R-CHOP

FOR UNTREATED DLBCL

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EMORY
WINSHIP
CANCER
INSTITUTE
National Cancer Institute Designated
Comprehensive Cancer Center

NCI
Designated
Comprehensive
Cancer Center

DISCLOSURES

Research funding: Lymphoma Research Foundation (underwritten by Celgene); Oncternal Therapeutics; Viracta Therapeutics; Atara Biotherapeutics

Consulting fees: Janssen / Pharmacyclics; MorphoSys; Gamida Cell; TG Therapeutics

I will be discussing non-FDA approved indications during my presentation.

THE MATCH-UP

- Professor of Hematology and Medical Oncology at Winship
- PI on pivotal trials leading to FDA approval of lenalidomide, ibrutinib, brentuximab vedotin, and idelalisib in lymphoma
- Member of the Alliance Lymphoma Core Committee
- Co-Director of Winship's Lymphoma Program
- On Dr. Koff's career development committee

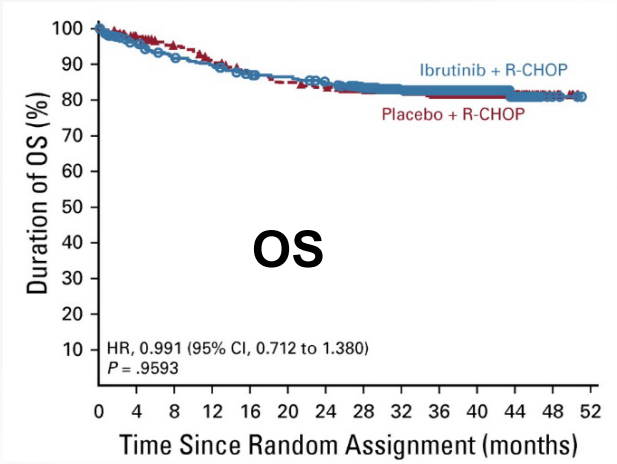
- Assistant Professor of Hematology and Medical Oncology at Winship
- Clinical and translational research focus in B-cell lymphoma
- Just happy to be out of the house at 6 weeks postpartum

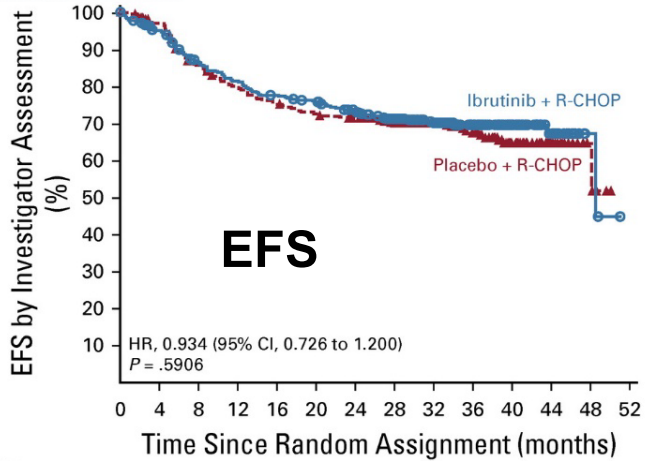
R-CHOP IS THE STANDARD 1L THERAPY IN DLBCL

- ~60% patients with DLBCL will be cured with R-CHOP

- Numerous approaches to improve outcomes with R-CHOP have **failed**:
  - Intensification of chemotherapy or rituximab
  - Addition of maintenance
  - Use of 2nd-gen anti-CD20
  - Incorporation of novel agents

E.g., PHOENIX:
R-CHOP ± ibrutinib in non-GCB DLBCL





POP QUIZ!

A randomized phase 3 trial recently showed PFS benefit in frontline DLBCL treatment with incorporation of a therapeutic agent *targeting which molecule?*

A. BTK

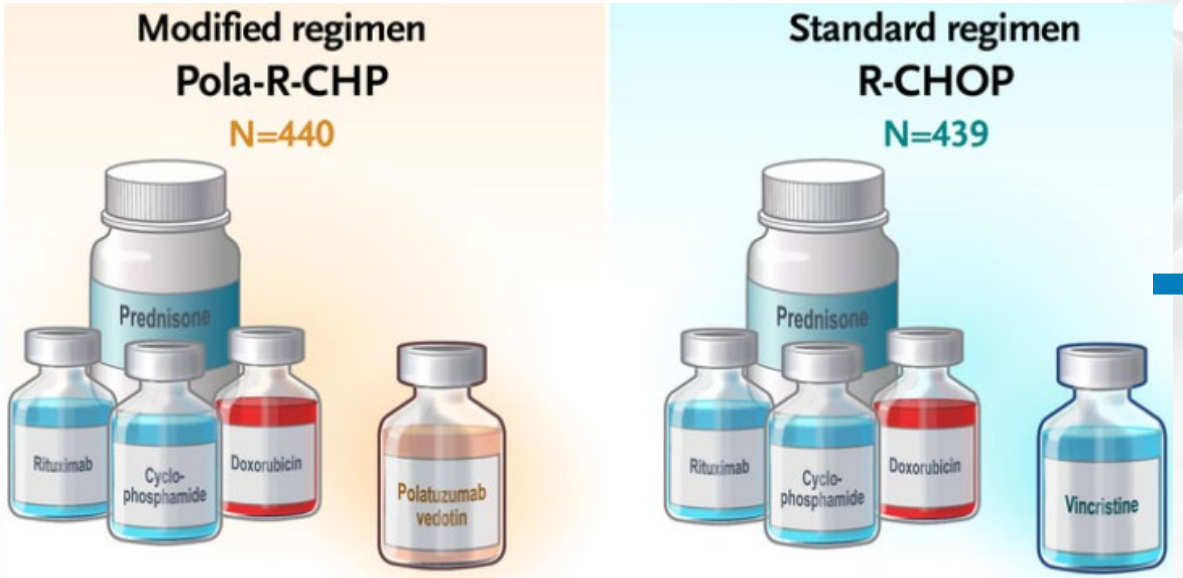
B. CD20

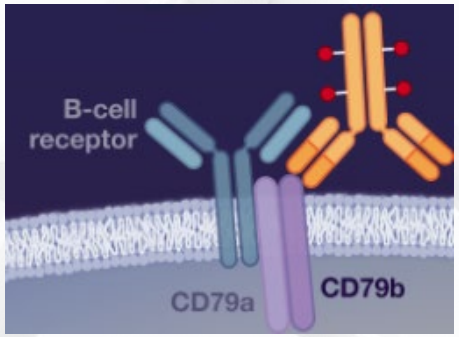
C. CD79b

D. BCL-2

R-CHOP HAS BEEN THE STANDARD 1L THERAPY IN DLBCL… UNTIL NOW?

Concession: The phase 3 trial POLARIX showed improved PFS in intermediate- and high-risk DLBCL patients treated with pola-R-CHP compared to R-CHOP in 1L

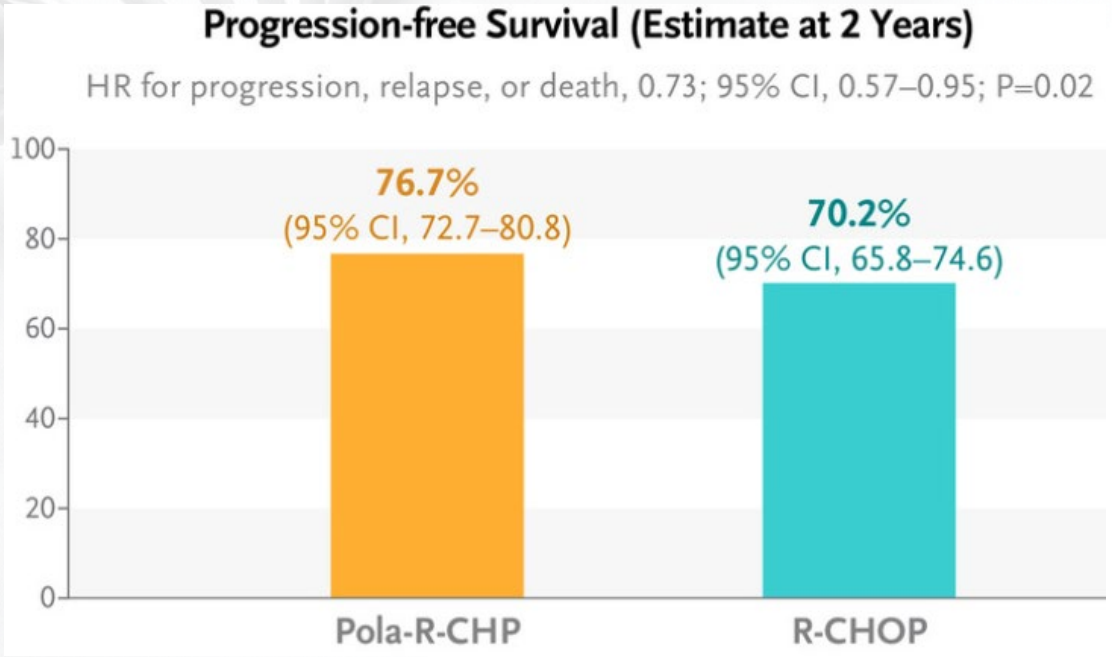




Clinical - International Prognostic Index (IPI)

- Age >60
- Stage III or IV
- Elevated LDH
- Performance status 2 or higher
- Two or more extranodal sites

(IPI 2 – 5 included on POLARIX)



H Tilly et al, *NEJM* 2022.

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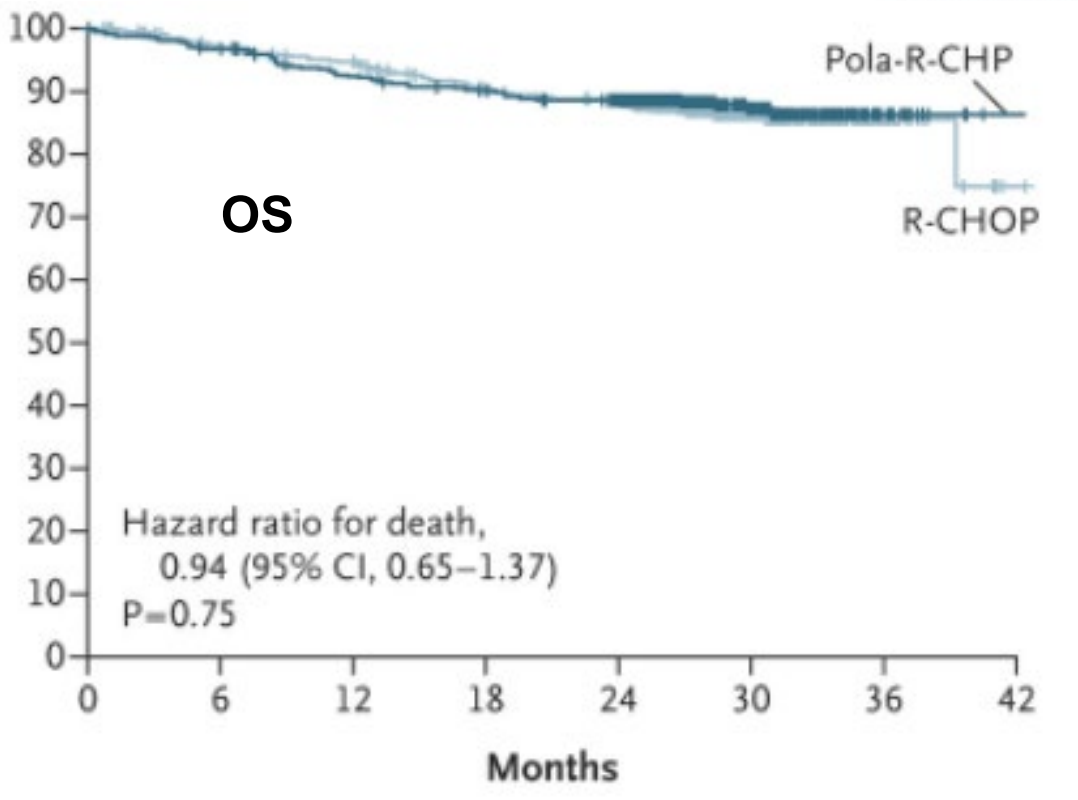
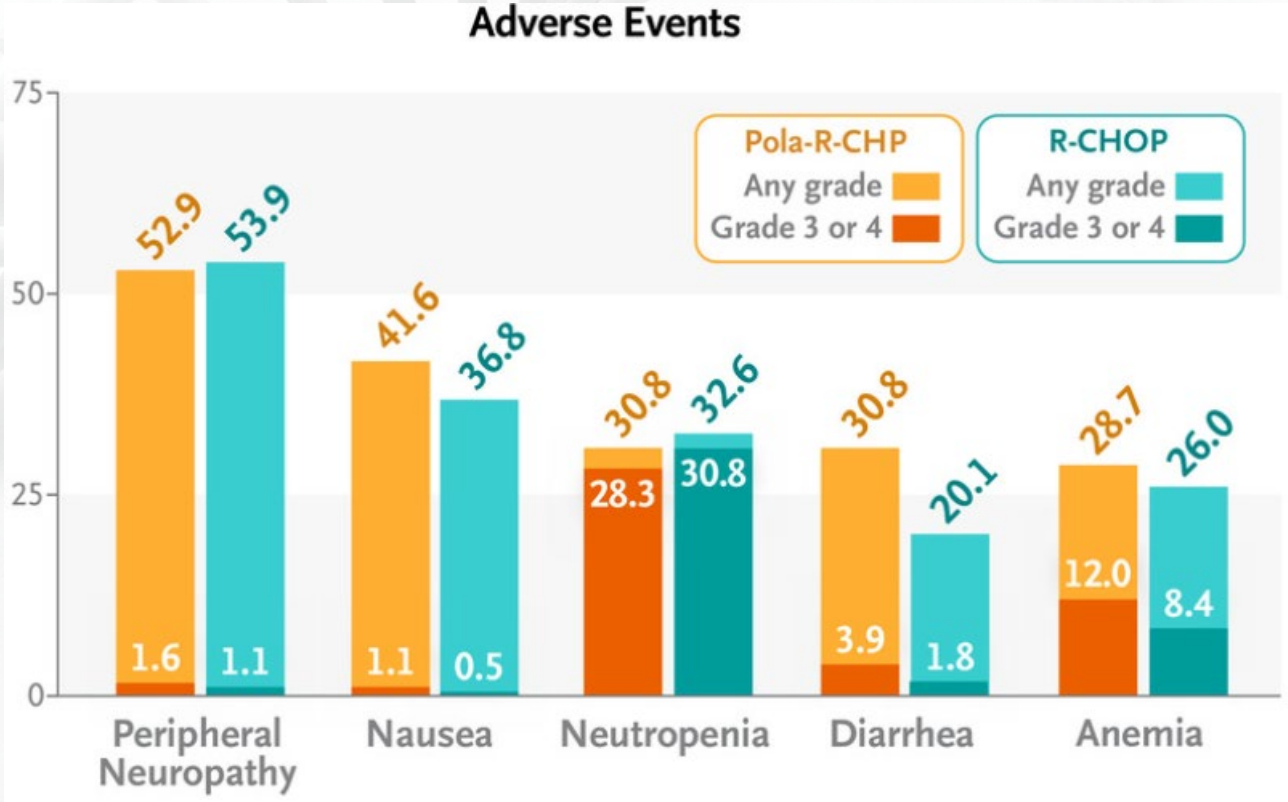
Concession: The phase 3 trial POLARIX showed improved PFS in intermediate- and high-risk DLBCL patients treated with pola-R-CHP compared to R-CHOP in 1L

But…

- PFS is not the only outcome of interest
- Trial population does not reflect **all** DLBCL
- DLBCL treatment often does not end at 1L

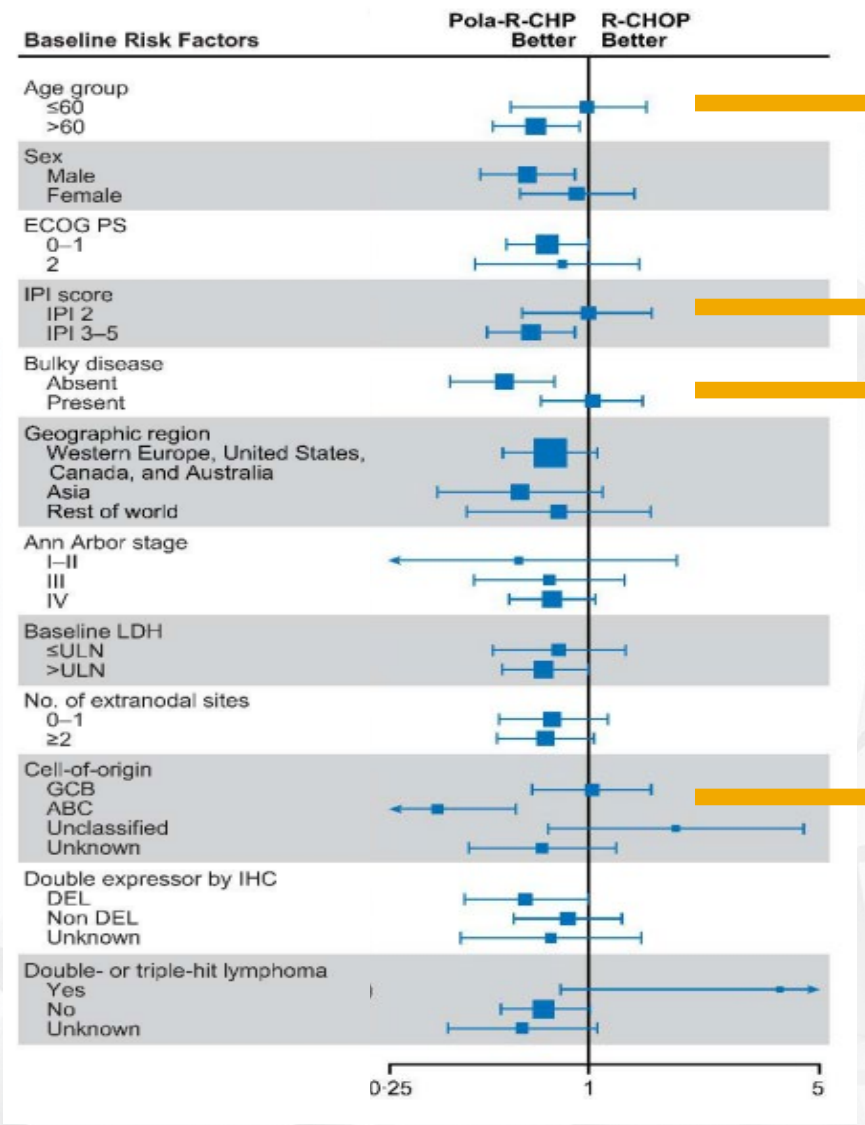
NO IMPROVEMENT IN OVERALL SURVIVAL OR ADVERSE EVENTS WITH POLA-R-CHP





Febrile neutropenia %: 14.3 (13.8) vs. 8 (8)

PFS BENEFIT OF POLA-R-CHP NOT OBSERVED IN ALL SUBGROUPS



Age ≤ 60

IPI 2

Bulky disease

GCB and unclassified subtypes

FINANCIAL COST OF POLATUZUMAB VEDOTIN VS. VINCRISTINE

- Average whole sale price of **pola** over 6 cycles: $112,320

- Average whole sale price of **vincristine** over 6 cycles: $96

KEY POPULATIONS NOT REPRESENTED IN POLARIX

- **IPI 0 – 1**
  - 3 cycles R-CHOP + ISRT vs. 4 cycles R-CHOP[1] = standard of care for non-bulky stage I/II
- **Age >80**
- **History / presence of indolent lymphoma** (e.g., follicular lymphoma)
- **Known CNS involvement**
  - Standard of care = R-CHOP +
    - HD-MTX for parenchymal disease
    - IT chemo for leptomeningeal disease

Characteristic	Pola-R-CHP (N=440)	R-CHOP (N=439)
Median age (range) — yr	65 (19–80)	66 (19–80)
Age category — no. (%)		
≤60 yr	140 (31.8)	131 (29.8)
>60 yr	300 (68.2)	308 (70.2)
Female sex — no. (%)	201 (45.7)	205 (46.7)
Geographic region — no. (%)†		
Western Europe, United States, Canada, and Australi	302 (68.6)	301 (68.6)
Asia	81 (18.4)	79 (18.0)
Rest of world	57 (13.0)	59 (13.4)
Ann Arbor stage — no. (%)‡		
I or II	47 (10.7)	52 (11.8)
III or IV	393 (89.3)	387 (88.2)
No. of extranodal sites — no. (%)		
0 or 1	227 (51.6)	226 (51.5)
≥2	213 (48.4)	213 (48.5)
Bulky disease — no. (%)†§	193 (43.9)	192 (43.7)
ECOG performance status score — no. (%)¶		
0 or 1	374 (85.0)	363 (82.7)
2	66 (15.0)	75 (17.1)

[1]V. Poeschel et al, *Lancet* 2019.

KEY POPULATIONS NOT (WELL) REPRESENTED IN POLARIX

- **Selection bias** towards patients with less aggressive disease?
  - ~16% pts with ECOG PS = 2
  - Average diagnosis-to-treatment interval = 26 days
    - Longer DTI associated with improved EFS24[1]
    - Median DTI = 15 days in non-clinical trial cohort

Given only modest improvement in PFS without OS or AE benefit in POLARIX's included population, extrapolation of findings to patient groups with different disease biology may be premature.

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[1]Maurer MJ et al, *JCO* 2018.

CONSIDERATIONS AFTER 1L TREATMENT

- Pola is a key component of salvage and bridging regimens in 2+L DLBCL.
  - On POLARIX, 8 patients in the R-CHOP group who relapsed received pola as part of subsequent therapy

- *It remains unknown whether patients treated with pola in 1L achieve similar response rates with pola retreatment in later lines*

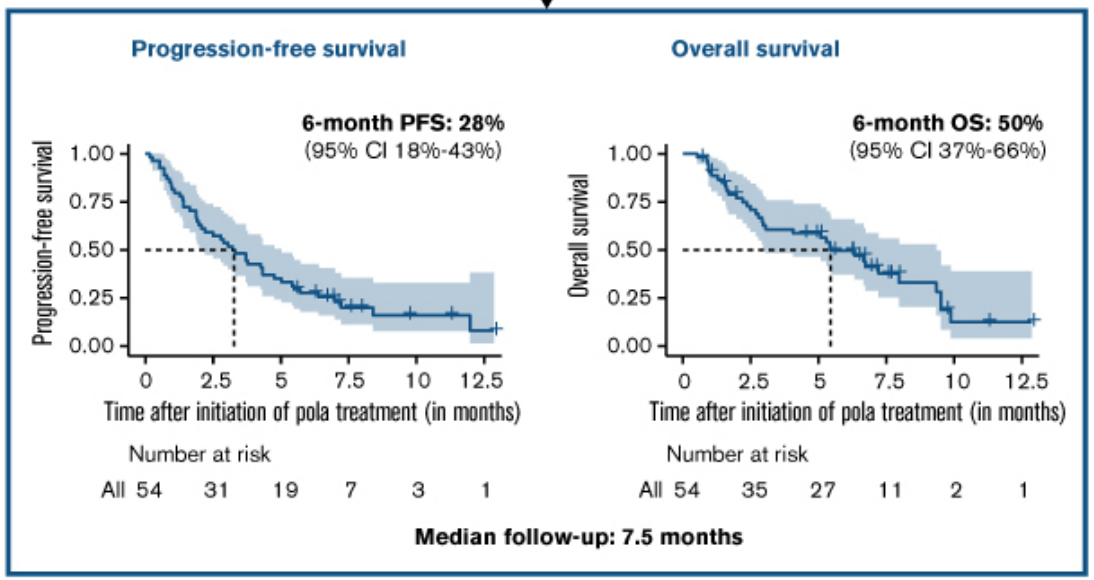
Polatuzumab vedotin (pola) ± BR
n=105
r/r LBCL with ≥ 2 prior treatment lines (CUP)

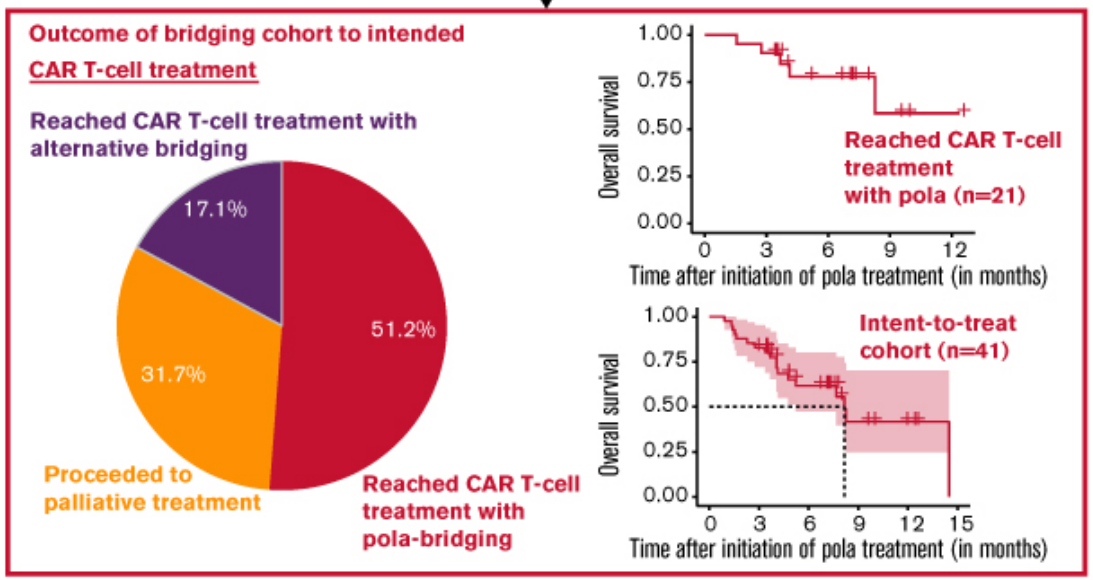
Salvage cohort
n=54

Median Pola cycles:
4

Bridging cohort
n=51
Intended CAR T-cell: n=41
Intended alloHCT: n=10

Median Pola cycles:
2





Liebers L et al, *Blood Advances* 2021.

SELECTED ONGOING CLINICAL TRIALS

- POLAR BEAR: R-Pola-mini-CHP vs. R-mini-CHOP in elderly/frail DLBCL
  - N = 200
  - Primary endpoint: PFS
- COALITION: Glofitamab + R-Pola-CHP vs. + R-CHOP in young, high-risk DLBCL
  - N = 80
  - Primary endpoints: safety, RDI, early chemo discontinuation
- POLARGO: Pola-R-Gem-Ox vs. R-Gem-Ox alone in R/R DLBCL
  - N = 206
  - Primary endpoint: OS
- Pola-R-ICE vs. R-ICE as salvage in R/R DLBCL
  - N = 324
  - Primary endpoint: EFS

Available at Winship

SUMMARY

- **R-CHOP remains a standard of care in 1L treatment of DLBCL**
  - *But pola-R-CHP should be considered for patients with IPI ≥2, especially if:*
    - IPI 3-5
    - Age 60 – 80
    - ABC subtype

- **Additional data is needed** regarding:
  - Safety/efficacy of pola-R-CHP in populations not (well) represented in POLARIX
  - 2+L outcomes in patients who receive pola in 1L