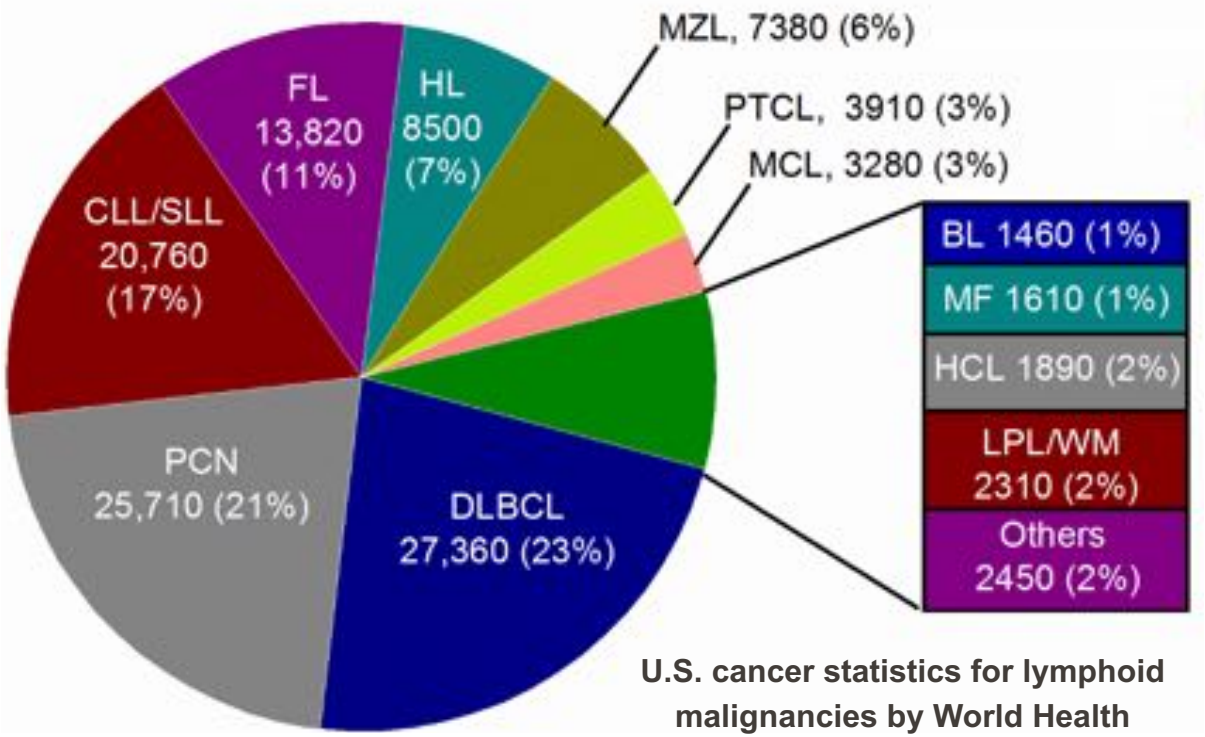
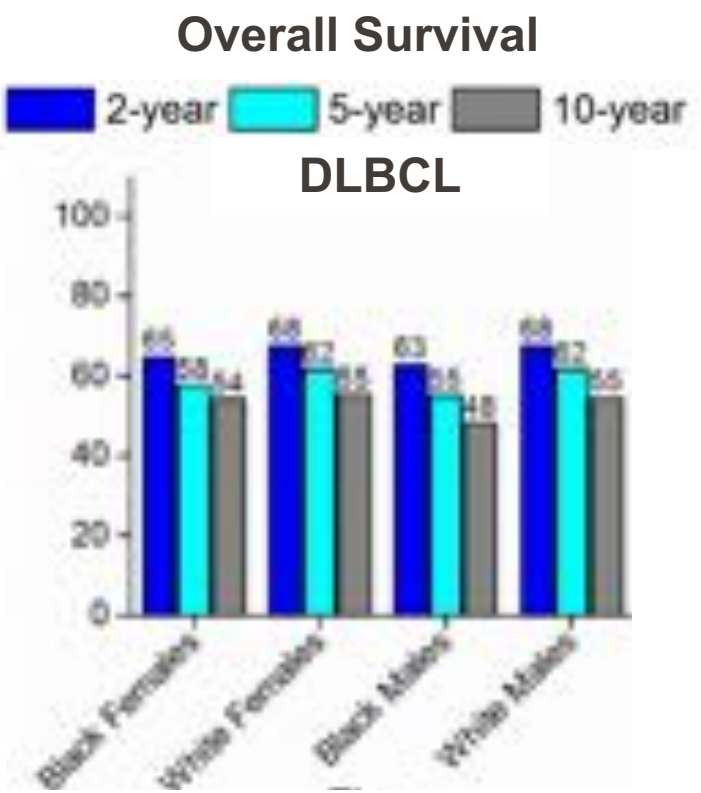
First-line DLBCL Therapy: What now and What's next?

Christopher Flowers, MD, MS, FASCO
Chair, Professor
Department of Lymphoma/Myeloma

Annual Incidence of Lymphoid Cancers in the United States



U.S. cancer statistics for lymphoid malignancies by World Health Organization subtypes



Teras LR, DeSantis CE, Morton LM, Cerhan JR, Jemal A, Flowers CR
CA Cancer J Clin. 2016

Patient Case

62-year-old woman diagnosed with DLBCL; Stage 4 involving liver & marrow

- Won tennis tournament at her local rec center in the February; now PS 3
- LDH >> ULN

Common approaches to improve her likelihood of cure include:

A. Whole genome sequencing of the tumor

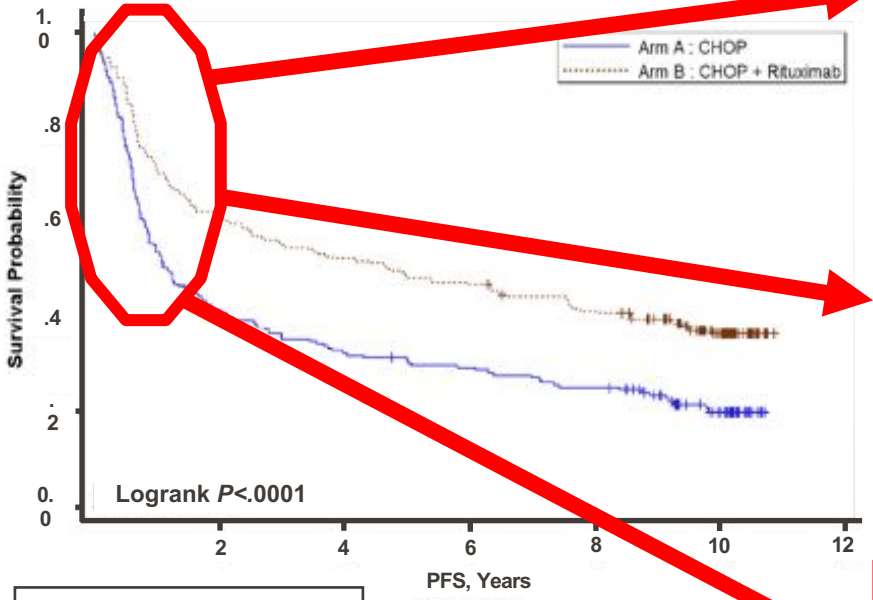
B. Cell free DNA analysis of the peripheral blood

C. Adding ibrutinib to R-CHOP

D. Adding lenalidomide to R-CHOP

E. None of the above

DLBCL: Strategies to Improve Beyond R-CHOP-21



Age>60 years
PS>2
Stage III-IV
Extranodal sites >2
LDH>Nml

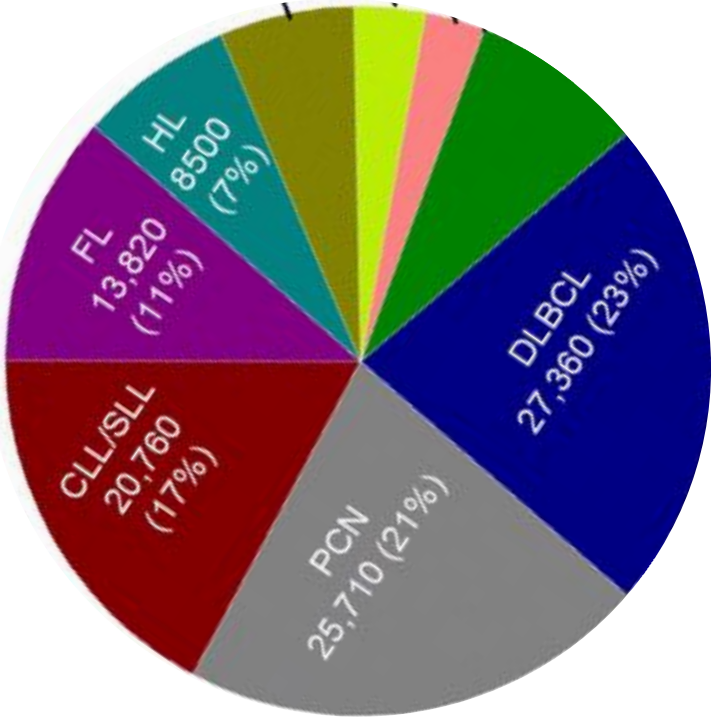
IPI

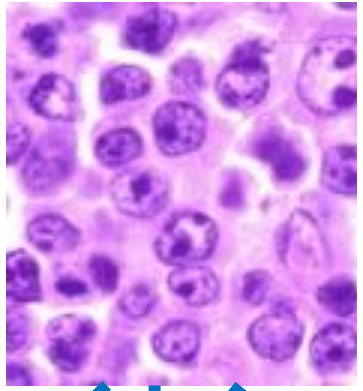
Intensification over R-CHOP-21?

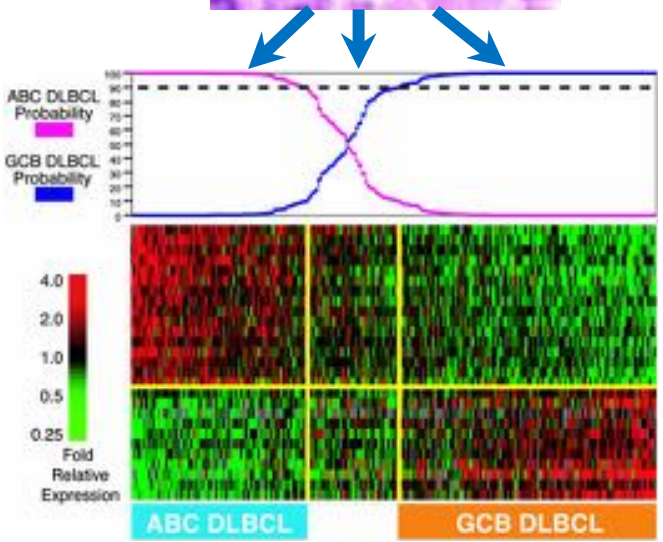
Better predict/evaluate quality of response?

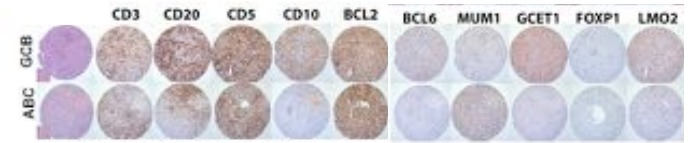
Take into consideration biological diversity of DLBCL

Diffuse Large B-cell Lymphoma







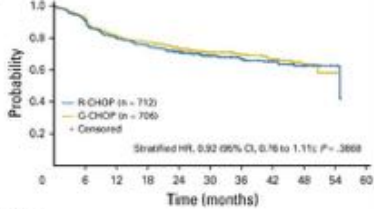


Retrospective studies identify DLBCL patient subgroups unlikely to be cured with R-CHOP

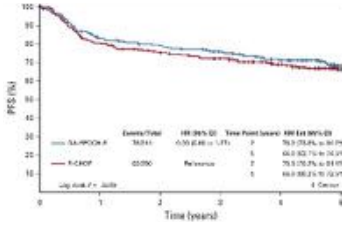
SUBSET	FREQ	R-CHOP		
		CR	PFS	OS
ABC DLBCL	30-50%	NR	2-yr 28%	2-yr 46%
Double-hit lymphoma	3-12%	40%	NR	<1yr
Dual expression of MYC, BCL2	21%	NR	5-yr 27%	5-yr 30%
Elderly DLBCL >60y	50%	70-80%	5-yr 50%	5-yr 58%
High IPI	45%	NR	4-yr 53%	4-yr 55%

Aukema Blood 2011; Hu Blood 2013; Feugier JCO 2005; Sehn Blood 2005; Nowakowski JCO 2014

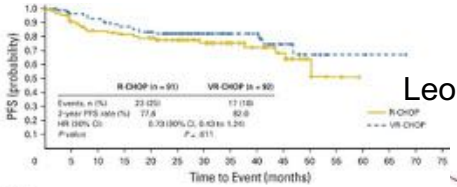
Trial	Comparison	Result
GOYA	R-CHOP vs. G-CHOP (n=1,418)	Negative
CALGB 50303	R-CHOP vs. R-DA-EPOCH (n=524)	Negative
PYRAMID (non-GCB)	R-CHOP vs. Bortezomib+R-CHOP (n=206)	Negative
REMoDL-B	R-CHOP vs. Bortezomib+R-CHOP (n=1,085)	Negative
LYM-2034 (non-GCB)	R-CHOP vs. Bortezomib+R-CHP (n=164)	Negative
PHOENIX (ABC)	R-CHOP vs. Ibrutinib+R-CHOP (n=838)	Negative
ECOG 1412	R-CHOP vs. Lenalidomide+R-CHOP (n=345)	*?Positive*
ROBUST (non-GCB)	R-CHOP vs. Lenalidomide+R-CHOP (n=570)	*Negative*



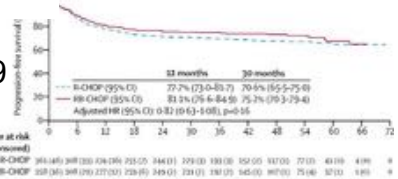
Vitolo *J Clin Oncol* 2017



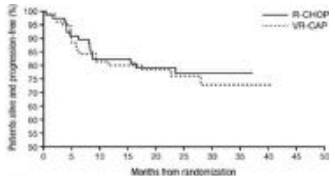
Bartlett *J Clin Oncol* 2019



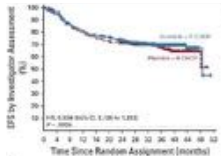
Leonard *J Clin Oncol* 2017



Davies Lancet Onc 2019



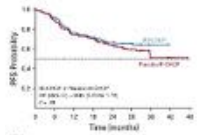
Offner *Blood* 2015



Younnes *J Clin Oncol* 2019

2-year OS: 87% len/R-CHOP
80% R-CHOP

Nowakowski *JCO* 2021



Nowakowski *J Clin Oncol* 2021

Progression-Free Survival as a Surrogate End Point for Overall Survival in First-Line Diffuse Large B-Cell Lymphoma: An Individual Patient - Level Analysis of Multiple Randomized Trials (SEAL)

Qian Shi, Norbert Schmitz, Fang-Shu Ou, Jesse G. Dixon, David Cunningham, Michael Pfreundschuh, John F. Seymour, Ulrich Jaeger, Thomas M. Habermann, Corinne Haioun, Hervé Tilly, Hervé Ghesquieres, Francesco Merli, Marita Ziepert, Raoul Herbrecht, Jocelyne Flament, Tommy Fu, Bertrand Coiffier, and Christopher R. Flowers

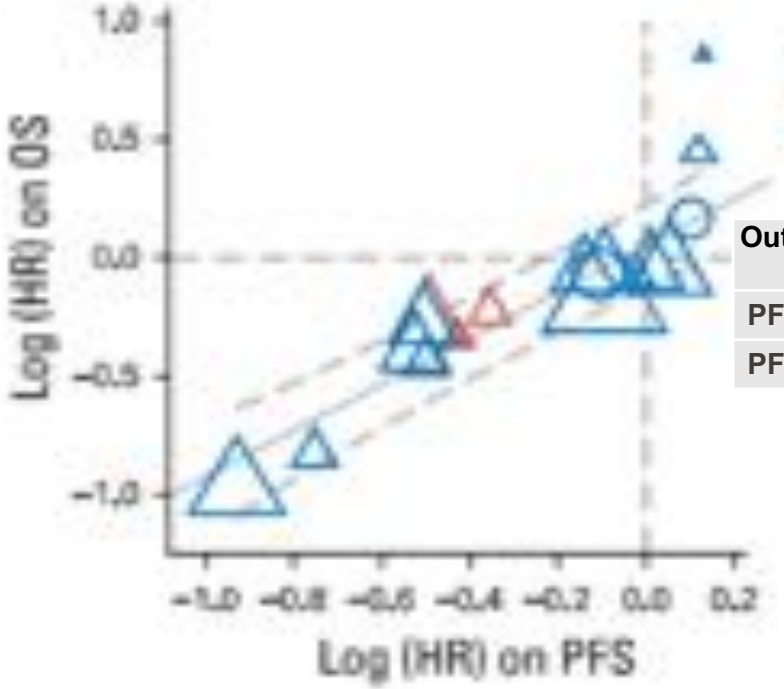
RCTs Included in the Analysis (n=13)

Age (categorical), years	Control (N=3,450)	Experimental (N=4,057)	Total (N=7,507)
<60	1,566 (45)	1,562 (39)	3,128 (42)
60-69	1,034 (30)	1,386 (34)	2,420 (32)
≥70	850 (25)	1,109 (27)	1,959 (26)
Sex			
Female	1,580 (46)	1,896 (47)	3,476 (46)
Male	1,870 (54)	2,161 (53)	4,031(54)
ECOG Performance Status			
Missing	3	1	4
0	1,627 (47)	1,837 (45)	3,464(46)
1	1,328 (38)	1,641 (40)	2,969 (40)
≥ 2	492 (14)	578 (14)	1,070 (14)
IPI score			
Missing	393	384	777
0-1	1,022(33)	1,217 (33)	2,239 (33)
2	734 (24)	968 (26)	1,702 (25)
3	768 (25)	878 (24)	1,646 (24)
4-5	533 (17)	610 (17)	1,143 (17)
Ann Arbor Stage			
Missing	14	9	23
I/II	1,223 (35)	1,492 (37)	2,715 (36)
III	787 (23)	1,022 (25)	1,809 (24)
IV	1,426 (41)	1,534 (38)	2,960 (40)

J Clin Oncol. 2018; 36(25): 2593-2602.

Progression-Free Survival is a Surrogate End Point for Overall Survival in First-Line Diffuse Large B-Cell Lymphoma

Trial-level treatment effect correlation between PFS and OS



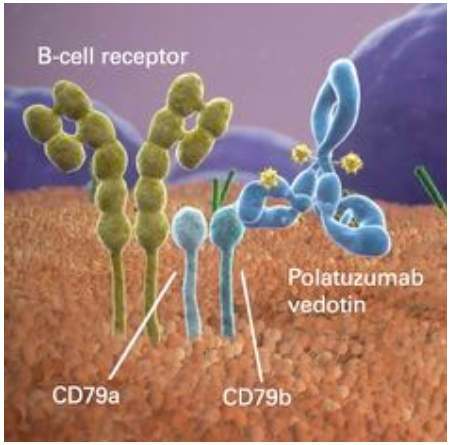
		Trial Level surrogacy:		Patient Level surrogacy:
Outcome	N Trials (N pts)	R^2WLS (95% CI)	R^2Copula (95% CI)	Global OR (95% CI)
PFS	17 (7,507)	0.83 (0.57-0.94)	**0.85 (0.73-0.98)**	0.85 (0.84-0.86)
PFS24	17 (6,882)	0.77 (0.51-0.92)	0.78 (0.59-0.96)	61.1 (52.6-69.6)

Prespecified criteria for surrogacy:

- R^2_{WLS} or $R^2_{Copula} \geq 0.80$ and neither < 0.7
- lower-bound 95% CI > 0.60

J Clin Oncol. 2018; 36(25): 2593-2602.

POLARIX: 1L DLBCL Phase 3



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Polatuzumab Vedotin in Previously Untreated Diffuse Large B-Cell Lymphoma

H. Tilly, F. Morschhauser, L.H. Sehn, J.W. Friedberg, M. Trněný, J.P. Sharman, C. Herbaux, J.M. Burke, M. Matasar, S. Rai, K. Izutsu, N. Mehta-Shah, L. Oberic, A. Chauchet, W. Jurczak, Y. Song, R. Greil, L. Mykhalska, J.M. Bergua-Burgués, M.C. Cheung, A. Pinto, H.-J. Shin, G. Hapgood, E. Munhoz, P. Abrisqueta, J.-P. Gau, J. Hirata, Y. Jiang, M. Yan, C. Lee, C.R. Flowers, and G. Salles

Patients

- Previously untreated DLBCL
- Age 18–80 years
- IPI 2–5
- ECOG PS 0–2

Stratification factors

- IPI score (2 vs 3–5)
- Bulky disease (<7.5 vs ≥7.5cm)
- Geographic region (Western Europe, US, Canada, & Australia vs Asia vs rest of world)

R 1:1

Pola-R-CHP

Polatuzumab vedotin (1.8mg/kg)* + **R-CHP + vincristine placebo**

R-CHOP

R-CHOP† + **polatuzumab vedotin placebo**

Cycles 1–6
(1 cycle=21 days)

Rituximab
375mg/m^2

Cycles 7 & 8

Primary endpoint

Progression-free survival (Investigator-assessed)

Secondary endpoints

- Event-free survival
- Complete response rate at end of treatment (PET/CT, IRC-assessed)
- Disease-free survival
- Overall survival

Safety endpoints

Incidence, nature, and severity of adverse events

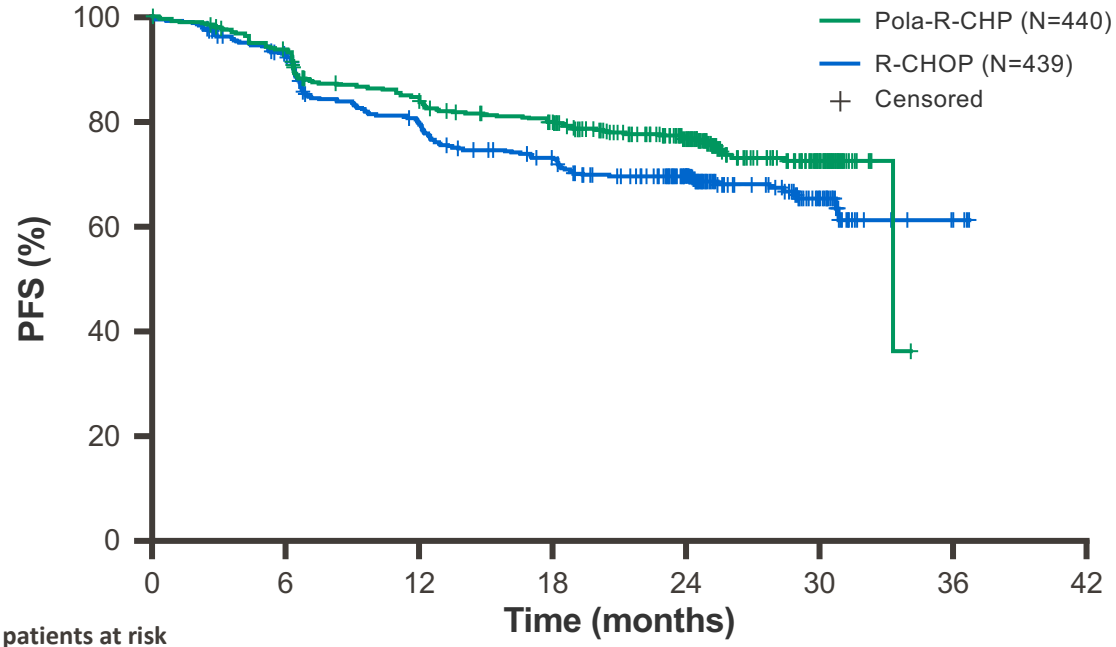
CCOD: June 28, 2021

Median follow up at the primary analysis: 28.2 months

Tilly et al. *NEJM* 2021

Primary endpoint: Progression-free survival

Pola-R-CHP significantly improved PFS vs R-CHOP



No. of patients at risk								
Pola-R-CHP	440	404	353	327	246	78	NE	NE
R-CHOP	439	389	330	296	220	78	3	NE

HR 0.73 **(P=0.02)**

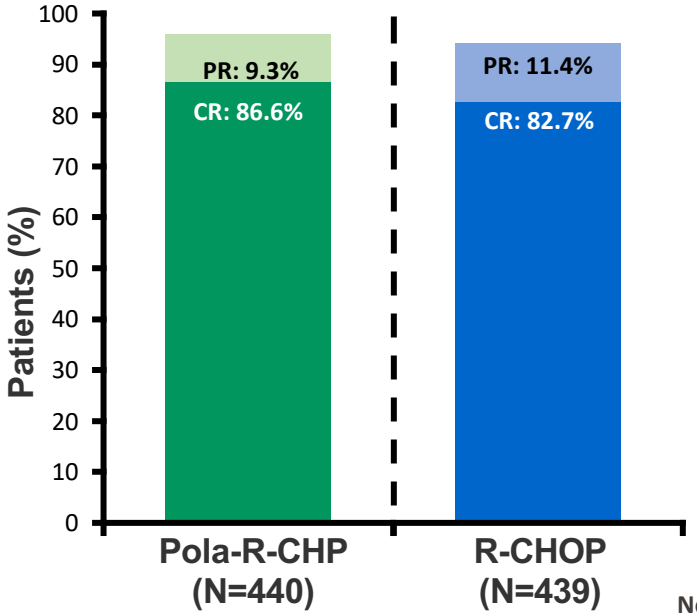
95% CI: 0.57, 0.95

- Pola-R-CHP demonstrated a **27% reduction in the relative risk of disease progression, relapse, or death** vs R-CHOP
- **24-month PFS:** 76.7% with Pola-R-CHP vs 70.2% with R-CHOP (**Δ=6.5%**)

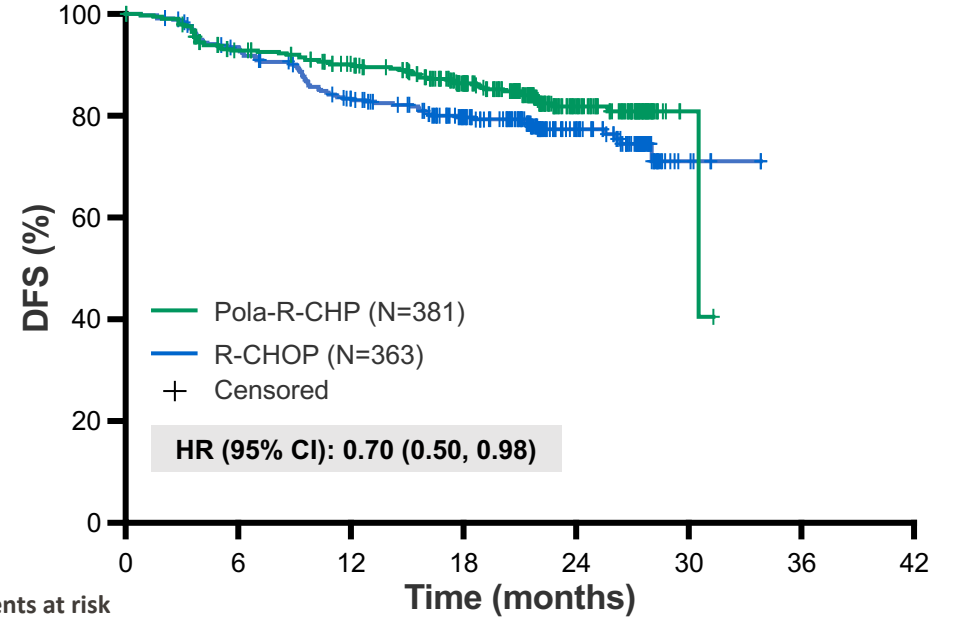
Tilly et al. *NEJM* 2021

Response rates and disease-free survival

Best overall response



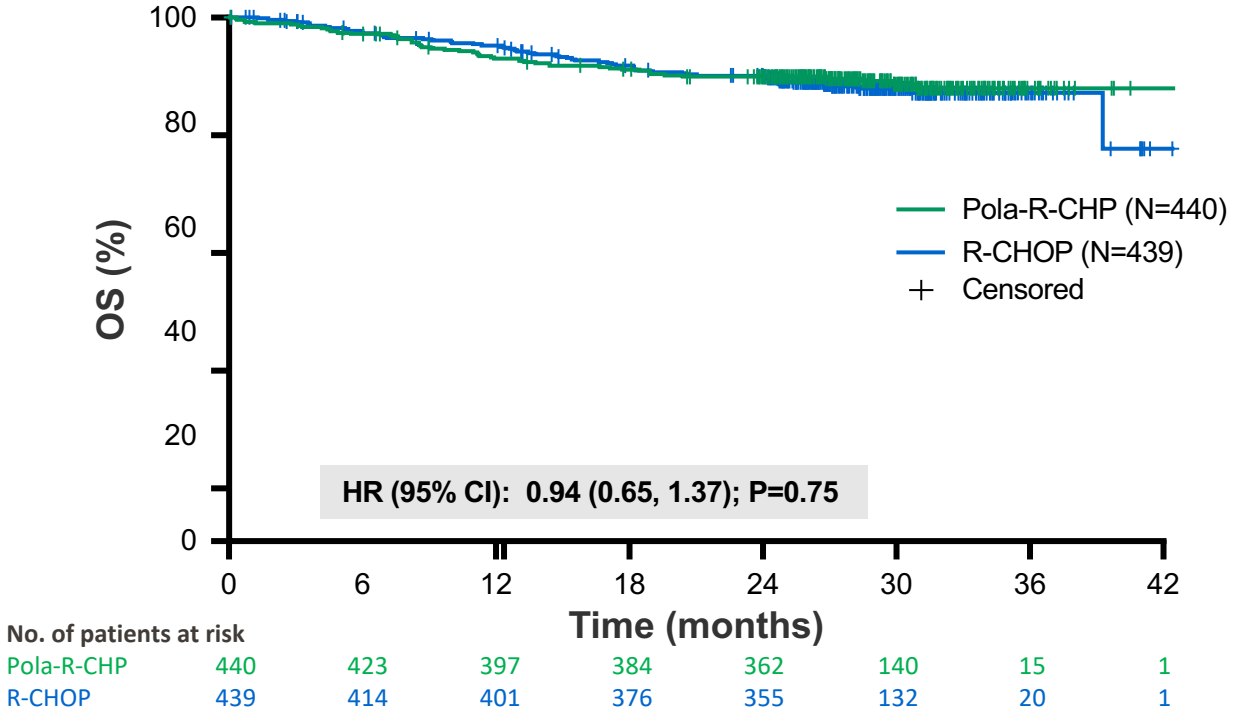
Disease-free survival



No. of patients at risk								
Pola-R-CHP	381	342	322	266	106	2	NE	NE
R-CHOP	363	326	282	238	96	5	NE	NE

Tilly et al. *NEJM* 2021

Overall survival



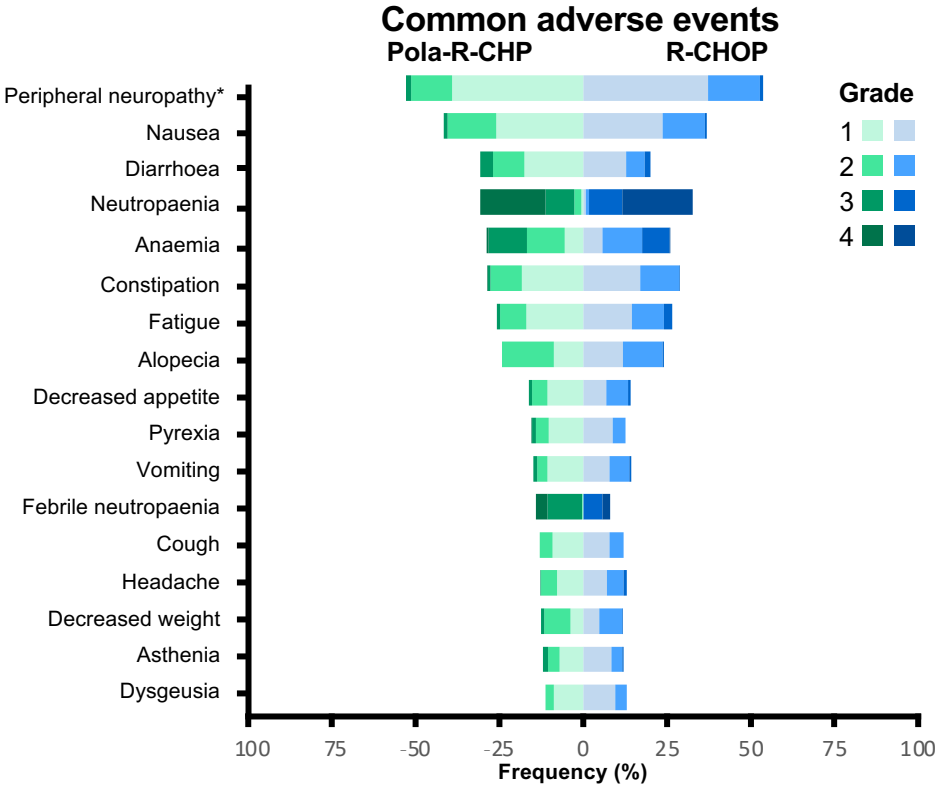
ITT population. Data cut-off: June 28, 2021; median 28.2 months' follow-up.
OS, overall survival.

Tilly et al. *NEJM* 2021

Safety summary

Safety profiles were similar with Pola-R-CHP and R-CHOP

n (%)	Pola-R-CHP (N=435)	R-CHOP (N=438)
Any-grade adverse events	426 (97.9)	431 (98.4)
Grade 3–4	251 (57.7)	252 (57.5)
Grade 5	13 (3.0)	10 (2.3)
Serious adverse events	148 (34.0)	134 (30.6)
Adverse events leading to:		
Discontinuation of any study drug	27 (6.2)	29 (6.6)
Polatuzumab vedotin / vincristine	19 (4.4)	22 (5.0)
Dose reduction of any study drug	40 (9.2)	57 (13.0)



- ITT population. Data cut-off: June 28, 2021; median 28.2 months' follow-up.
  CI, confidence interval; HR, hazard ratio; NE, not evaluable; PFS, progression-free survival.

Tilly et al. *NEJM* 2021

POLARIX: Conclusions

Pola-R-CHP significantly prolongs PFS compared with R-CHOP (HR 0.73) in patients with intermediate- and high-risk previously untreated DLBCL

The **safety profiles** of Pola-R-CHP and R-CHOP were **comparable**

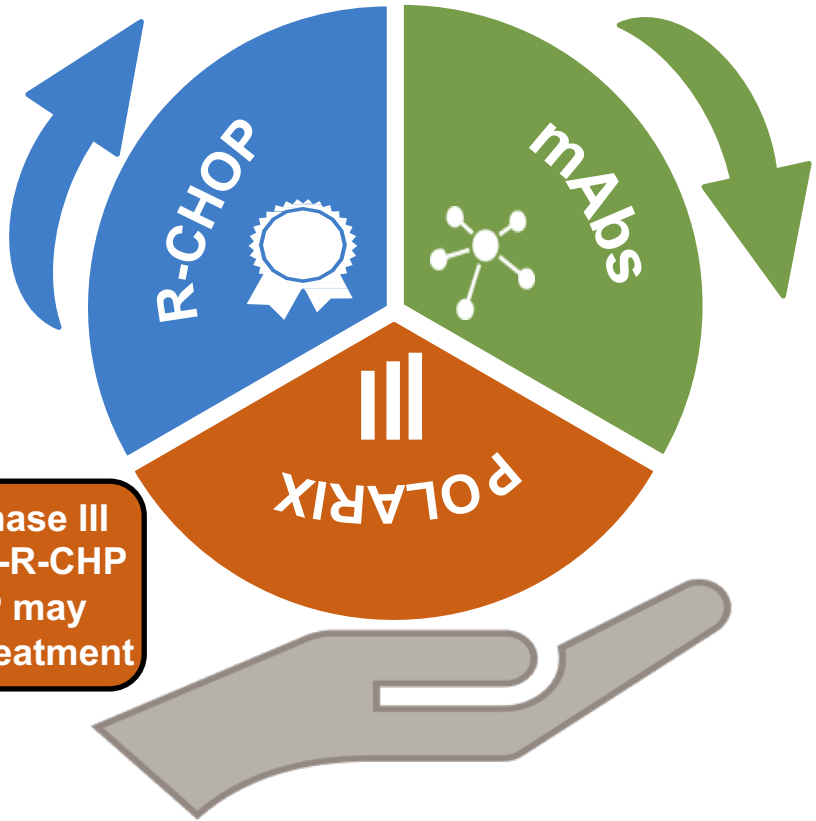
Exploratory analyses are ongoing with regard to various subgroups and other prognostic classification systems

These results **support the use of Pola-R-CHP** in the initial management of patients with DLBCL

Tilly et al. *NEJM* 2021

First-line DLBCL: what does the future hold?

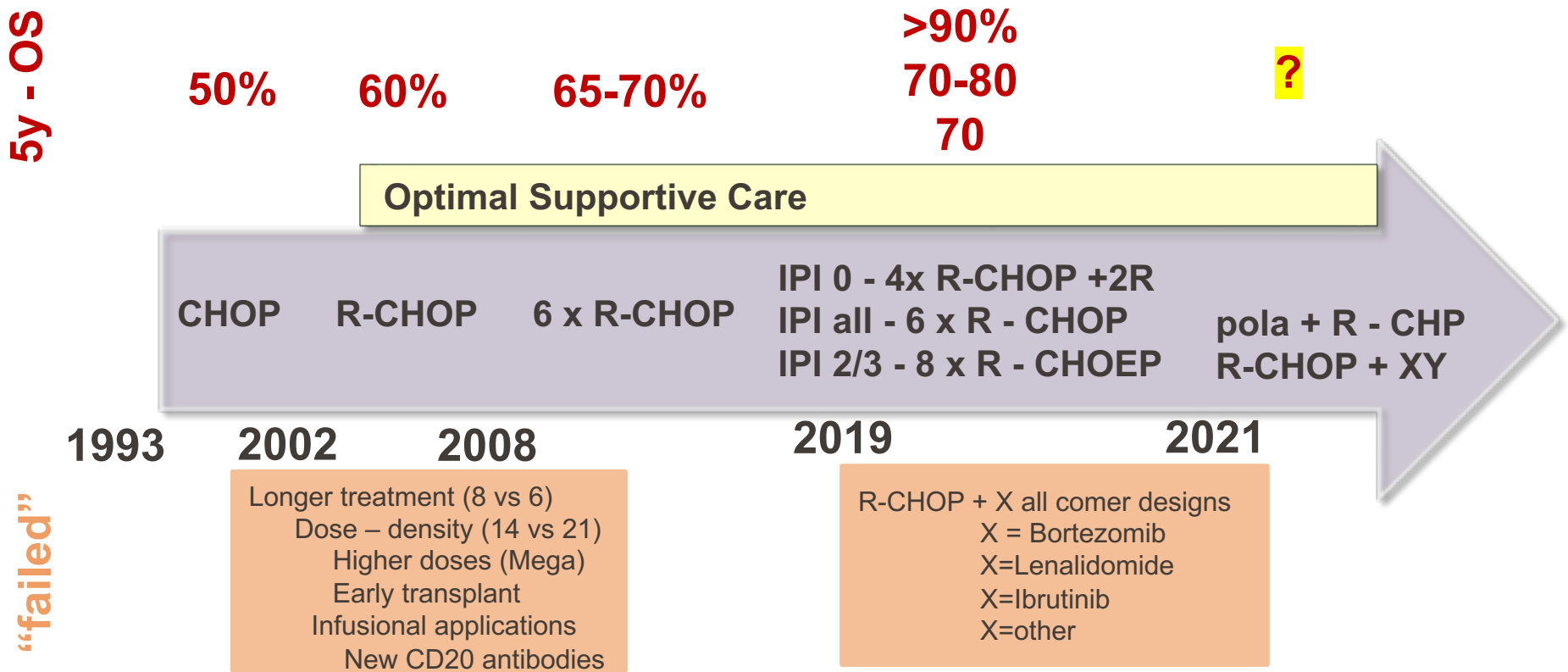
R-CHOP remains gold standard, but an unmet need to increase the cure



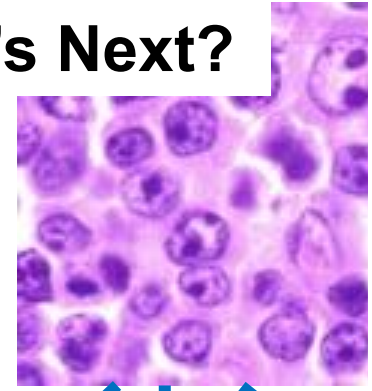
Targeted therapies and small molecules have been investigated

POLARIX Phase III study of Pola-R-CHP vs R-CHOP may improve 1L treatment

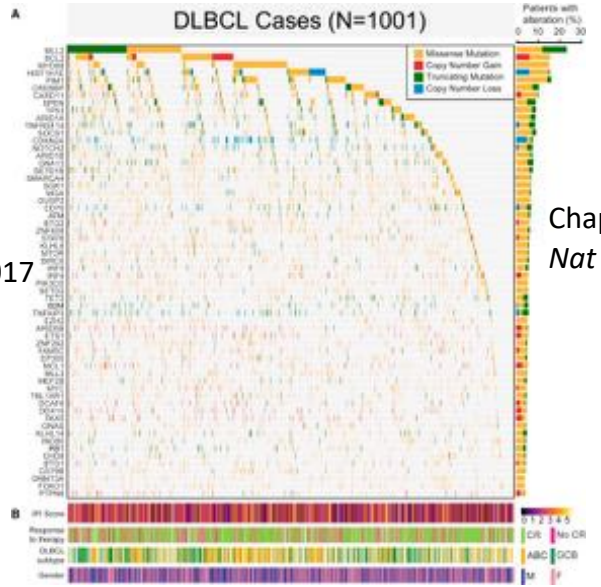
Empirical Development/Optimization of R-CHOP



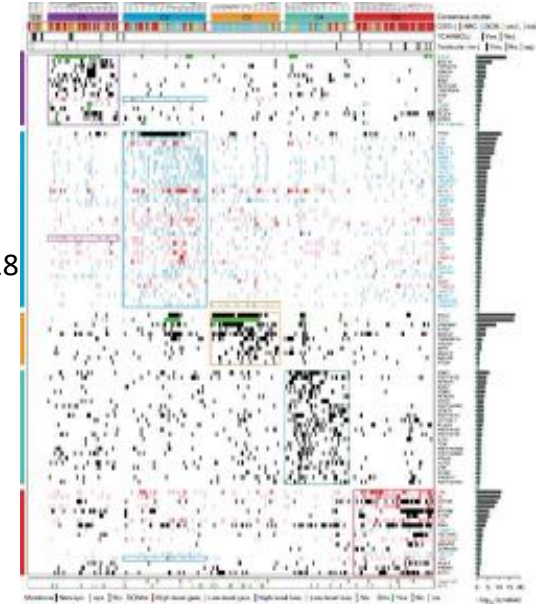
What's Next?

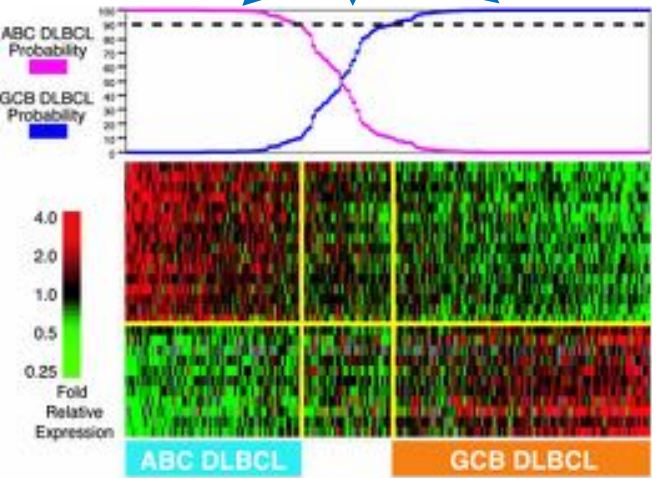


Reddy
Cell 2017

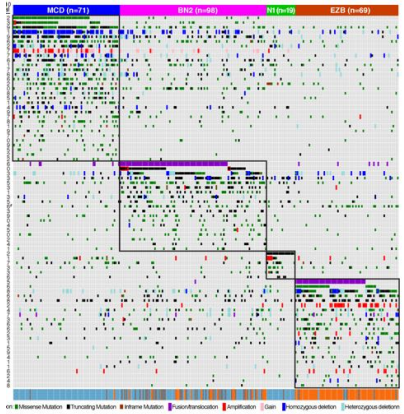


Chapuy
Nat Med 2018

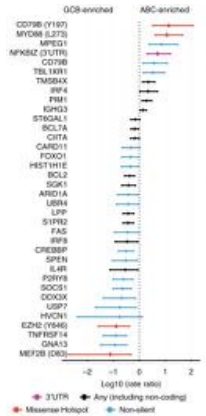


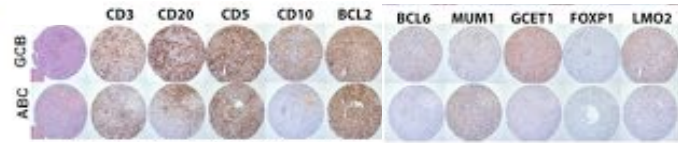


Schmitz NEJM 2018

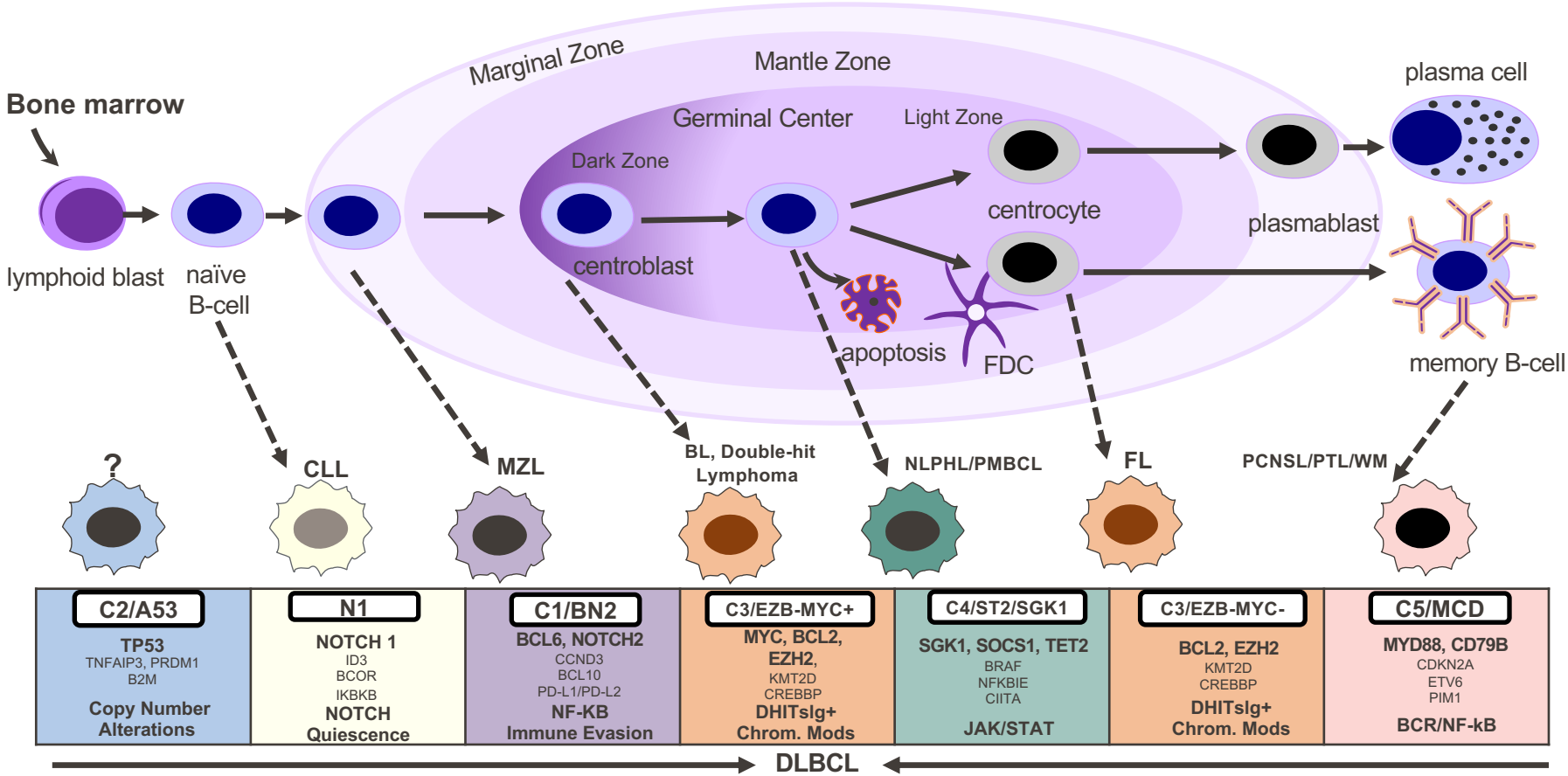


Arthur *Nat Commun* 2018



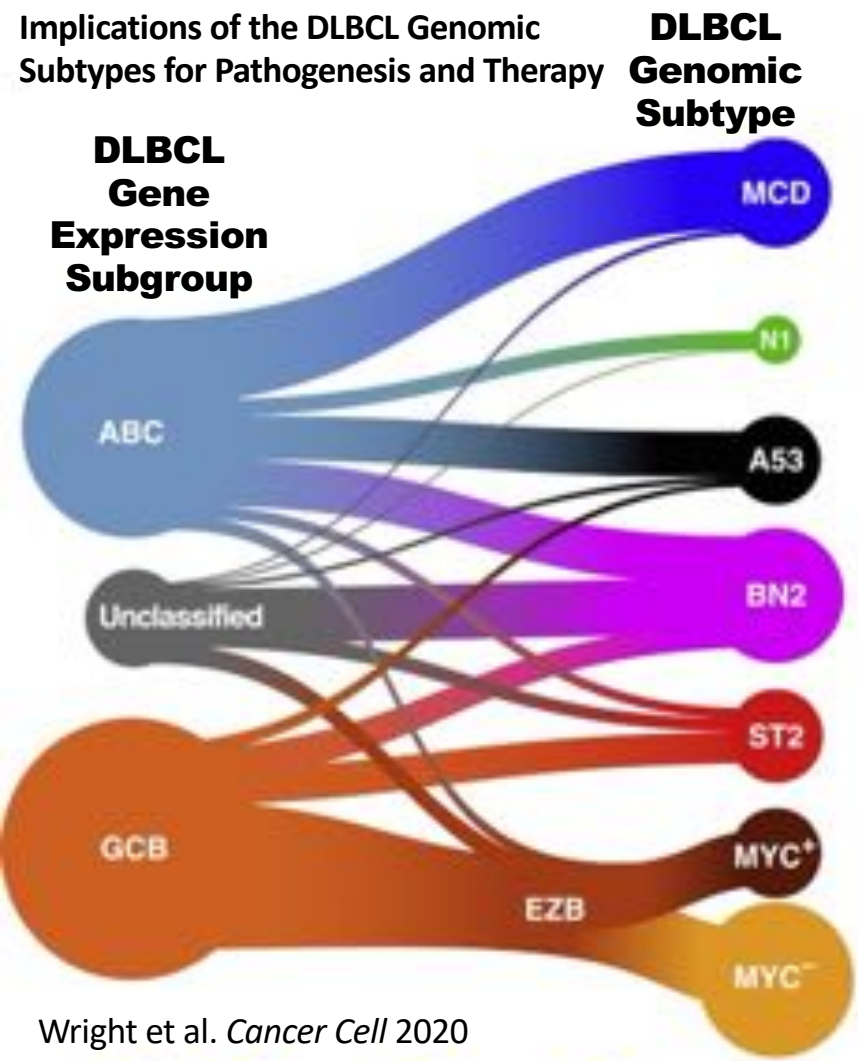


Linking Genomic Subtypes to Cell Biology



Morin, Walker, Hodson, BrJH 2021

Implications of the DLBCL Genomic Subtypes for Pathogenesis and Therapy



Prevalence	5-yr overall survival	Genetically related lymphomas
8.7%	40% (All) 37% (ABC)	Primary extranodal DLBCL Transformed WM
1.7%	27% (All) 22% (ABC)	NOTCH1-mutant CLL
5.8%	63% (All) 33% (ABC) 100% (GCB)	–
13.3%	67% (All) 76% (ABC) 100% (GCB) 38% (UC)	MZL Transformed MZL
6.4%	84% (All) 81% (GCB)	NLPHD THRLBCL
5.9% (MYC+) 17.8% (MYC−)	48% (MYC+) 82% (MYC−)	FL Transformed FL BL (EZB-MYC+)

Drug Target					
BTK	PI3K	BCL2	JAK	IRF4	EZH2
X	X	X	X	X	
X					
X	X	X			
	X		X		
	X	X			X

Wright et al. *Cancer Cell* 2020

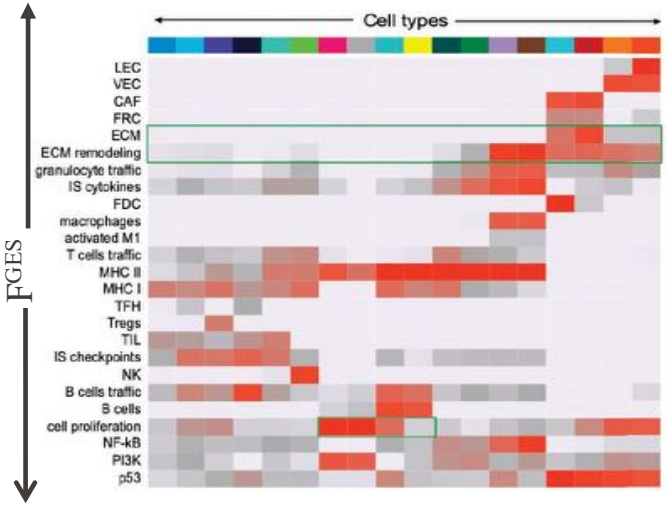
Using transcriptomics to distinguish subtypes of the DLBCL microenvironment

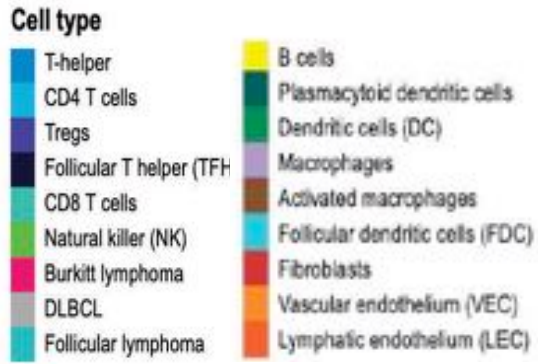
Development of 25(FGES)

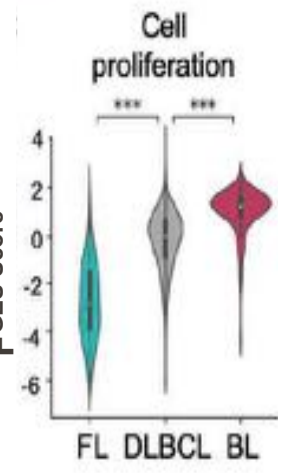
DLBCL Samples Correlation

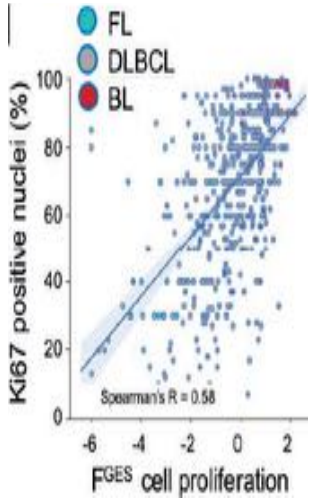
Communities Detection

LME Clusters



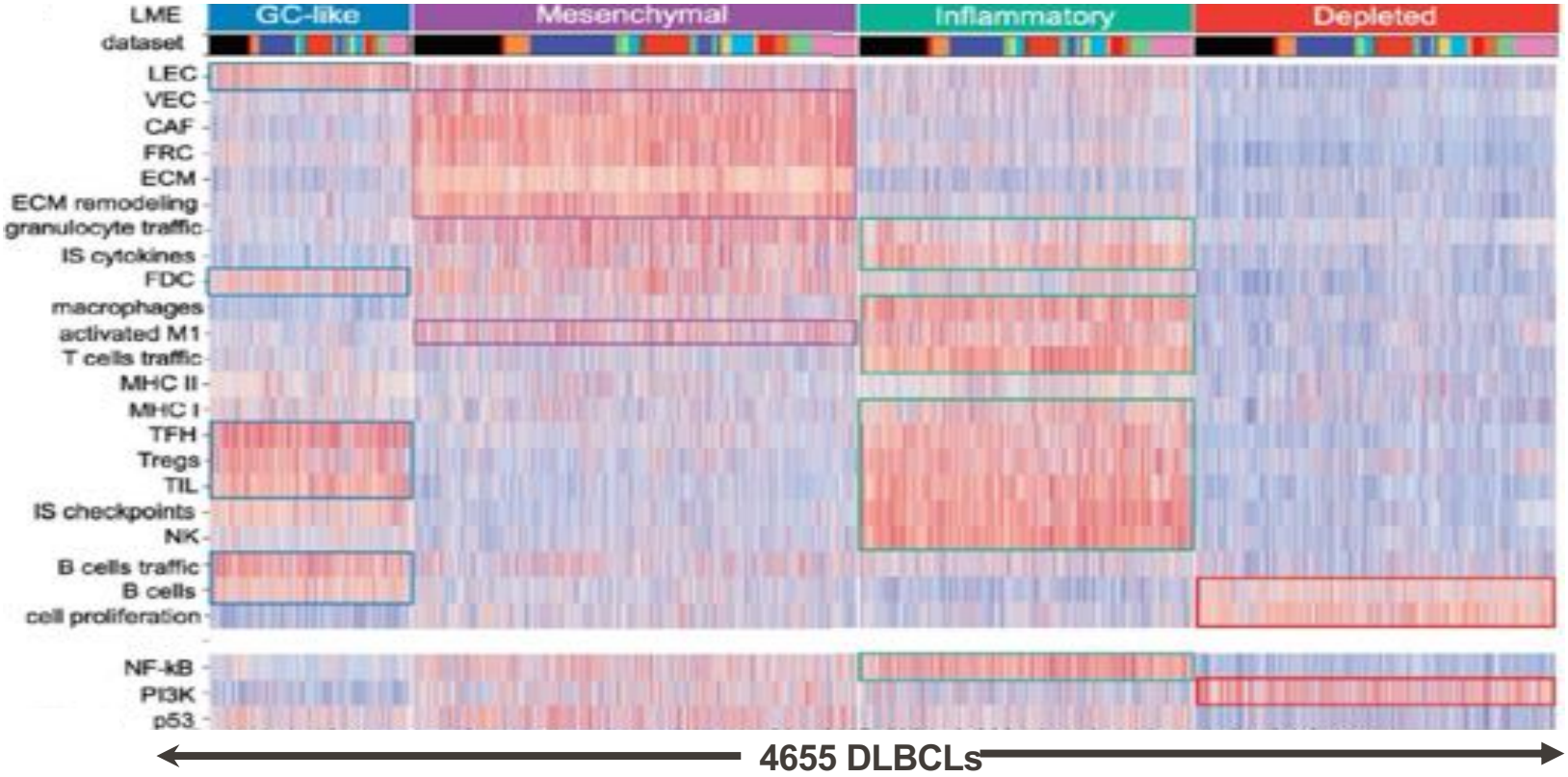






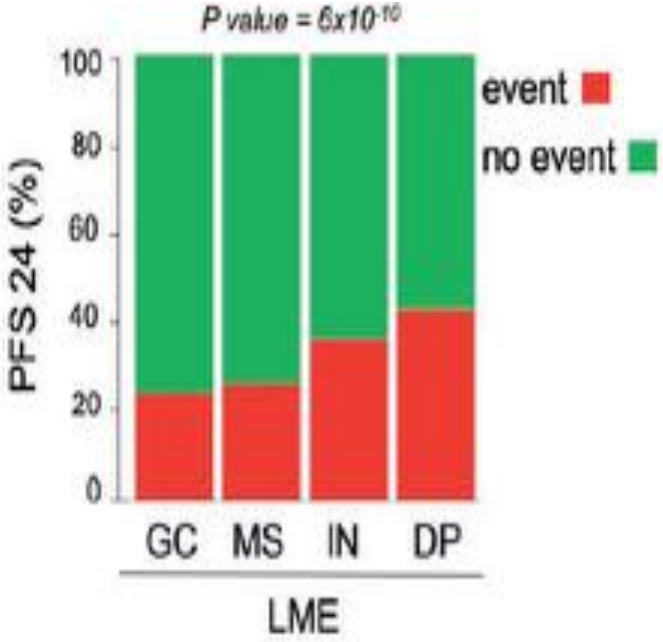
Kotlov N e al. *Cancer Discov*. 2021

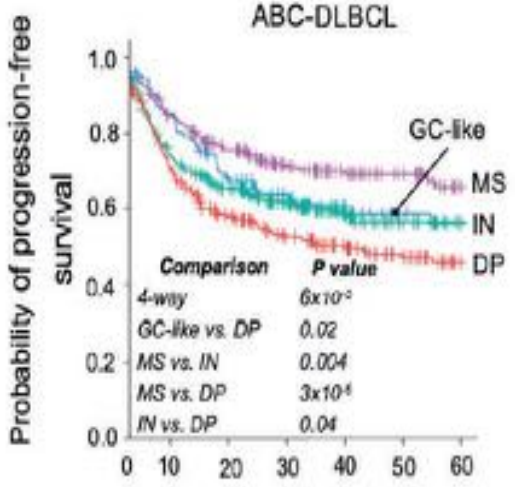
Heat map of the activity scores of 25 FGES (x-axis) denoting four major LME clusters termed as GC-like, mesenchymal, inflammatory and depleted



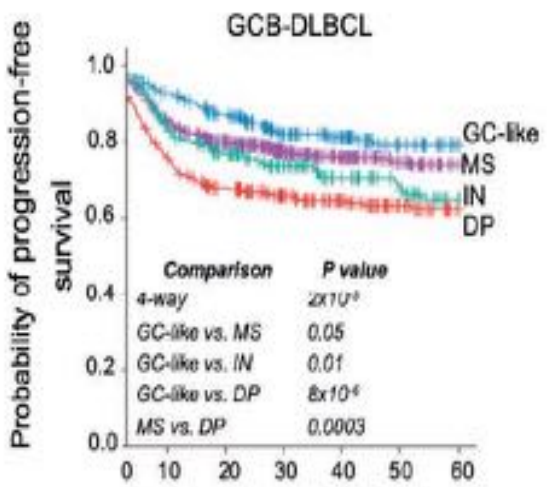
Kotlov N e al. *Cancer Discov*. 2021

PFS at 24 months (PFS24) in DLBCL patients according to the LME category
Kaplan-Meier models of PFS according to LME category in ABC- and GCB DLBCL





No. at risk							
GC-like	105	88	66	51	35	26	21
MS	224	178	148	108	87	69	50
IN	326	234	186	142	98	71	57
DP	258	176	126	93	69	50	31

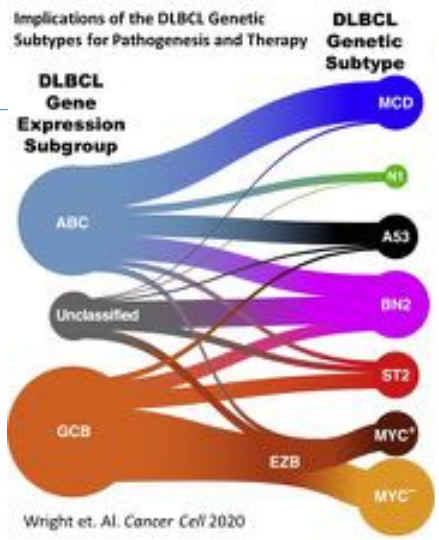


No. at risk							
GC-like	224	218	214	207	203	203	200
MS	558	525	489	473	464	457	451
IN	206	193	176	172	165	154	146
DP	300	259	227	214	211	205	199

Kotlov N e al. *Cancer Discov*. 2021

What's Next?: Improve DLBCL Risk Prediction and Treatment Strategies

Improved Probabilistic Algorithm



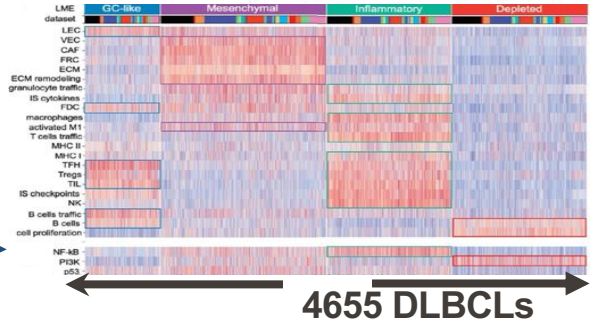
Define Additional Biological subsets (40.6%)

Prediction of Subtype with estimate of uncertainty

Reduce Uncertainty in Prediction of Outcome Adding Large Database and RWE

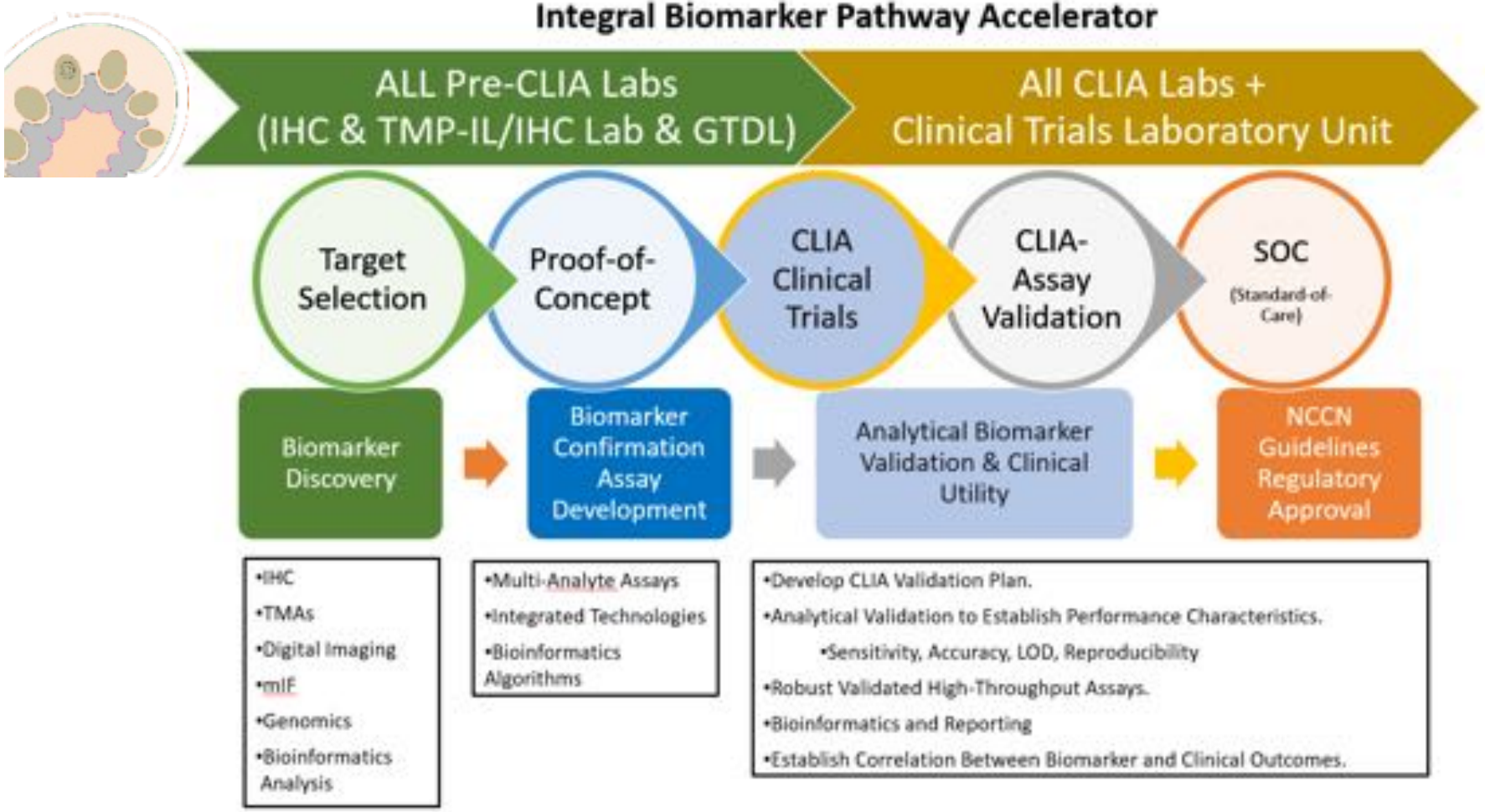
Drug Target					
BTK	PI3K	BCL2	JAK	IRF4	EZH2
X	X	X	X	X	
X					
X	X	X			
	X		X		
	X	X			X

Design Frontline and Relapsed DLBCL Trials based on subtype directed targets



Identify New Therapeutic Targets / Cellular Therapy for Additional Subtypes

Integral Biomarker Pathway Accelerator



“Test the test” Trial in DLBCL – Molecular Testing to Shorten DTI

Protocol: 2022-0396; RCTS 61163

Study Design:

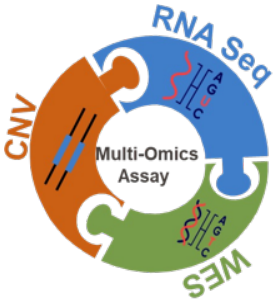
DLBCL

Initial Diagnosis (n=40)

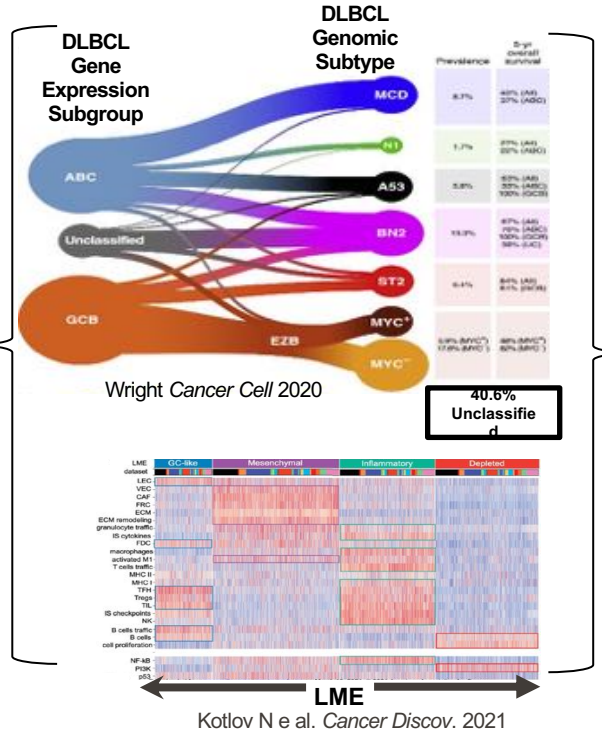
Relapsed / Refractory (n=40)

FFPE

Tissue Biopsy



LymphGen and LME Classification



Wright *Cancer Cell* 2020

Kotlov N e al. *Cancer Discov*. 2021

Results available (≤7 days) from submission ?

Yes

Target: >65% results

Evaluate:
- **DTI Prevalence/response by:**
- **NCI / DFCI Clusters**
- **LME subgroups**

No

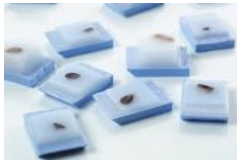
What's Next?: Genomic Subtyping Evaluation of Diffuse Large B-cell Lymphoma

Tissue Biopsy

Blood Sample

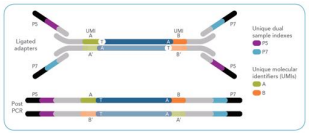
Cell free tumor DNA

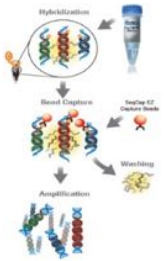
FFPE Sample → Isolate DNA



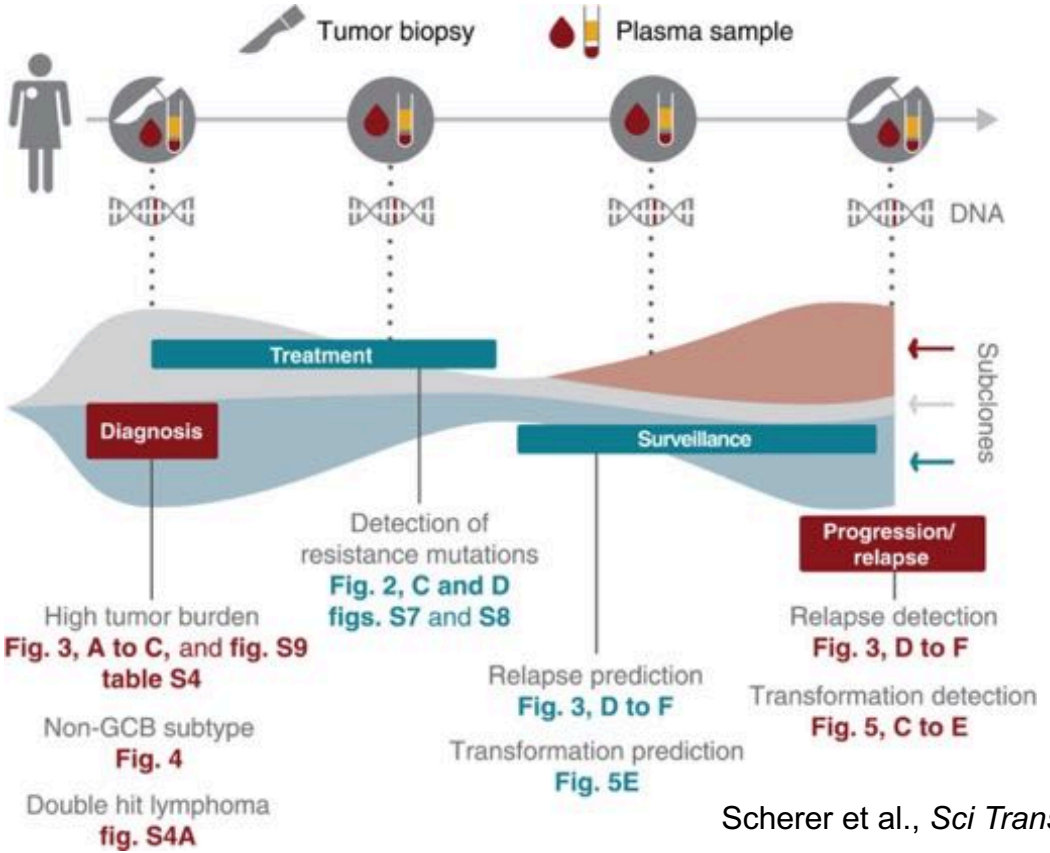
Blood Sample → Isolate plasma → Isolate cfDNA

Quality control → duplex-UMI NGS library prep → Hybrid capture → Sequence → Analyze





Less invasive identification of DLBCL poor-risk groups

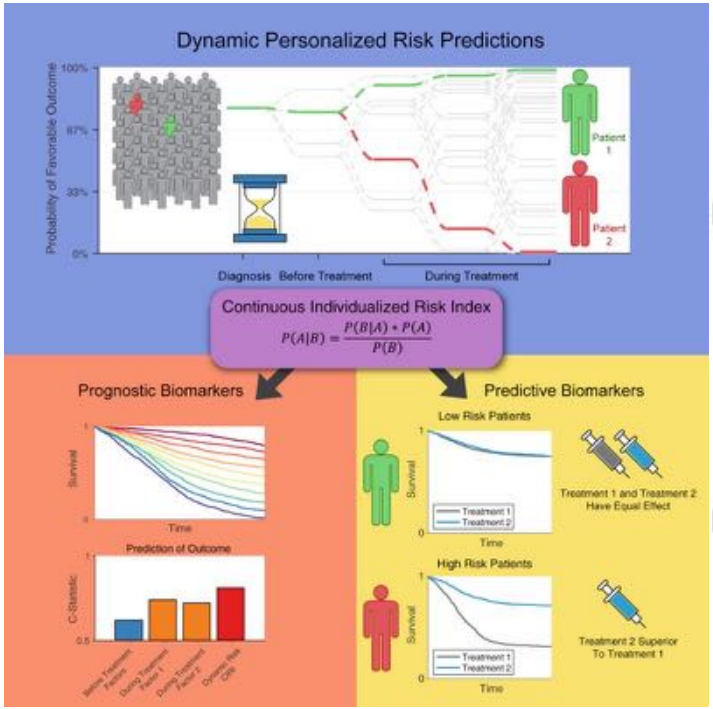


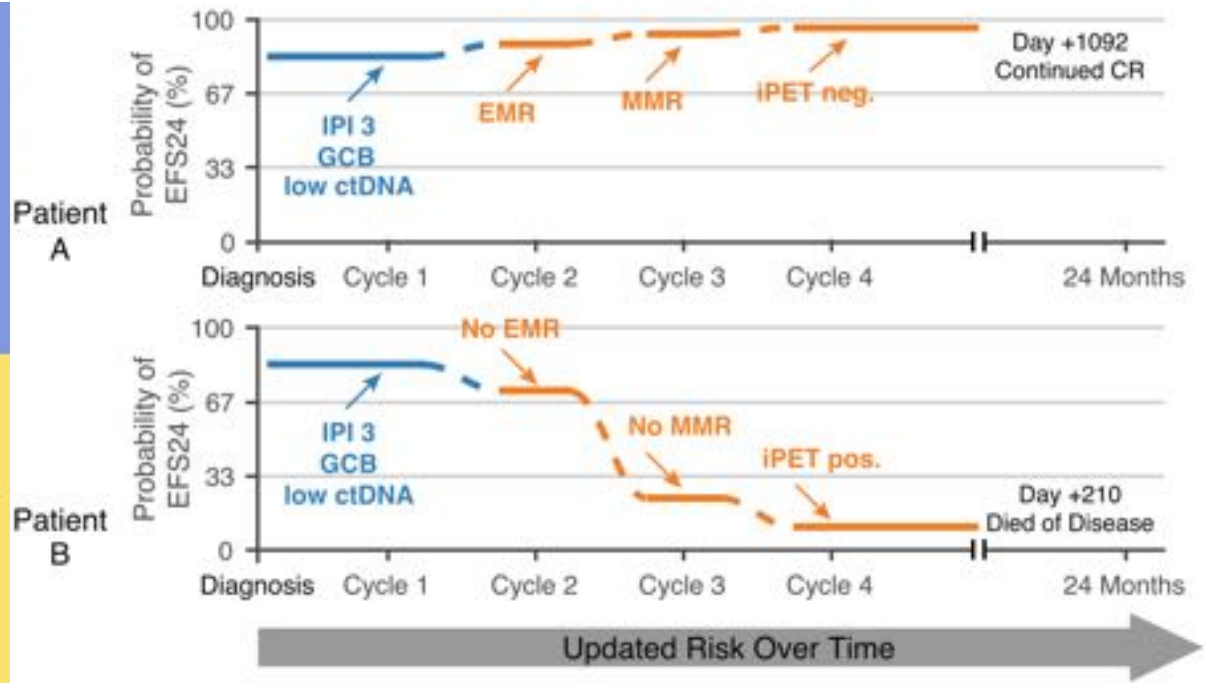
Which ctDNA technology?

- Adaptive (Sequenta)
  - VDJ “idiotype” sequencing
  - requires tumor tissue
- CAPP-Seq
  - Sequencing ~200 most common mutations
  - No need for tumor tissue

Scherer et al., *Sci Transl Med* 2016

Dynamic ”real time” updated risk prediction based upon ctDNA changes





Kurtz *Cell* 2019

Evaluation of cfDNA collection for Diffuse Large B-cell Lymphoma: in academic and community settings

Protocol: 2022-0603

1L Therapy DLCBL R-Chemotherapy

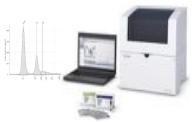
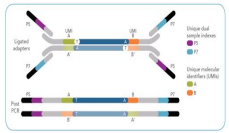
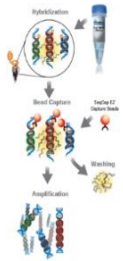
Baseline
C1D1 Pre-Tx
C2D1 Prae-Tx
C3D1 Pre-Tx

Blood Sample
Cell free tumor DNA

Blood Sample → Isolate plasma → Isolate cfDNA

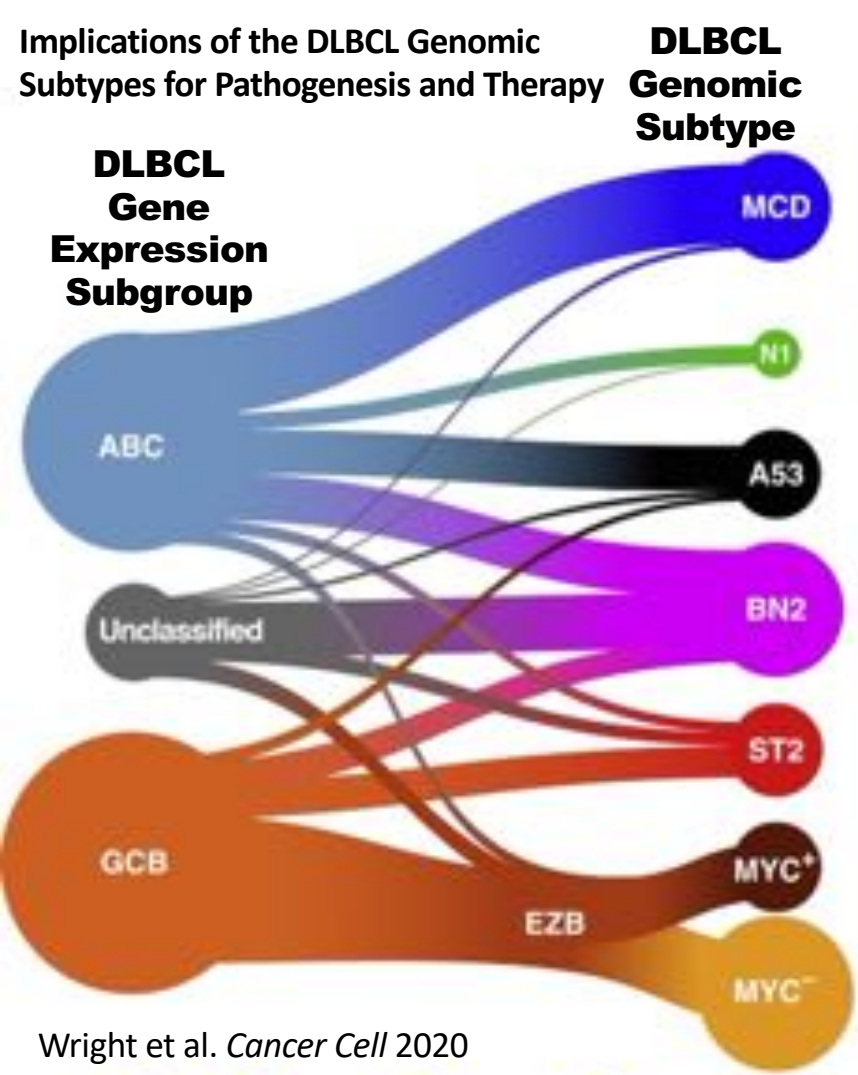


Quality control → duplex-UMI NGS library prep → Hybrid capture → Sequence → Analyze

Feasible to collect cfDNA in community settings?

Implications of the DLBCL Genomic Subtypes for Pathogenesis and Therapy

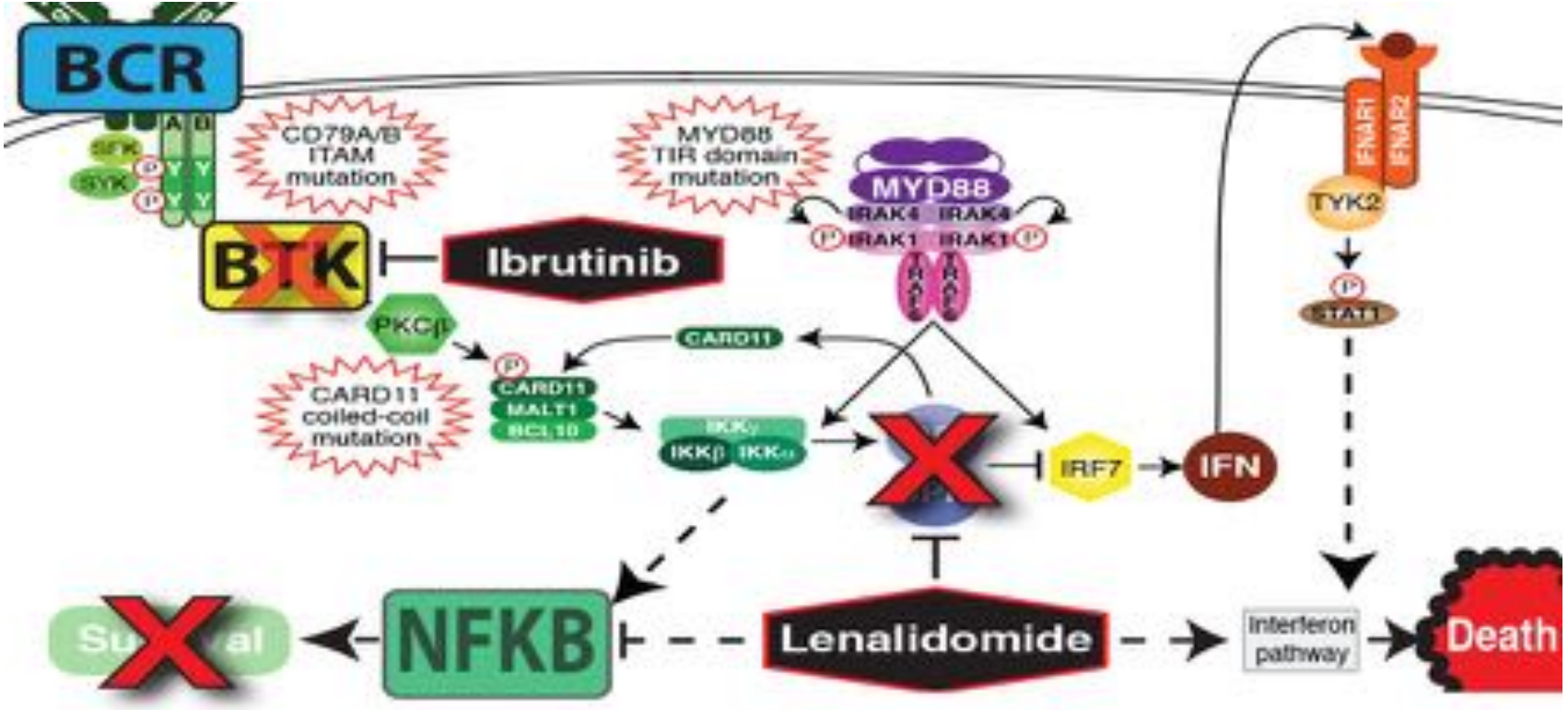


Prevalence	5-yr overall survival	Genetically related lymphomas
8.7%	40% (All) 37% (ABC)	Primary extranodal DLBCL Transformed WM
1.7%	27% (All) 22% (ABC)	NOTCH1-mutant CLL
5.8%	63% (All) 33% (ABC) 100% (GCB)	–
13.3%	67% (All) 76% (ABC) 100% (GCB) 38% (UC)	MZL Transformed MZL
6.4%	84% (All) 81% (GCB)	NLPHD THRLBCL
5.9% (MYC+) 17.8% (MYC−)	48% (MYC+) 82% (MYC−)	FL Transformed FL BL (EZB-MYC+)

Drug Target					
BTK	PI3K	BCL2	JAK	IRF4	EZH2
X	X	X	X	X	
X					
X	X	X			
	X		X		
	X	X			X

Wright et al. *Cancer Cell* 2020

What's Next?: DLBCL Molecular Targeted Therapy



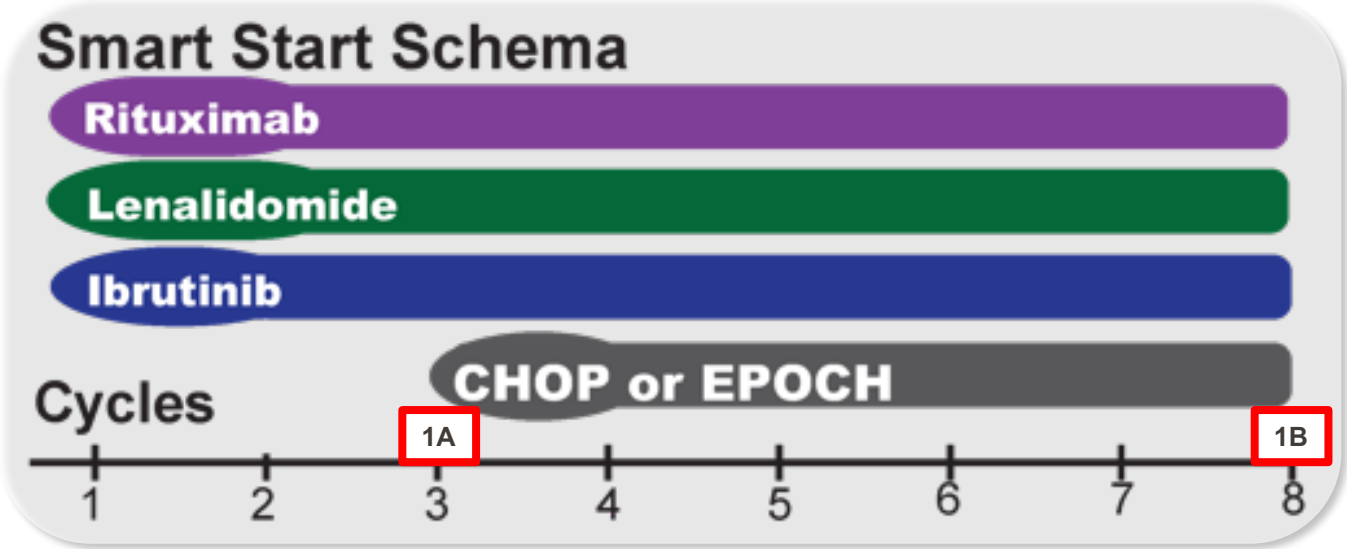
Yang, Staudt Cancer Cell 2012

Lenalidomide: Upregulate IL2 in T-cells
Ibrutinib: ITK inhibition shift Th2 to Th1

Study Design

First 2 cycles of RLI are without chemotherapy

- Phase 2 single arm, single center, investigator-initiated trial



CHOP or EPOCH selected by MD for reasons including high ki-67, high IPI,

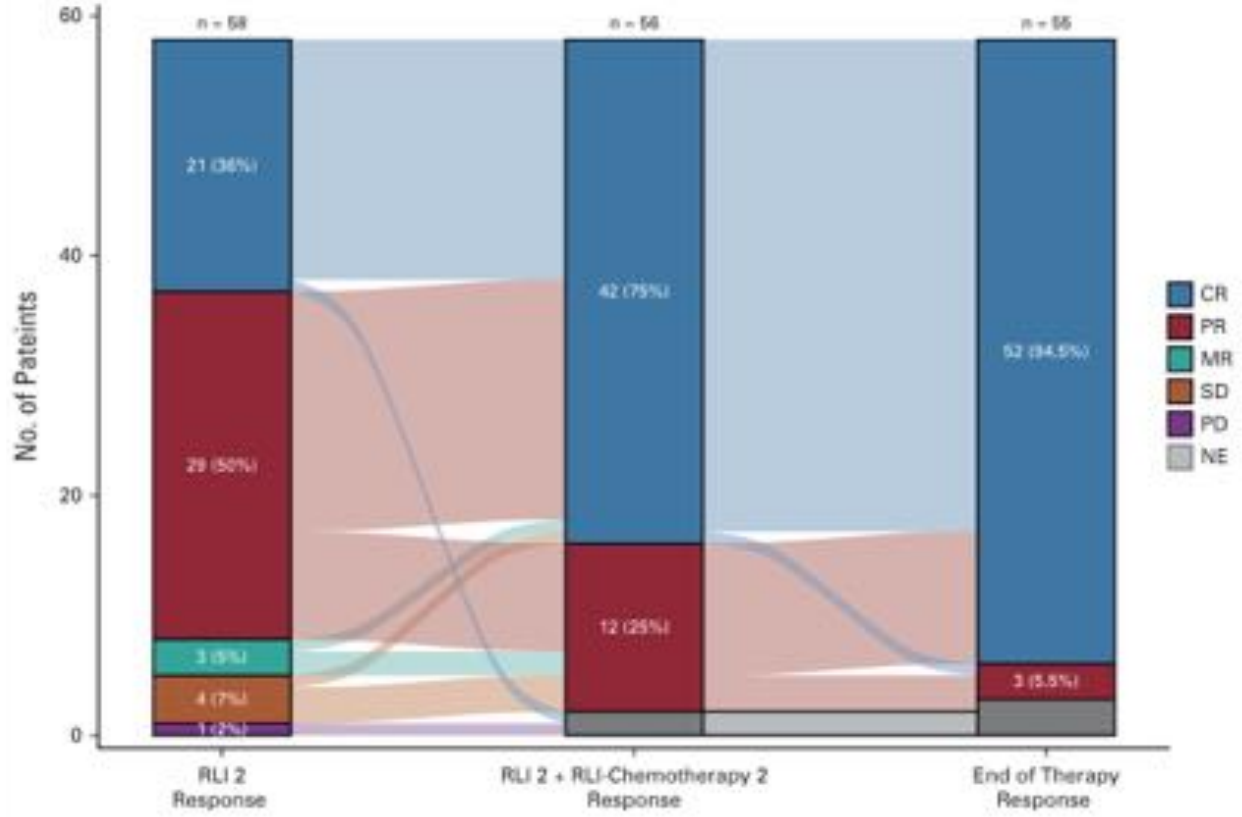
Mandatory GCSF, VTE, PJP & VZV prophylaxis

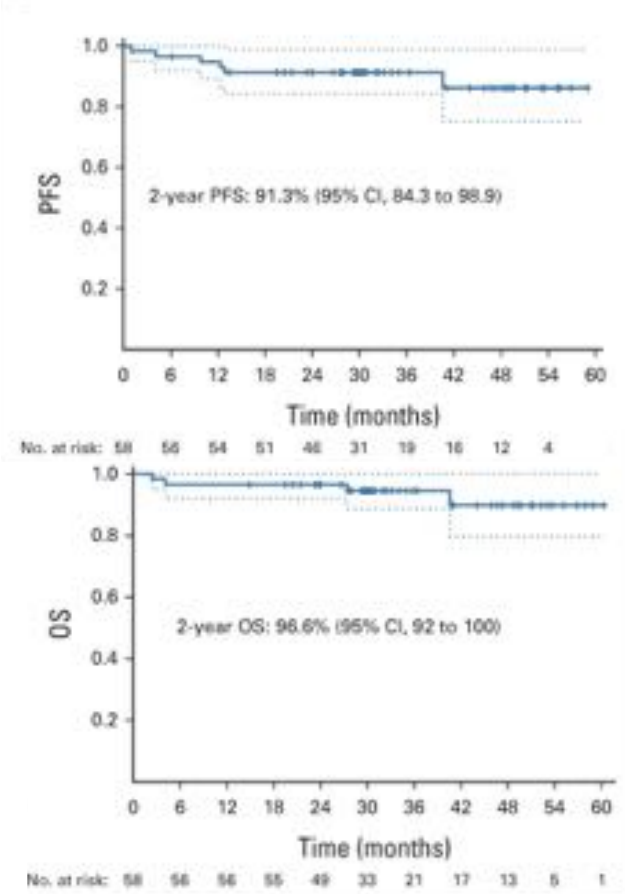
July 2018:
Dosing for 65+y was amended to Ibrutinib 420mg with chemotherapy
N = 9

- Primary Objectives
  - 1A: To determine the ORR at the end of 2 cycles of RLI alone
  - 1B: To determine the CR rate at the end of RLI x 2 + RLI combined with chemotherapy x 6

Westin et al. J Clin Oncol. 2022

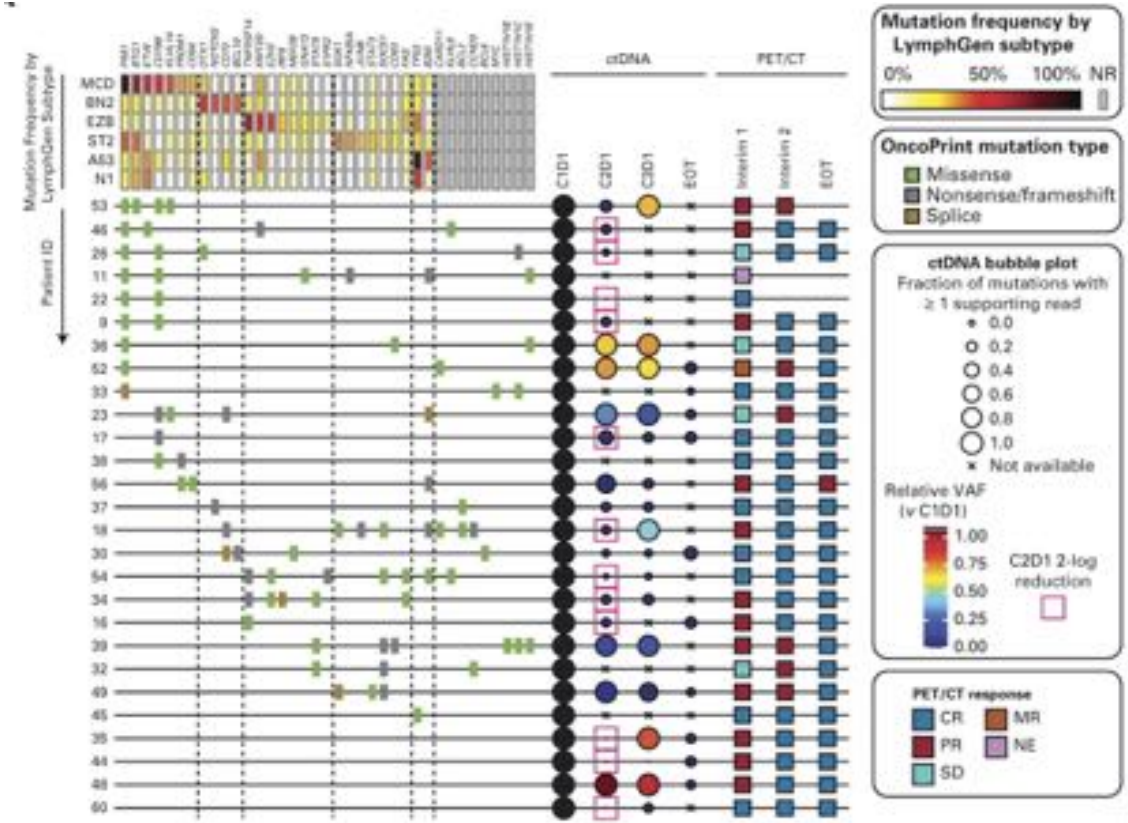
Smart Start: Results





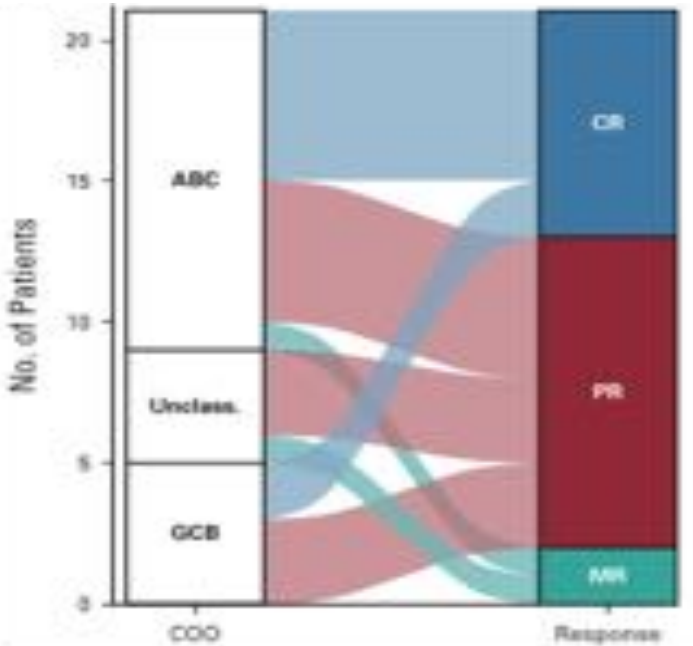
Westin et al. J Clin Oncol. 2022

Smart Start: Results



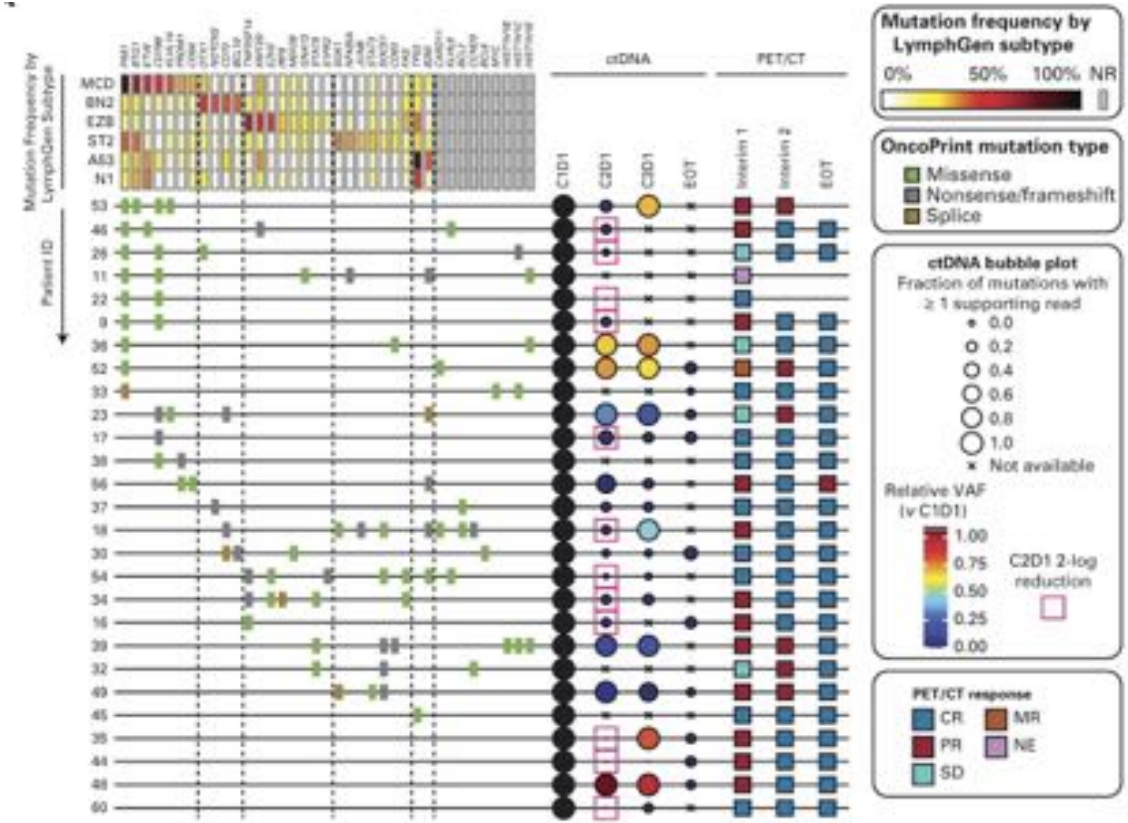
Response after RLI by subtype

PET/CT after 2 cycles



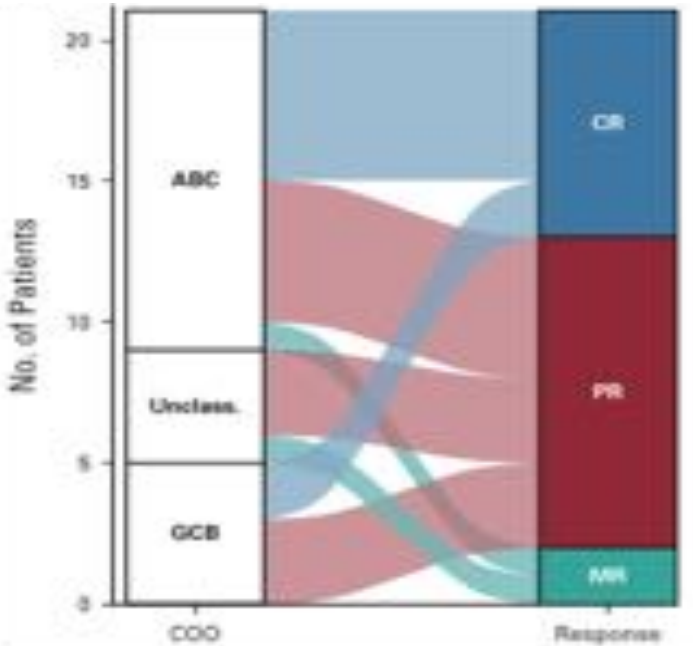
Westin et al. J Clin Oncol. 2022

Smart Start: Results



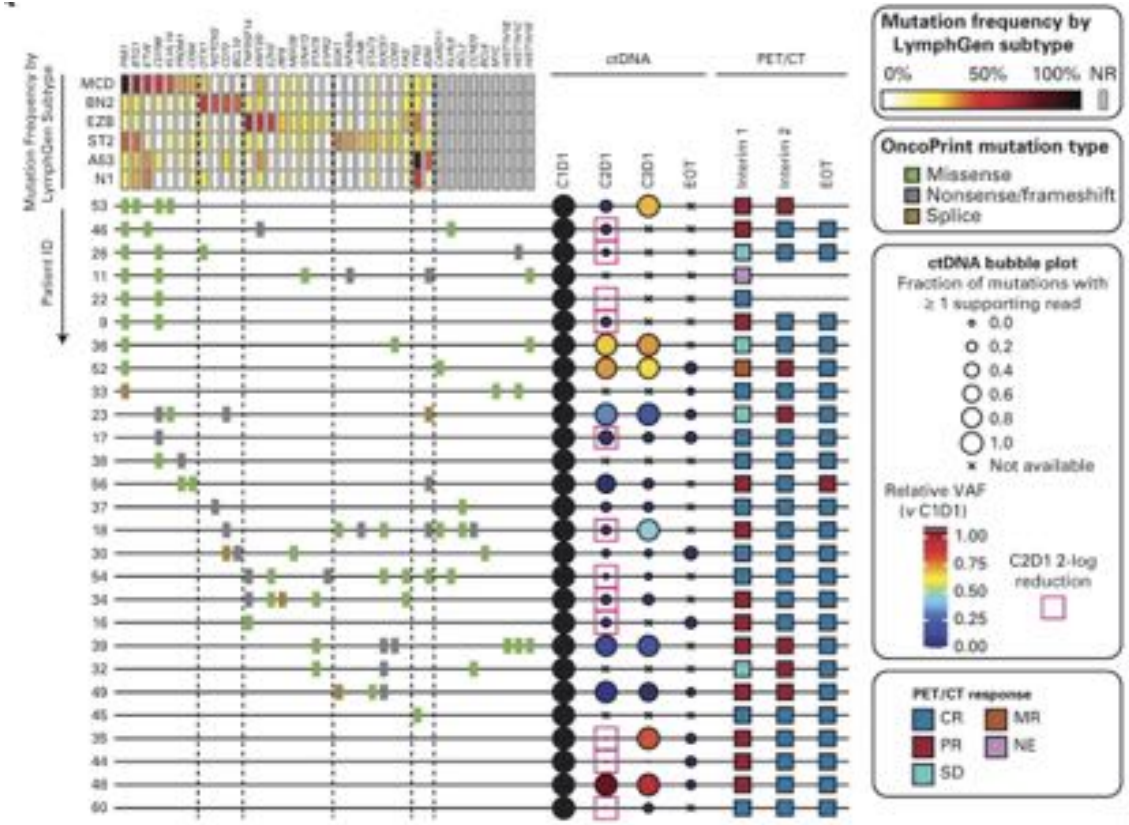
Response after RLI by subtype

PET/CT after 2 cycles



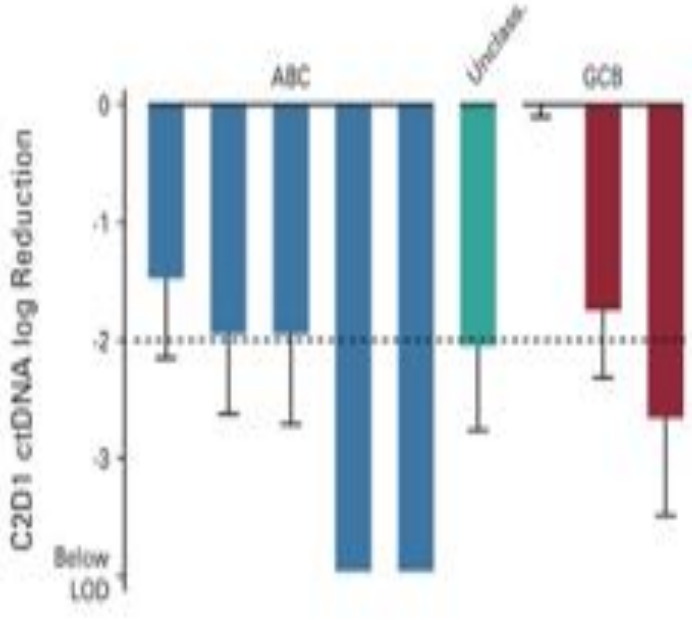
Westin et al. J Clin Oncol. 2022

Smart Start: Results

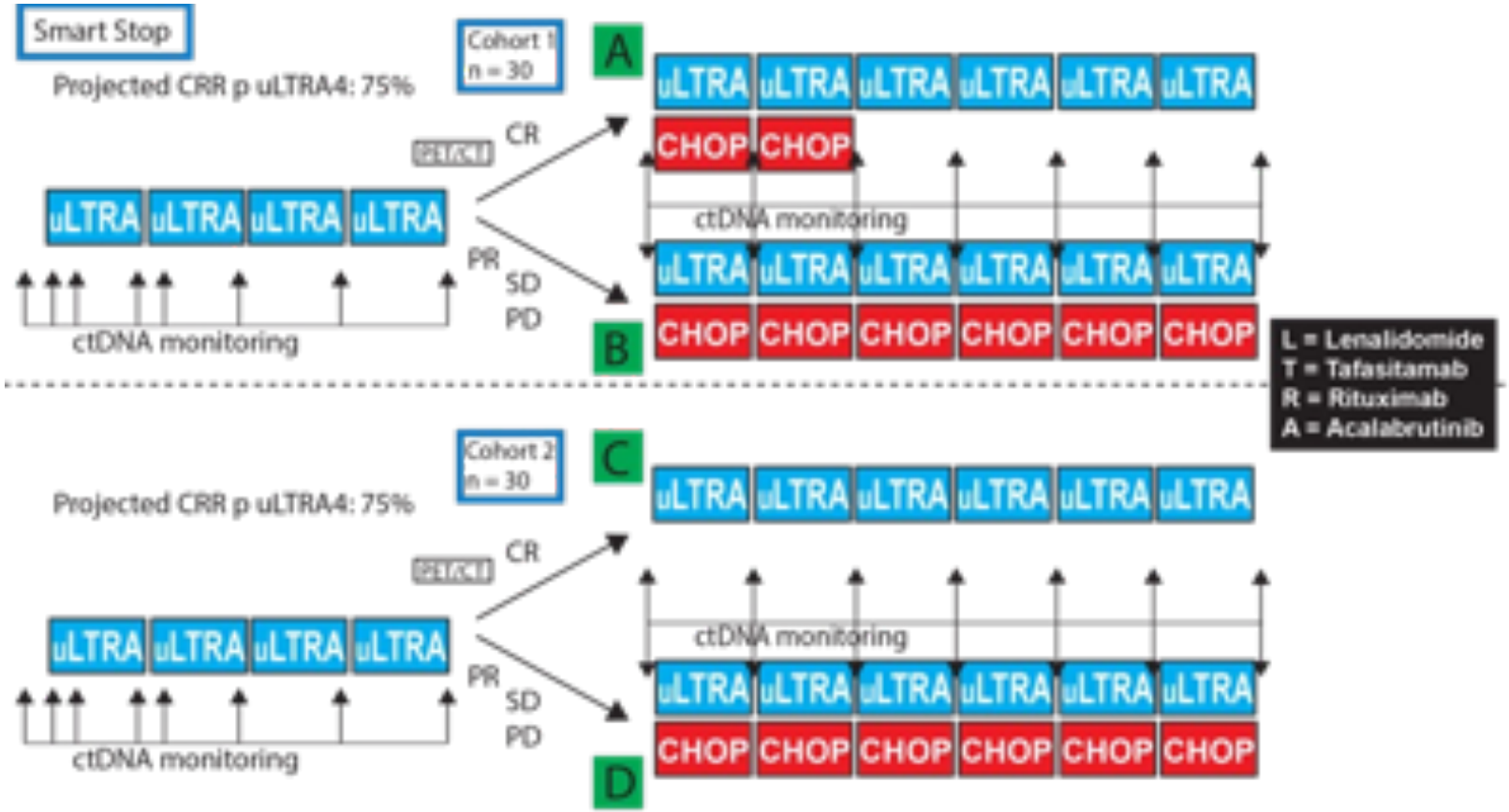


Response after RLI by subtype

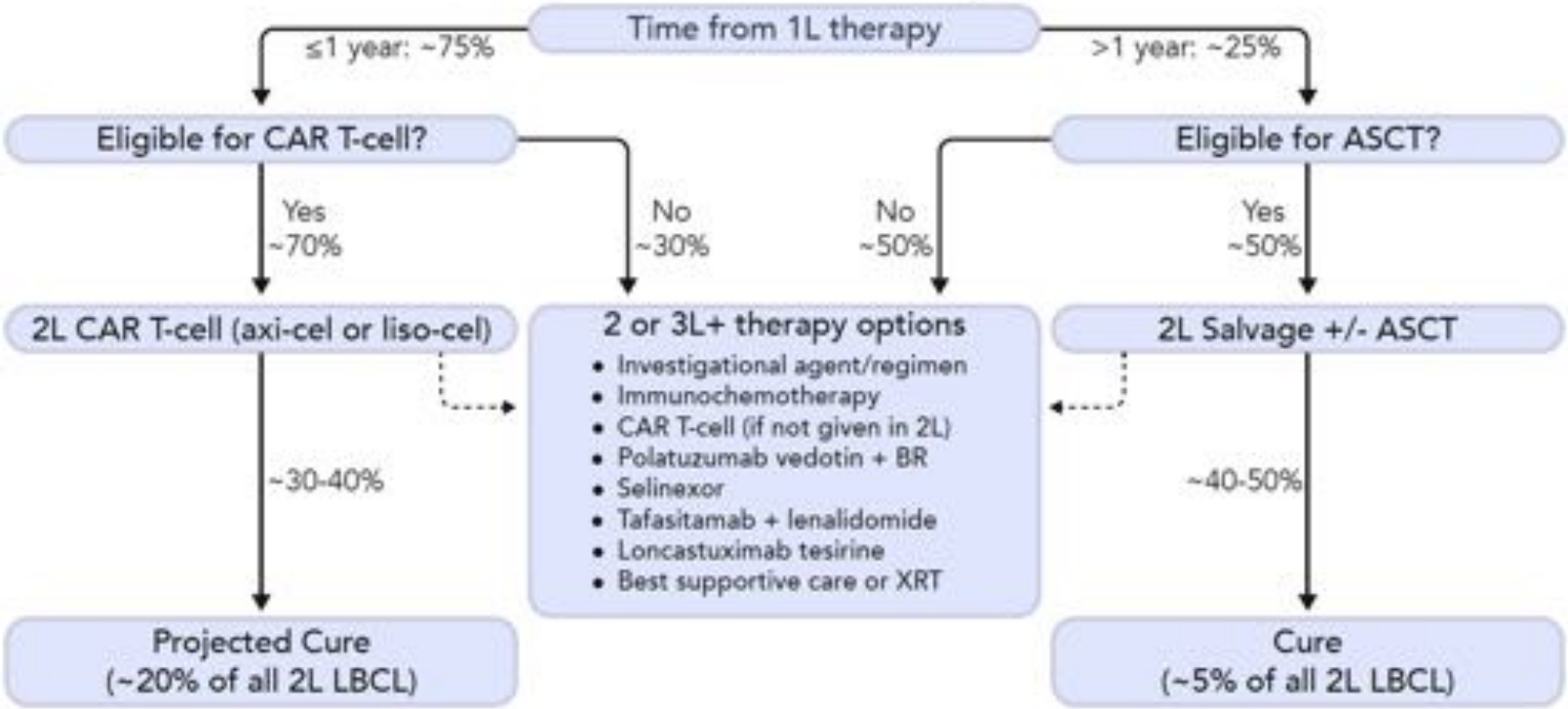
cfDNA after 1 cycles



Smart Stop: Study Design



What Now: Algorithm for R/R LBCL



1L, first-line; 2L, second-line; ASCT, autologous stem cell transplant; axi-cel, axicabtagene ciloleucel; BR, bendamustine, rituximab; CAR T-cell, chimeric antigen receptor T cell; LBCL, large B-cell lymphoma; liso-cel, R/R, relapsed/refractory; XRT, radiotherapy.

Westin J, Sehn LH. *Blood.* 2022;139(18):2737-2746.

Summary of 3 Randomized Second-line CAR T-cell Therapy Trials

Patient population similar: R/R within 12 months of therapy
Definition of EFS (Primary Endpoint) differed between trials

	Bridging Allowed	% Bridging	% CAR-T	% ASCT	Cross-Over Planned*	% Cross-Over	EFS	OS
ZUMA-7	NO	0	94	36	NO	56	✓	NS
TRANSFORM	YES	63	97	46	YES	51	✓	NS
Belinda	YES	83	96	33	YES	51	NS	NS

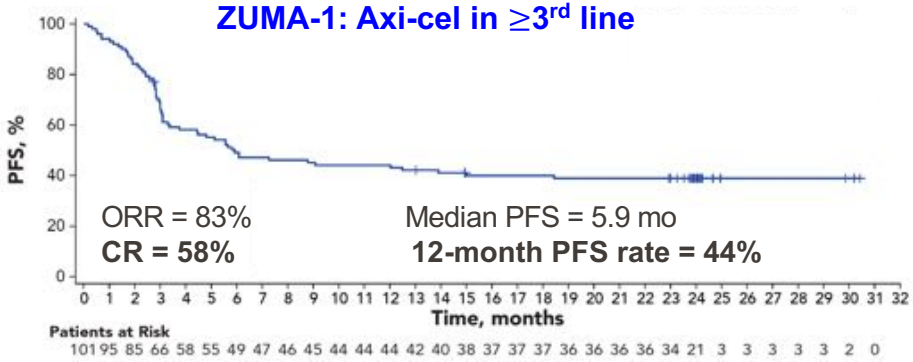
*Belinda permitted cross-over only after 2 lines of salvage

ASCT, autologous stem cell transplant; CAR-T, chimeric antigen receptor T cell; EFS, event-free survival; NS, not significant; OS, overall survival; R/R, relapsed/refractory

Locke FL et al. *New Engl J Med.* 2022;386:640-654. Kamdar M et al. ASH 2021. Abstract 91. Bishop MR et al. *New Engl J Med.* 2022;386:629-639.

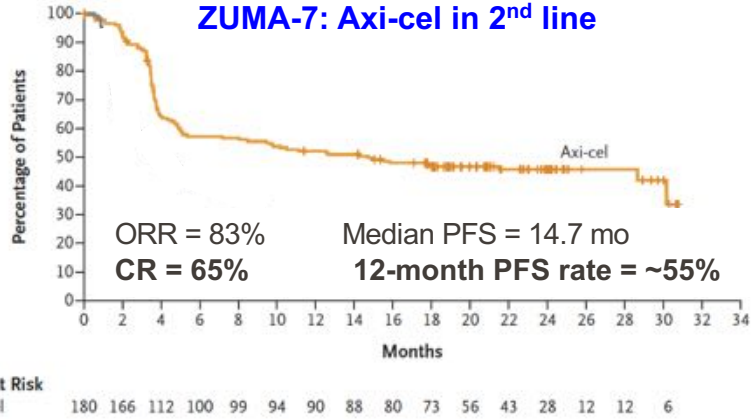
Axi-cel in LBCL: 3rd line vs. 2nd line vs. 1st line

ZUMA-1: Axi-cel in ≥3rd line



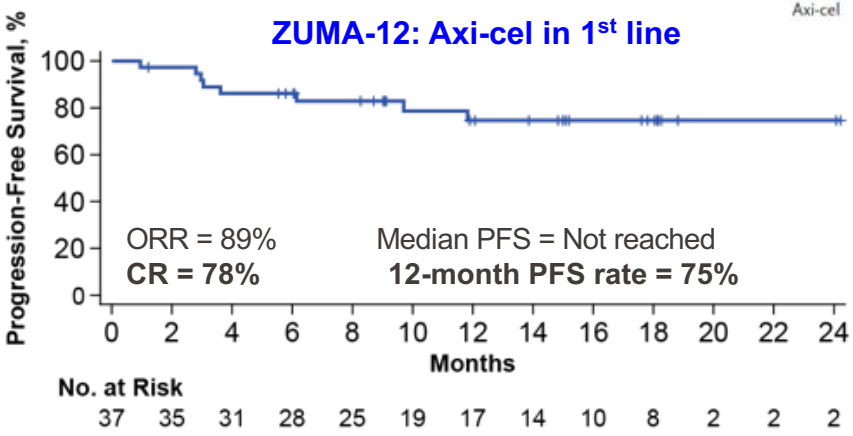
ORR = 83%
CR = 58%
Median PFS = 5.9 mo
12-month PFS rate = 44%

ZUMA-7: Axi-cel in 2nd line



ORR = 83%
CR = 65%
Median PFS = 14.7 mo
12-month PFS rate = ~55%

ZUMA-12: Axi-cel in 1st line

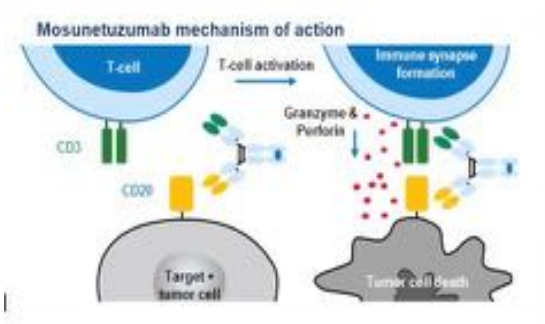


ORR = 89%
CR = 78%
Median PFS = Not reached
12-month PFS rate = 75%

Neelapu et al, *N Eng J Med* 2017
Locke et al, *Lancet Oncol* 2019
Locke et al, *N Eng J Med* 2021
Neelapu et al, *Nat Med* 2022

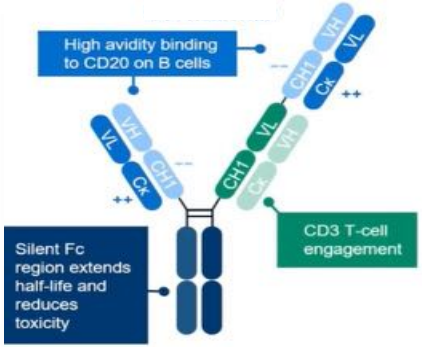
What's Next?: CD3/CD20 Bispecific Antibodies

Mosunetuzumab



IV, SQ

Glofitamab

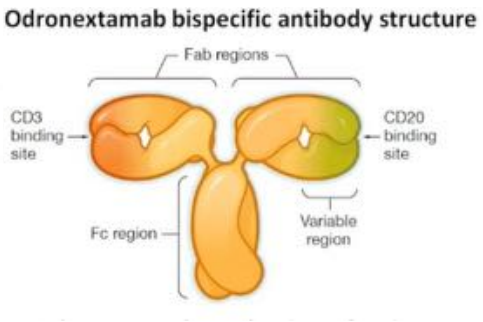


IV

Epcoritamab

SQ

Odronextamab



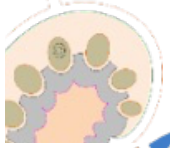
IV

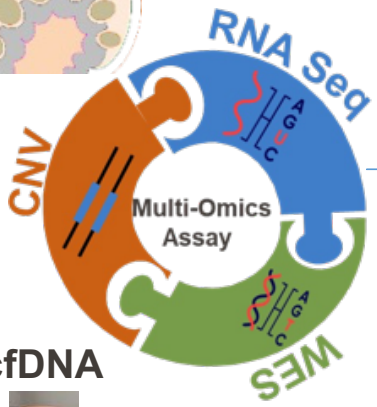
Some *specific* CD20-CD3 bispecific abs for B-NHL

		Odronextamab	Mosunetuzumab	Glofitamab	Plamotamab	Epcoritamab
	Study Phase	**Phase 1/2**	**Phase 1/1b**	**Phase 1b**	**Phase 1**	**Phase 1/2**
	Study Population	R/R B-NHL patients with aggressive disease after at least 2 prior therapies	R/R NHL patients with at least 2 prior therapies	R/R NHL patients with aggressive disease after at least 1 prior systemic therapy	Transplant ineligible R/R NHL patients	R/R DLBCL and aggressive NHL patients after anti-CD20 treatment and/or ASCT
	Administration	IV	IV	IV	IV	SC
	Sample Size	DLBCL = 71 FL = 37	DLBCL = 119 FL = 62	DLBCL = 85, FL = 18 (fixed dosing)	DLBCL = 18 FL = 5	DLBCL = 46 FL = 12
Efficacy	**DLBCL: ORR, CR, mDoR/DoCR**	60% ORR, 60% CR, mDOR 10.3 mo, mDoCR 9.5 mo	35% ORR, 19% CR	49% ORR, 34% CR, mDoCR NR	39% ORR, 28% CR	68% ORR, 46% CR (dose 12-60 mg)
Efficacy	**FL: ORR, CR, mDoR/DoCR**	93% ORR, 75% CR, mDOR 7.7 mo, mDoCR 8.1 mo	68% ORR 50% CR, mDoR 20.4 mo	67% ORR, 50% CR, mDoR NR	ORR N/A, 20% CR	80% ORR, 60% CR (dose 12-48 mg)
Safety	**All CRS**	62%	28.4% (Group B); 23% (FL population)	56%	56%	59%
Safety	**Grade 3+ CRS**	7%	1.4%; 6%	2%	4%	0%

Future Direction: Improving Lymphoma Trial and Treatment Strategies

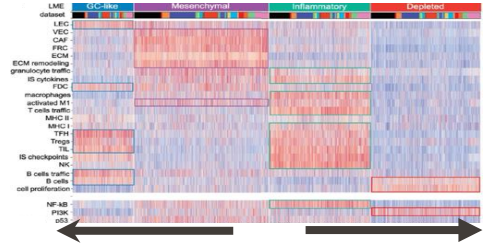
FFPE Tissue Biopsy





cfDNA

	NCI		Drug Target					
	Prevalence	5-yr OS	BTK	PI3K	BCL2	JAK	IRF4	EZH2
BN2 C1	13.3%	All (67%) ABC (76%) GCB (100%) Unclassified (38%)	X	X	X			
A53 C2	5.8%	All (63%) ABC (33%) GCB (100%)	X?					
EZB MYC+ C3	5.9%	All 48%		X	X			X
EZB MYC+ C3	17.6%	All 82%		X	X			X
ST2 C4	6.4%	All (84%) GCB (81%)		X		X		
MCD C5	8.7%	All (40%) ABC (37%)	X	X	X	X	X	
N1 C5	1.7%	All (27%) ABC (22%)						

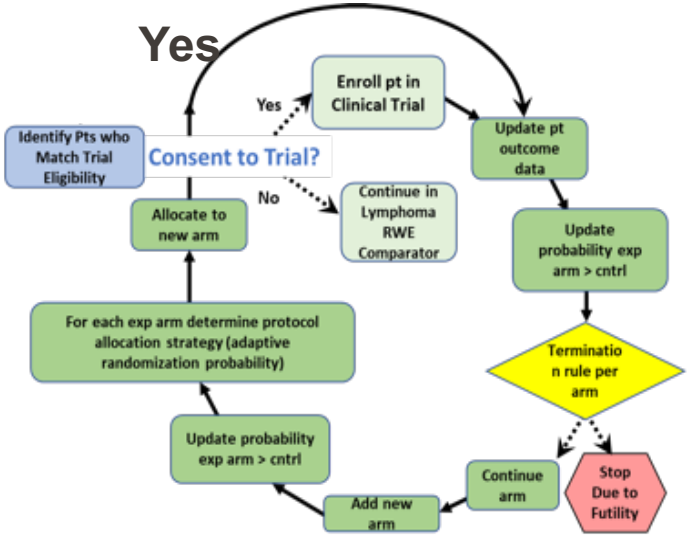


LymphGen and LME Classification

Results Adequate for Trial Enrollment? (0-7 days)

No

Yes



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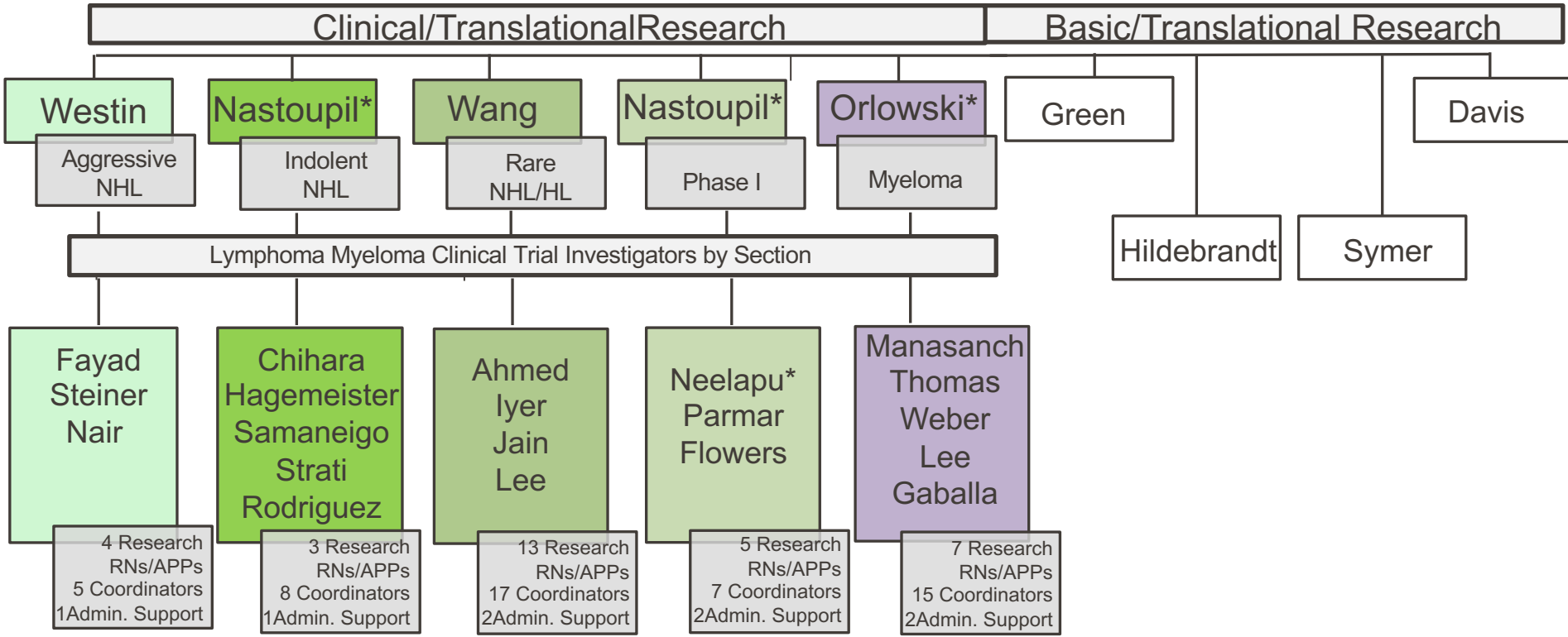
Research Leaders in Lymphoma/Myeloma



*Deputy Chair

Thank you!

Lymphoma Epidemiology of Outcomes

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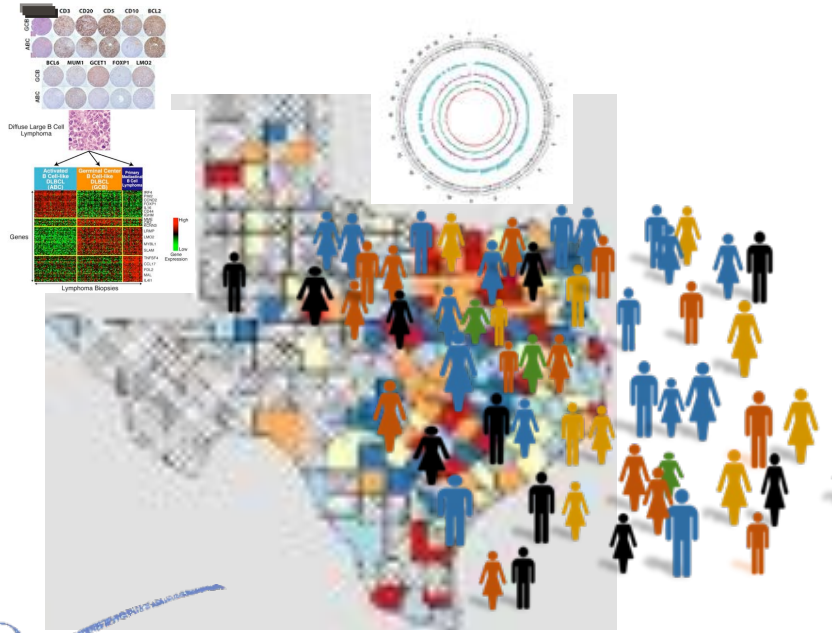

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