Great Debates & Updates Hematologic Malignancies

How Do We Choose among non-CAR T Options for Patients with Recurrent Aggressive Lymphoma?

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Disclosures

- Astra Zeneca - consultant

Choosing a Non-CAR-T Treatment Strategy Decision Factors

- Disease course
  - Bridging to ASCT?
  - Consider CAR-T in future?
  - Relapse after CAR-T
- Disease biology
  - High-grade/Double-Hit?
  - Concerned for CNS disease?
  - GCB vs ABC

CAR-T = chimeric antigen T-cell; ASCT = autologous stem cell transplant; CNS = central nervous system; GCB = germinal-center B-cell; ABC = activated B-cell.

Learning Objectives

After completing this activity, learners should be able to:

1. Assess the mechanisms, safety, and efficacy of new and emerging agents for the treatment of R/R DLBCL

2. Evaluate new and emerging agents for proper sequencing in the individualized care of R/R DLBCL patients

3. Devise strategies to properly sequence therapy for individualized patient care and to mitigate potential adverse effects and toxicities associated with new and emerging R/R DLBCL treatments

R/R DLBCL = relapsed/refractory diffuse large B-cell lymphoma.

Disease Course

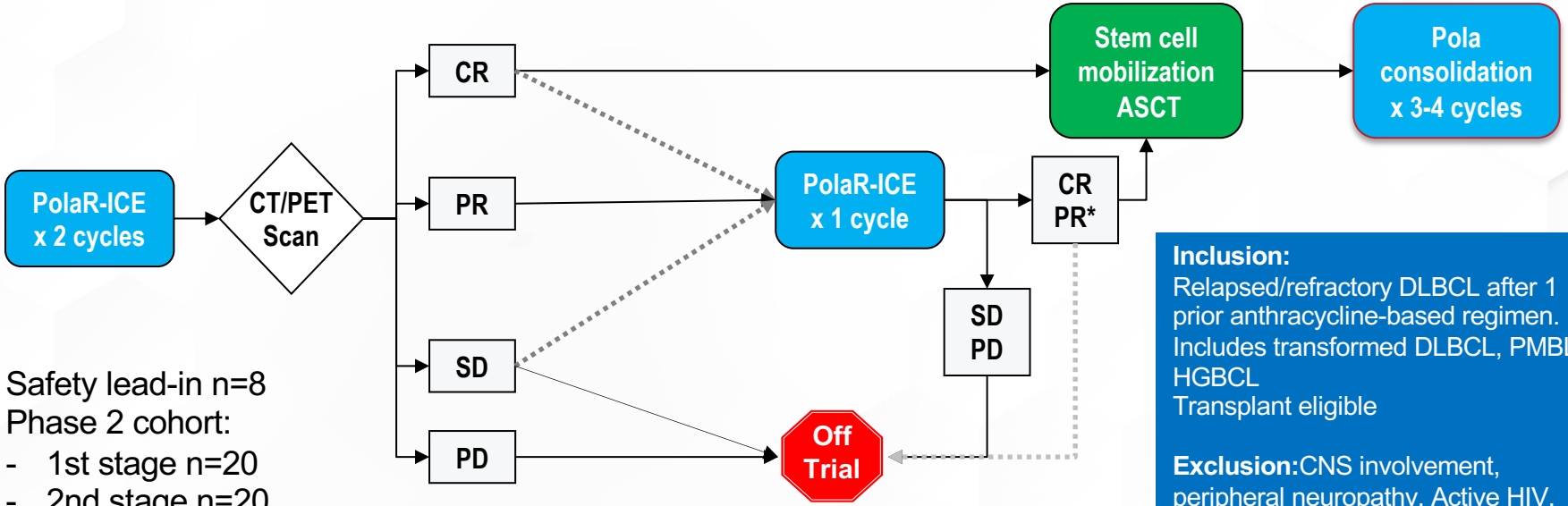
Case 1

- A 52-year-old man with AIDs-associated, triple-hit DLBCL was treated with R-EPOCH. He was successfully treated and remained disease-free for nearly 2 years after which he began to notice new cervical LAD. The patient was found to have relapsed disease

- Given the time to relapse was greater than 1 year, he was determined not to be a candidate for CART

- Plans for ASCT were made, and salvage chemotherapy was initiated

Polatuzumab Vedotin Plus R-ICE (PolaR-ICE) as Second-line Therapy in Relapsed/Refractory DLBCL



Safety lead-in n=8
Phase 2 cohort:
- 1st stage n=20
- 2nd stage n=20

Inclusion:
Relapsed/refractory DLBCL after 1 prior anthracycline-based regimen.
Includes transformed DLBCL, PMBL, HGBCL
Transplant eligible

Exclusion:CNS involvement, peripheral neuropathy, Active HIV, HBV, HCV.

Hypothesis: Improvement in CR rate from 40% with R-ICE to 60% with Pola-RICE

R-ICE = rituximab, ifosfamide, carboplatin, and etoposide.
Herrera AF, et al. Presented at: ASH;2022. Abstract 442.

Characteristics and Outcomes

49% Primary refractory

Histology:

- 66% DLBCL
- 27% Transformed from indolent lymphoma
- 59% non-GCB
- 17% Double hit

Disposition:

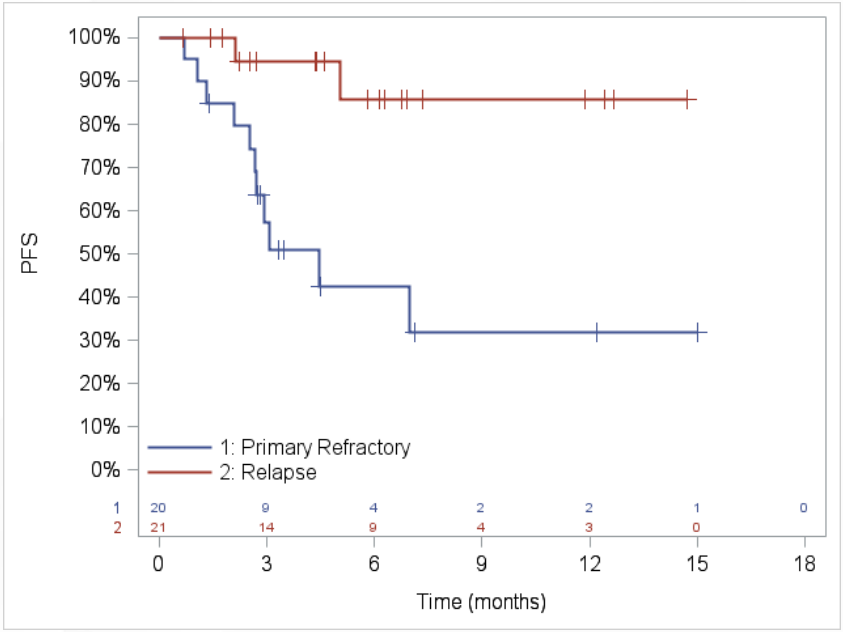
- 22/41 patients proceeded to transplant,
- - 16 of these had pola consolidation
  - 16 did not proceed to transplant.
  - Most common reasons were lack of response/death (n=7), PD before collection (n=5), Toxicity/MD decision (n=5)
  - 5 went to Car-T in PD
  - 1 collection failure

Response	Overall (n=41)	Refractory (n=20)	Relapsed (n=21)
After 2 cycles			
ORR	36 (88%)	16 (80%)	20 (95%)
CR	22 (54%)	6 (30%)	16 (76%)
End of treatment			
ORR	33 (80%)	14 (70%)	19 (90%)
CR	23 (56%)	7 (35%)	16 (76%)

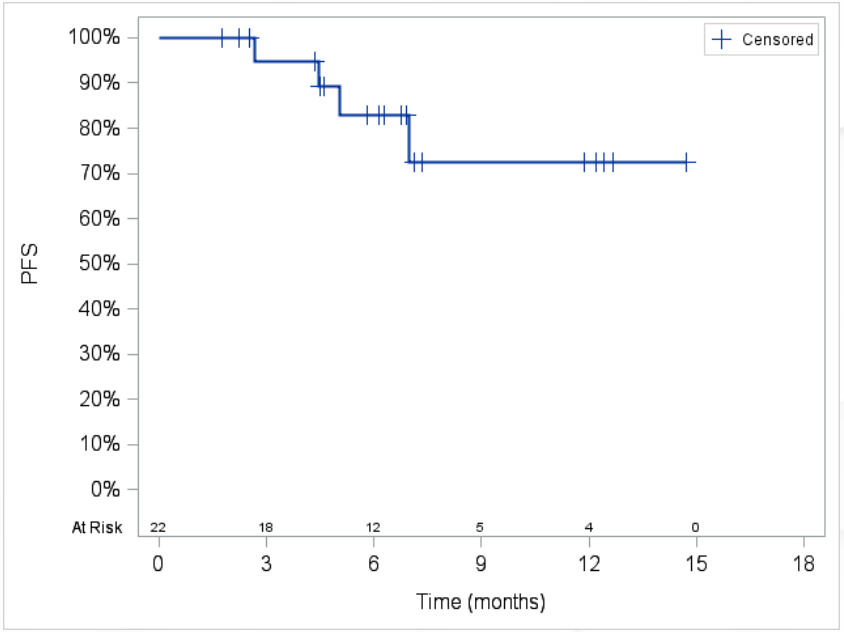
Herrera AF, et al. Presented at: ASH;2022. Abstract 442.

PFS According to Subgroups

PFS by response to 1L tx (n=41)



PFS in pts who went to ASCT (n=22)



Median follow-up in survivors, 6.6 months (range, 0.7-20.2)

Herrera AF, et al. Presented at: ASH;2022. Abstract 442.

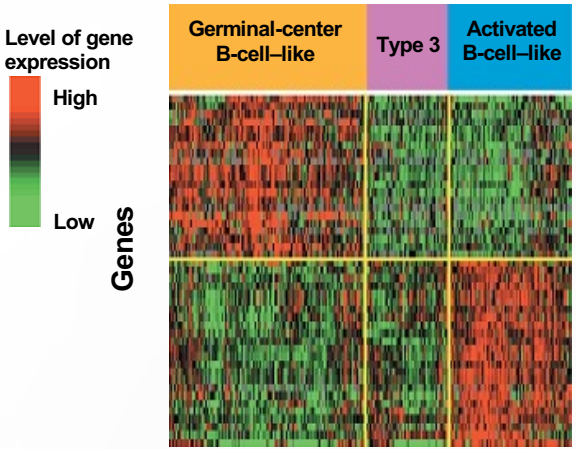
Conclusions: PolaR-ICE

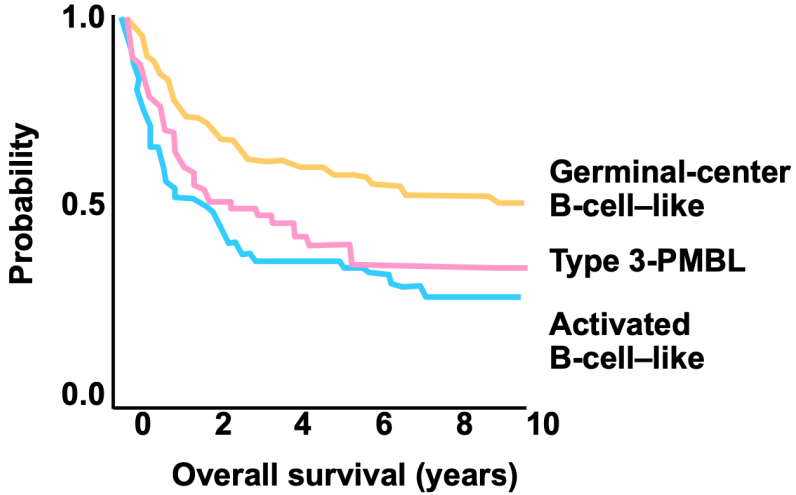
- PolaR-ICE produced high CR rate
  - CR rate: Relapse >> Primary refractory
- No excess toxicity compared to RICE historically.
- 61% bridged to ASCT vs 36-47% (ZUMA-7, TRANSFORM)
- BUT Pola-RICE included fewer patients with primary refractory disease

Herrera AF, et al. Presented at: ASH;2022. Abstract 442.

Consideration of Biology

DLBCL Cell of Origin



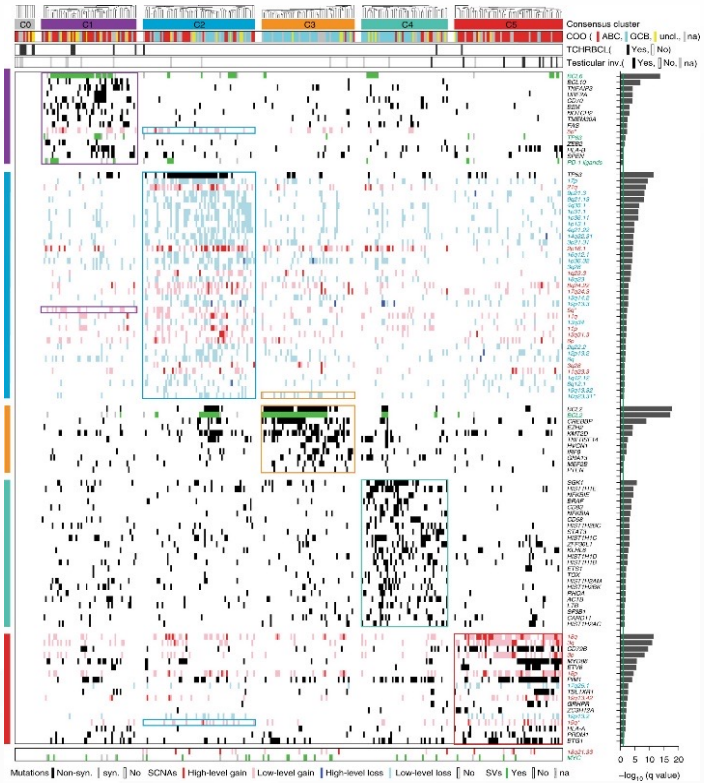


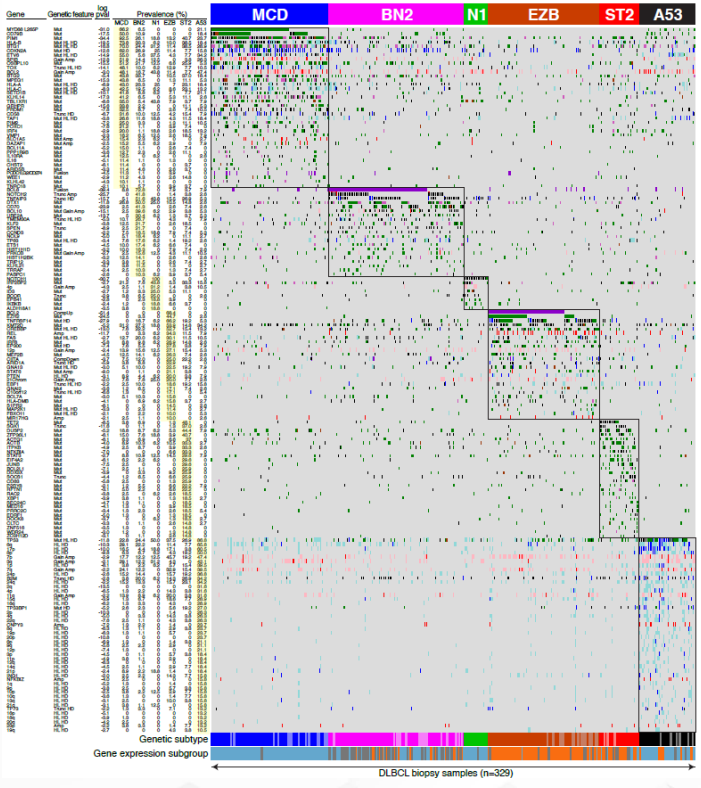
In *germinal center-type*, mutations of BCL6, histone acetyltransferases and EZH2 lead to a repressed transcriptional state

In *ABC-type*, mutations in the B-cell receptor pathway lead to unchecked activation of NFkB

Rosenwald A, et al. Accessed April 3, 2023. https://www.nejm.org/doi/full/10.1056/nejmoa012914.

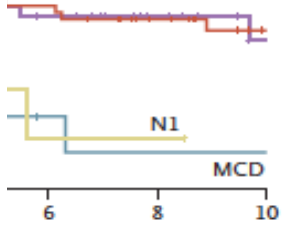
DLBCL Cell of Origin





umors Were Genetically

Comparison	P Value
4-Way	1.70×10^{-4}
EZB vs. MCD	2.13×10^{-4}
EZB vs. N1	0.005
EZB vs. BN2	0.86
N1 vs. BN2	0.008
MCD vs. N1	0.93
MCD vs. BN2	0.001

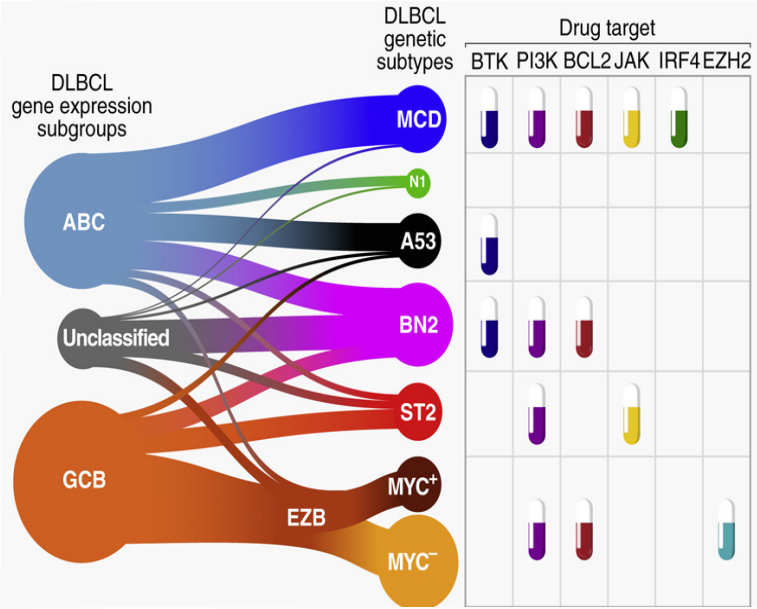


rs

2	1	1
18	11	5
1	1	0
27	19	11

Wright GW, et al. *Cancer Cell*. 2020;37(4):551-568.e14. Chapuy B, et al. *Nat Med*. 2018;24(5):679-690.

DLBCL Cell of Origin
LymphGen Classification



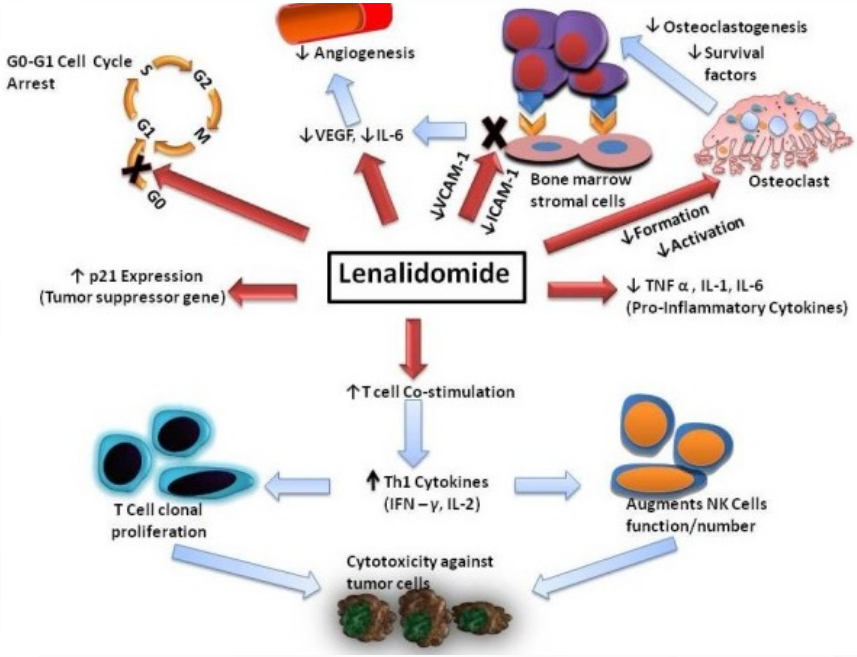
Characteristics	OS
MYD88 L265P mutations and CD79B mutations CDKN2A deletions	40%
OTCH1 mutations. BCOR, IkB kinase β mutations	27%
TP53 mutations/deletions Aneuploidy	63%
NOTCH2 mutations, BCL6 translocation, TNFAIP3 (A20), BCL10, PRKCB mutations	67%
SGK1 and TET2 mutated	84%
EZH2, CREBBP, KMT2D, EP300 mutations and BCL2, MYC, TP53, GNA13, FOXO1 alterations	48%
EZH2, CREBBP, KMT2D, EP300 mutations and BCL2 translocations CARD11, TNFAIP3 (A2) alterations	82%

Schmitz R, et al. *N Engl J Med*. 2018;378(15):1396-1407. Wright GW, et al. *Cancer Cell*. 2020;37(4):551-568.

Case 2

- An 82-year-old patient was found to have FL transformed to DLBCL. He was initially treated with mini R-CHOP chemotherapy and obtained a complete remission
- Eight months later, the patient presented with fatigue, weight loss and night sweats. Imaging and biopsy confirmed relapsed disease
- The patient was considered unfit for transplant or CART
- What strategies could we use?

Treatment Strategies for ABC-DLBCL
Lenalidomide

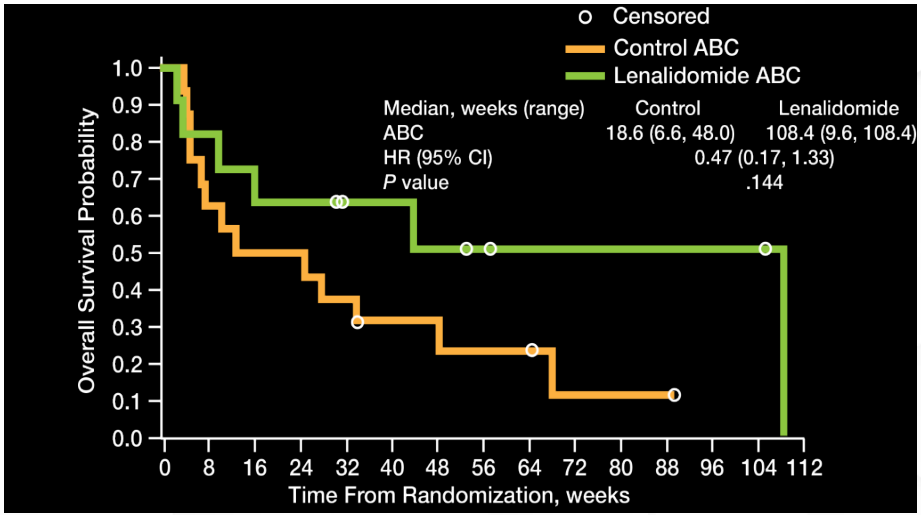


- Lenalidomide is an IMID (immunomudulatory drug)
- FDA approved for mantle cell lymphoma, multiple myeloma, myelodysplastic syndrome (MDS)
- Given orally, cousin to thalidomide
- Side effects: thrombosis, cytopenias, ?? secondary malignancies

Kotla V, et al. *J Hematol Oncol*. 2009;2:36.

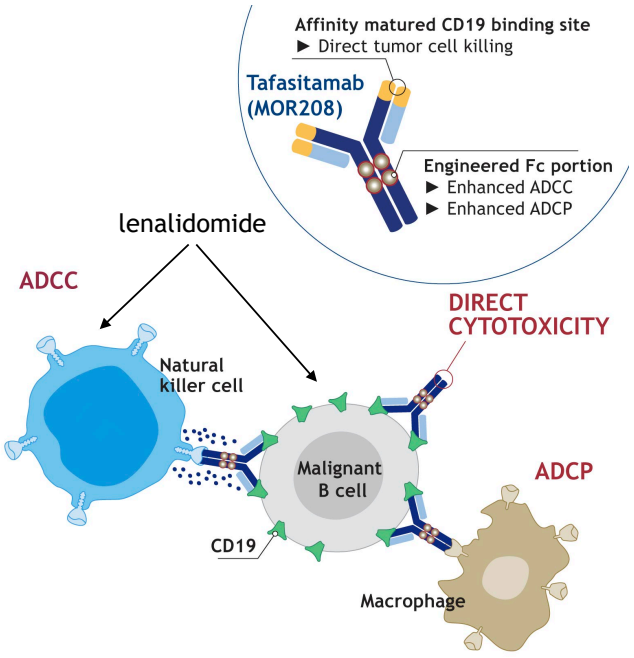
Treatment Strategies for ABC-DLBCL
Lenalidomide

- DLBCL Relapsed Setting
  - Lenalidomide worked as a single agent in patients with relapse DLBCL of both GC and ABC subtypes
  - Lenalidomide demonstrated enriched activity in relapsed ABC DLBCL compared to other drugs



Czuczman MS, et al. *Clin Cancer Res*. 2017;23(15):4127-4137.

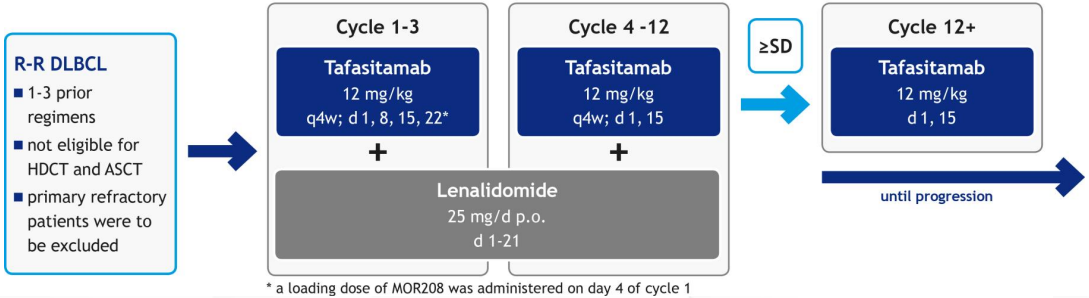
New Treatment Strategies for R/R DLBCL
Tafasitamab + Lenalidomide



ADCC: Antibody-Dependent Cell-Mediated Cytotoxicity
ADCP: Antibody-Dependent Cell-Mediated Phagocytosis

L-MIND: Study Design

phase 2, single-arm, open-label, multicenter study (NCT02399085)



* a loading dose of MOR208 was administered on day 4 of cycle 1

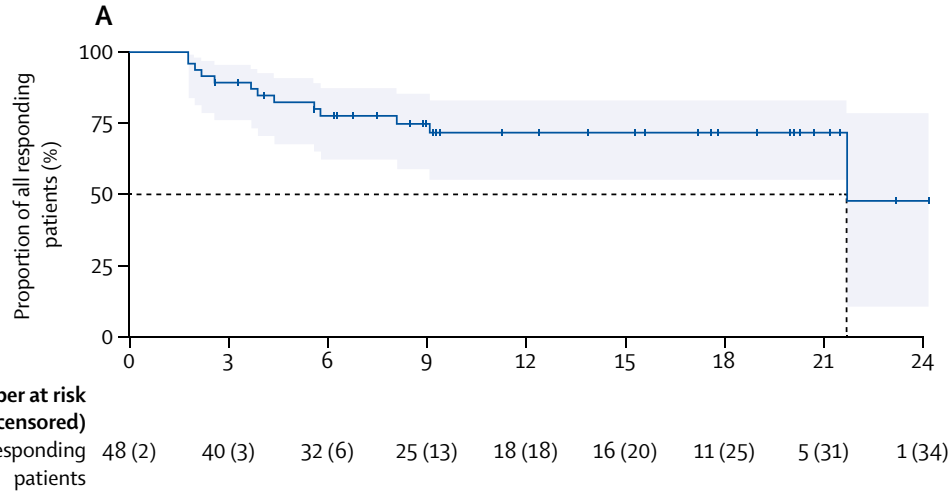
Salles G, et al. *Lancet Oncol*. 2020;21(7):978-988.

New Treatment Strategies for R/R DLBCL

Tafasitamab + Lenalidomide

	Grade 1–2	Grade 3	Grade 4	Grade 5
Haematological events				
Neutropenia	1 (1%)	22 (27%)	17 (21%)	0
Anaemia	22 (27%)	6 (7%)	0	0
Thrombocytopenia	11 (14%)	10 (12%)	4 (5%)	0
Leukopenia	5 (6%)	6 (7%)	1 (1%)	0
Febrile neutropenia	0	8 (10%)	2 (2%)	0
Lymphopenia	2 (2%)	2 (2%)	1 (1%)	0
Agranulocytosis	0	0	1 (1%)	0
Non-haematological events				
All rash*	22 (27%)	7 (9%)	0	0
Diarrhoea	26 (32%)	1 (1%)	0	0
Asthenia	17 (21%)	2 (2%)	0	0
Cough	17 (21%)	1 (1%)	0	0
Peripheral oedema	18 (22%)	0	0	0
Pyrexia	16 (20%)	1 (1%)	0	0
Decreased appetite	16 (20%)	0	0	0
Hypokalaemia	10 (12%)	4 (5%)	1 (1%)	0
Back pain†	11 (14%)	2 (2%)	0	0
Fatigue	12 (15%)	2 (2%)	0	0
All urinary tract infection*	9 (11%)	3 (4%)	1 (1%)	0
Constipation	13 (16%)	0	0	0
Muscle spasms	12 (15%)	0	0	0
Nausea	12 (15%)	0	0	0
Bronchitis	10 (12%)	0	1 (1%)	0
Vomiting	11 (14%)	0	0	0
Dyspnea	9 (11%)	1 (1%)	0	0

- ORR 60.0% (95% CI 48.4% - 70.8%)
- CR-rate 42.5%



At 5 yr Follow-up:
PFS 11.6 m
OS 33.5 m, >60 m in 25% of pts

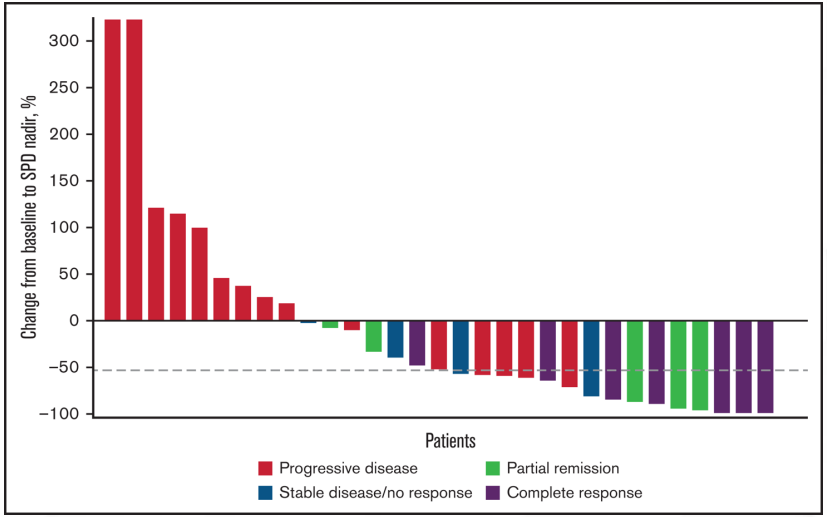
Salles G, et al. *Lancet Oncol*. 2020;21(7):978-988. , Duell AACR 2023

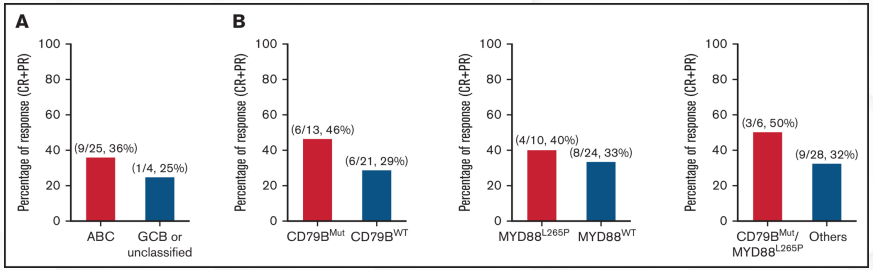
Treatment Strategies of ABC-DLBCL
Zanubrutinib

- Phase 2 study N=41
- Zanu 160 mg BID
- ORR 29%, CR 17%
- DOR 4.5 m
- PFS 2.8 m
- OS 8.4 m
- Grade 3 adverse events (AEs) in 48.8%

- Responses enriched in patients with both CD79b and MYD88 mutations

- Perhaps ideal use will be in combination

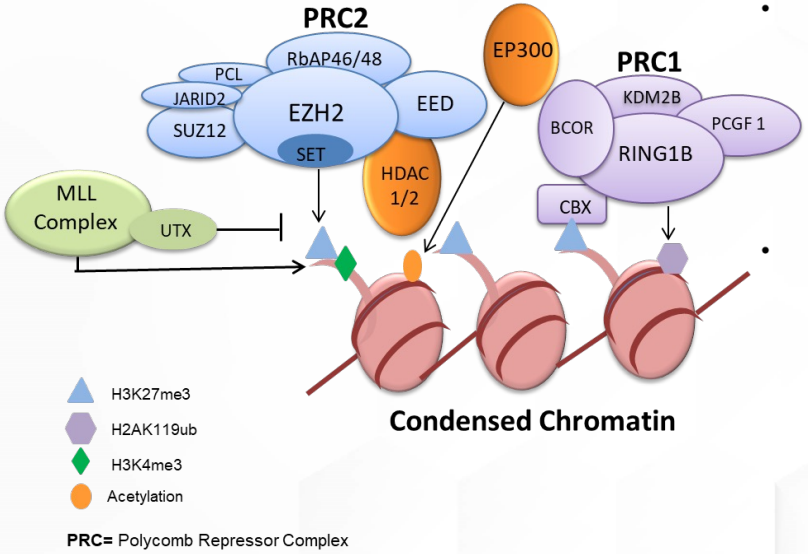




Yang H, et al. *Blood Adv*. 2022;6(6):1629-1636.

Targeting the Germinal Center
Tazemetostat Plus Belinostat

- Lymphomas derived from the germinal center harbor epigenetic derangements driving disease



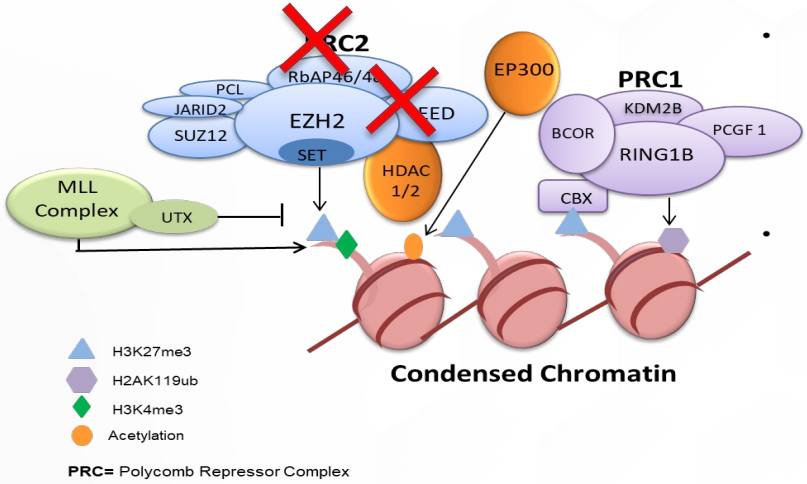
PRC= Polycomb Repressor Complex

- **EZH2:**
  Histone Methyltransferase
  - Activating Mutations
  - 30% of GC-DLBCL
  - 27% of FL
- **EP300 and CREBBP:**
  Histone Acetyltransferases
  - Loss of function
  - 39% of GC-DLBCL
  - 41% of FL

Lue JK, et al. *Clin Cancer Res*. 2019;25(17):5271-5283.

Tazemetostat Plus Belinostat
Background and Rationale

- Lymphomas derived from the germinal center harbor epigenetic derangements driving disease



- **EZH2:**
  Histone Methyltransferase
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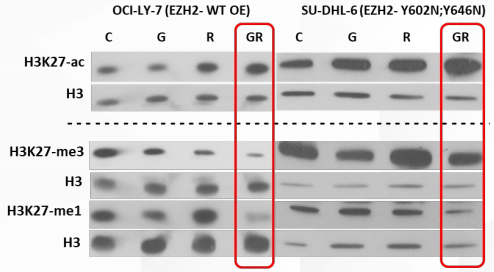
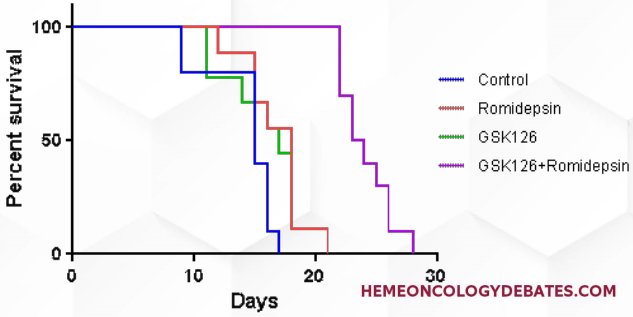
  - 30% of GC-DLBCL
  - 27% of FL
- **EP300 and CREBBP:**
  Histone Acetyltransferases
  - Loss of function
  - 39% of GC-DLBCL
  - 41% of FL

- Dual targeting of EZH2 and HDAC in pre-clinical models
  - Modulation of histone methylation and acetylation
  - Prolonged survival

Increase Ac- and Decreased Me3- of Histone

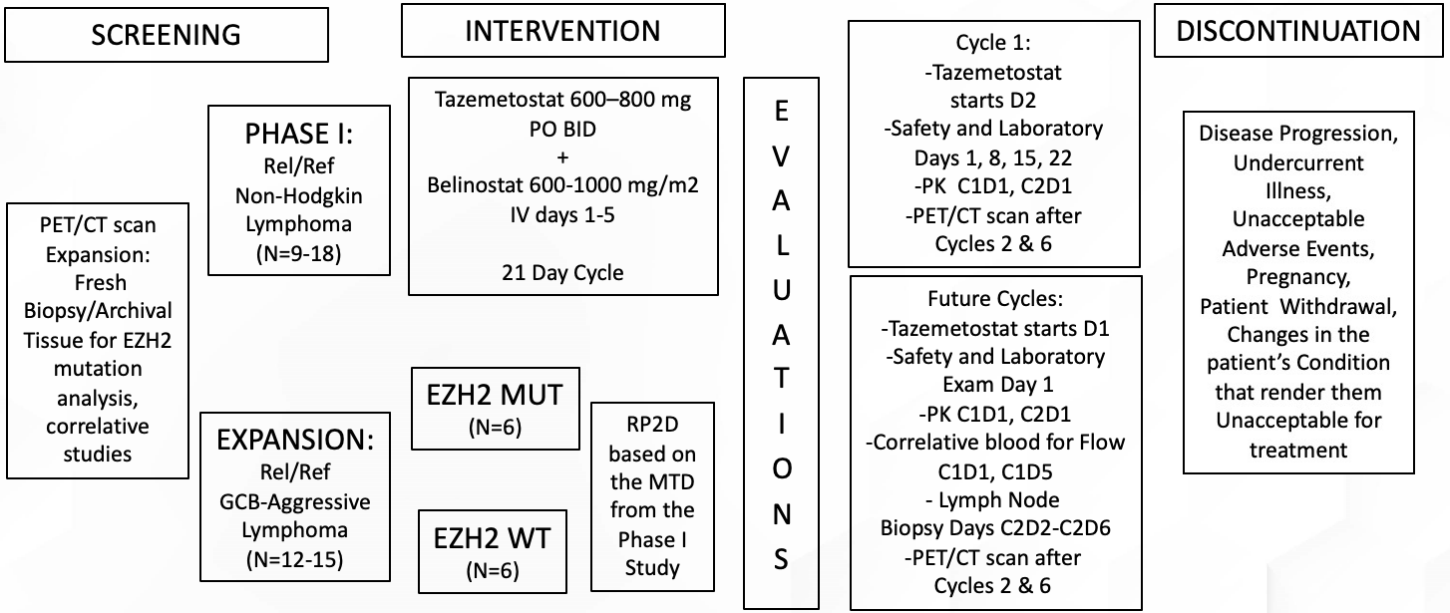


Survival in Xenograft Mouse Model



Lue JK, et al. *Clin Cancer Res*. 2019;25(17):5271-5283.

Tazemetostat Plus Belinostat ETCTN 10500
Study Design



EZH2/HAT mutational analysis (Integral/Integrated biomarker)
Pretreatment/archival tissue will be prospectively evaluated for EZH2(integral) / HAT(integrated) mutations and correlated to response.
CUMC

Epiproteomic Histone Modification (Integrated biomarker)
Paired samples will be assessed via mass spectrometry at the Northwestern Proteomics Core Facility (N=12).

Epigenetic gene signature to inform combination therapy (Exploratory biomarker)
A gene expression signature will be developed as a tool to identify response to epigenetic therapy.
NCLN

Dual Epigenetic Therapy Effects on Gene Expression (Integrated biomarker)
Paired samples will be assessed via RNA seq to determine changed in GEP following EZH2/HDAC inhibition (N=12).
NCLN

Modulation of T-cell Activation (Exploratory biomarker)
Paired peripheral blood will be collected to assess for changes in T-cell activation following exposure to dual epigenetic therapy.
CUMC

Lue JK, et al. *Clin Cancer Res*. 2019;25(17):5271-5283.

Biology Agnostic

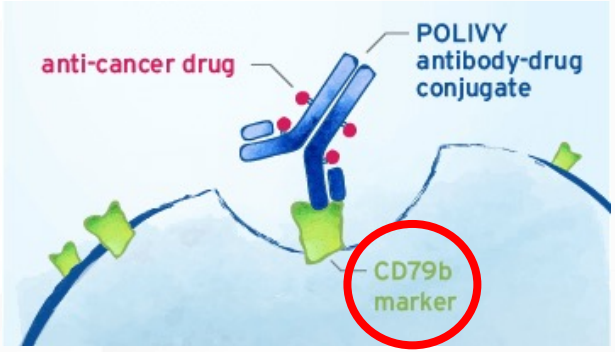
Case 3

- A 56-year-old patient was diagnosed with DLBCL and treated with RCHOP chemotherapy. She obtained a complete remission but less than one year later was found to have anthracycline-induced cardiomyopathy. In addition, she suffered from diabetes, with several negative sequelae from this
- Eight years later the patient again was found to have a new de novo DLBCL. She was treated with R-CEPP, however, could not tolerate procarbazine therefore the dosing was foreshortened and ultimately discontinued
- She obtained a CR but 3 years later relapsed with omental caking. She was highly symptomatic due to burden of disease
- She was evaluated for CAR-T however given her significant comorbidities she was deemed ineligible

New Treatment Strategies for R/R DLBCL

Polatuzumab

- Polatuzumab targets CD79b with MMAE warhead
- 80 patients randomized with rituxan-bendamustine in R/R DLBCL in phase 2



	Pola-BR (n = 39)*		BR (n = 39)*	
Adverse Event	**All Grades, No. (%)**	**Grades 3-4, No. (%)**	**All Grades, No. (%)**	**Grades 3-4, No. (%)**
Blood and lymphatic system disorders				
Anemia	21 (53.8)	11 (28.2)	10 (25.6)	7 (17.9)
Neutropenia	21 (53.8)	18 (46.2)	15 (38.5)	13 (33.3)
Thrombocytopenia	19 (48.7)	16 (41.0)	11 (28.2)	9 (23.1)
Lymphopenia	5 (12.8)	5 (12.8)	0	0
Febrile neutropenia	4 (10.3)	4 (10.3)	5 (12.8)	5 (12.8)
GI disorders				
Diarrhea	15 (38.5)	1 (2.6)	11 (28.2)	1 (2.6)
Nausea	12 (30.8)	0	16 (41.0)	0
Constipation	7 (17.9)	0	8 (20.5)	1 (2.6)
General disorders and administration site conditions				
Fatigue	14 (35.9)	1 (2.6)	14 (35.9)	1 (2.6)
Pyrexia	13 (33.3)	1 (2.6)	9 (23.1)	0
Metabolism and nutrition disorders				
Decreased appetite	10 (25.6)	1 (2.6)	8 (20.5)	0
Peripheral neuropathy				
Peripheral neuropathy†	17 (43.6)	0	3 (7.7)	0

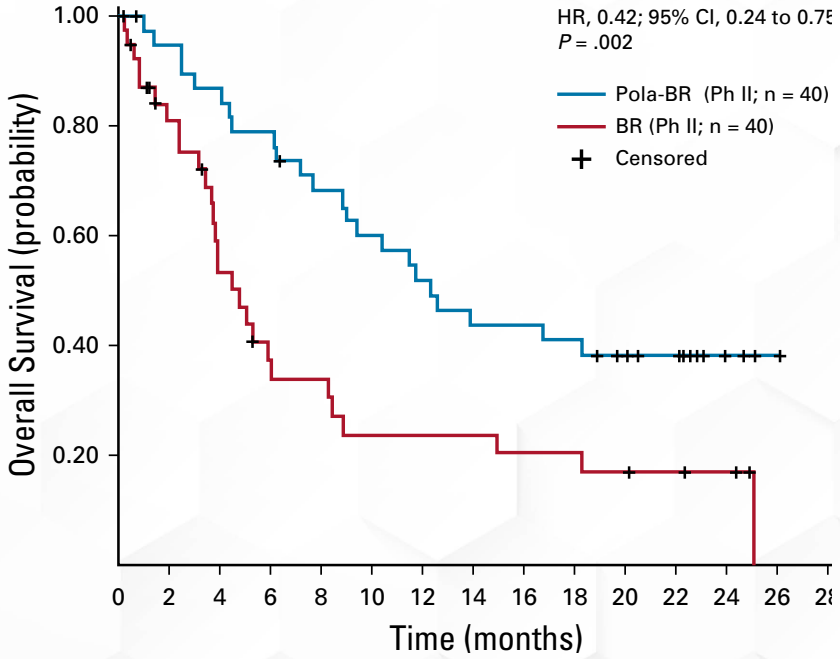
MMAE = monomethyl auristatin E.

Sehn LH, et al. *J Clin Oncol*. 2020;38(2):155-165.

New Treatment Strategies for R/R DLBCL

Polatuzumab

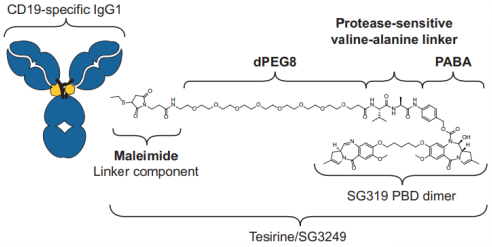
	Phase II Randomized	
Outcome	**Pola-BR (n = 40)**	**BR (n = 40)**
End of treatment		
IRC, objective response	18 (45.0)	7 (17.5)
Complete response	16 (40.0)	7 (17.5)
Partial response	2 (5.0)	0
Stable disease	6 (15.0)	1 (2.5)
Progressive disease	8 (20.0)	10 (25.0)
Missing or unevaluable†	8 (20.0)	22 (55.0)
Median duration of response, months (95% CI)		
IRC	12.6 (7.2 to NE)	7.7 (4.0 to 18.9)
INV assessed	10.3 (5.6 to NE)	4.1 (2.6 to 12.7)
Median progression-free survival, months (95% CI)		
IRC	9.5 (6.2 to 13.9)	3.7 (2.1 to 4.5)
INV assessed	7.6 (6.0 to 17.0)	2.0 (1.5 to 3.7)
Median overall survival, months (95% CI)	12.4 (9.0 to NE)	4.7 (3.7 to 8.3)

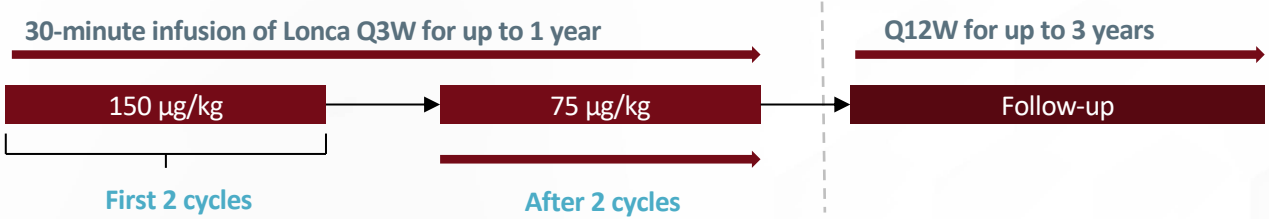


Sehn LH, et al. *J Clin Oncol*. 2020;38(2):155-165.

Loncastuximab Tesirine (ADCT-402)

- Patients with R/R DLBCL have a poor prognosis and unmet need for new treatment options
- Lonca had substantial antitumor activity and an acceptable safety profile in this single-arm open-label Phase 2 study (NCT03589469) in adult patients with R/R DLBCL, who had failed ≥2 established therapies





Most common (≥10%) grade ≥3 TEAEs were:

- Neutropenia (38 patients; 26.2%)
- Thrombocytopenia (26 patients; 17.9%)
- GGT increased (25 patients; 17.2%)
- Anemia (15 patients; 10.3%)

Treatment-related TEAEs leading to treatment discontinuation occurred in 26 (17.9%) patients, most commonly (≥2%):

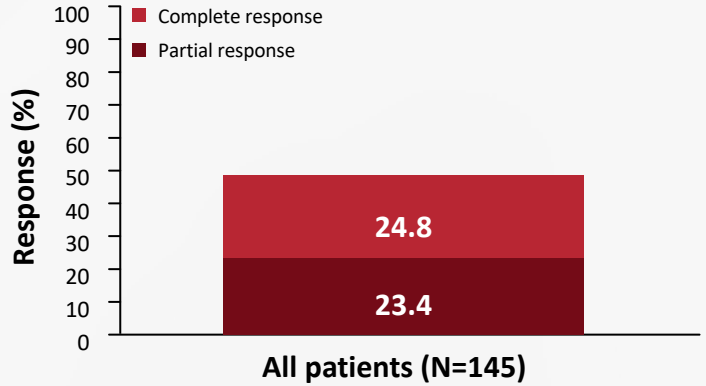
- GGT increased (16 patients; 11.0%)
- Peripheral edema (4 patients; 2.8%)
- Localized edema (3 patients; 2.1%)

Dexamethasone 4mg BID Days -1 to +1

No increase in toxicity was seen in patients aged ≥65 years compared with younger patients

Caimi PF, et al. *Blood.* 2020;136(Suppl 1):35-37.

Loncastuximab Tesirine (ADCT-402)



Lonca ORR:

48.3%

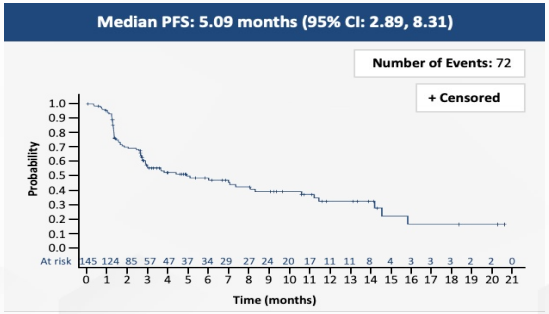
(95% CI: 39.9, 56.7)

Lonca CRR:

24.8%

(95% CI: 18.0, 32.7)

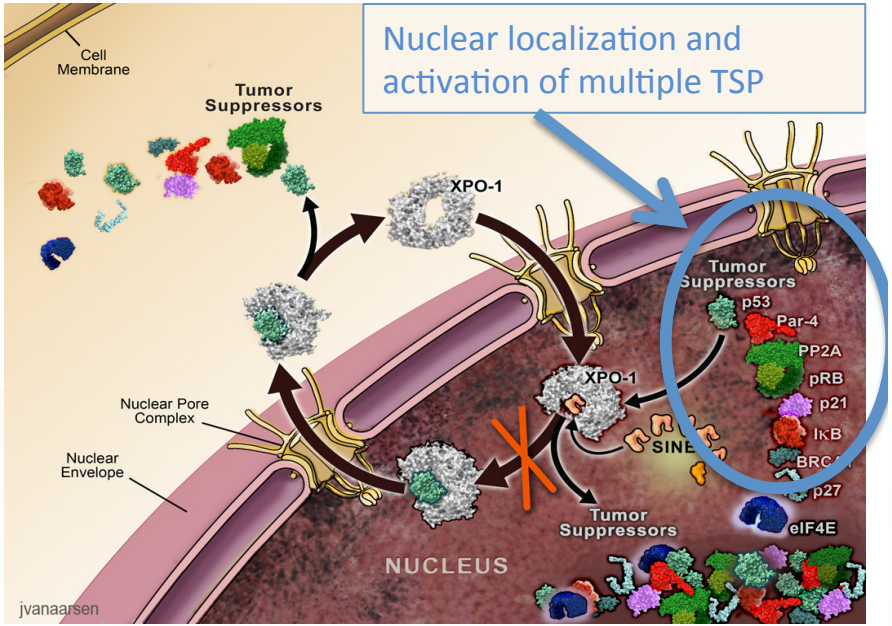
Most responders had a response after 2 cycles; median time to first response was 41.0 days (range: 35–247)
Mean Lonca cycles: 4.5 (Std: ± 3.89) (Min, max: 1, 18)*



- **15 patients** received CD19-directed CAR-T therapy with an investigator-assessed ORR of 46.7% (6 CR; 1 PR)
- **9 patients** proceeded to SCT as consolidation after Lonca response

Caimi PF, et al. *Blood.* 2020;136(Suppl 1):35-37.

New Treatment Strategies for R/R DLBCL
Selective Nuclear Export Inhibitors



Selective Nuclear Export Inhibitors (SINE) or exportin inhibitors block the exit of proteins from the nucleus

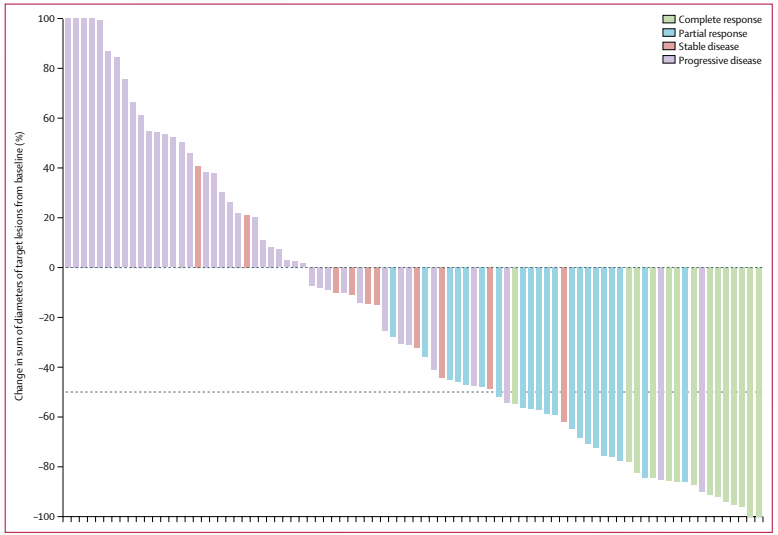
Forces retention of tumor suppressors: p53, p21 in the nucleus

Reduces the entry oncogenes: Myc, Bcl2, Bcl6 into the nucleus

New Treatment Strategies for R/R DLBCL
Selective Nuclear Export Inhibitors

Selinexor given 60 mg PO days 1 and 3 each week
Responses seen regardless of subtype
Median duration of response 9.3 months

	Grade 1–2	Grade 3	Grade 4
Thrombocytopenia	20 (16%)	39 (31%)	19 (15%)
Nausea	66 (52%)	8 (6%)	0
Fatigue	46 (36%)	14 (11%)	0
Anaemia	26 (21%)	27 (21%)	1 (1%)
Decreased appetite	42 (33%)	5 (4%)	0
Diarrhoea	41 (32%)	4 (3%)	0
Constipation	39 (31%)	0	0
Neutropenia	7 (6%)	20 (16%)	11 (9%)
Weight loss	38 (30%)	0	0
Vomiting	35 (28%)	2 (2%)	0
Pyrexia	23 (18%)	5 (4%)	0
Asthenia	21 (17%)	6 (5%)	0
Cough	23 (18%)	0	0
Upper respiratory tract infection	18 (14%)	1 (1%)	0
Dizziness	18 (14%)	0	0
Hypotension	13 (10%)	4 (3%)	0
Oedema peripheral	14 (11%)	1 (1%)	0
Dyspnoea	12 (10%)	1 (1%)	1 (1%)
Hyponatraemia	4 (3%)	10 (8%)	0



	Overall response rate	Complete response	Partial response	Stable disease	Progressive disease or no response recorded
All patients	36/127 (28%) (20·7–37·0)	15 (12%) (6·8–18·7)	21 (17%) (10·5–24·2)	11 (9%) (4·4–15·0)	80 (63%) (54·0–71·4)
GCB subtype	20/59 (34%) (22·1–47·4)	8 (14%) (6·0–25·0)	12 (20%) (11·0–32·8)	7 (12%) (4·9–22·9)	32 (54%) (40·8–67·3)
Non-GCB subtype	13/63 (21%) (11·5–32·7)	6 (10%) (3·6–19·6)	7 (11%) (4·6–21·6)	3 (5%) (1·0–13·3)	47 (75%) (62·1–84·7)
Unclassified	3/5 (60%) (14·7–94·7)	1 (20%) (0·5–71·6)	2 (40%) (5·3–85·3)	1 (20%) (0·5–71·6)	1 (20%) (0·5–71·6)

Data are n/N (%; 95% CI). Responses were adjudicated according to central imaging assessment. GCB=germinal centre B cell. See results section in main text for one-sided 97·5% CI.

Table 2: **Responses in evaluable patients**

Kalakonda N, et al. *Lancet Hematol*. 2020;7(7):e511-e522.

Trying to Convert PR to CR After CAR-T

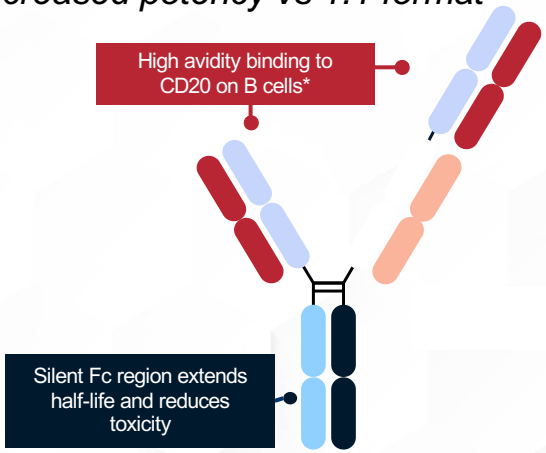
Case 4

- A 42-year-old patient was diagnosed with high-grade DLBCL PTLD following kidney transplant. He was treated with R-EPOCH and obtained a complete remission
- Three months after completion of therapy he was found to have relapse of disease. He was eligible for CAR-T and received Liso-cel
- At his 30 day scan he was found to have a partial response
- What strategies can we use to convert this PR to a CR?

Fixed-course Glofitamab in Relapsed/Refractory DLBCL: Study Updates

- **Glofitamab**
  - Redirects T cells to eliminate B cells
  - Off-the-shelf treatment, administered for a fixed duration of up to 12 cycles
- **Phase I/II experience (NCT03075696)**
  - Glofitamab has induced frequent and durable complete responses (CRs) and demonstrated a manageable safety profile in patients with R/R LBCL and other B-cell NHL subtypes

Glofitamab: *CD20xCD3 bispecific antibody with 2:1 format for increased potency vs 1:1 format*



Hutchings M, et al. Presented at: ASH;2022. Abstract 441.

Study Design and Baseline Characteristics

- **Study Design**
- Glofitamab IV administration fixed dose (0.6–25mg) or with step-up dosing during C1 (target dose: 16mg or 30mg) every three weeks, maximum 13 infusions
- Obinutuzumab pretreatment (1 x 1000mg) to mitigate CRS
- Fixed duration treatment maximum 12 cycles (8.3 months)
- Optional re-treatment in patients with PD after prior response

Baseline Characteristics	N=154
Median age (range)	66 (21-90)
Median prior tx (range)	3 (2-7)
Prior ASCT	28 (18%)
Prior CAR	51 (33%)
Refractory to last tx	132 (86%)

Hutchings M, et al. Presented at: ASH;2022. Abstract 441.

Phase 2 Study Update for Glofitamab in R/R DLBCL

Most common adverse events

CRS: 63% (grade 3-4: 4%)

ICANS: 8% (grade 3-4: 3%)

Neutropenia: 38%

Tumor flare grade ≥2: 7%

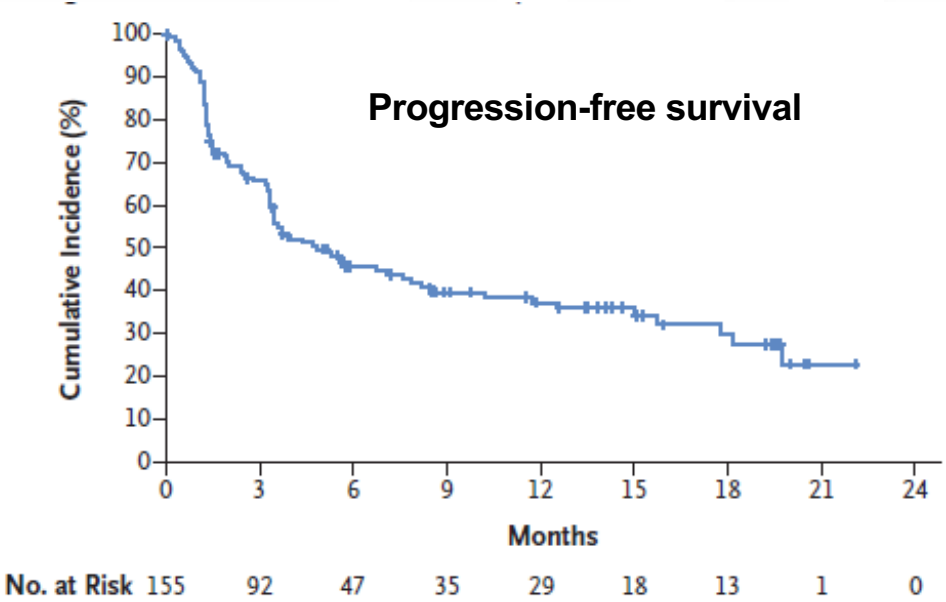
Best IRC-assessed overall response

ORR: 52%

CR: 39%

Median DoR: 18.4 mo

Median DoCR: NR, 24m DoCR 79%

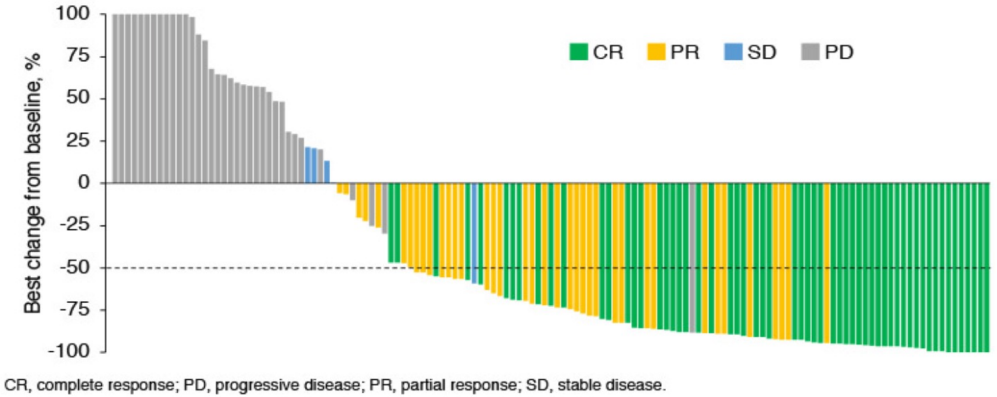


Median 4.9 months

Dickinson MJ, et al. Accessed May 17, 2023. https://www.nejm.org/doi/10.1056/NEJMoa2206913.

Epcoritamab - Subcutaneous

- SC CD3/CD20 bispecific
- Phase 2 EPCORE NHL-1 study
- N=157 DLBCL, FL3B, PMBCL
- Priming and intermediate doses followed by full doses of 48 mg
- QW C1-3, Q2W C4-9, Q4W C>9



CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.

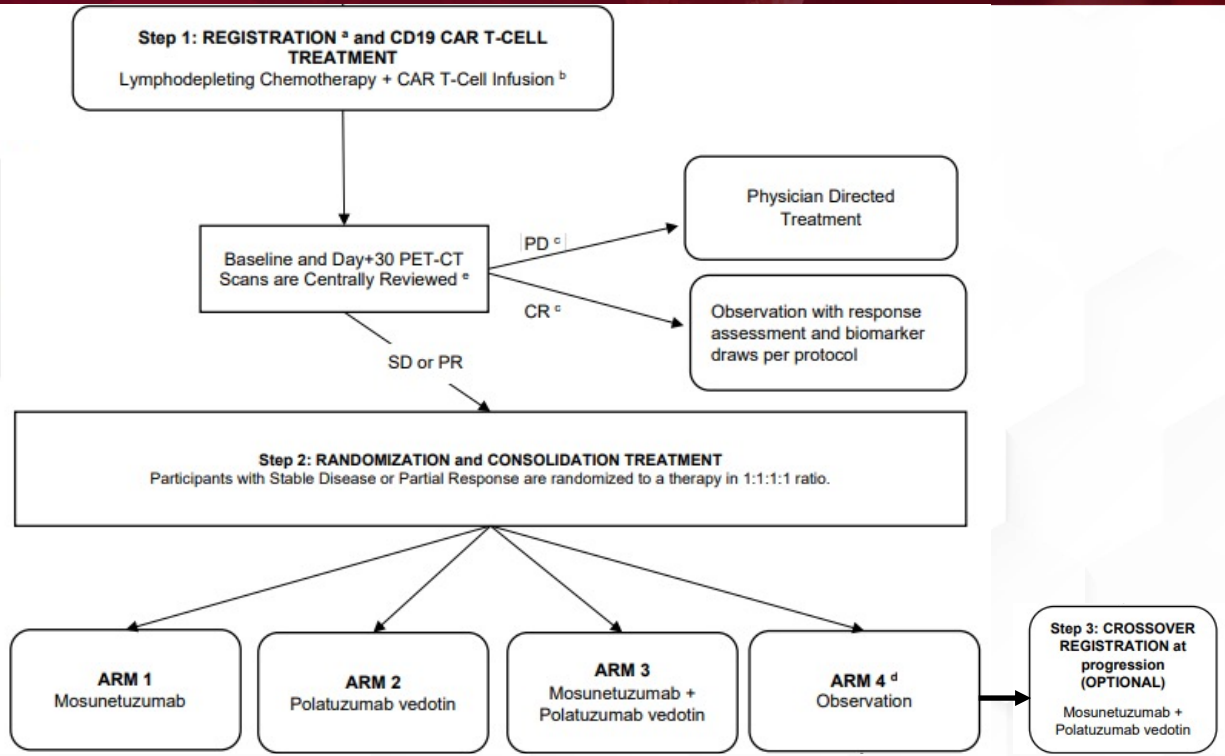
- N=61 had prior CAR TN=31 prior ASCT
- 61% Primary Refractory
- ORR 63%
- CR 39%
- mDOR 12 m
- mCR DOR not reached

- AEs: CRS 49.7% (only 2.5% G3), pyrexia 23.6%, fatigue 22.9%, neutropenia 21.7%, diarrhea 20.4%, ICANS 6.4%
- CRS mainly occurred C1D15 (20 h after first full dose)

Thieblemont C, et al. Presented at: EHA;2022. Abstract LB2364.

SWOG 2114

Participants with Relapsed/Refractory Large B-Cell Lymphoma or Grade IIIB Follicular Lymphoma

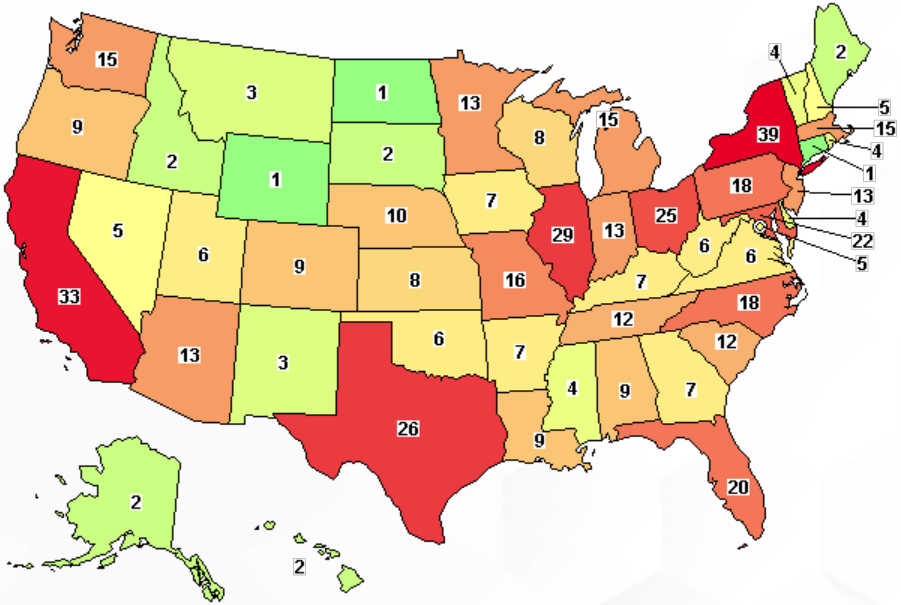


NCT05633615. Updated March 15, 2023. Accessed April 3, 2023. https://clinicaltrials.gov/ct2/show/NCT05633615.

Non-CAR-T Treatment Strategy
Decision Factors

- Bridging to ASCT?
  - Consider chemotherapy containing regimen: PolaR-ICE
- Consider CAR-T in future?
  - Perhaps avoid CD19 targeting agents
- Relapse after CAR-T?
  - Consider targeted agents, polatuzumab vedotin+benda, bispecifics
- Not a candidate for CAR-T or ASCT?
  - Avoid chemo containing regimens, consider tafa+len, lonca-T, bispecifics
- GCB vs ABC?
  - Consider drugs specifically targeting biology: lenalidomide or BTK vs epigenetic

ClinicalTrials.gov
A service of the U.S. National Institutes of Health



Clinical trials are a tool to get the most ground-breaking scientific advances to patients

Thank You!

Contact: Jennifer Amengual
jea2149@columbia.edu

Q&A Session