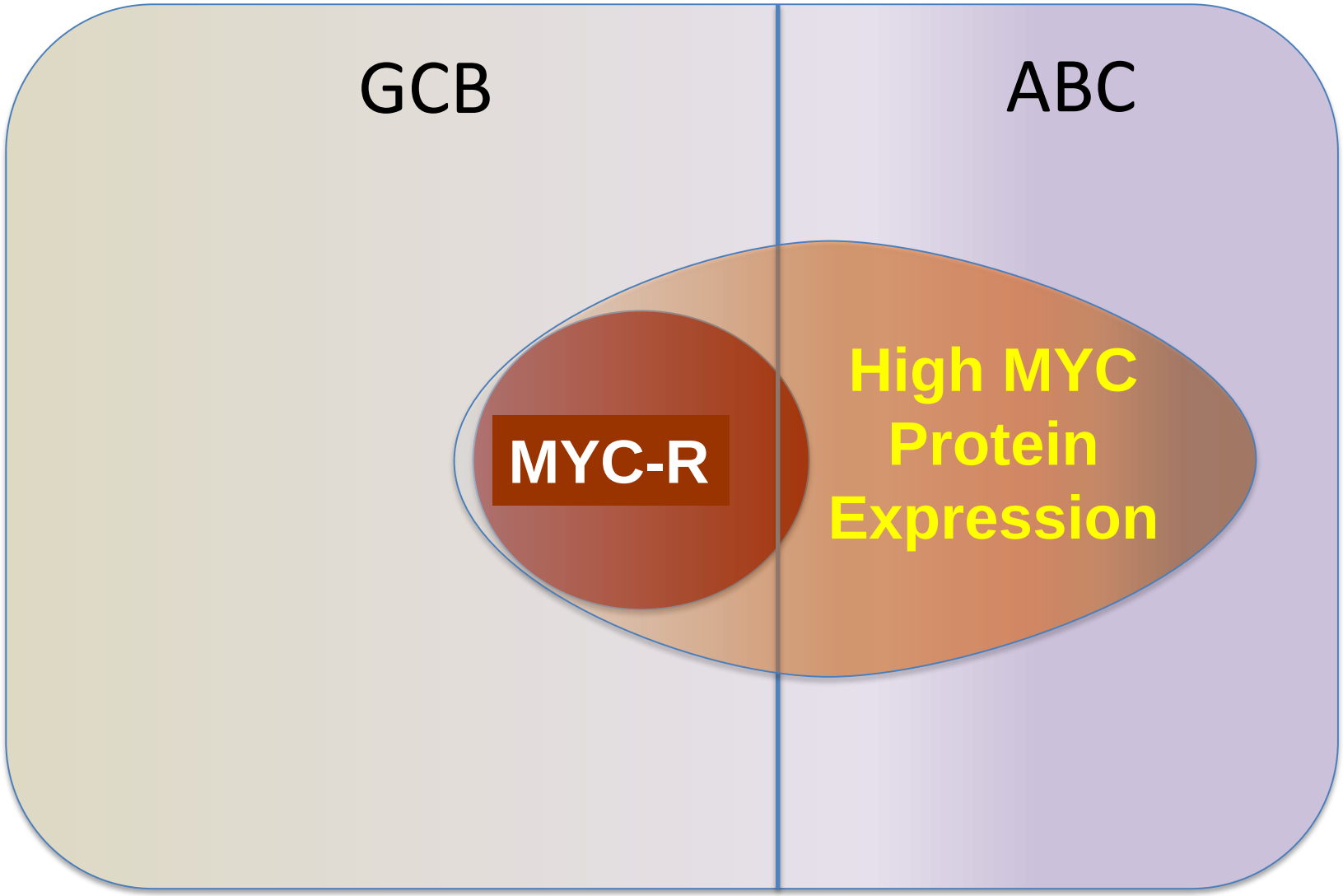


Adapted from Lenz and Staudt, NEJM, 2010

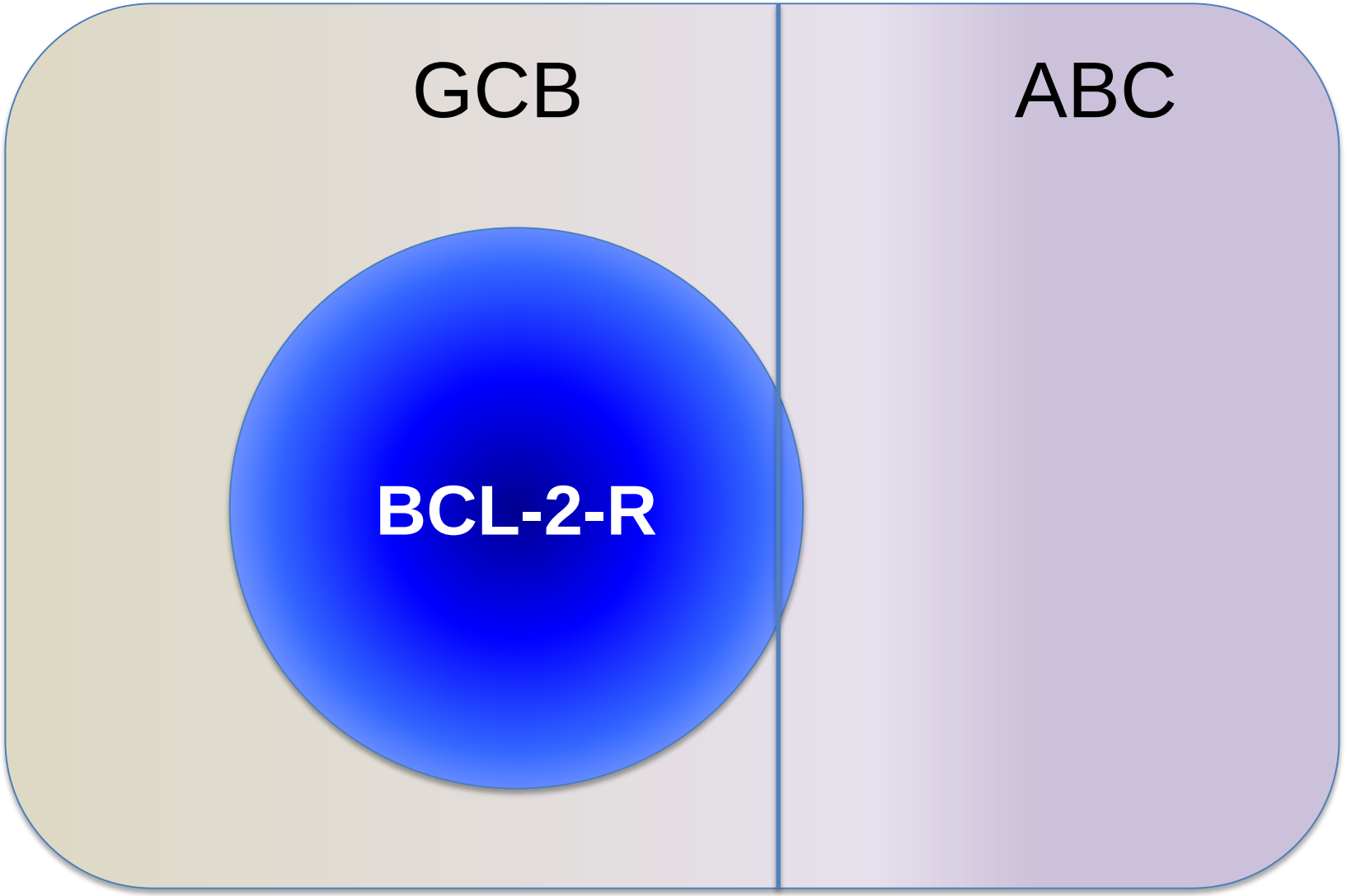
Essentially ALL Myc - Rearrangements Reside in the GCB Subtype



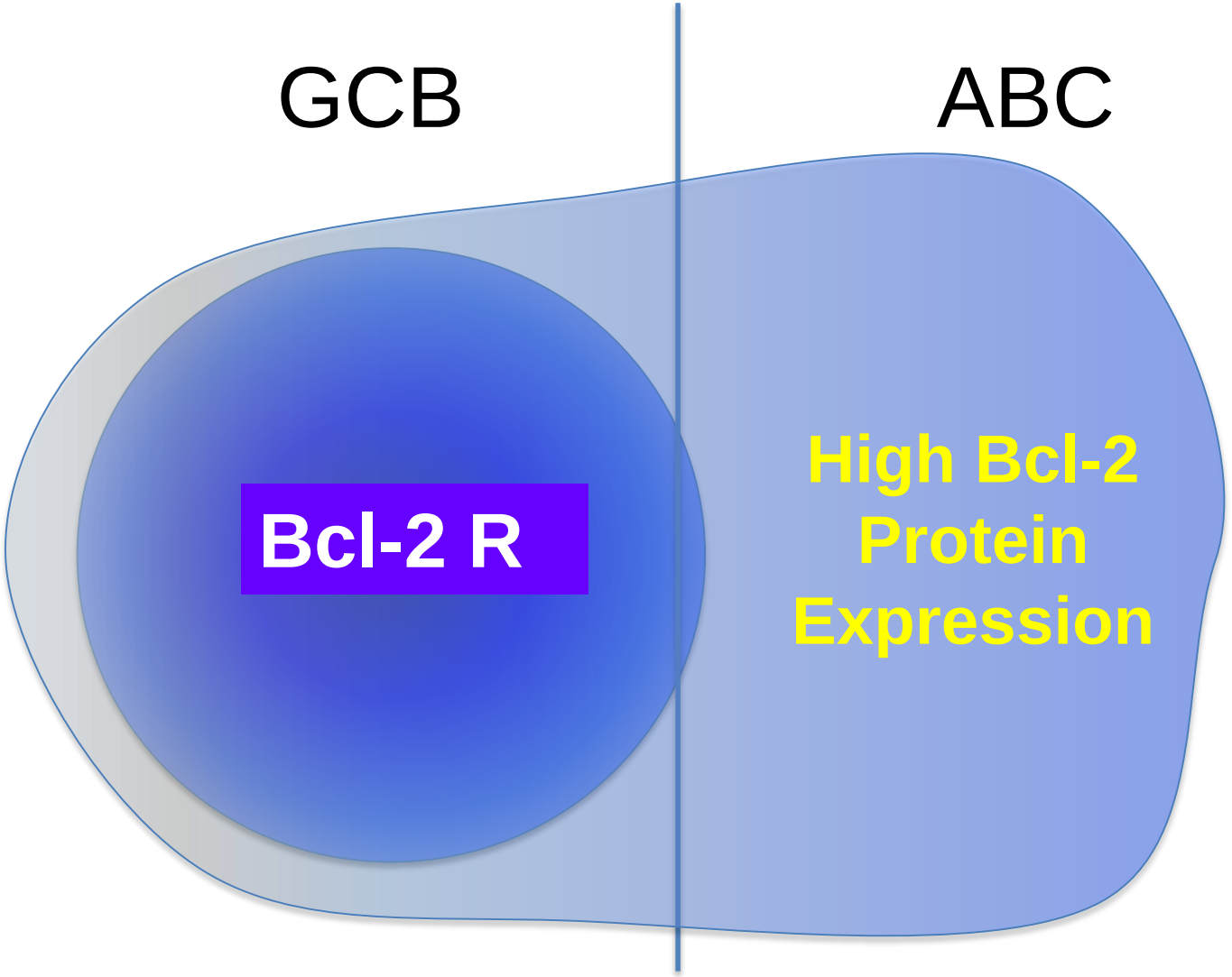
….While MYC High Expressors Without Rearrangement Tend to be ABC



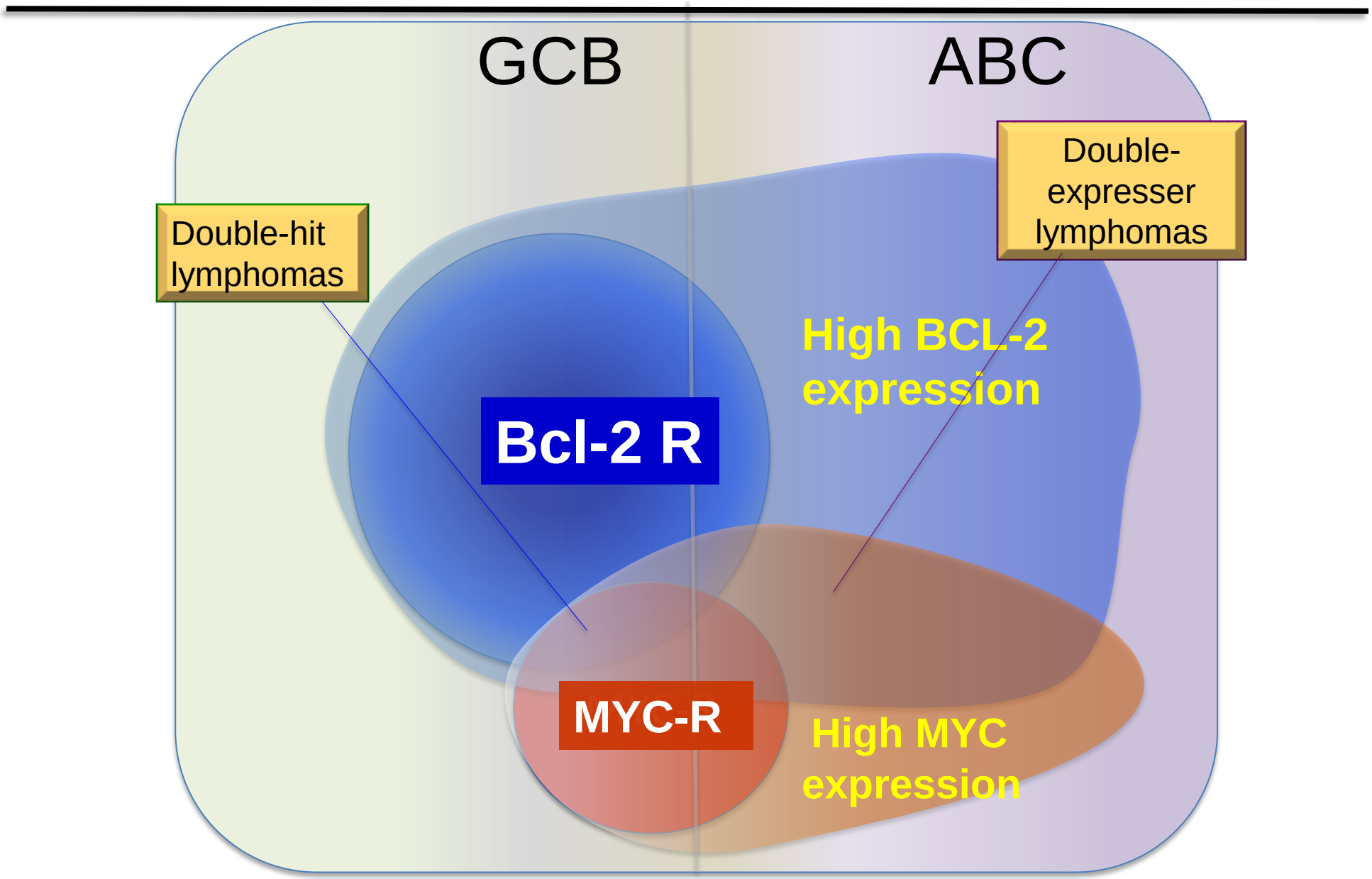
Almost ALL BCL-2 Rearrangements are of GCB Origin



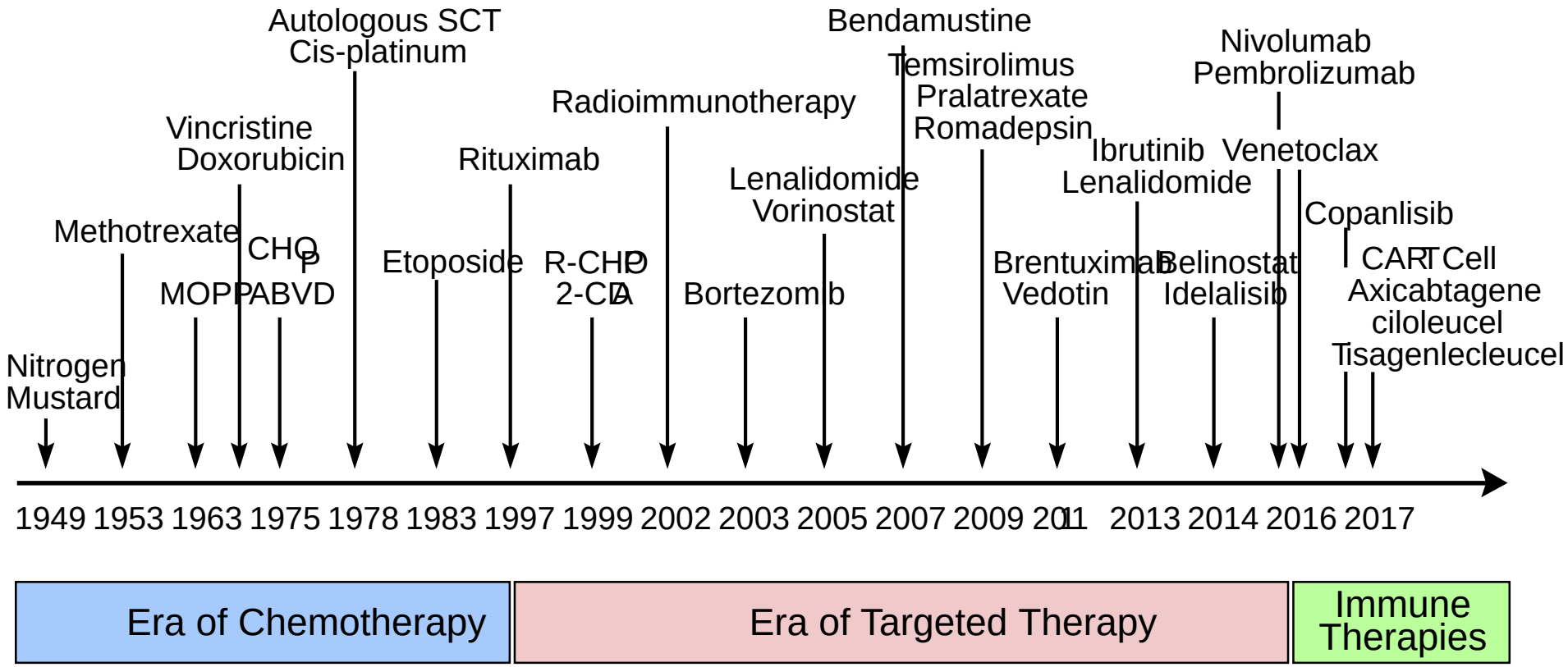
…..While BCL-2 High Expressors Cluster in ABC



How Does One Risk Stratify These Patients and 'Tailor' Treatment



Nearly 70 Years of Lymphoma Treatment



*Modified from T.E. Witzig, MD

Trends in Five-year Relative Cancer Survival Rates (%), 1975-2011

Site	1975-1977	1987-1989	2005-2011
All sites	49	55	69
Breast (female)	75	84	91
Colorectum	50	60	66
Leukemia	34	43	62
Lung & bronchus	12	13	18
Melanoma of the skin	82	88	93
Non-Hodgkin lymphoma	47	51	72
Ovary	36	38	46
Pancreas	3	4	8
Prostate	68	83	99
Urinary bladder	72	79	79

A Misleading Statistic… *Essentially all of the improvement in NHL is in B-cell lymphoma*

5-year relative survival rates based on patients diagnosed in the SEER 9 areas from 1975-1977, 1987-1989, and 2005-2011, all followed through 2012.
Source: Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, 2015.

1993 – 50% Chemotherapy Era

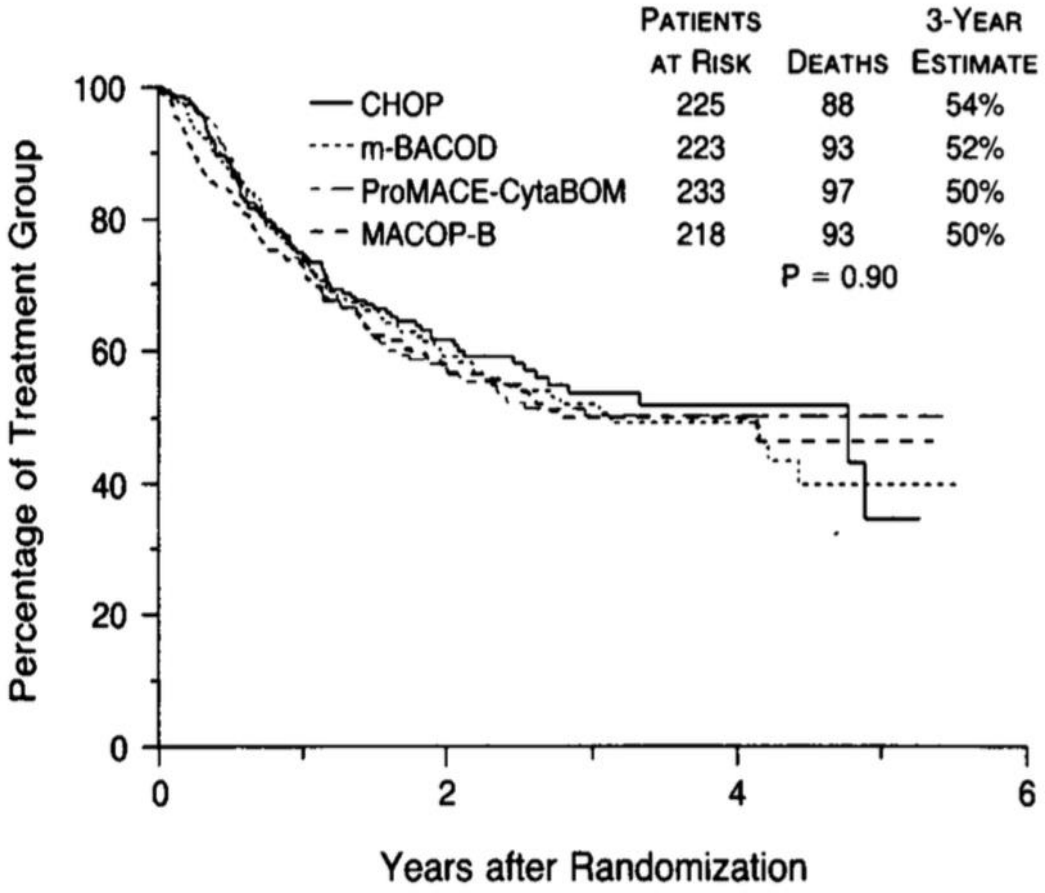


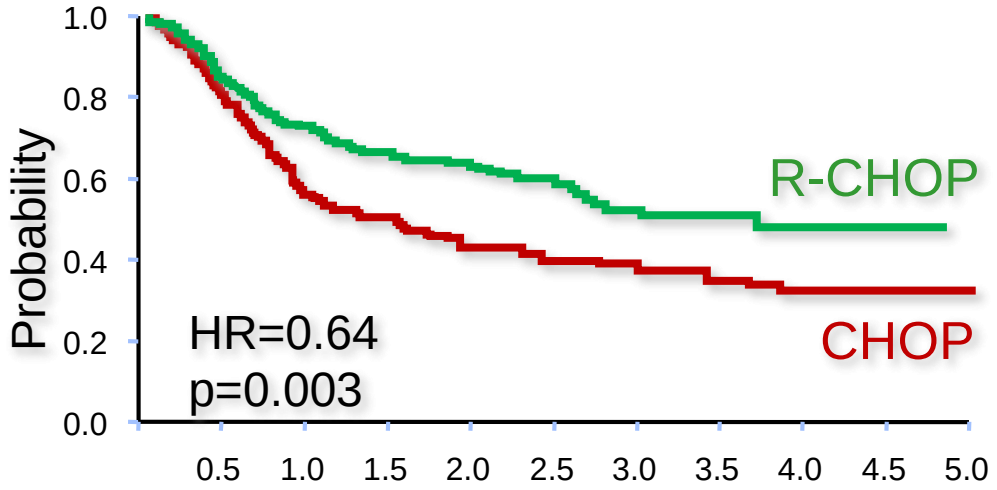
Figure 2. Overall Survival in the Treatment Groups. The three-year estimate is of overall survival.

50% Overall Survival

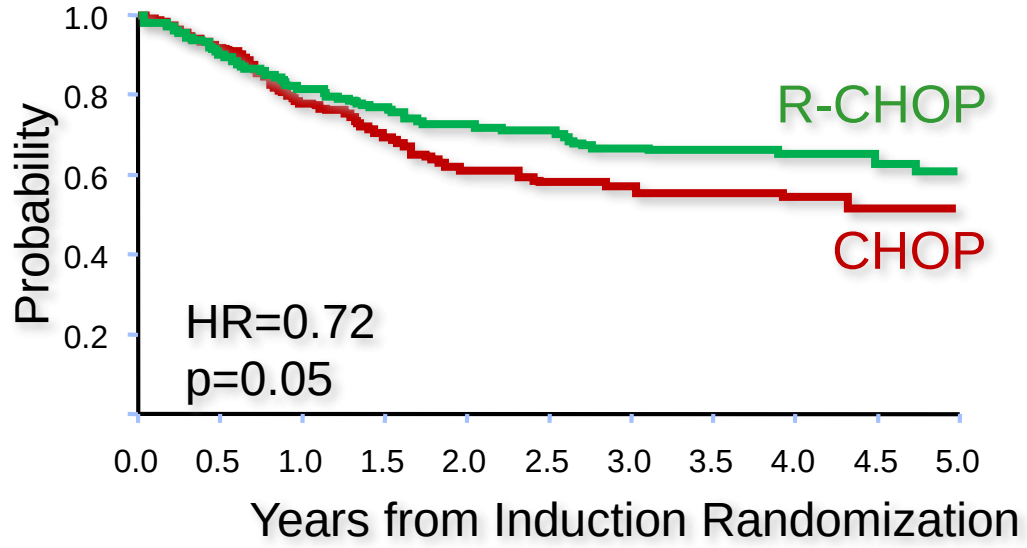
More intense regimens more toxic and no more effective

Fisher R et al NEJM 1993

2002 – 2006 The Rituximab Era
About a 15% Improvement Over CHOP



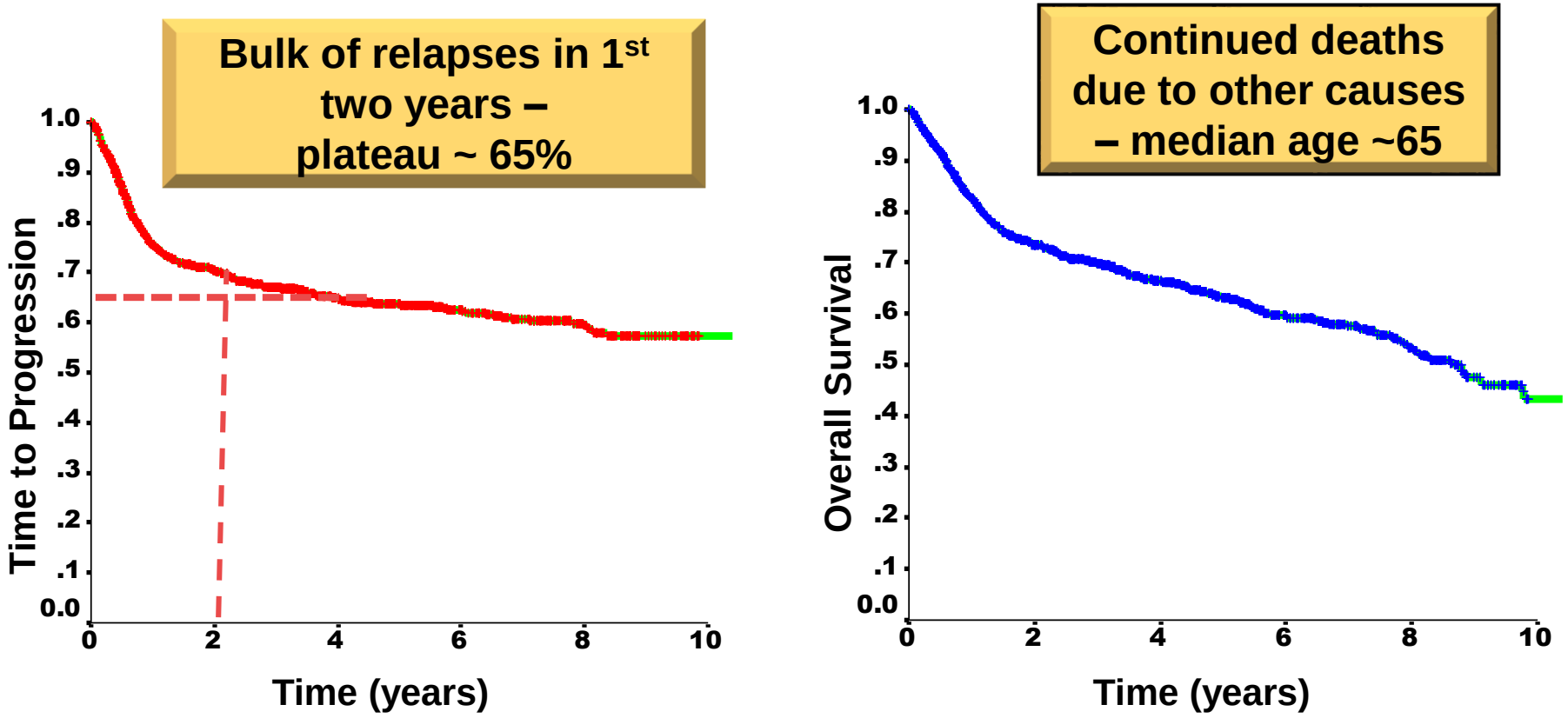
Failure-Free Survival



Overall Survival

Coiffier et al N Engl J Med. 2002; Habermann et al J Clin Oncol 2006

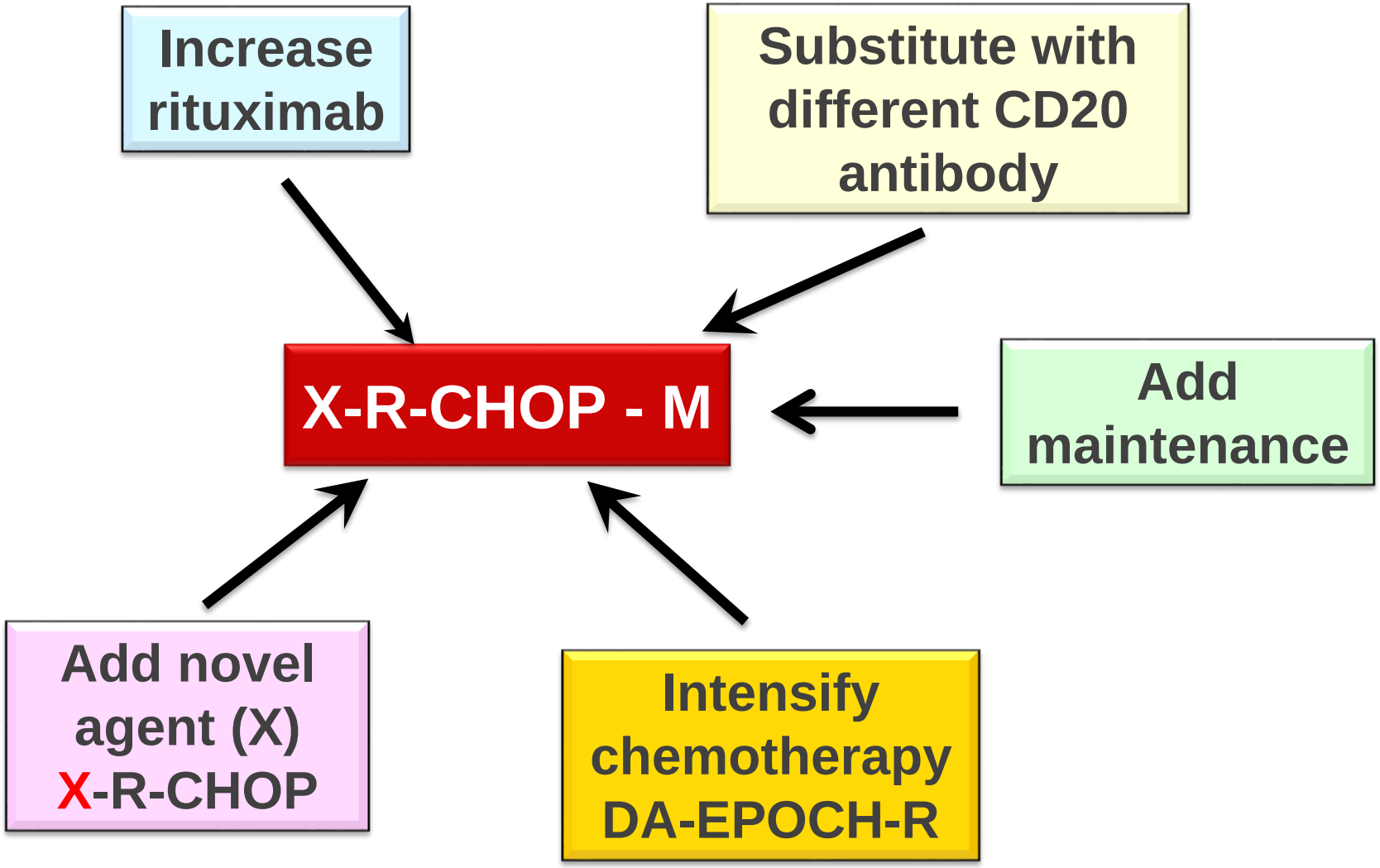
Time-to-Progression and Overall Survival of Patients with DLBCL Following R-CHOP at BCCA (n=1476)



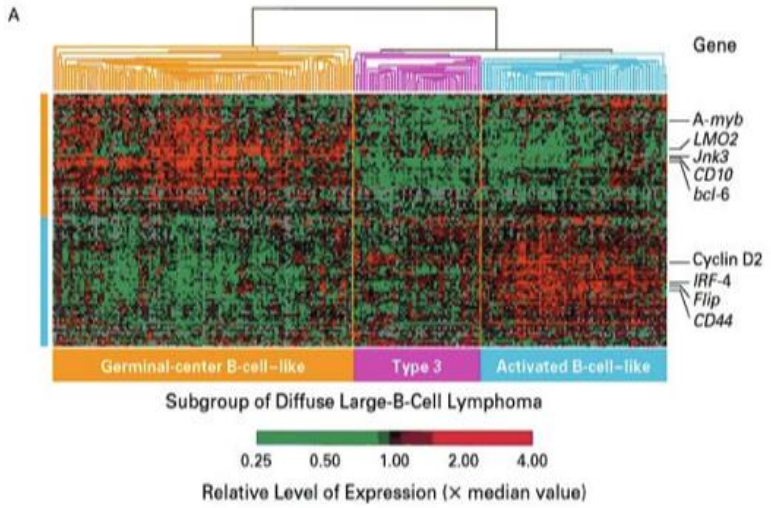
Median follow-up: 45 months (range 1-171)

Sehn et al. BC Cancer Agency

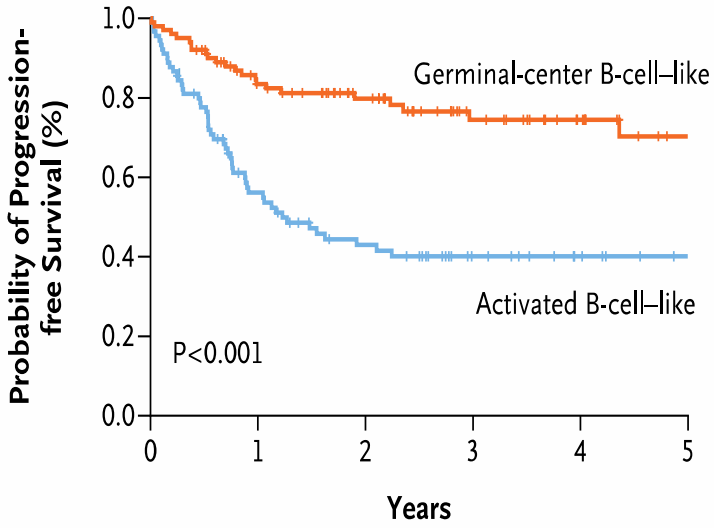
STRATEGIES TO IMPROVE R-CHOP

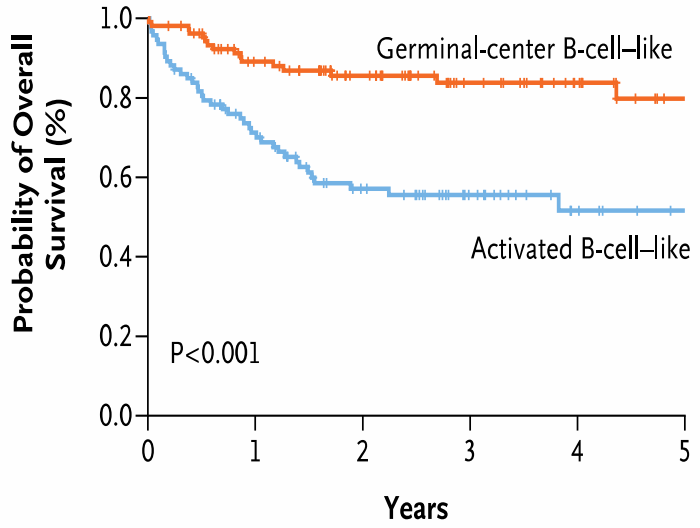


…AND / OR, DEFINE THE PATIENT POPULATION BETTER



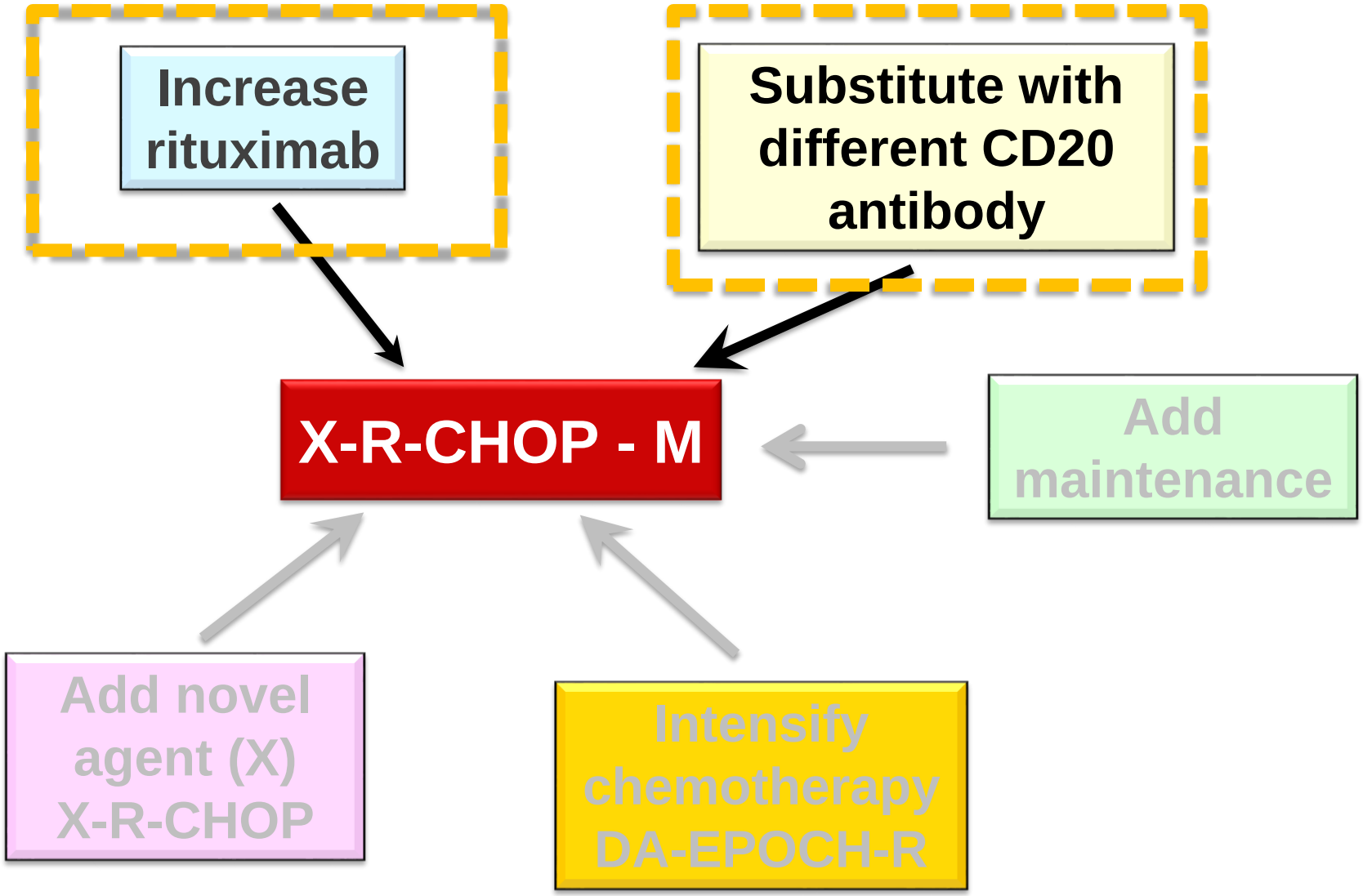
- Two major molecular subtypes:
- Activated B-cell like (ABC)
  - B-cell receptor driven
- Germinal center B-cell like (GCB)





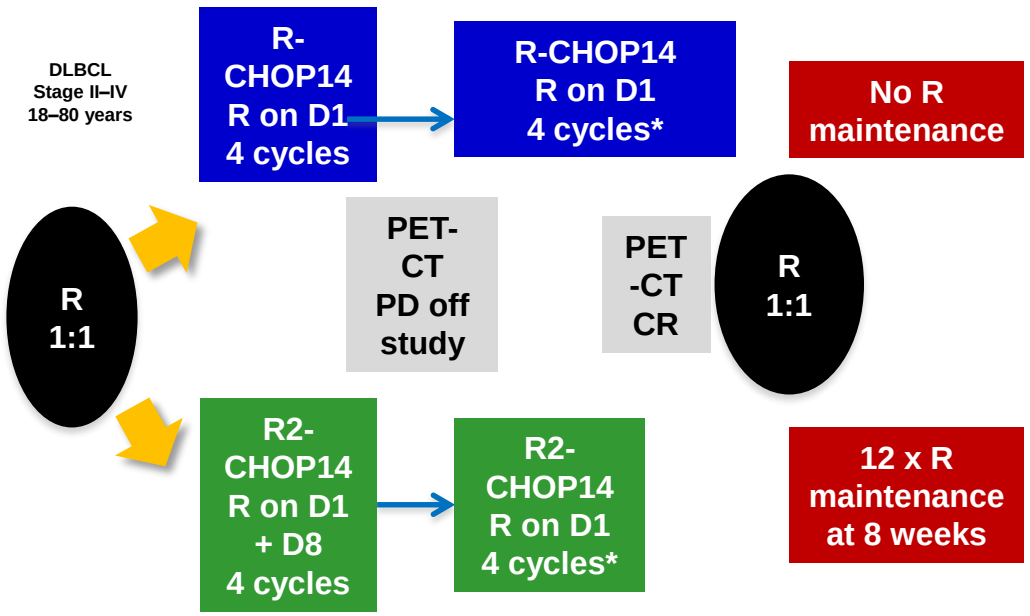
Lenz et al. N Engl J Med 2008;359:2313–2323.

STRATEGIES TO IMPROVE R-CHOP

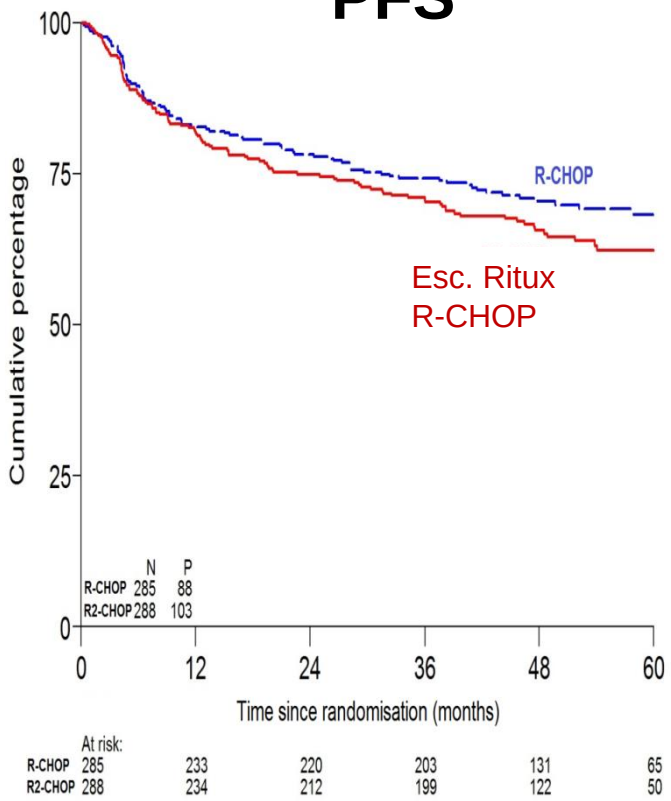


INTENSIFIED RITUXIMAB IN HOVON STUDY

Study design



PFS



Presented by: PJ Lugtenburg ASCO 2016.

OR TRY A DIFFERENT (? BETTER ?) ANTI-CD20: RITUXIMAB VS OBINOTUZUMAB

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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

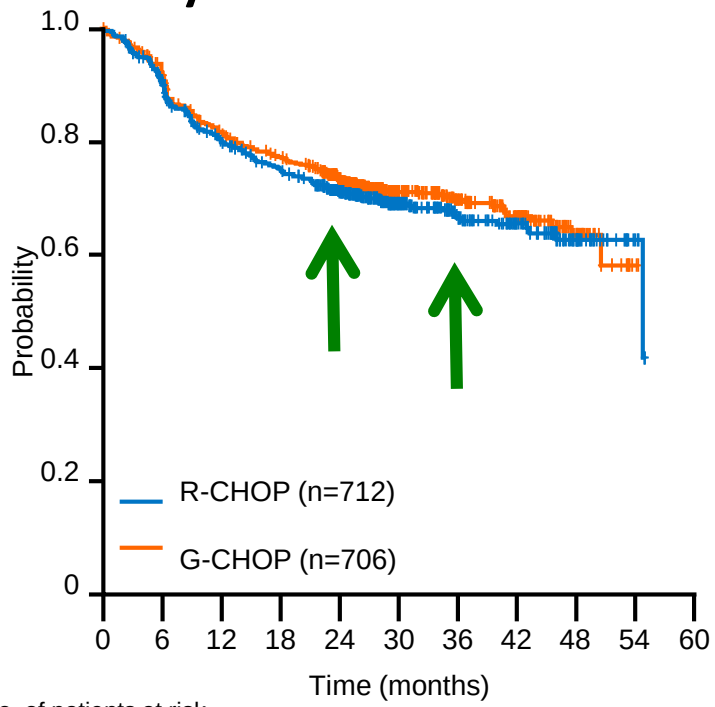
Obinutuzumab or Rituximab Plus Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone in Previously Untreated Diffuse Large B-Cell Lymphoma

Umberto Vitolo, Marek Trněný, David Belada, John M. Burke, Angelo Michele Carella, Neil Chua, Pau Abrisqueta, Judit Demeter, Ian Flinn, Xiaonan Hong, Won Seog Kim, Antonio Pinto, Yuan-Kai Shi, Yoichi Tatsumi, Mikkel Z. Oestergaard, Michael Wenger, Günter Fingerle-Rowson, Olivier Catalani, Tina Nielsen, Maurizio Martelli, and Laurie H. Sehn

INVESTIGATOR-ASSESSED PFS

J Clin Oncol 35:3529-3537. 2017

Kaplan-Meier plot of investigator-assessed PFS by treatment arm

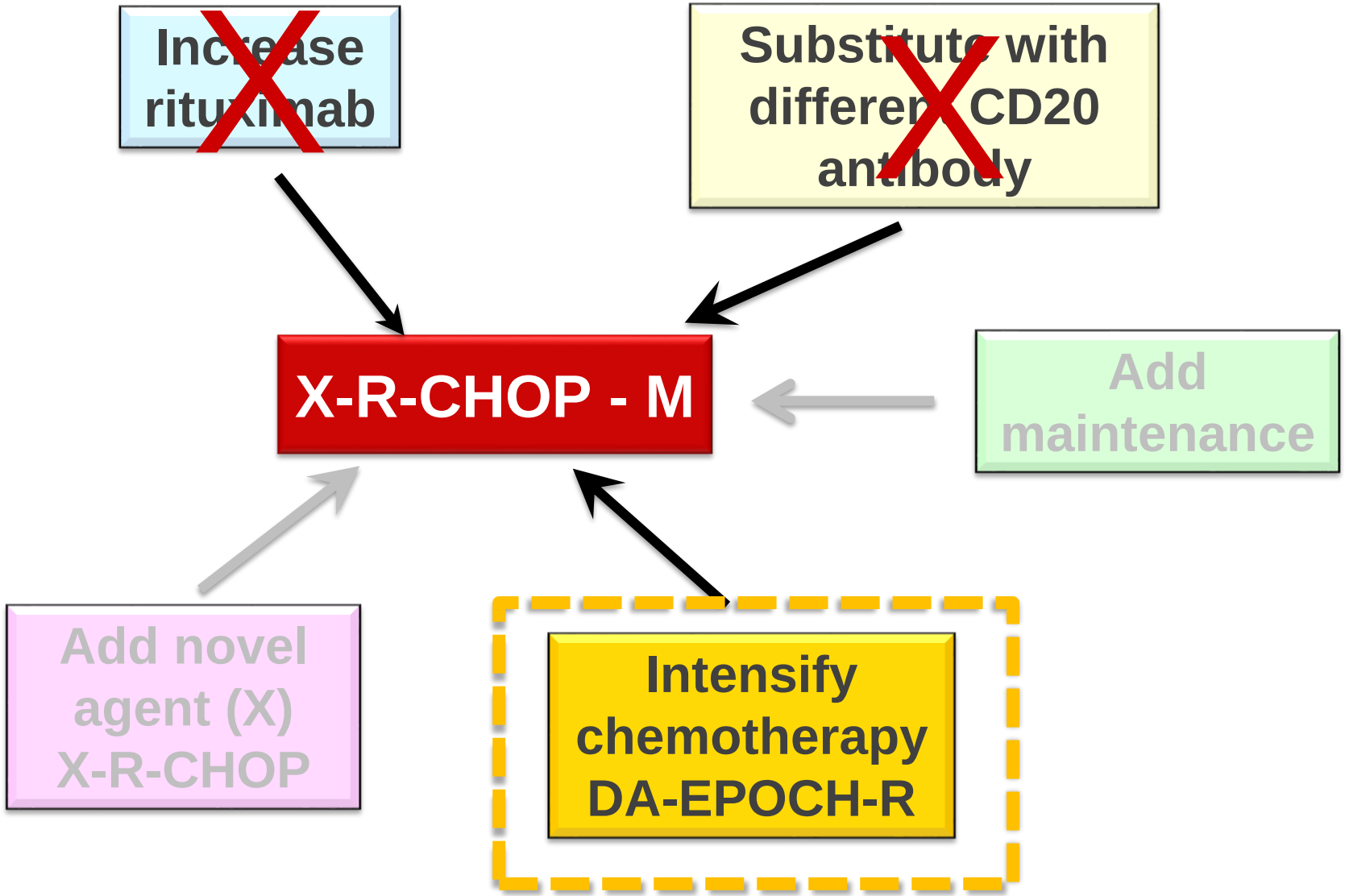


	R-CHOP, n=712	*G-CHOP, n=706*
Pts with event, n (%)	215 (30.2)	201 (28.5)
1-yr PFS, %	79.8	81.6
2-yr PFS, %	71.3	73.4
3-yr PFS, %	66.9	69.6
HR (95% CI), p-value*	0.92 (0.76, 1.11), p=0.3868	

Median follow-up: 29 months

*Stratified analysis; stratification factors: IPI score, number of planned chemotherapy cycles

STRATEGIES TO IMPROVE R-CHOP

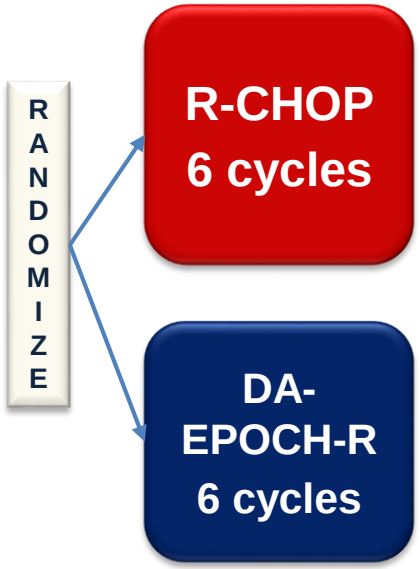


Phase III Study of R-CHOP vs DA-EPOCH-R in patients with untreated DLBCL (CALGB/Alliance 50303)

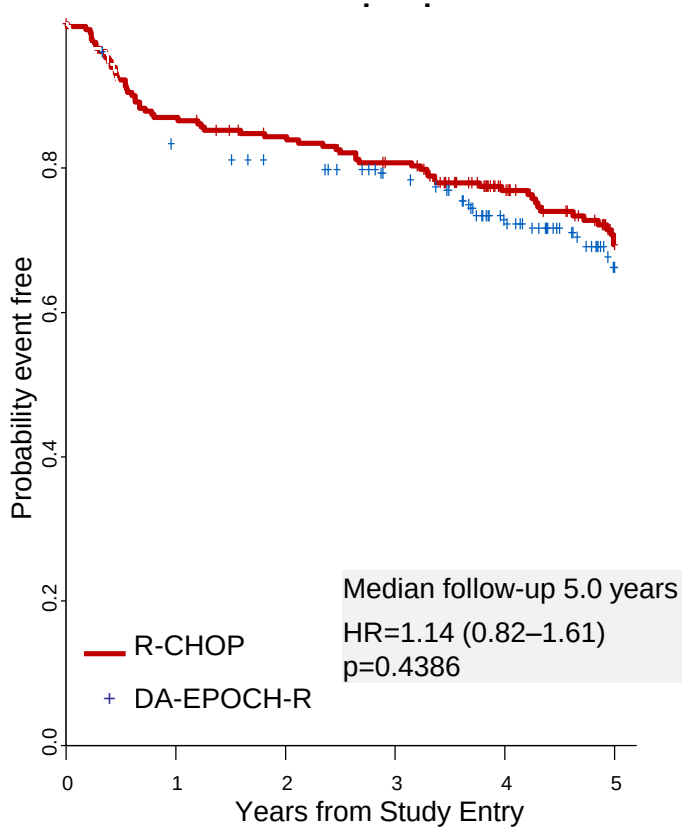
Study schema

Key eligibility criteria (N=524)

- Age ≥18 years
- Stage II or higher newly diagnosed DLBCL (Stage I PMBCL)
- ECOG PS 0–2
- Fresh/frozen tumor biopsy (4 cores)

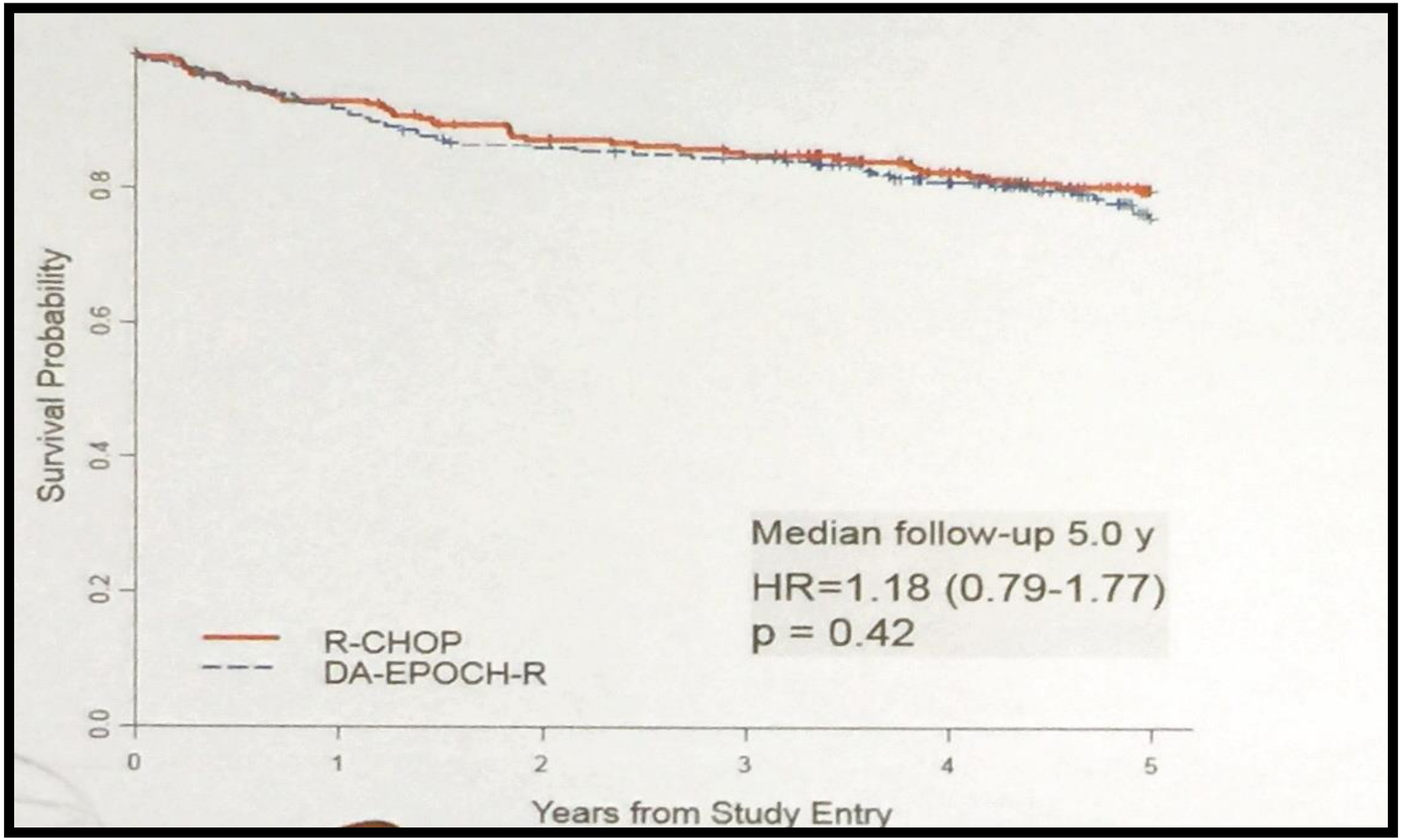


Event-free



Bartlett, Wilson et al. ASH 2016. Abstract 469.

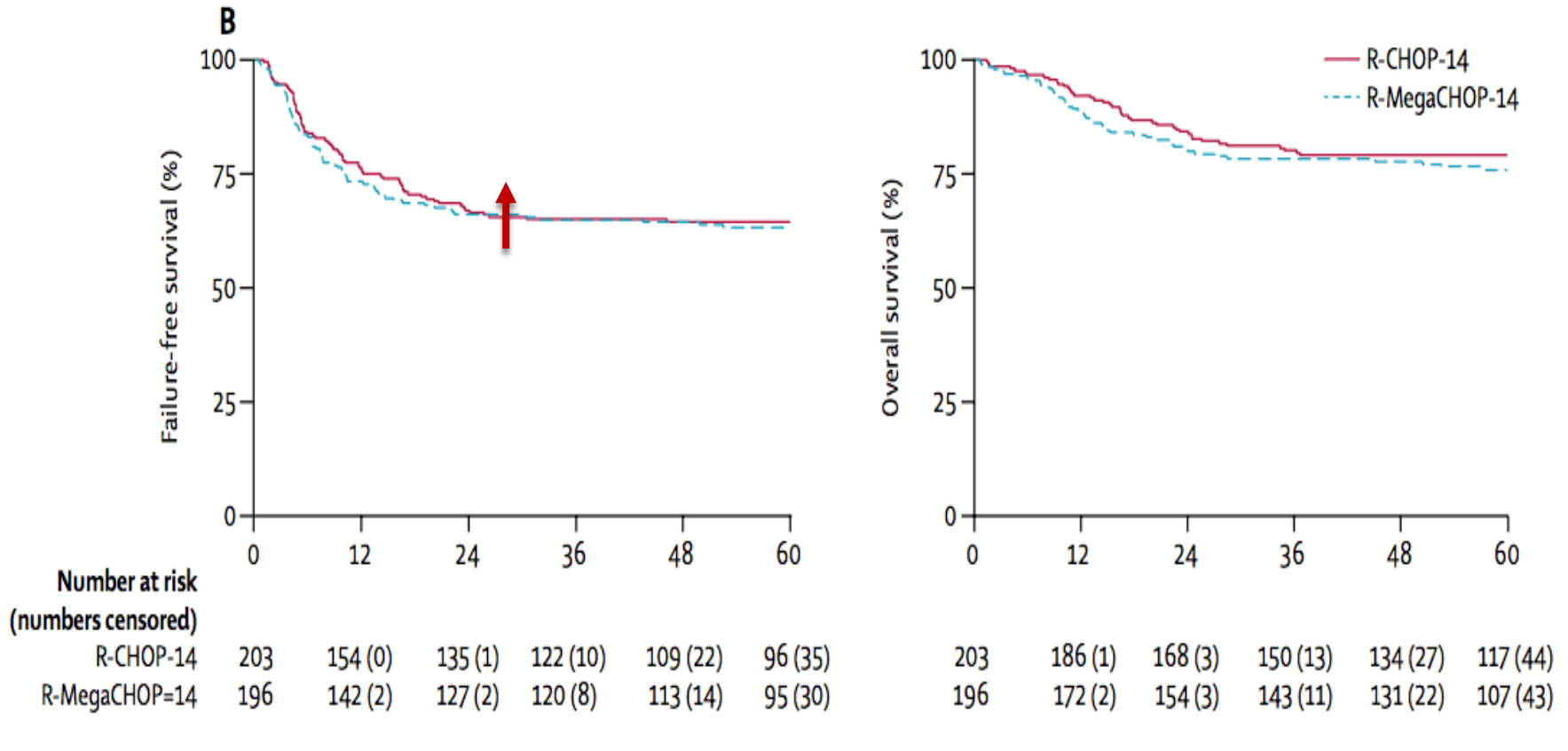
…..And, More Chemotherapy Did Not Improve Overall Survival Either



Bartlett, Wilson et al. ASH 2016. Abstract 469.

R-CHOP-14 vs R-MegaCHOP-14

More Chemotherapy Was *Not* Better



Lancet Oncol 2017; 18: 1076–88

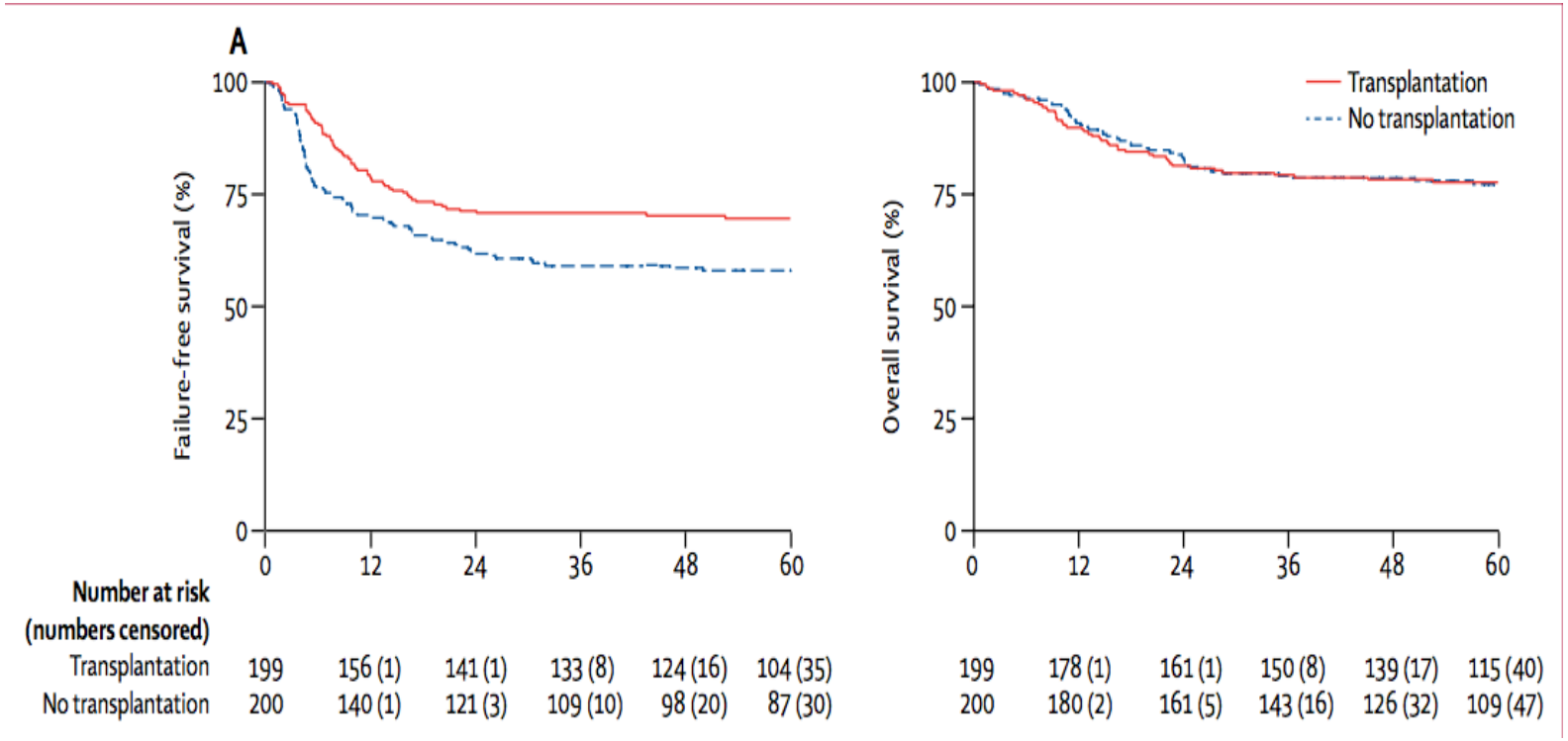
Rituximab-dose-dense chemotherapy with or without high-dose chemotherapy plus autologous stem-cell transplantation in high-risk diffuse large B-cell lymphoma (DLCL04): final results of a multicentre, open-label, randomised, controlled, phase 3 study

Annalisa Chiappella, Maurizio Martelli*, Emanuele Angelucci, Ercole Brusamolino†, Andrea Evangelista, Angelo Michele Carella, Caterina Stelitano, Giuseppe Rossi, Monica Balzarotti, Francesco Merli, Gianluca Gaidano, Vincenzo Pavone, Luigi Rigacci, Francesco Zaja, Alfonso D'Arco, Nicola Cascavilla, Eleonora Russo, Alessia Castellino, Manuel Gotti, Angela Giovanna Congiu, Maria Giuseppina Cabras, Alessandra Tucci, Claudio Agostinelli, Giovannino Ciccone, Stefano A Pileri, Umberto Vitolo*

Lancet Oncol 2017; 18: 1076–88

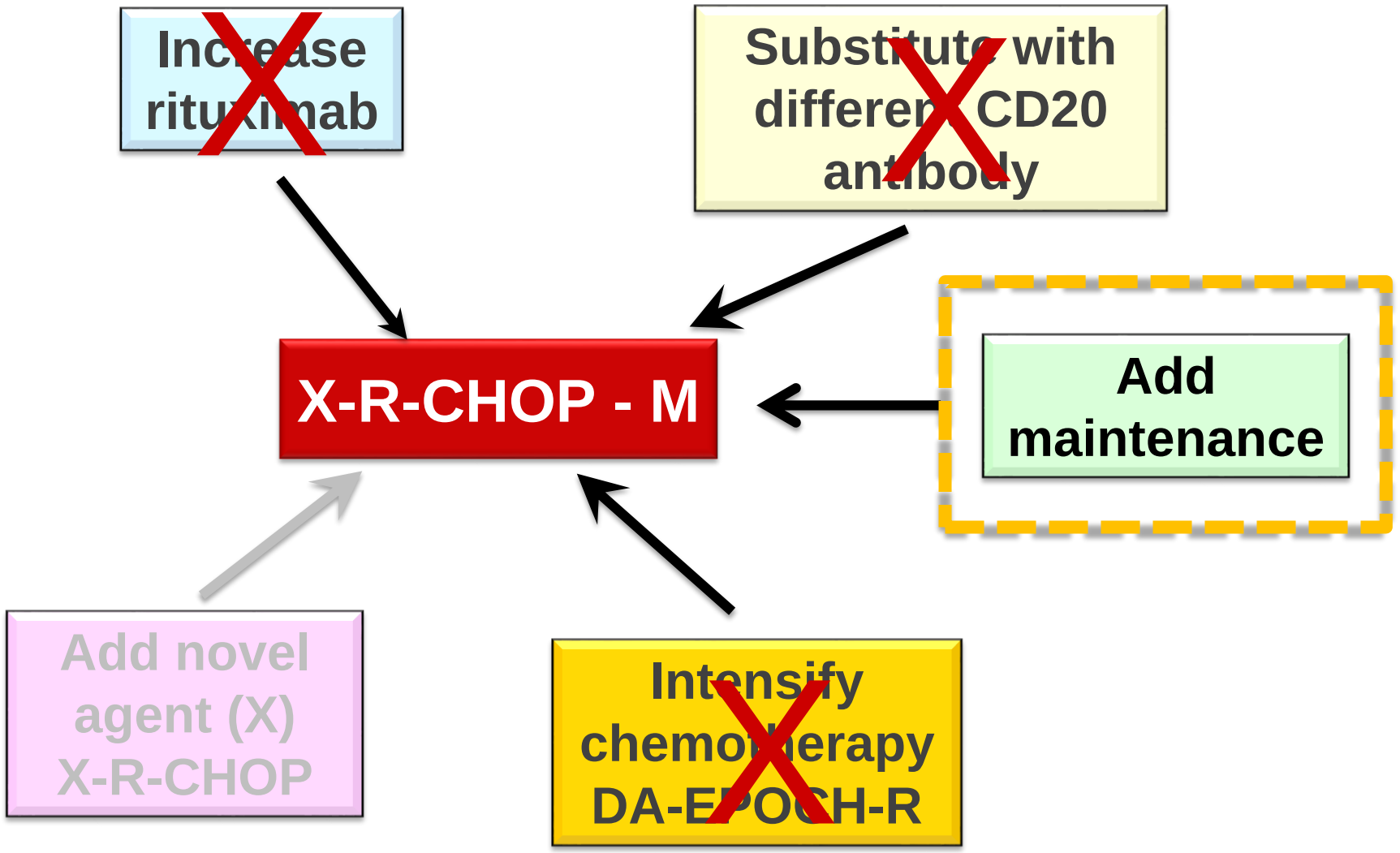
TRANSPLANT VS NO TRANSPLANT

You Can Wait and Get Your Transplant Later



Lancet Oncol 2017; 18: 1076–88

Strategies to Improve R-CHOP



PILLAR-2 Study Design: Adjuvant Everolimus

Stratification by R-chemo
- **R-CHOP, n=725**
- **R-EPOCH, n=17**

Patients
- **Age ≥18 years**
- **Stage 2 bulky disease, stage 3, or stage 4 DLBCL**
- **Poor risk (IPI, 3-5)**
- **First-line therapy with R-chemo (5-8 cycles)**
- **PET confirmed CR to first-line R-chemo**
- **ECOG PS 0-2**

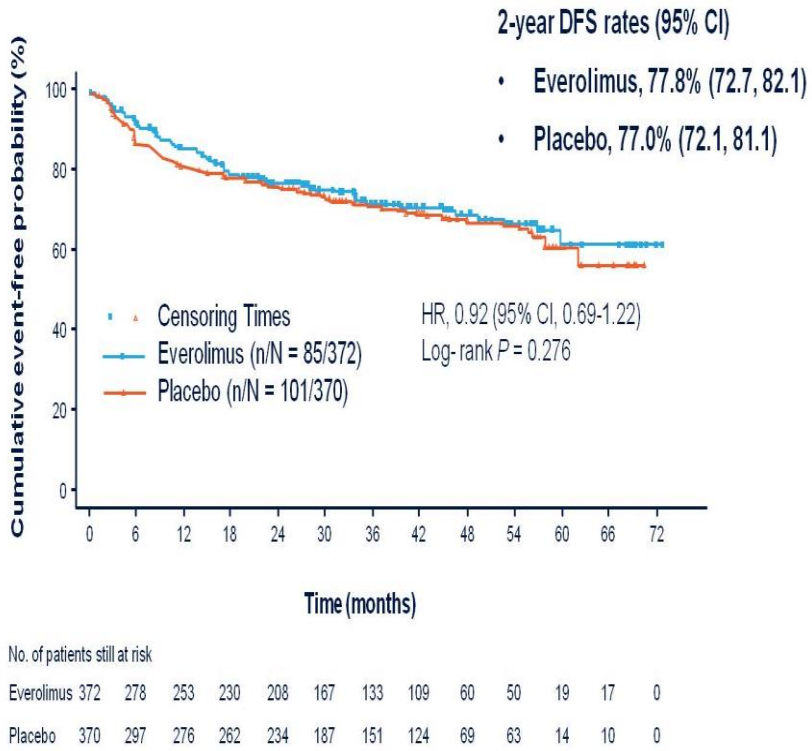
Randomization (1:1)

N=742

Everolimus 10 mg PO daily for 1 year N=372

Placebo PO daily for 1 year N=370

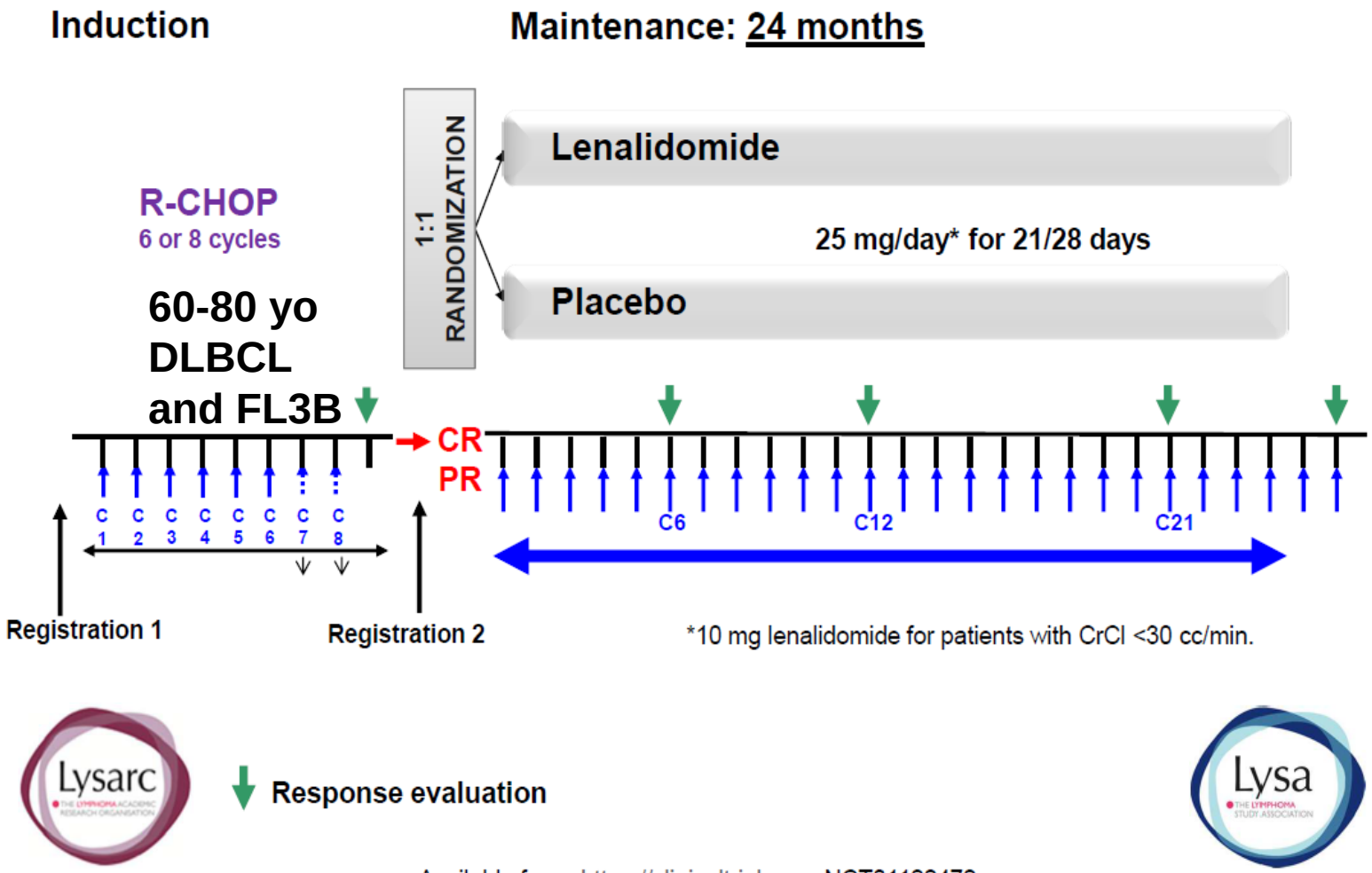
Disease-free survival



No Benefit to Maintenance Everolimus

Witzig 2016 Ann Oncol. 2017

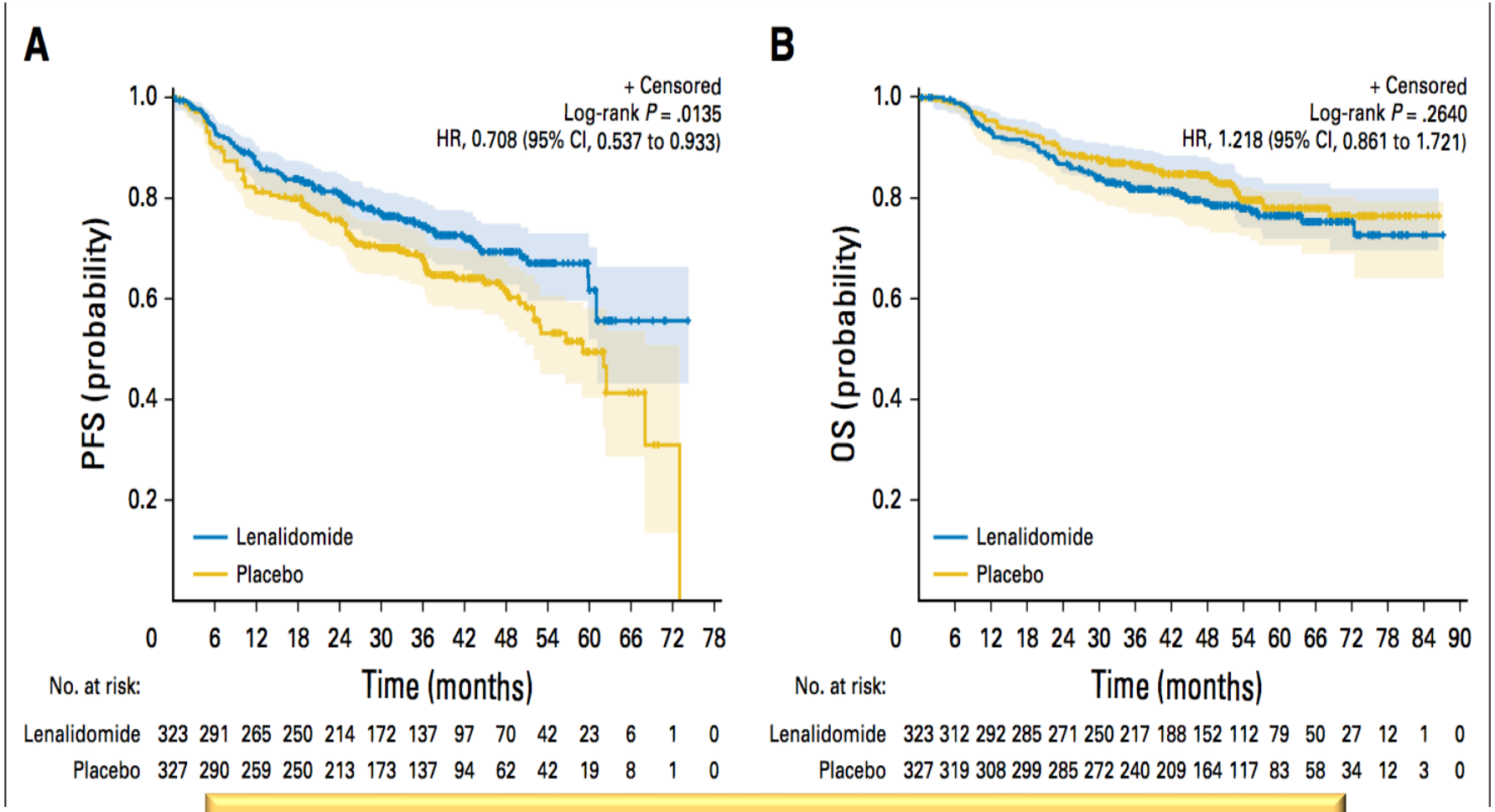
REMARC Study Design



Available from: https://clinicaltrials.gov NCT01122472

Thieblemont C et al J Clin Oncol. 2017 Aug 1;35(22):2473-2481.

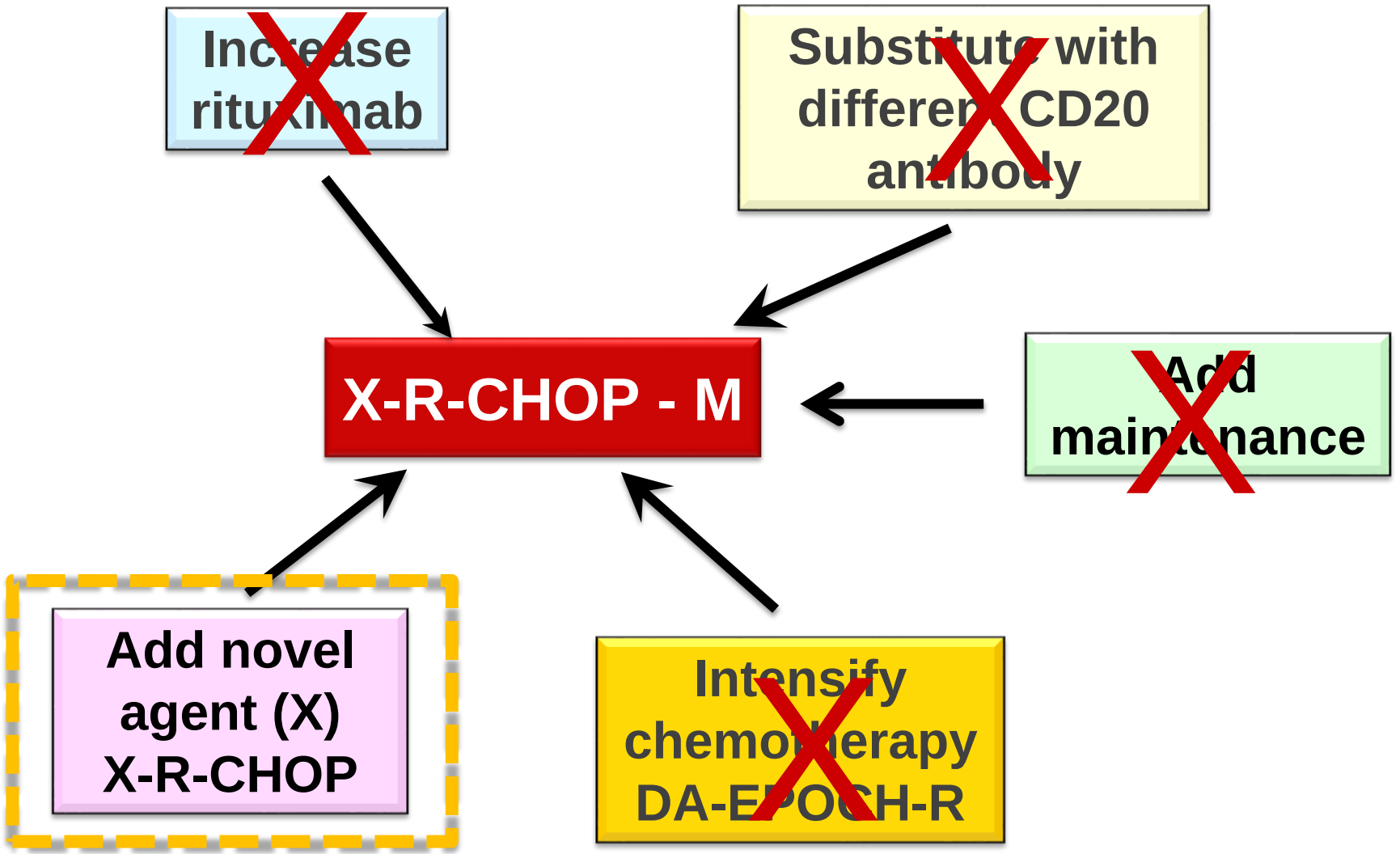
LENALIDOMIDE MAINTENANCE



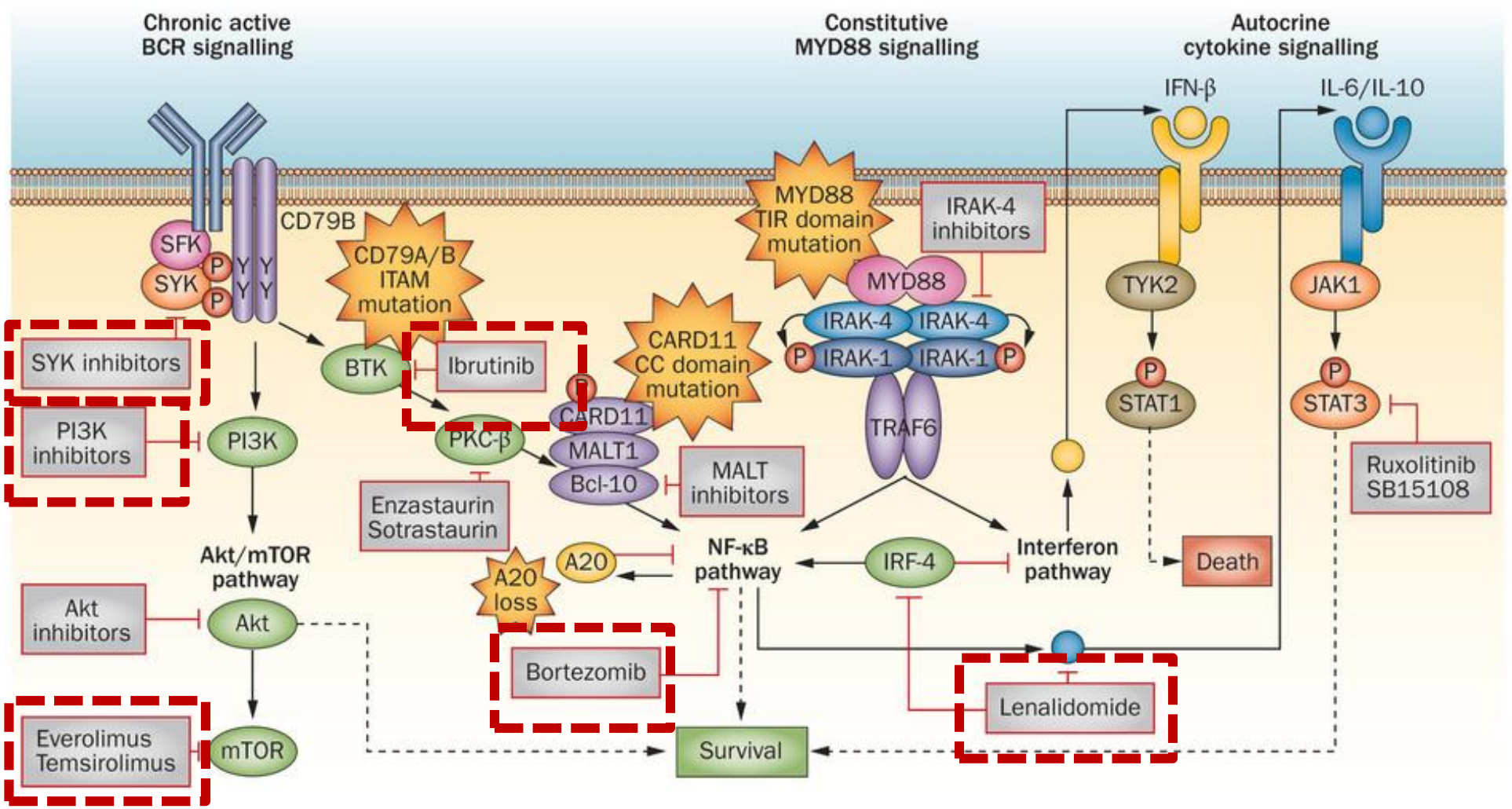
Modest Improvement in PFS but No Difference in Survival

Thieblemont C et al J Clin Oncol. 2017 Aug 1;35(22):2473-2481

Strategies to Improve R-CHOP



PATHWAYS WITH THERAPEUTIC POTENTIAL DLBCL



Mark Roszewski et al. *Nature Reviews Clinical Oncology 2014*

From Relapsed Setting to Front Line:
X-R-CHOP

Drug	Combination	Phase	Result
Epratuzumab	ER_CHOP	Phase 2	Not promising
Bortezomib	Bor-CHOP	Phase 3's	ALL Negative
Everolimus	EverCHOP	Phase 1	Not Promising and toxic
Ibrutinib	Phoenix	Phase 3	NEGATIVE (July 2018)
Lenalidomide	ROBUST	Phase 3	Last Hope (Early 2019)

VOLUME 35 · NUMBER 31 · NOVEMBER 1, 2017

JOURNAL OF CLINICAL ONCOLOGY

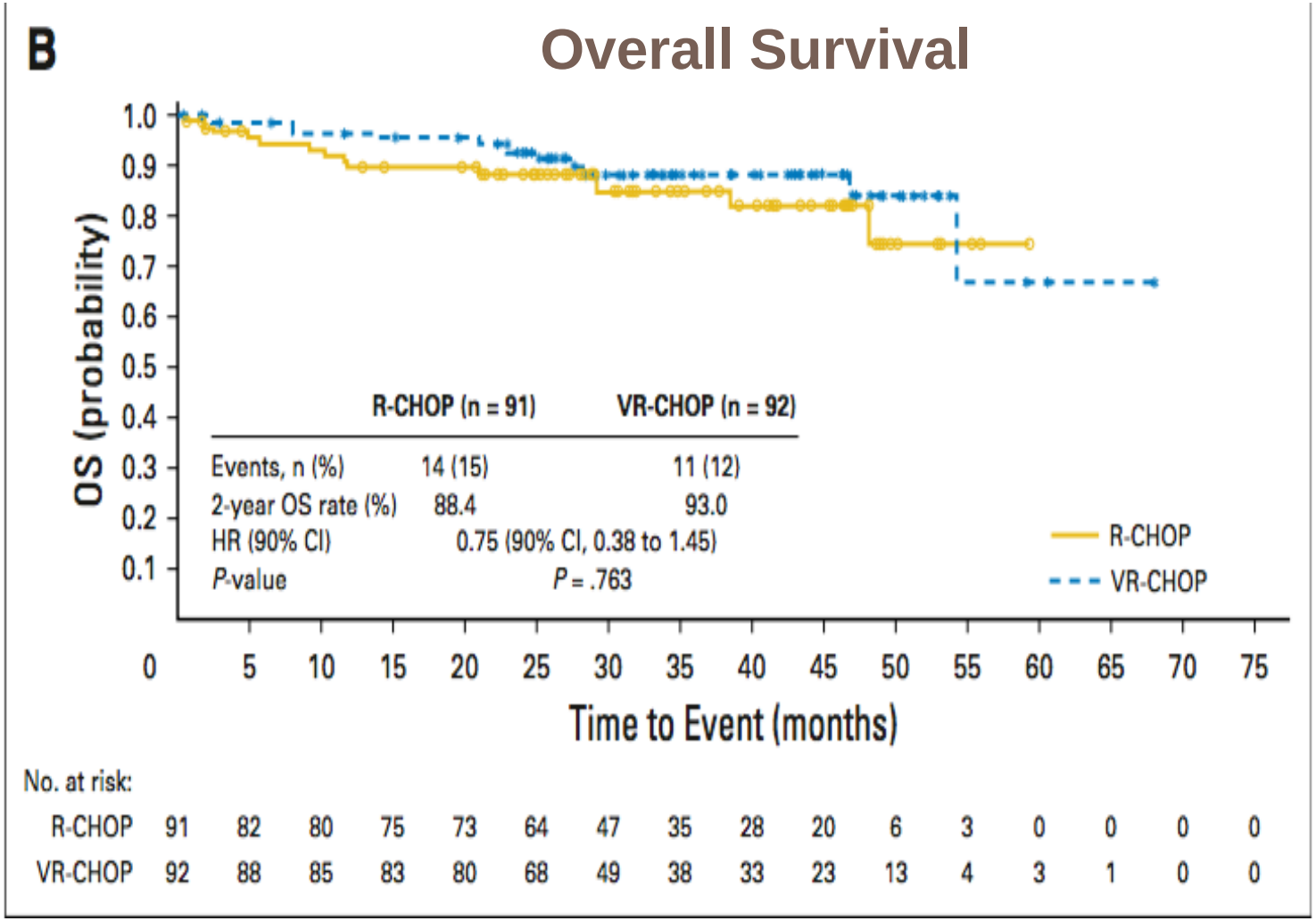
ORIGINAL REPORT

Randomized Phase II Study of R-CHOP With or Without Bortezomib in Previously Untreated Patients With Non–Germinal Center B-Cell–Like Diffuse Large B-Cell Lymphoma

John P. Leonard, Kathryn S. Kolibaba, James A. Reeves, Anil Tulpule, Ian W. Flinn, Tatjana Kolevska, Robert Robles, Christopher R. Flowers, Robert Collins, Nicholas J. DiBella, Steven W. Papish, Parameswaran Venugopal, Andrew Horodner, Amir Tabatabai, Julio Hajdenberg, Jaehong Park, Rachel Neuwirth, George Mulligan, Kaveri Suryanarayan, Dixie-Lee Esseltine, and Sven de Vos

J Clin Oncol 35:3538-3546 2017

Bortezomib Plus R-CHOP – No Improvement in OS



J Clin Oncol 35:3538-3546 2017

A Prospective Randomised Trial of Targeted Therapy for Diffuse Large B-Cell Lymphoma (DLBCL) Based upon Real-Time Gene Expression Profiling.

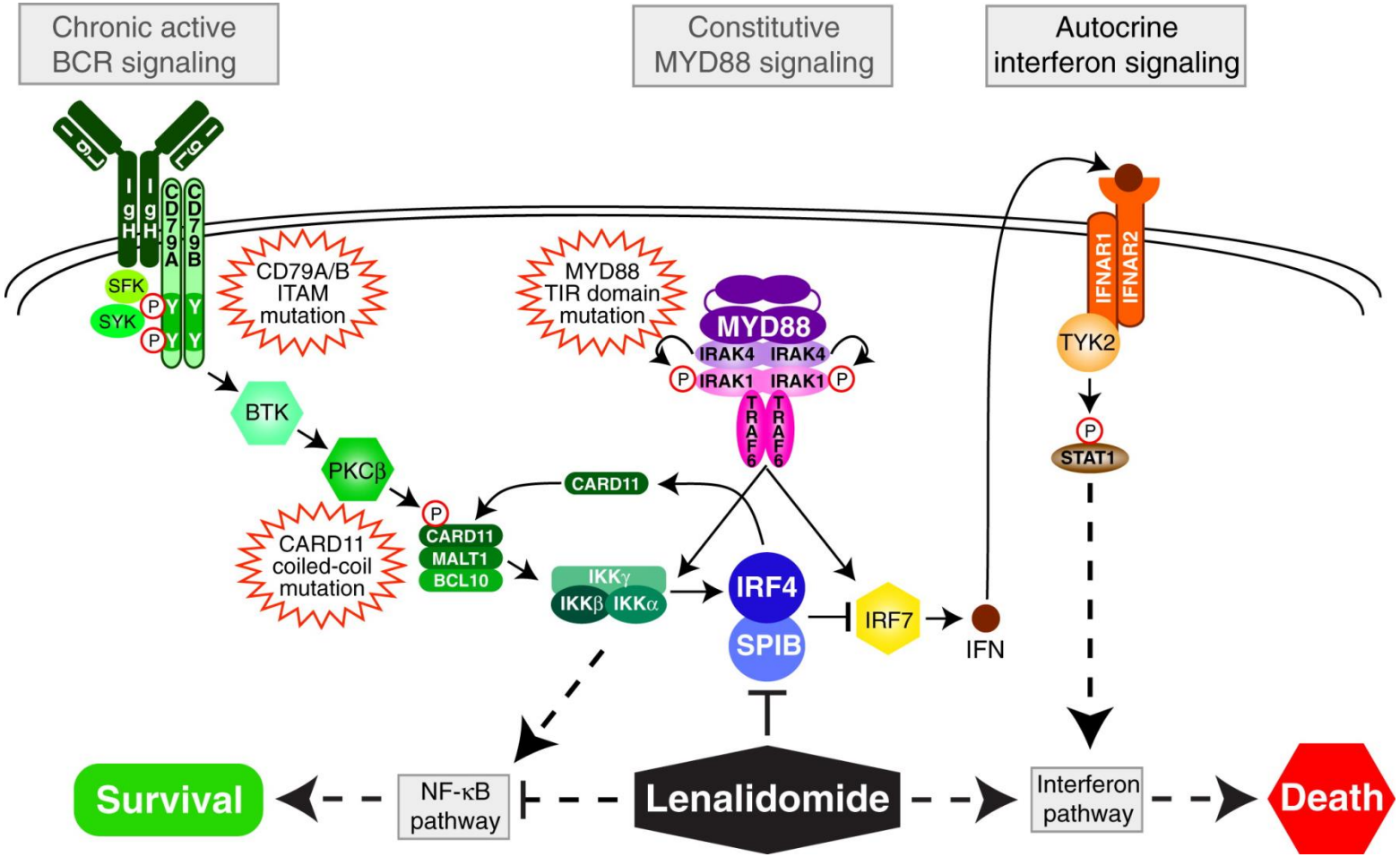
The REMoDL-B Study of the UK NCRI and SAKK Lymphoma Groups

REMoDL-B

Andrew J Davies[1], Josh Caddy[2], Tom Maishman[2], Sharon Barrans[3], Christoph Mamot[4], Matthew Care[5], Christopher Pocock[6], Louise Stanton,[2], Debbie Hamid[2], Keith Pugh[2], Andrew McMillan,[7], Paul Fields[8], Anton Kruger[9], Andrew Jack[10] and Peter W.M. Johnson[1]

[1]Cancer Research UK Centre, University of Southampton, Southampton, United Kingdom [2]Southampton Clinical Trials Unit, University of Southampton, Southampton, United Kingdom [3]St James Institute of Oncology, HMDS, Leeds, United Kingdom [4], Cantonal Hospital of Aarau, Aarau, Switzerland [5]University of Leeds, Leeds Institute of Cancer and Pathology, Leeds, United Kingdom [6]East Kent Hospitals, Canterbury, United Kingdom 7Nottingham City Hospital, Nottingham, United Kingdom [8]Department of Haematology, Guy's and St Thomas' Hospitals NHS Trust, London, United Kingdom [9]Royal Cornwall Hospital, Truro, United Kingdom [10]HMDS, Leeds Cancer Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

Synthetic Lethality of Lenalidomide in ABC DLBCL



CELGENE CLINICAL EFFICACY DATA FOR ABC PATIENTS*

- CC-5013-DLC-001 Open label, Phase 2 study of lenalidomide versus single agent control in relapsed/refractory DLBCL patients
- FFPE sample subtyped by IHC (Hans algorithm)
- Fresh frozen biopsy sample subtyped by GEP (Randy Gascoyne; Affymetrix U133 Plus 2.0 GeneChip microarrays)

	Non-GCB by IHC (n=28)	ABC by GEP (n=11)
	Lenalidomide patients	
ORR	8 (28.6%)	5 (45.5%)
CR	4 (14.3%)	3 (27.3%)
PFS median	15.1 wks	82.0 wks
OS median	32.3 wks	108.4 wks

Includes ABC + **unclassified**

ROBUST uses **GEP**

*Czuczman *et al*. ASH2014 Oral Session, abstract #628

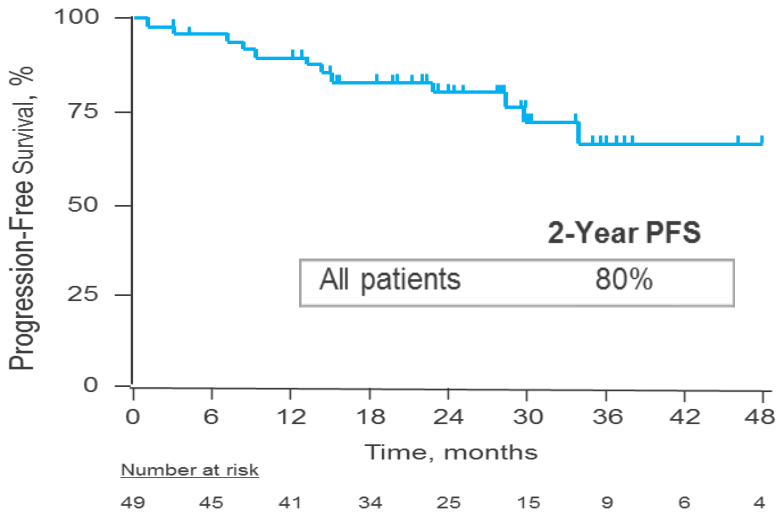
Addition of Lenalidomide to R-CHOP in Untreated DLBCL Improves non-GCB Outcomes

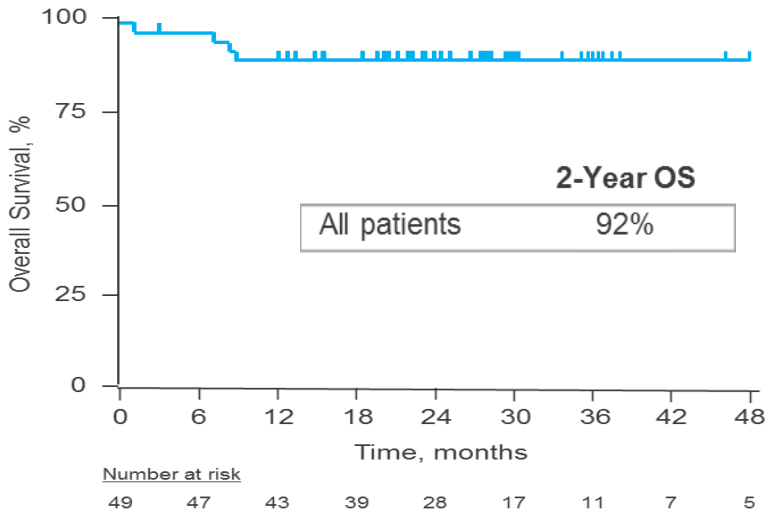
	Mayo Clinic MC078E*				FIL REAL07**	
	R2-CHOP		R-CHOP		R2-CHOP	
N	55 (51 evaluable)		87 (83 evaluable)		49	
Regimen	R-CHOP21 + lenalidomide 25mg days 1-10		R-CHOP21		R-CHOP21 + lenalidomide 15mg days 1-14	
ORR	51 (100%)		68 (83%)		45 (92%)	
CR	37 (73%)		56 (67%)		42 (86%)	
PFS at 24 mo	59%		52%		80%	
	GCB n = 31	**Non-GCB n = 20**	GCB n = 57	**Non-GCB n = 26**	GCB n = 16	**Non-GCB n = 16**
ORR	31 (100%)	20 (100%)	50 (88%)	18 (69%)	14 (88%)	14 (88%)
CR	23 (74%)	16 (80%)	43 (75%)	13 (50%)	13 (81%)	14 (88%)
PFS at 24 mo	59%	**60%**	64%	**28%**	71%	**81%**
OS at 24 mo	75%	**83%**	74%	**46%**	88%	**94%**

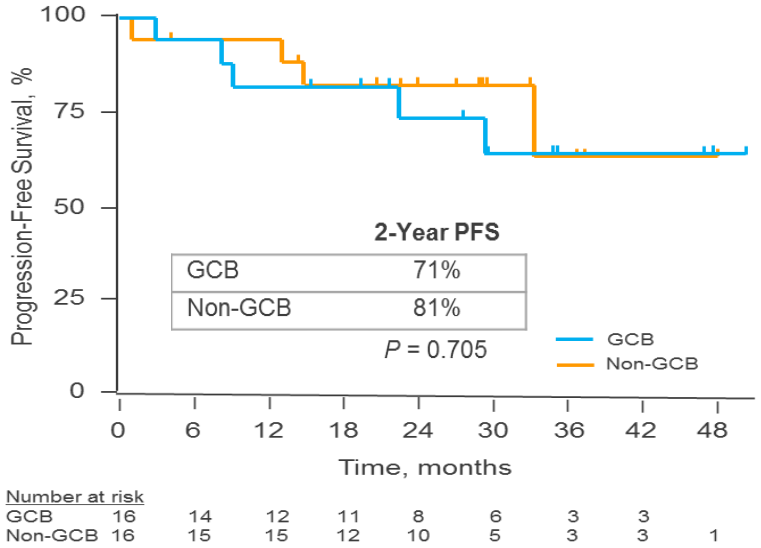
Two independent studies generate similar results

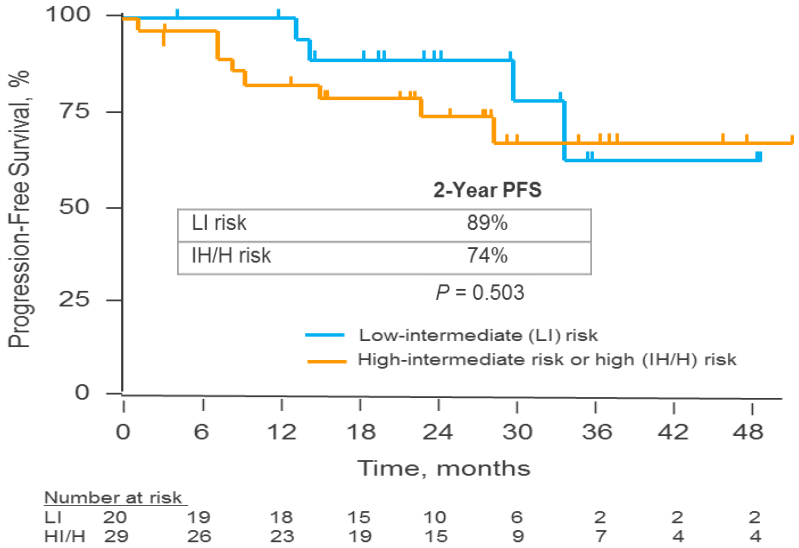
*Nowakowski *et al*. ASCO 2014 Oral Session
**Vitolo, et al. Lancet Oncol 2014;15:730-37

REAL07 Phase II R^2-CHOP21 in Elderly Untreated DLBCL: PFS and OS[1] PFS by COO and PFS by IPI







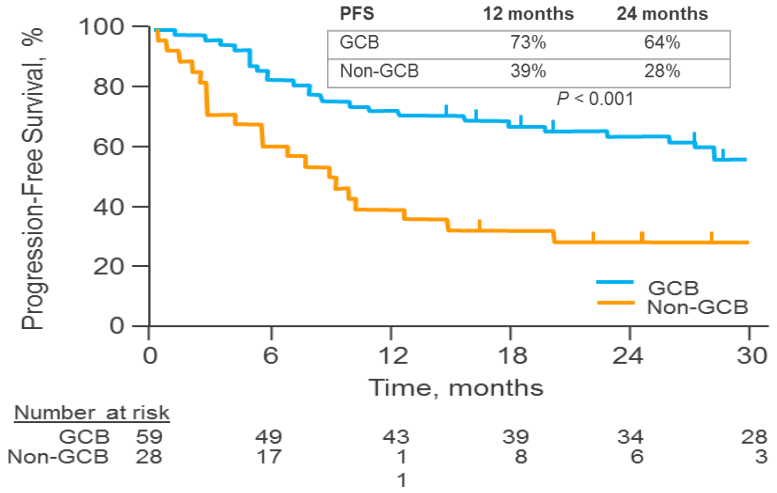


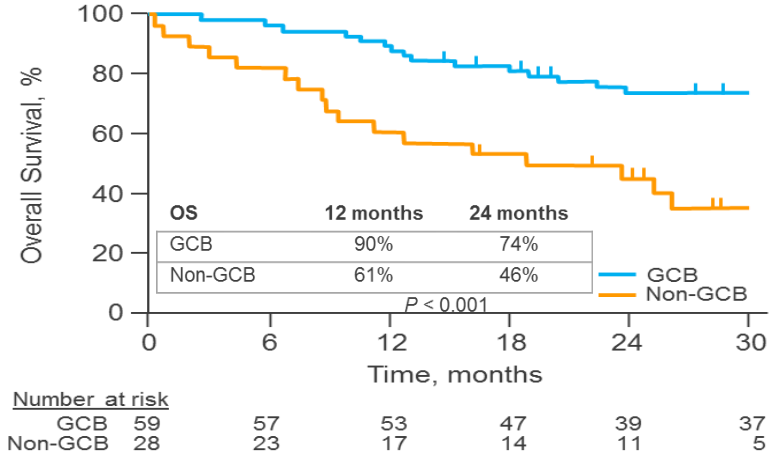
Median follow-up of 28 months.

1. Vitolo et al. *Lancet Oncol*. 2014;15:730-737.

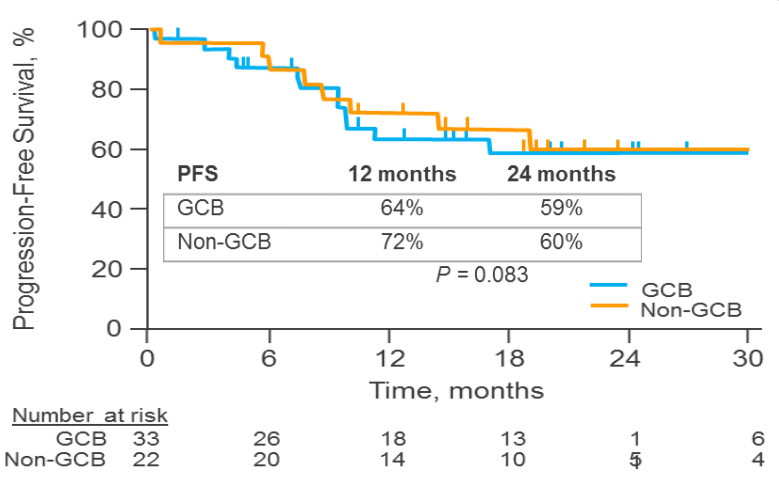
PFS and OS in GCB and Non-GCB DLBCL For Patients Treated With R-CHOP and R2-CHOP

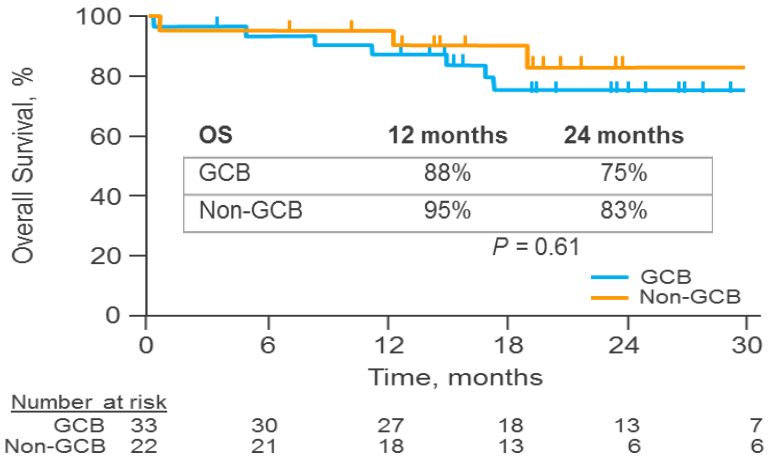
Historical R-CHOP





R²-CHOP





*Non-GCB subtype was defined by Hans algorithm.

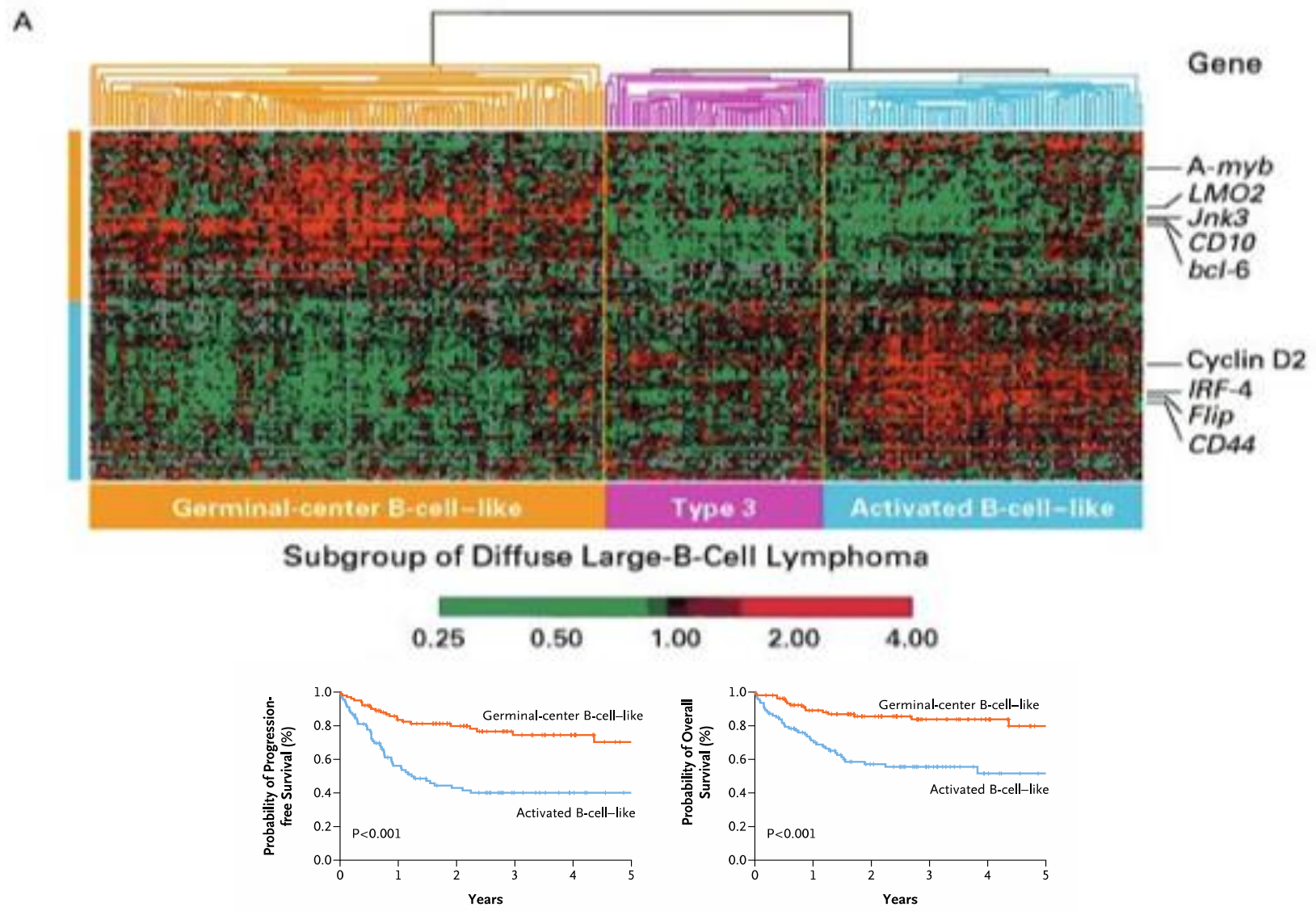
1.Nowakowski et al. *J Clin Oncol*. 2015;33:251-257. 2. Hans et al. *Blood*. 2004;103:275-282.

Evolution of Cell of Origin Determination Methods
Not All Equally as Accurate

15 Years of Research

- Gene expression profiling (GEP)
  - Usually fresh tissue required
  - 2-3 weeks to results, maybe difficult to standardize
- Immunohistochemical (IHC) method (Hans algorithm and others)
  - Rapid, on paraffin tissue (FFPE)
  - Difficult to standardize, non-GCB contains ABC and “unclassified” cases
- GEP by Nonostring platform (Lymph2Cx)
  - Done of paraffin (FFPE)
  - Rapid (2-3 days)

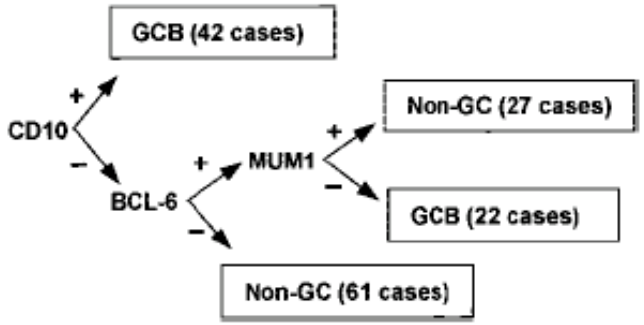
Gene Expression Profiling Defines DLBCL Subtypes

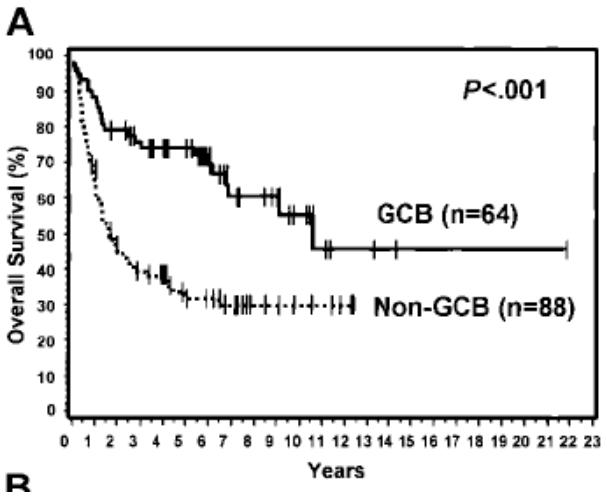


Lenz et al. N Engl J Med 2008;359:2313–2323.

Immunohistochemical Methods are Easy and Cheap but Least Accurate

Hans Method





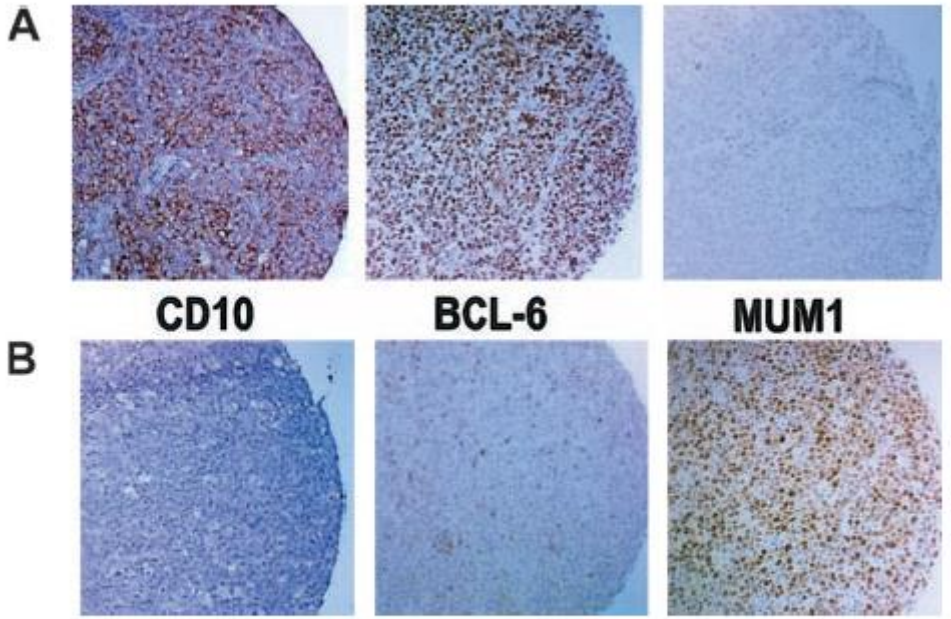
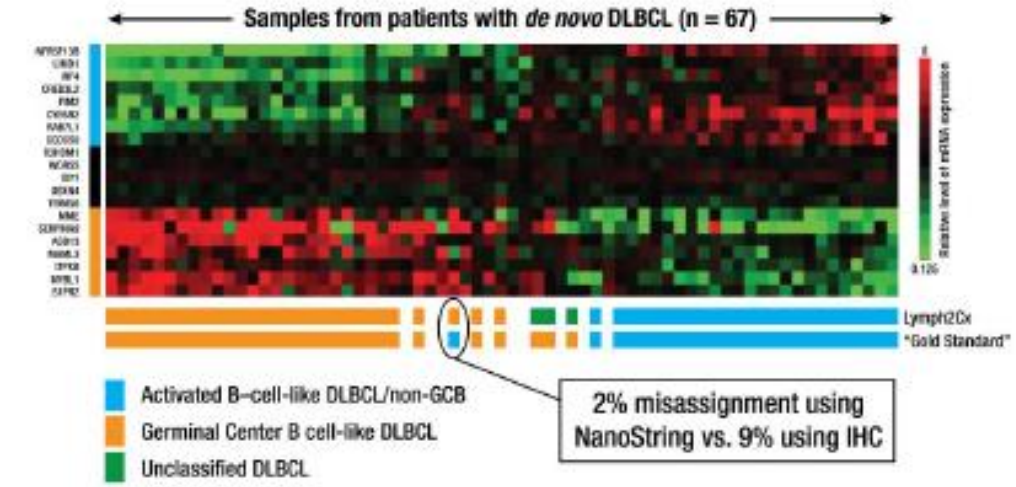
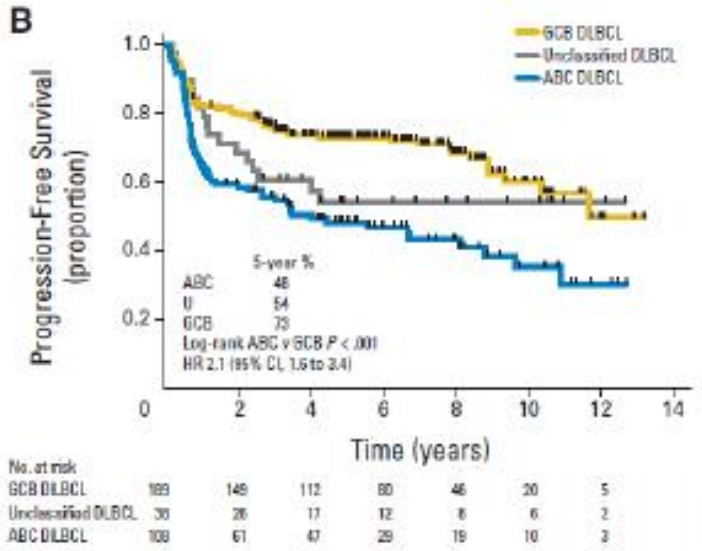
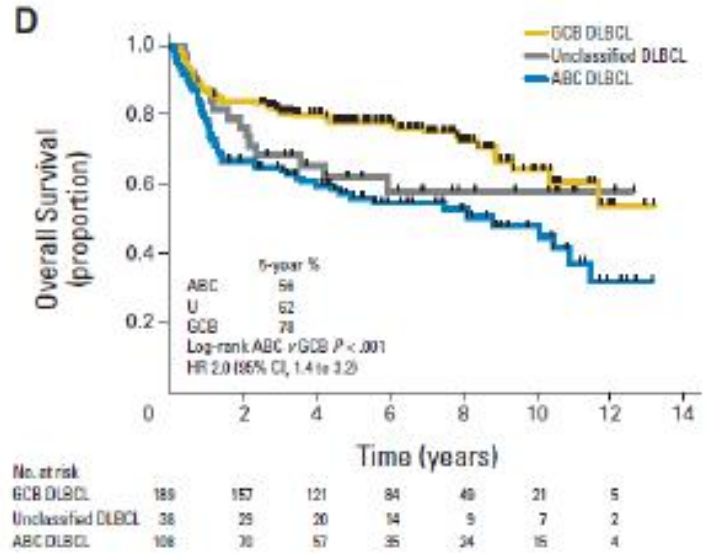


Figure 2. Results of Immunoperoxidase staining. (A) Immunoperoxidase stains of a GCB case that is positive for CD10 and bcl-6 but negative for MUM1. (B) Immunoperoxidase stains of a non-GCB case that is negative for CD10 but shows rare bcl-6$^+$ cells and is positive for MUM1. Original magnification, × 100.

NANOSTRING TECHNOLOGY PREDICTS SURVIVAL IN DLBCL TREATED WITH R-CHOP

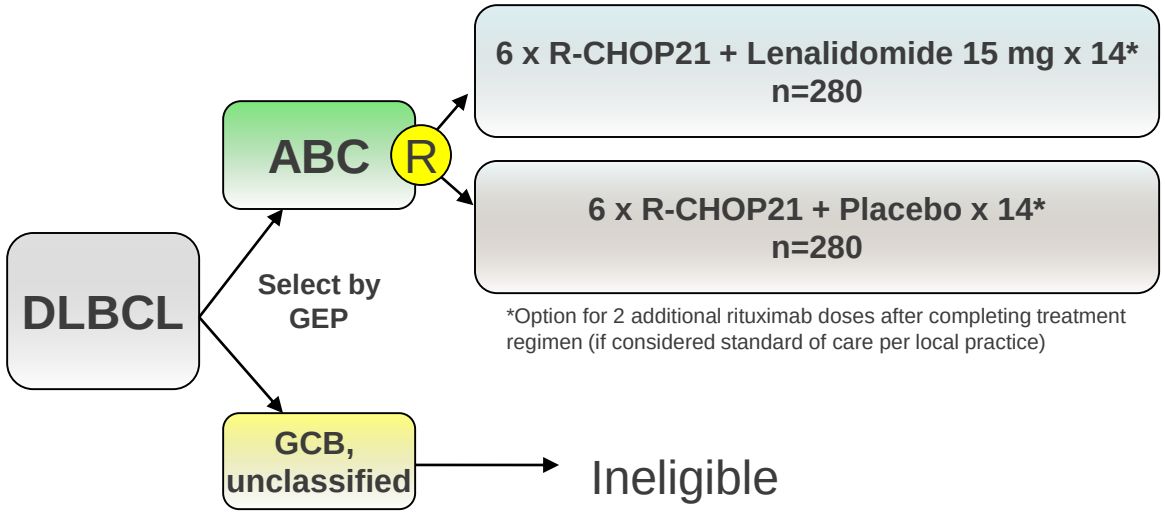






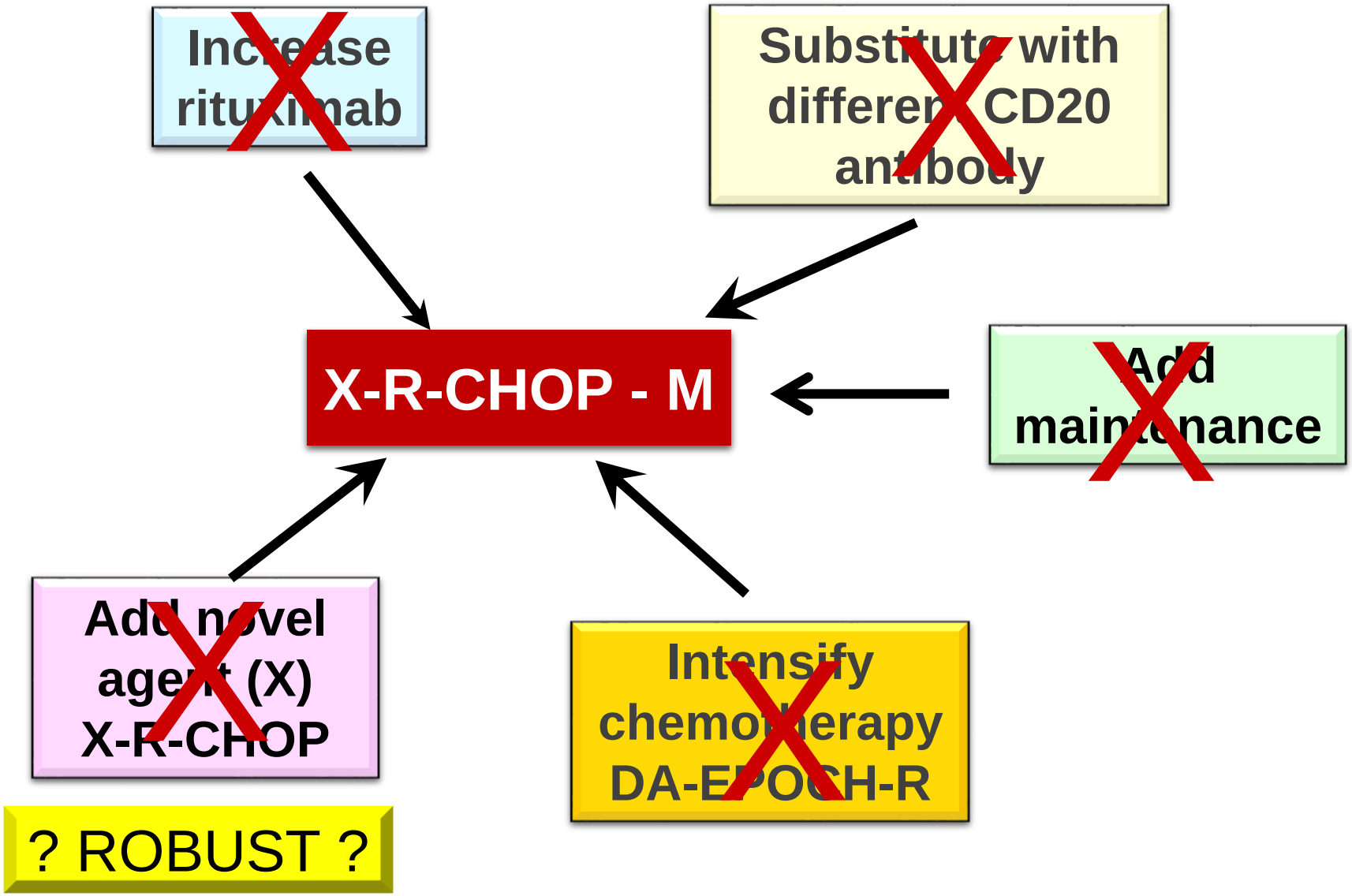
1. Scott et al. *Blood*. 2014;123:1214-1217. 2. Scott D et al. J Clin Oncol 2015; 33: 2848-56.

ROBUST Clinical Study Schema
Results Expected 2019



- Newly diagnosed DLBCL of ABC type
- IPI ≥ 2; ECOG PS ≤ 2; Age 18–80
- Primary Endpoint = PFS
- N = 560
- 90% power to detect 60% difference in PFS (control median PFS estimate = 24 mo)

STRATEGIES TO IMPROVE R-CHOP



So, What's New in the Standard of Care in DLBCL?

Not much has changed
despite a lot of effort.

Intensifying Anti-CD-20 → **No benefit**

Intensifying Chemotherapy → No Benefit

Adding Maintenance Therapy → No Benefit

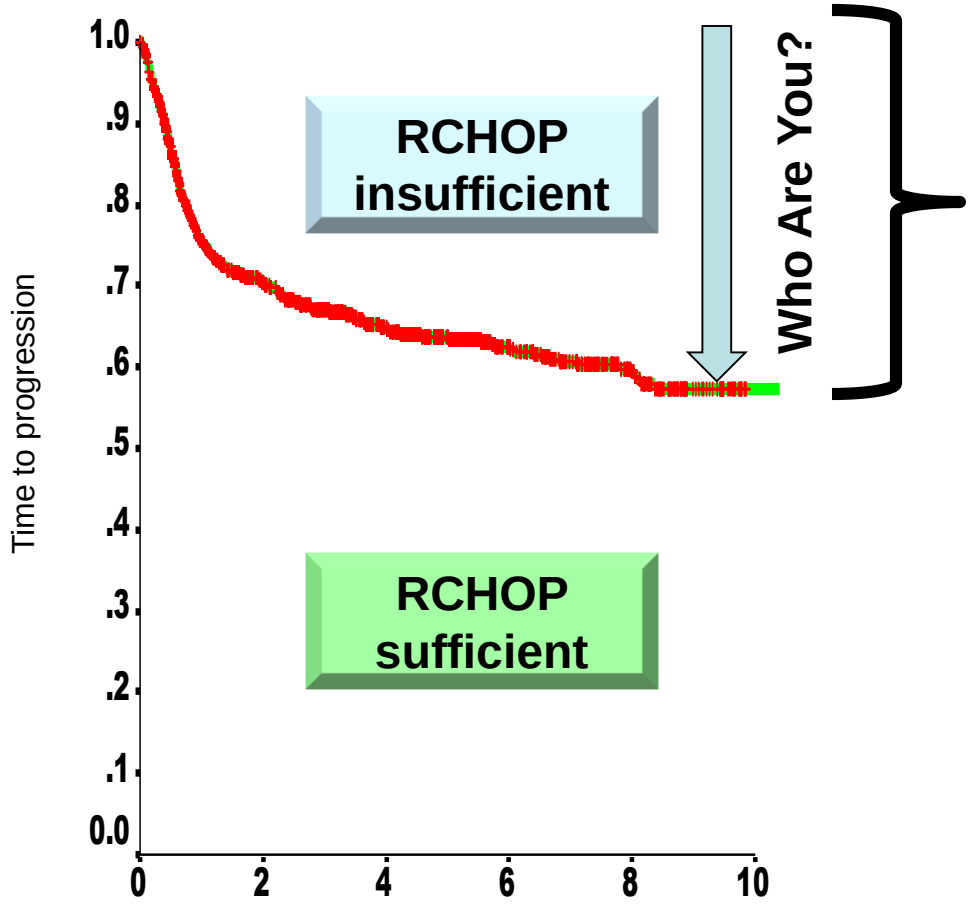
Adding 'Targeted' Molecules →
So far, No Benefit – Await ROBUST

R-CHOP x 6 is Standard of Care

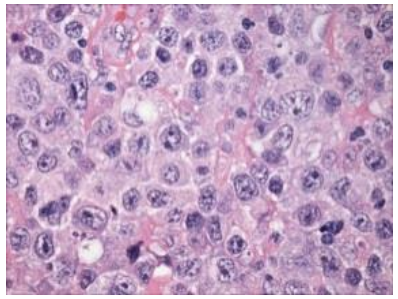
So Whats Next?
How Can We Make the Next Advance

- How do we identify those patients who don't do well with the SOC?
- Can we more precisely target the Achilles heal of that disease?
- In the era of evolving immunotherapy, how do we leverage those advances?

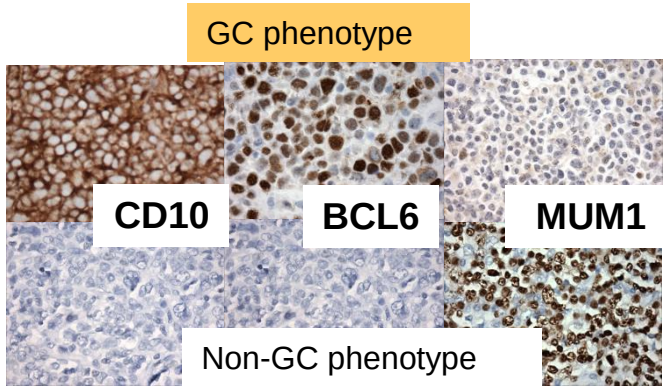
HETEROGENEITY OF OUTCOMES IN DLBCL



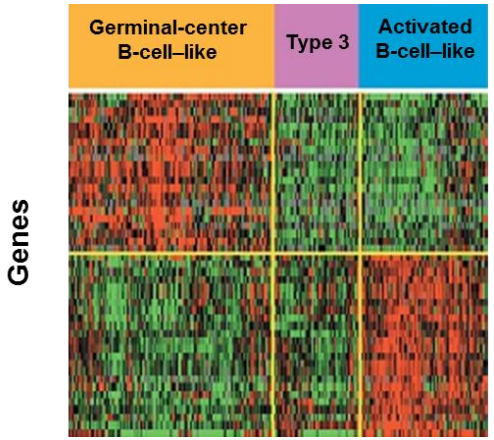
- **Clinical factors**
  - IPI (R-IPI)
- **GEP**
  - ACB vs GCB
- **Protein expression**
  - MYC and BCL2
- **Chromosomal alterations**
  - MYC, BCL2, BCL6
- **Somatic mutations**
  - MYD88, EZH2



Tissue cytomorphology

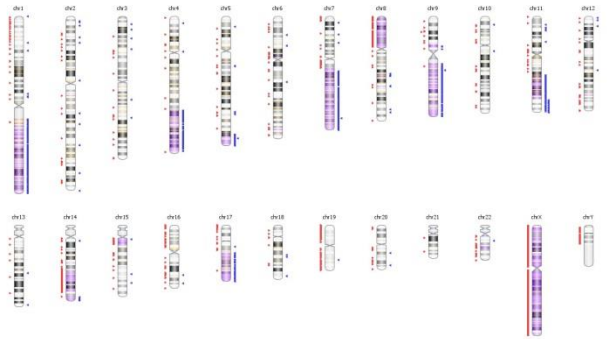


Immunohistochemistry

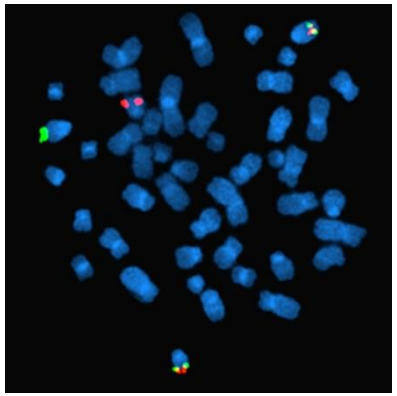


Current chromosome and genetic analysis techniques

Gene Expression Profiling



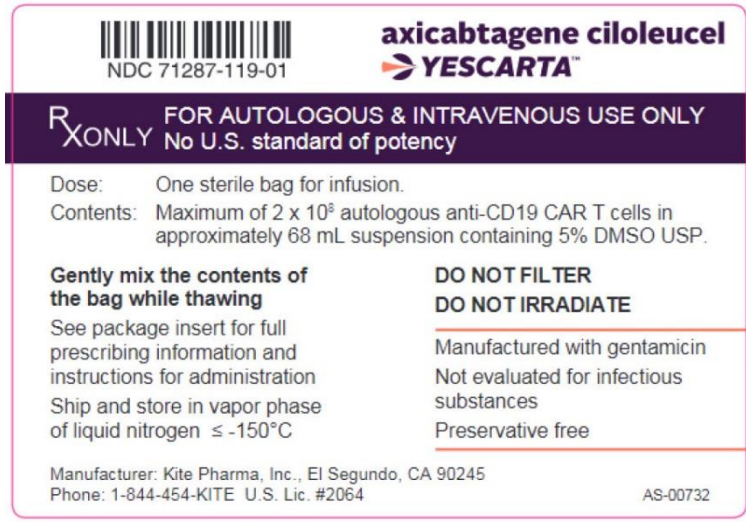
Comparative Genomic Hybridization (CGH)



Fluorescent In-Situ Hybridization (FISH)

The Future
Next Generation Sequencing
Single Nucleotide Polymorphisms (SNPs)

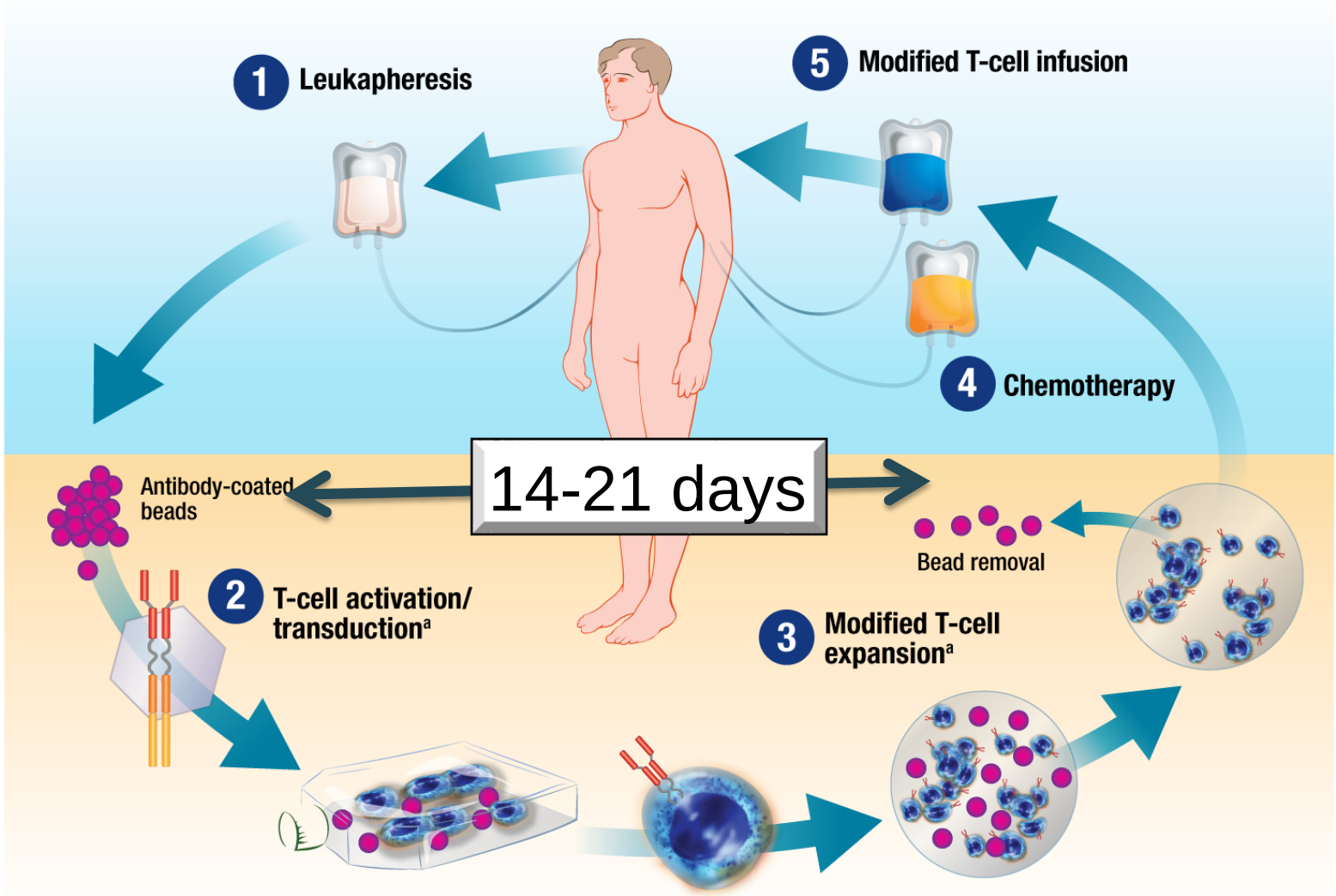
First Approved CAR-T cells



Oct. 17, 2017 – adult lymphoma

Aug. 30, 2017 – ALL up to age 25
May 1, 2018 – adult lymphoma

THE PATIENT'S JOURNEY



Courtesy Ran Reshef

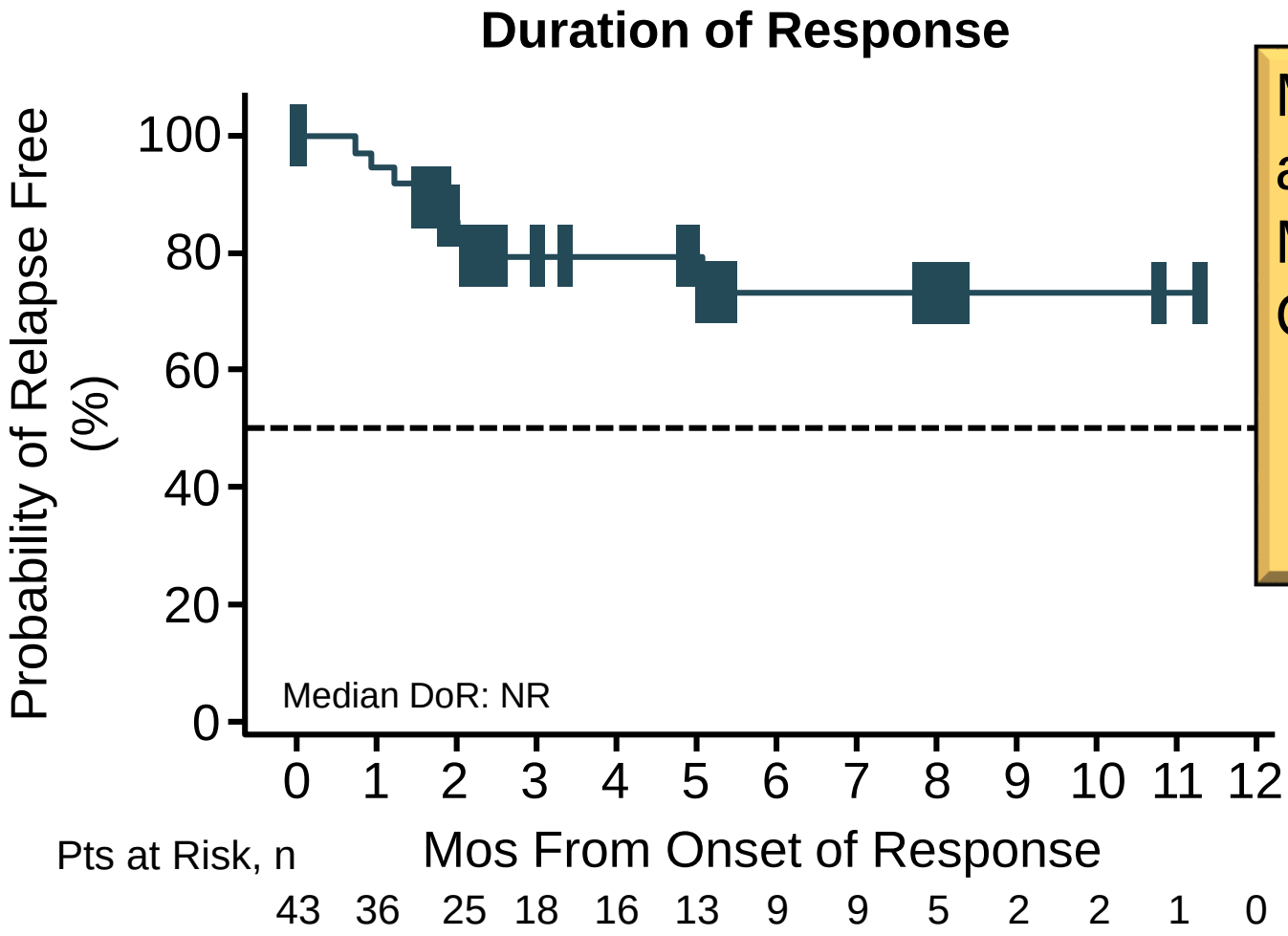
CD19 CAR in Adult Lymphoma (tisagenlecleucel): Patients with No Options

Response, %	Best ORR (n = 81)	3-Mo Response (n = 81)	6-Mo Response (n = 46)
ORR (CR + PR)	53	38	37
▪ CR	40	32	30
▪ PR	14	6	7

- **Study met primary endpoint with ORR of 53% (95% CI: 42% to 64%)**
  - **No relationship apparent between tisagenlecleucel dose and 3-mo response**
- **Follow up beyond 6 months not published yet**

Courtesy Ran Reshef

CD19 CAR IN ADULT LYMPHOMA (tisagenlecleucel)



Most pts achieving CR at Mo 3 remained in CR

- 74% of pts relapse free at 6 mos

CD19 CAR in Adult Lymphoma (tisagenlecleucel)
Summary of Risk : Benefit

- **EHA 2018 Update** (data cutoff December 2017)
- 165 enrolled; 111 infused
- Median follow up 13.9 mo
- Best ORR 52%; CR 40%; PR 12%
- At 12 mo: RFS 65% OS 49%
- Grade3/4 (Penn scale) CRS 14%
- Grade 3/4 Neurotoxicity 12%
- Prolonged cytopenias 32%
- Tocilizumab (Il-6 inhibitor) 15%
- No deaths attributed to CAR-T therapy

Courtesy Ran Reshef

How Can We Make the Next Advance

- Need to precisely identify those patients who don't achieve cure with conventional therapy
- Need to identify a targeted agent that can mitigate that adverse impact (ibrutinib was to be that promise – maybe assay not drug!)
- Utilize the most sensitive rapid-turn around tools possible to discriminate those patient
- Optimize new generation immunologics

  (CAR-T; ADC, bispecifics, etc.)
- Be cognizant of the added toxicity,

Some men see things as they are
and ask, Why?
I dream of things that never were,
and ask, Why not?

Center for Lymphoid Malignancies at Columbia University Medical Center

Columbia University Medical Center

Physicians

Owen A. O'Connor, M.D., Ph.D.
Jennifer Amengual, M.D.
Changchun Deng, M.D., Ph.D.
Jennifer Lue, M.D.
Francesca Montanari, M.D.
Ahmed Sawas, M.D.

Nurses/Clinical Staff

Laine Atkins, RN
Karen Khan, RN
Hyea Kim, NP
Aishling Rada, RN
Alice O'Rielly

Administrative Staff

Victoria Serrano, MPH
Carolyn Baldwin, MPH
Melissa Osorio
Tyler Williams
.

Research Study Coordinators

Hager Elgedawe, BS
Freddy Loffredo, MS
Michele Malanga, BA

Laboratory Staff

Luigi Scotto, Ph.D.
Jennifer Amengual, M.D.
Changchun Deng, M.D., Ph.D.
Yuxuan Liu, Ph.D.
Ipsita Pal, Ph.D..
Yulissa Gonzalez, B.S.
Cristina, Kinahan, M.S
Andre M. Sardinha Grilo, Ph.D.

Fellows

Enrica Marchi, M.D., Ph.D. Lorenzo Falchi, M.D.

Thank You!

Columbia University Medical Center

NCI CCC
A Comprehensive Cancer Center Designated by the National Cancer Institute

NewYork-Presbyterian
The University Hospital of Columbia and Cornell

Vinita Khanna, LCSW, ACHP-SW, OSW-C

MPH Candidate
Licensed Clinical Social Worker
Hematology/Bone Marrow Transplantation
University of Southern California
Keck Hospital of USC/Norris Comprehensive Cancer Center

Cancer

Cancer has profound biopsychosocial effects on patients and caregivers.

The Interdisciplinary Team Approach

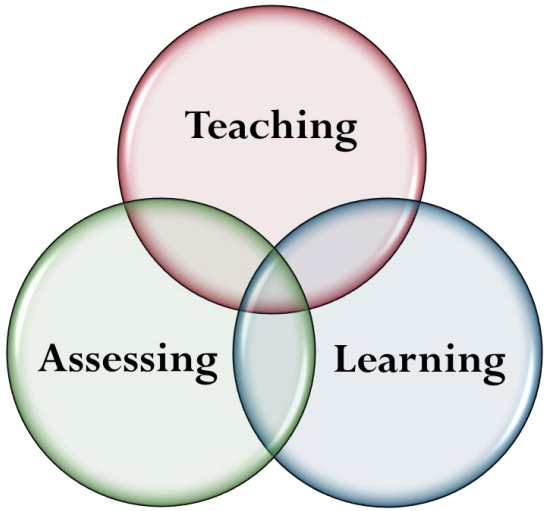
"I'm right there in the room, and no one even acknowledges me."

ARTIST: Leo Cullum

Pre Transplant Psychosocial Evaluation

Key components:

- Social history
- History of psychiatric illness
- History of alcohol or drug abuse
- Responsibility to treatment and understanding
- Patient's history of compliance or non-compliance
- Ability to engage in activities of daily living
- Faith-based or cultural concerns
- Advance directives
- Consider geriatric assessment



Caregiver Evaluation

- Health status
- Express understanding of role
- Aware of responsibilities
- Ability to care for themselves and patient
- Health literacy

- Special Considerations:
  - Children turning into caregivers
  - Older adults caring for their loved ones

Pre Admission Preparation

- Patient goals and expectations
- Understanding and responsibilities
- Preparing for an inpatient stay
- Coping within the inpatient unit
- Be The Match educational videos
- The Leukemia & Lymphoma Society

Chemotherapy-Related Cognitive Impairment (CRCI)

Deficits in:

- Memory
- Attention
- Clarity of thought
- Executive functioning
- Information processing

Mental Health Considerations

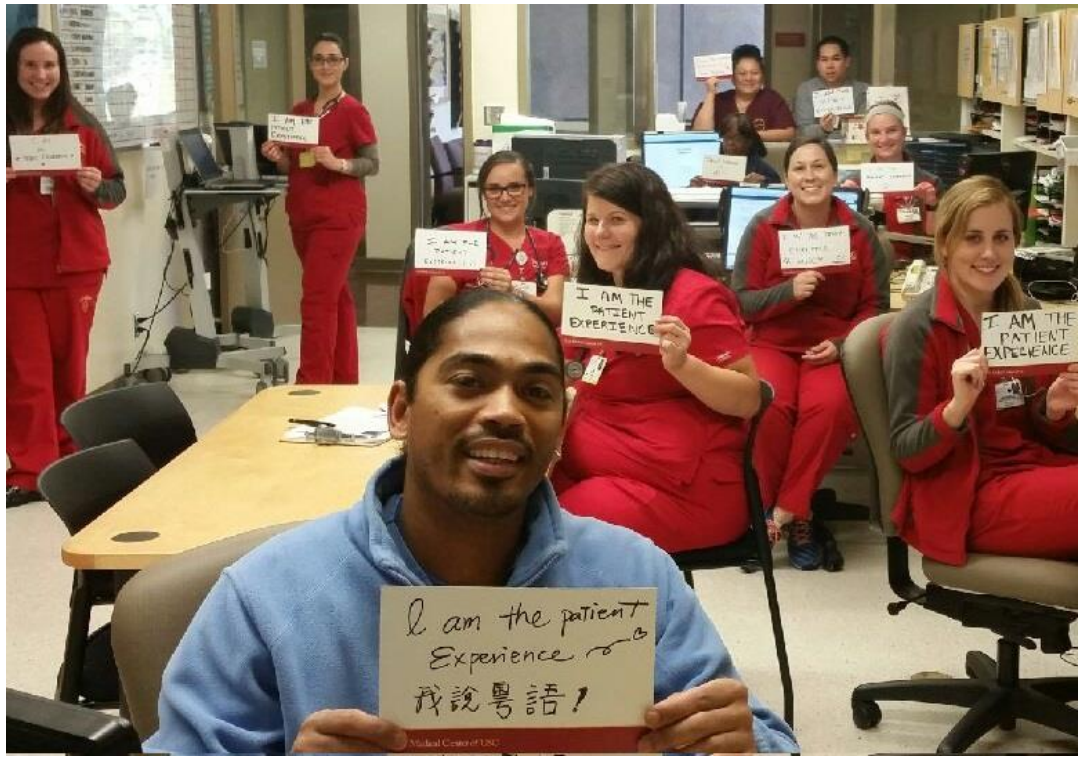
- Depression
- Anxiety
- PTSD
- Independence vs dependence
- Adjustment Concerns:
  - Family role changes
  - Children becoming caregivers
  - Adjusting to diagnosis related care

Interventions

- Psychoeducation
- Consultative services collaboration
- Gatekeeper of psychosocial needs
- Discussion in multidisciplinary rounds
- Goals of Care Discussions
- Life review/reminisce – Erickson
- Empty chair theory – Gestalt

Our Model

- Provided with an initial consult by MD
- Provided with a psychosocial assessment
- Discussed in hem/BMT selection committee
- Admission preparation
- Inpatient follow up
- Daily huddle with the interdisciplinary team
- Preparation for Discharge
- Clinic Follow up visit



Transitions to Palliative Care and End of Life

- Family meetings / Goals of care
- Support during Decision Making
- Options of care i.e., Home health, full treatment, palliative care, and/or hospice
- Advance directives, code status and POLST forms

Recommendations

- Team communication, collaboration and consistency are key
- Standardize processes of care and education provided
- Create unique educational material for patients and families
- Virtualization!
- Keep growing, learning, dreaming, and creating to continuously improve

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Thank you!

Lauren Berger, MPH
Senior Director, Professional Education & Engagement,
The Leukemia & Lymphoma Society

OUR MISSION

The mission of The Leukemia & Lymphoma Society (LLS) is: Cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families.

We fund **RESEARCH** to advance lifesaving treatments

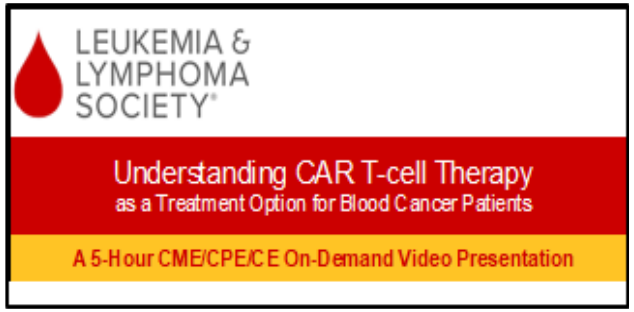
We drive **ADVOCACY** for policies that protect patient access to lifesaving treatment

We provide patients and families with hope, guidance, education and **SUPPORT**

LEUKEMIA & LYMPHOMA SOCIETY®

FREE HCP RESOURCES

Online & in-person webinars, symposia, rounds, publications CME & CE: www.LLS.org/CE



Refer patients to LLS for support
via phone, email, fax & online referral form:
http://www.lls.org/article/patient-referral-form

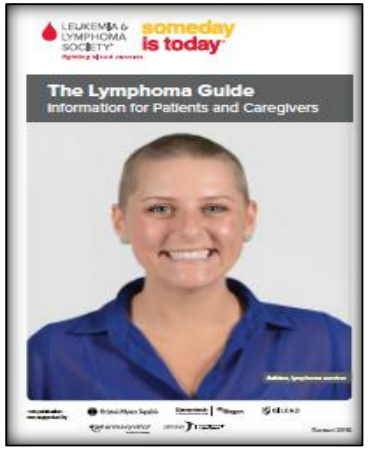
Research focused on finding cures:
www.LLS.org/research

BEATING CANCER IS IN OUR BLOOD.

LEUKEMIA & LYMPHOMA SOCIETY®

FREE PATIENT AND CAREGIVER RESOURCES

Webinars & videos:
www.LLS.org/programs and www.LLS.org/educationvideos



Booklets on disease, treatment, & support:
www.LLS.org/booklets

Lymphoma resources: www.LLS.org/lymphoma

LLS Community online social network: www.LLS.org/community

Blood cancer conferences:
www.LLS.org/BCC

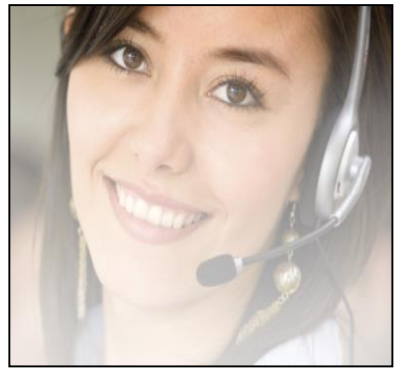
BEATING CANCER IS IN OUR BLOOD.

LEUKEMIA & LYMPHOMA SOCIETY®

FREE PATIENT AND CAREGIVER RESOURCES

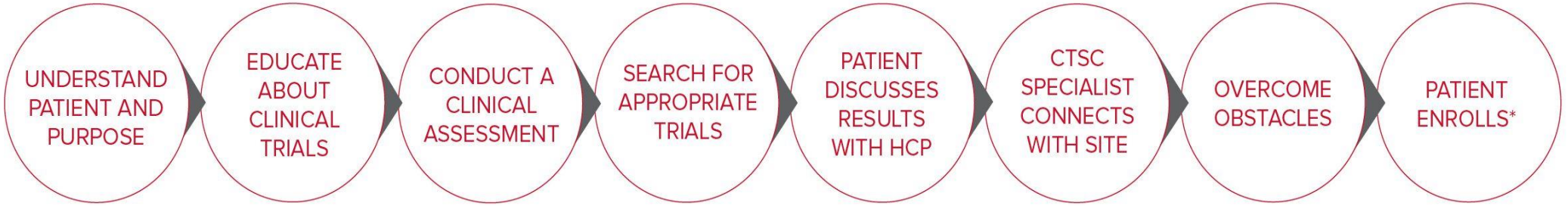
Information Specialists

Oncology social workers, health educators & nurses with expertise in blood cancers assist through treatment, financial & social challenges
call: 800.955.4572 or **email:** infocenter@LLS.org



Financial and psychosocial support and disease information:
www.LLS.org/support

CLINICAL TRIAL SUPPORT CENTER (CTSC)



*The majority of eligible patients enter into clinical trials.

LLS offers help for patients and caregivers in understanding, identifying, and accessing clinical trials. When appropriate, patients and caregivers can work one-on-one with nurses specially trained in hematological malignancies to assist them throughout the entire clinical trial.

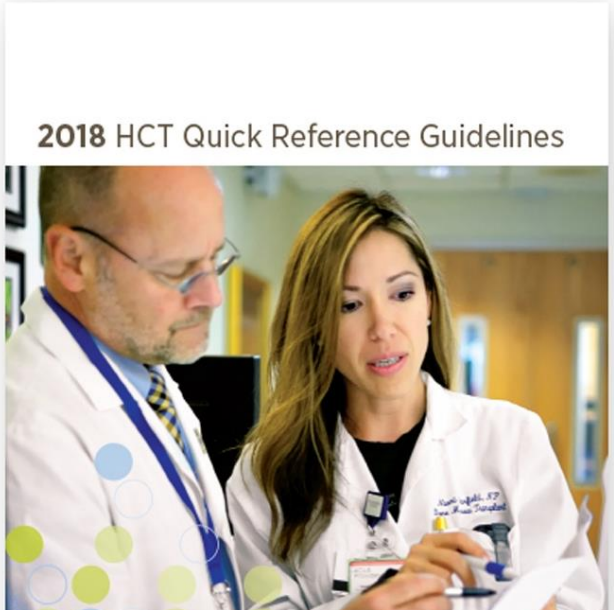
Call: 1-800-955-4572

visit: www.LLS.org/clinicaltrials

NMDP /Be The Match
Programs and resources for you and your patients

Stacy Stickney Ferguson, MSW, LICSW
Manager, Education and Outreach,
Patient and Health Professional Services
National Marrow Donor Program /Be The Match

HCT Quick Reference Guidelines



2018 Clinical Guidelines include:

- HCT referral guide for autologous and allogeneic transplant for 20+ diseases
- Recommended post-transplant screening, preventive practices, and vaccination schedules
- Clinical screening and prognostic tools for early detection of chronic GVHD, with photo atlas

Available in mobile app, print and online:

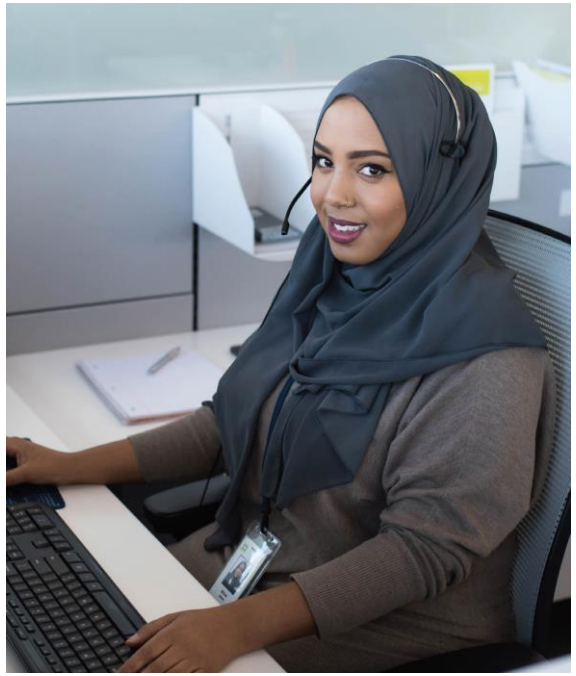
BeTheMatchClinical.org/guidelines

Be The Match *Patient Support Center*

Our services include:

- Confidential telephone counseling and one-on-one support for your patients and families
- Financial grants for patients
- Support groups and telephone workshops
- Caregiver support
- Information and support in many languages
- Educational books, DVDs, newsletters and fact sheets

Order, view or download: BeTheMatchClinical.org/order



Bilan, MSW, BMT Patient Navigator

Phone: 1 (888) 999-6743

Email: patientinfo@nmdp.org

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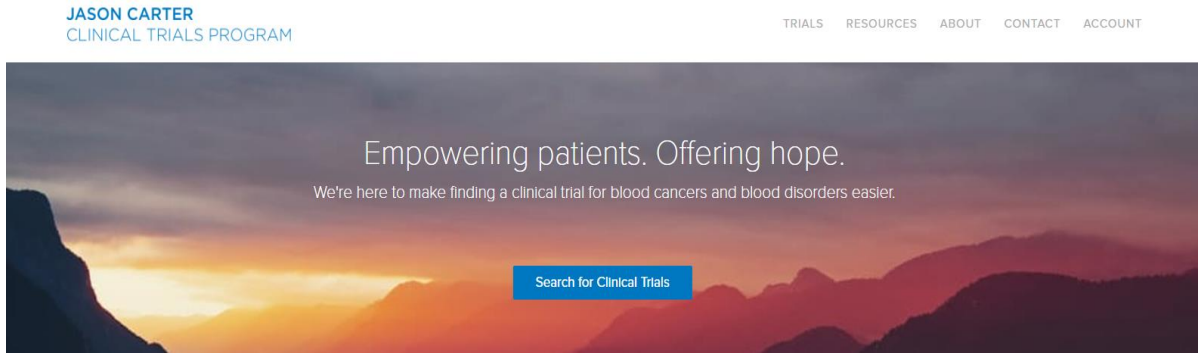
BE THE MATCH®

Jason Carter Clinical Trials Program

To help your patients with blood cancers, blood disorders, and immune systems diseases find and join clinical trials

- **One-on-one support** for patients & families to help answers questions and guide their clinical trials search
- **Online search tool**: JasonCarterClinicalTrialsProgram.org
- **Easy-to-understand resources** to learn about cancer treatments and clinical trials



Contact: Scott Kerwin, RN, MN, CCRC, CCRN
Clinical Trial Patient Education Specialist

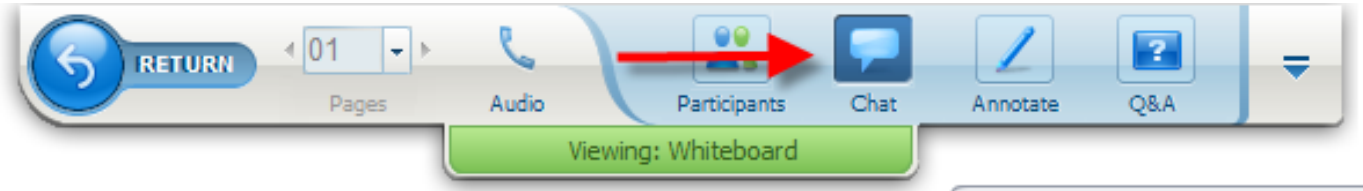
Phone: 1 (888) 814-8610

Email: clinicaltrials@jcctp.org

Questions

Owen A. O'Connor, MD, PhD

Vinita Khanna, LCSW, ACHP-SW, OSW-C

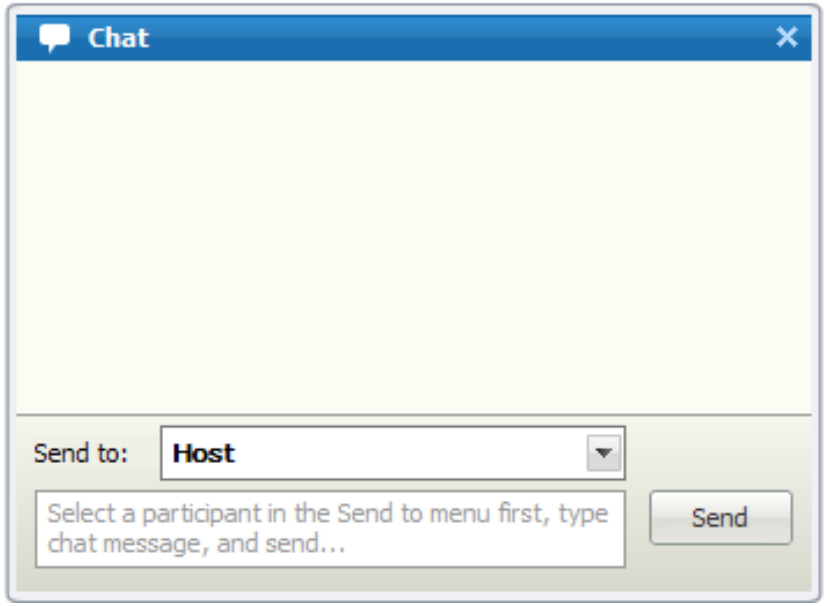


To ask a question, use the chat  icon

or

General questions / technical support

Email: nmdpeducation@nmdp.org



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- All attendees completing the online program evaluation will receive a statement of continuing education or a certificate of attendance within 30 days.

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