Southeastern Multidisciplinary Approaches to Cancer Symposium

Updates in Lymphoma

Beyond Chemoimmunotherapy: Navigating the Next Generation of Lymphoma Therapeutics

Clinical Insights, Emerging Trial Data, and Paradigm Shifts

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Disclosures

I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

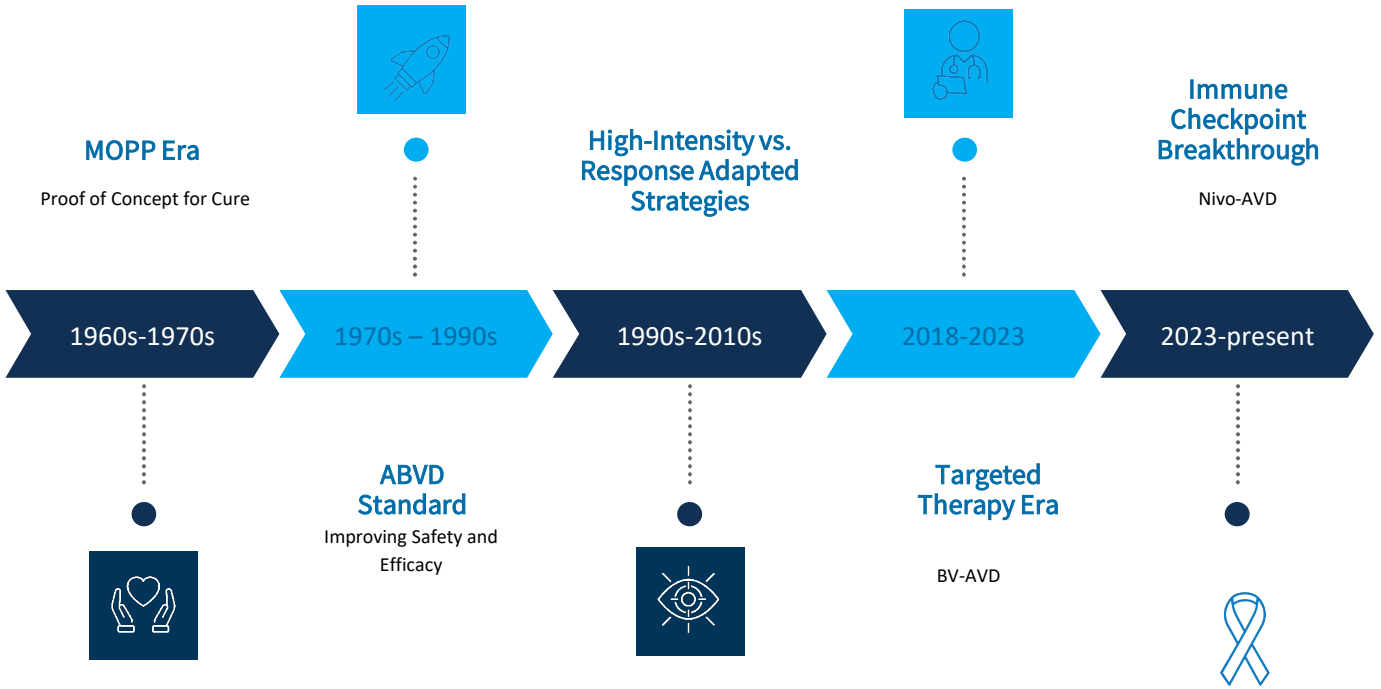
STATE LAW:
The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:
Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

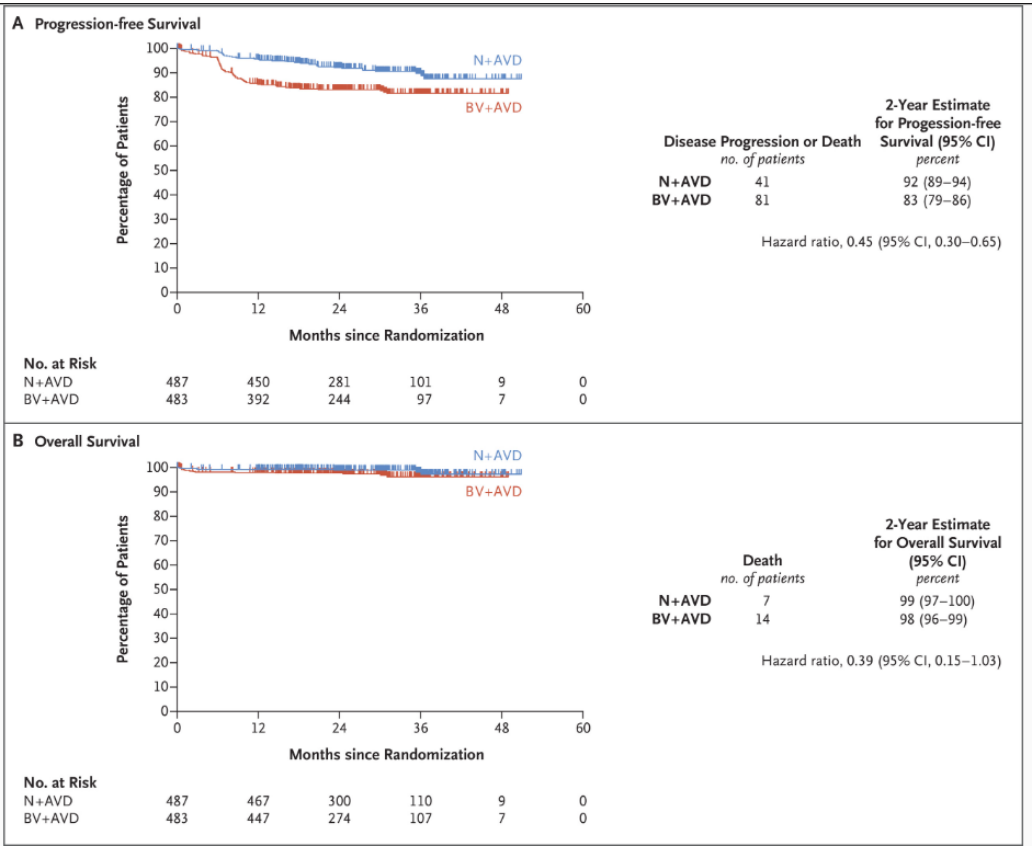
This presentation is dedicated solely to research or other issues that do not contain a direct patient care component.

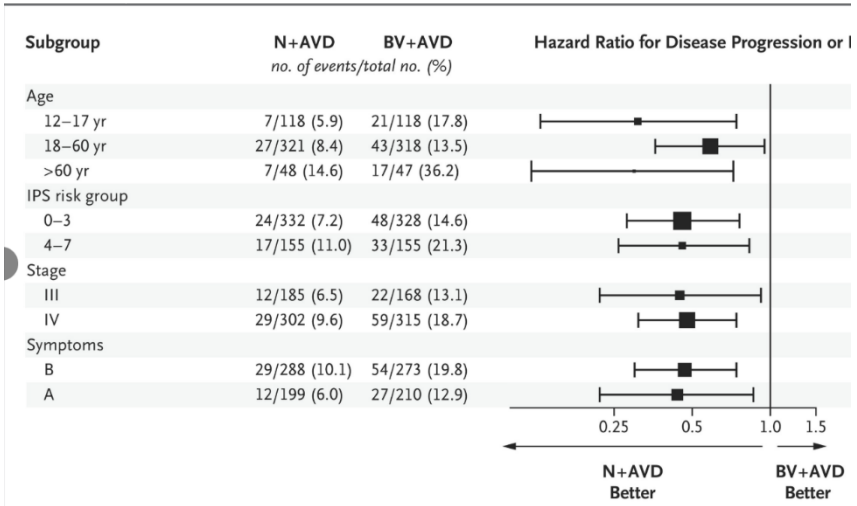
Evolution of Hodgkin Lymphoma Therapy



1. Frontline Advanced Hodgkin Lymphoma

Trial Design: Randomized Phase III N-AVD vs BV-AVD





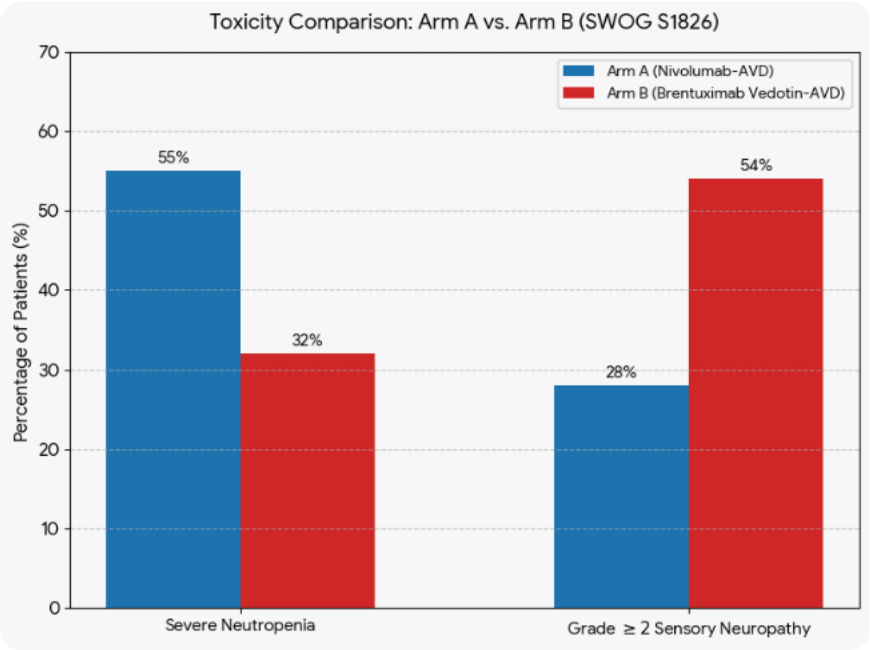
S1826 Patient Populations:

Population		
HIV+	Goyal et al JCO Onc Adv 2026	2Y F/U PFS 77.9% vs. 75% OS 85.7% vs 75%
>60 yr.	Rutherford et al JCO 2025	2Y F/U PFS 89% vs 64% OS 96% vs 85%
12-17y.o.	Castellino et al JCO 2026	3Y F/U PFS 93% vs 82%

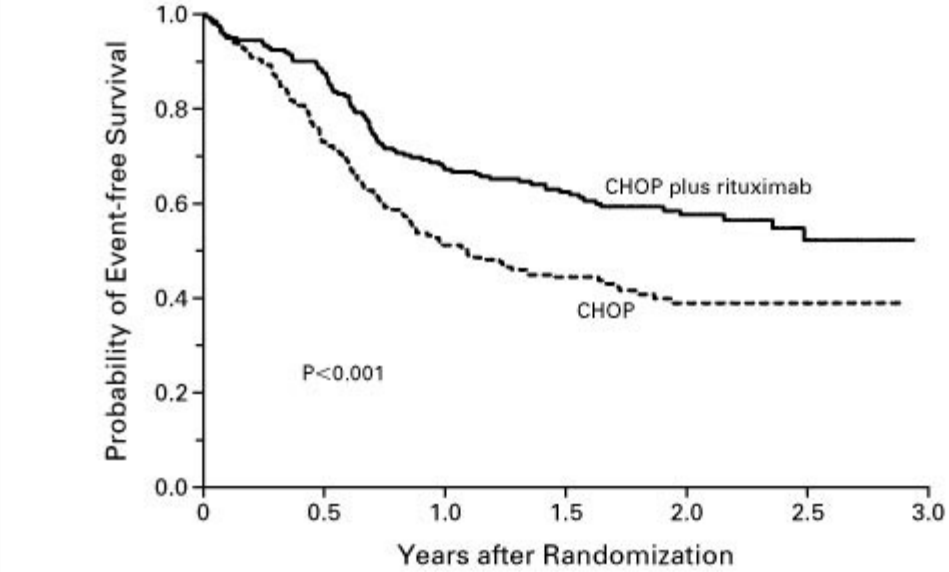
2. Frontline Advanced Hodgkin Lymphoma

S1826: Unprecedented 3-Year PFS and Reduced Neuropathy

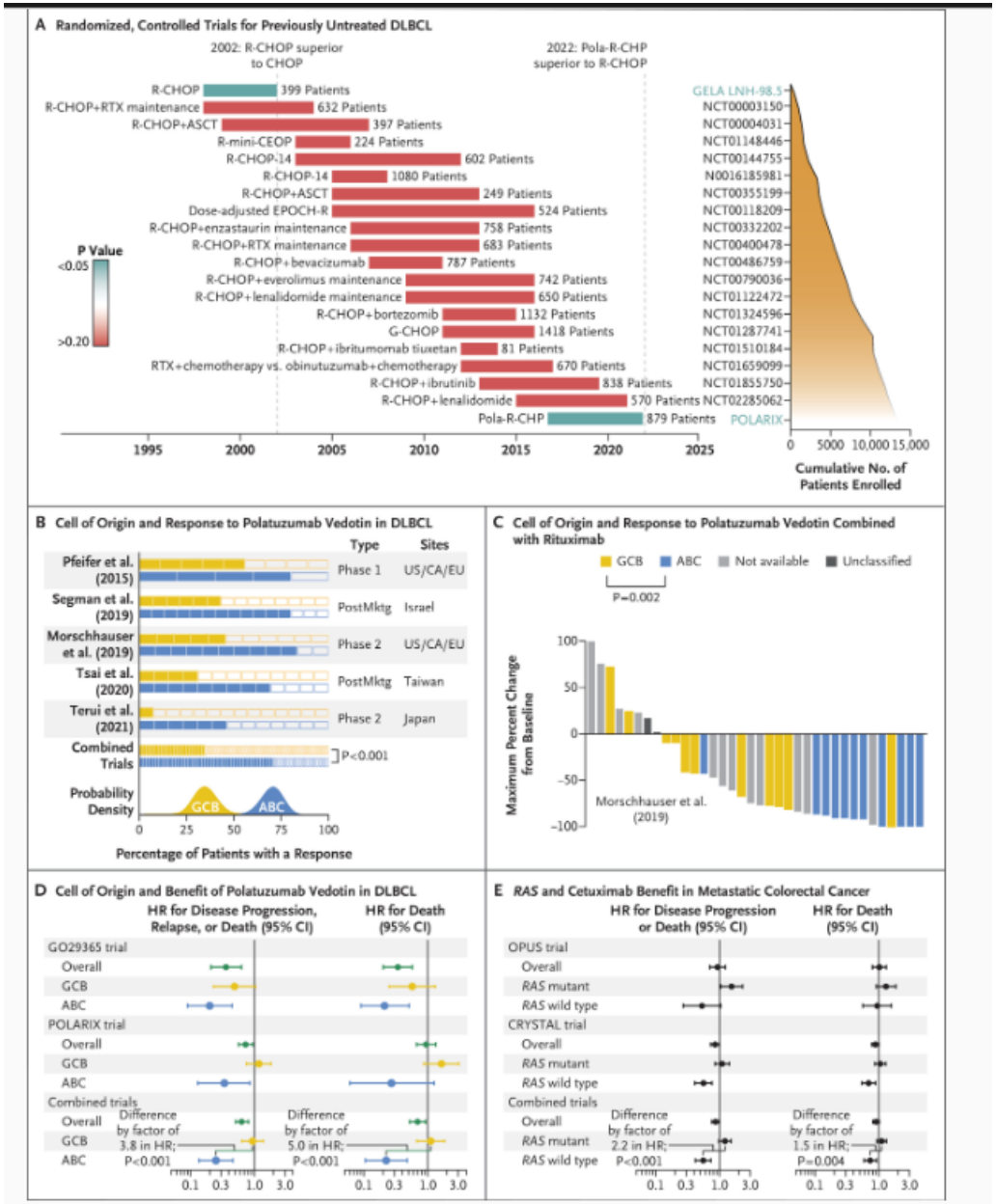
- **3-Year Follow-Up PFS: 93%** (N-AVD) vs. **82%** (BV-AVD)
- **Hazard Ratio (HR):** High statistical significance favoring the immunotherapy-forward arm.
- **Sensory Neuropathy (Grade ≥ 2):** Cut in half: **7%** (N-AVD) vs. **14%** (BV-AVD)

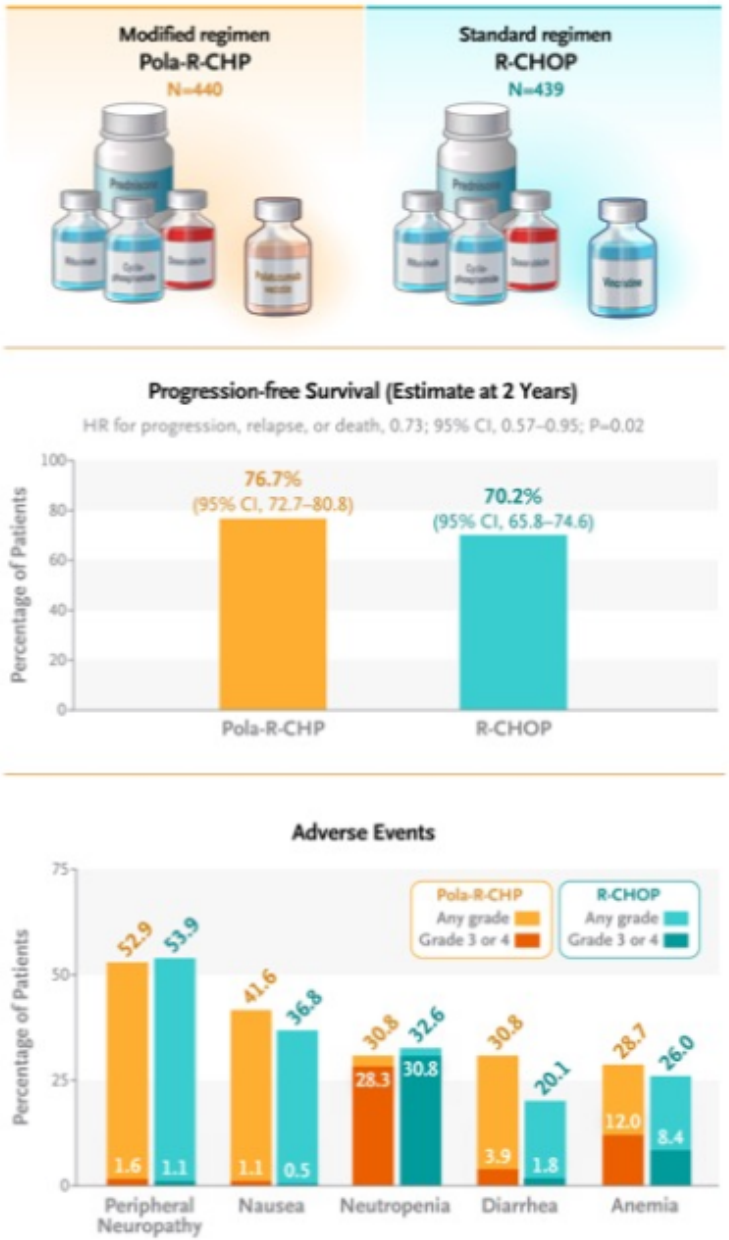


2002 --RCHOP became the standard of care for front-line



No. at Risk						
CHOP plus rituximab	202	177	137	108	63	19
CHOP	197	144	101	72	42	17

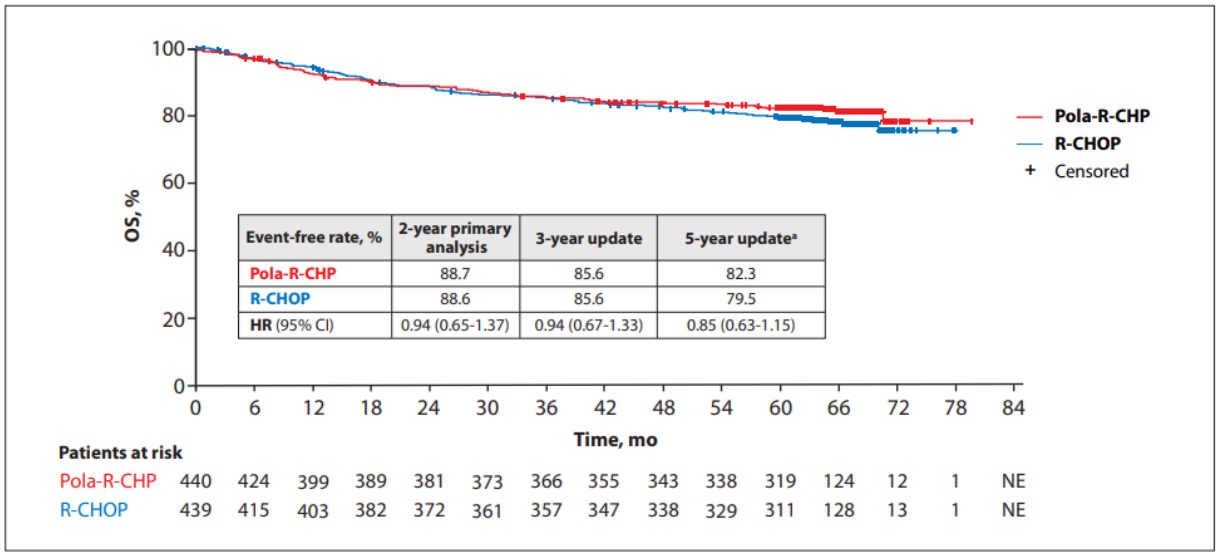

A Randomized, Controlled Trials for Previously Untreated DLBCL
2002: R-CHOP superior to CHOP
2022: Pola-R-CHP superior to R-CHOP
R-CHOP 399 Patients
R-CHOP+RTX maintenance 632 Patients
R-CHOP+ASCT 397 Patients
R-mini-CEOP 224 Patients
R-CHOP-14 602 Patients
R-CHOP-14 1080 Patients
R-CHOP+ASCT 249 Patients
Dose-adjusted EPOCH-R 524 Patients
R-CHOP+enzastaurin maintenance 758 Patients
R-CHOP+RTX maintenance 683 Patients
R-CHOP+bevacizumab 787 Patients
R-CHOP+everolimus maintenance 742 Patients
R-CHOP+lenalidomide maintenance 650 Patients
R-CHOP+bortezomib 1132 Patients
G-CHOP 1418 Patients
R-CHOP+ibritumomab tiuxetan 81 Patients
RTX+chemotherapy vs. obinutuzumab+chemotherapy 670 Patients
R-CHOP+ibrutinib 838 Patients
R-CHOP+lenalidomide 570 Patients
Pola-R-CHP 879 Patients
GELA LNH-98.5
NCT00003150
NCT00004031
NCT01148446
NCT00144755
N0016185981
NCT00355199
NCT00118209
NCT00332202
NCT00400478
NCT00486759
NCT00790036
NCT01122472
NCT01324596
NCT01287741
NCT01510184
NCT01659099
NCT01855750
NCT02285062
POLARIX
P Value
<0.05
>0.20
1995 2000 2005 2010 2015 2020 2025
0 5000 10,000 15,000
Cumulative No. of Patients Enrolled
B Cell of Origin and Response to Polatuzumab Vedotin in DLBCL
Type Sites
Pfeifer et al. (2015) Phase 1 US/CA/EU
Segman et al. (2019) PostMktg Israel
Morschhauser et al. (2019) Phase 2 US/CA/EU
Tsai et al. (2020) PostMktg Taiwan
Terui et al. (2021) Phase 2 Japan
Combined Trials P<0.001
Probability Density
GCB
ABC
0 25 50 75 100
Percentage of Patients with a Response
C Cell of Origin and Response to Polatuzumab Vedotin Combined with Rituximab
GCB ABC Not available Unclassified
P=0.002
Maximum Percent Change from Baseline
100 50 0 −50 −100
Morschhauser et al. (2019)
D Cell of Origin and Benefit of Polatuzumab Vedotin in DLBCL
HR for Disease Progression, Relapse, or Death (95% CI)
HR for Death (95% CI)
GO29365 trial
Overall
GCB
ABC
POLARIX trial
Overall
GCB
ABC
Combined trials
Overall
GCB
ABC
Difference by factor of 3.8 in HR; P<0.001
Difference by factor of 5.0 in HR; P<0.001
0.1 0.3 1.0 3.0
E RAS and Cetuximab Benefit in Metastatic Colorectal Cancer
HR for Disease Progression or Death (95% CI)
HR for Death (95% CI)
OPUS trial
Overall
RAS mutant
RAS wild type
CRYSTAL trial
Overall
RAS mutant
RAS wild type
Combined trials
Overall
RAS mutant
RAS wild type
Difference by factor of 2.2 in HR; P<0.001
Difference by factor of 1.5 in HR; P=0.004
0.1 0.3 1.0 3.0


Modified regimen
Pola-R-CHP
N=440
Standard regimen
R-CHOP
N=439
Progression-free Survival (Estimate at 2 Years)
HR for progression, relapse, or death, 0.73; 95% CI, 0.57–0.95; P=0.02
Percentage of Patients
100 80 60 40 20 0
76.7%
(95% CI, 72.7–80.8)
70.2%
(95% CI, 65.8–74.6)
Pola-R-CHP
R-CHOP
Adverse Events
Pola-R-CHP
Any grade
Grade 3 or 4
R-CHOP
Any grade
Grade 3 or 4
Percentage of Patients
75 50 25 0
52.9 53.9
41.6 36.8
30.8 32.6
30.8 20.1
28.7 26.0
1.6 1.1
1.1 0.5
28.3 30.8
3.9 1.8
12.0 8.4
Peripheral Neuropathy
Nausea
Neutropenia
Diarrhea
Anemia

5-year followup POLARIX

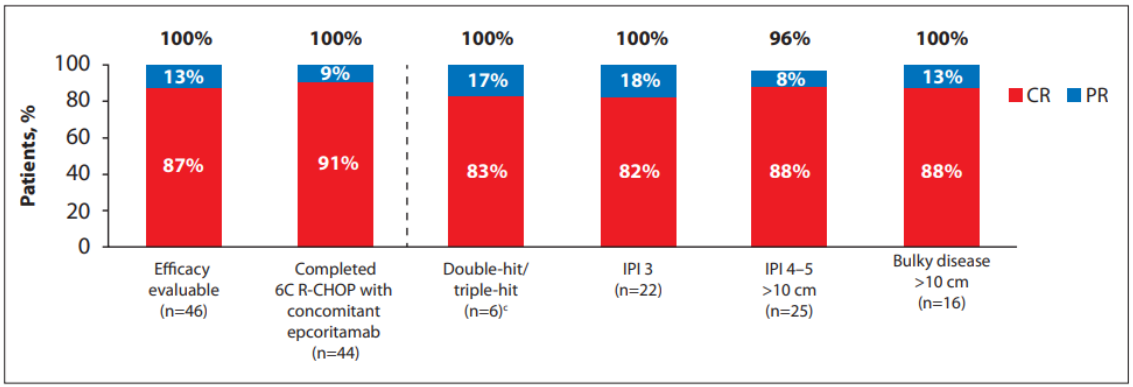
Improvement in PFS over RCHOP persisted at 5 years with PFS of 64.9% vs 59.1%

OS at 5 years 82.3% vs 79.5%



Event-free rate, %	2-year primary analysis	3-year update	5-year update[a]
Pola-R-CHP	88.7	85.6	82.3
R-CHOP	88.6	85.6	79.5
HR (95% CI)	0.94 (0.65-1.37)	0.94 (0.67-1.33)	0.85 (0.63-1.15)

Fixed-Duration Epicoritamab + RCHOP for newly diagnosed DLBCL



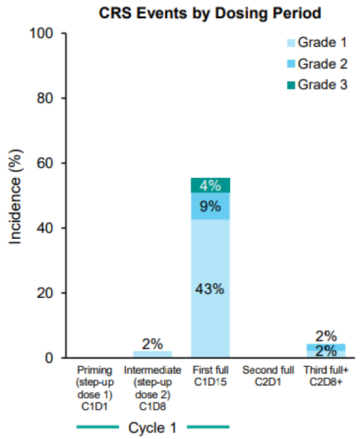
- **Arm 1 EPCORE NHL-2 trial**
- **Long-term results median F/U 27.4 months**
- **47 subjects, IPI 3+**
- **Epcoritamab weekly C1-4, q3w C5-6, and monthly for up to 1 year.**
- **MRD negativity attained in 91% of evaluable patients (83% by D1/C3)**
- **CR durable in 94% of patients who completed treatment**

EPCORE NHL-2 Arm 1

- **Most frequent grade 3/4 TEAE were hematologic**
- **CRS developed in 60% of patients overall but was primarily grade 1/2**
- **4% with grade 3 CRS**
- **ICANS 4% (was grade 1 or 2)**

CRS and ICANS Mostly Low Grade

CRS	N=47
CRS, n (%)[a]	28 (60)
Grade 1	21 (45)
Grade 2	5 (11)
Grade 3	2 (4)
CRS resolution, n/n (%)	28/28 (100)
Median time to CRS onset from first full dose, d (range)	2 (1–7)
Median time to CRS resolution, d (range)[b]	2 (1–11)
Treated with tocilizumab for CRS, n (%)	5 (11)
CRS leading to treatment discontinuation, n (%)	0
ICANS	**N=47**
ICANS, n (%)[a,c]	2 (4)
Grade 1	1 (2)
Grade 2	1 (2)
ICANS resolution, n/n (%)	2/2 (100)
Median time to ICANS resolution, d (range)[b]	2.5 (1–4)
ICANS leading to treatment discontinuation, n (%)	0

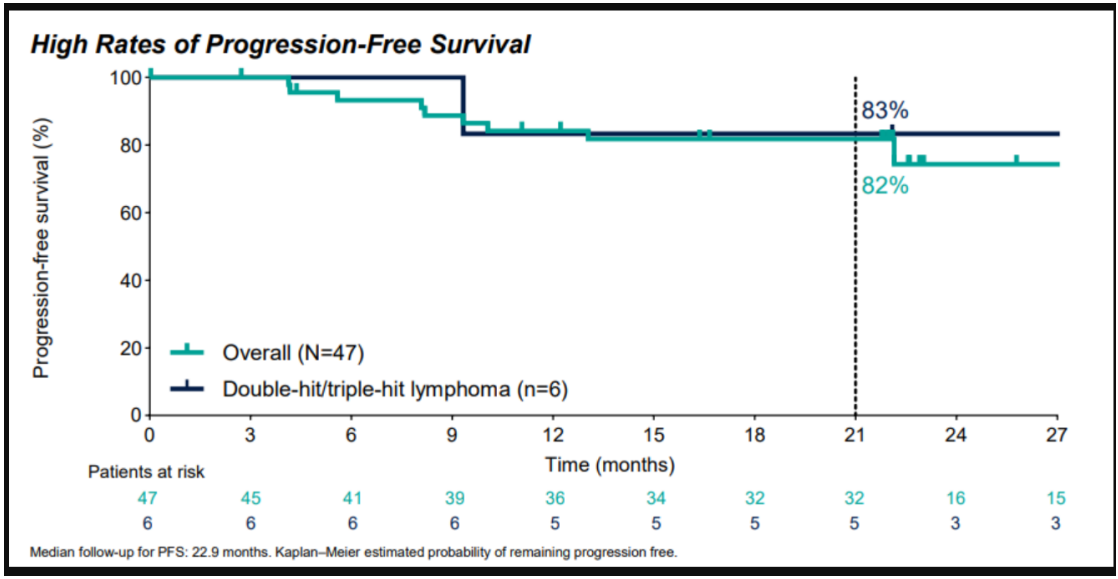


[a]Graded by Lee et al 2019 criteria. [b]Median is based on longest event duration in patients with >1 event. [c]Signs and symptoms included confusional state, disorientation, and dysmetria.

EPCORE NHL-2 Arm 1

24M OS rate was 87% overall and 83% in patients with DHL or THL.

After 21M, PFS was 82%



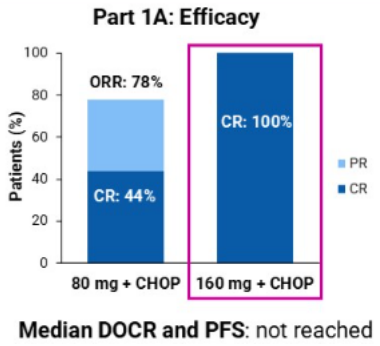
3. Bispecific T-Cell Engagers (BiTEs) in Frontline DLBCL

Frontline Bispecifics: The Phase III OLYMPIA-3 Trial odronextamab/CHOP.
Part 1B results (dose optimization) ASCO 2026

Efficacy Metrics: 85% Complete Response (CR) rate across optimized cohorts; **6-month event-free probability is 90.0%**. Median PFS not yet reached. Complete response (CR) rates are **upwards of 80% so far**, disrupting historic benchmarks set by traditional R-CHOP.

Cytokine Release Syndrome (CRS): High incidence (33%–77%) but **strictly Grade 1 or 2** via step-up dosing; 0% Grade ≥ 3 CRS.

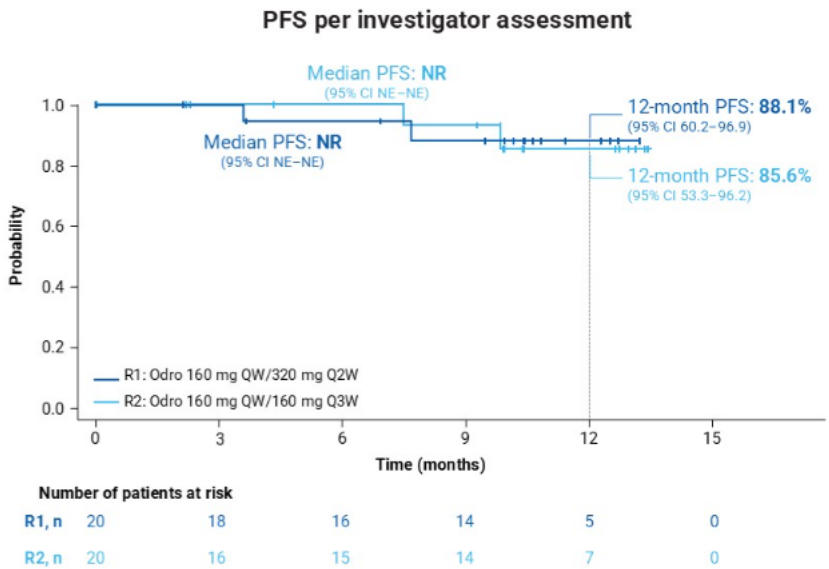
Infection Profile: Grade ≥ 3 infections noted in 22% to 62%. High rate of low-grade opportunistic reactivations.



Median DOCR and PFS: not reached

Key eligibility criteria:

- Previously untreated CD20+ DLBCL NOS or HGBL[1]
- ECOG PS ≤2
- ≥1 high-risk feature, including:
  - IPI score 3–5
  - Non-GCB COO (IPI ≥2)
  - *MYC*, *BCL-2*, and/or *BCL-6* rearrangements (IPI ≥2)

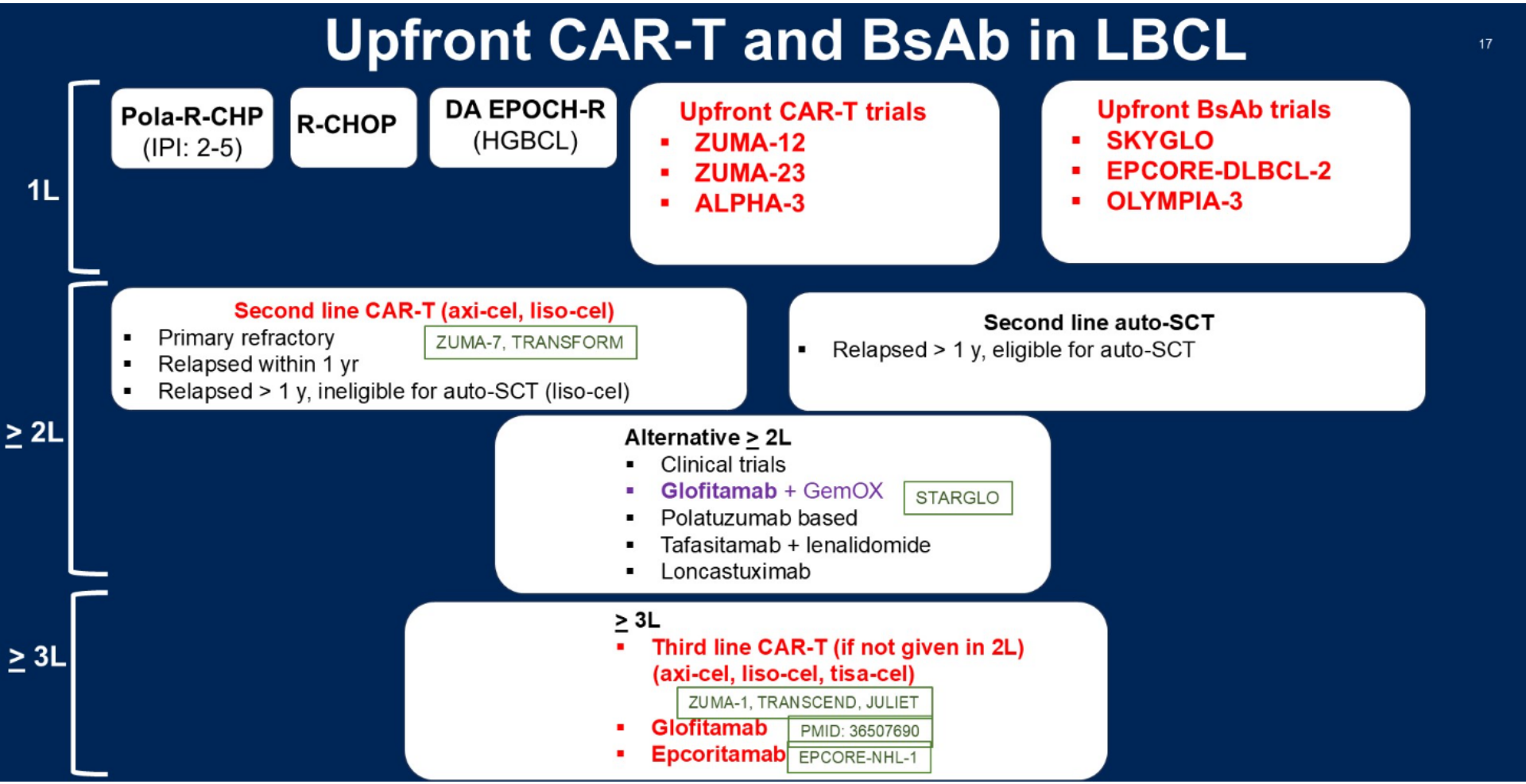


4. OLYMPIA-3 – Efficacy and Safety Profile

- **Efficacy Metrics: 85% Complete Response (CR) rate** across optimized cohorts; **6-month event-free probability is 90.0%**. Median PFS not yet reached.
- **Cytokine Release Syndrome (CRS):** High incidence (33%–77%) but **strictly Grade 1 or 2** via step-up dosing; 0% Grade ≥ 3 CRS.
- **Infection Profile:** Grade ≥ 3 infections noted in 22% to 62%. High rate of low-grade opportunistic reactivations.

Fixed-duration Odro-CHOP in frontline high-risk DLBCL achieved a high CR rate (85%) and a generally manageable safety profile

A Phase 3, randomized study of OLYMPIA-3 is underway to evaluate Odro 160 mg QW/160 mg Q3W + CHOP vs R-CHOP



Ghobadi, ASCO 2025

Upfront Randomized Phase 3 Trials of BsAbs in LBCL

	SKYGLO (NCT06047080)	EPCORE-DLBCL-2 (NCT05578976)	OLYMPIA-3 (NCT06091865)
Phase	III	III	III
Experimental arm	**Glofitamab + Pola-R-CHP**	**Epcoritamab + R-CHOP**	**Odronextamab + CHOP**
Control arm	Pola-R-CHP	R-CHOP	R-CHOP
Population	CD20+ LBCL, age 18-80, IPI ≥2 (excluding grade 3B FL or transformed indolent lymphoma)	CD20+ LBCL (DLBCL, HGBCL, Grade 3B FL, tFL) with IPI ≥2	CD20+ DLBCL, IPI ≥2
Primary endpoint	PFS	PFS	PFS
Target enrollment	1130	900	904

Ghobadi, ASCO 2025

Thank You

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