# The Annual
# National General Medical Oncology Summit

## Saturday, March 23, 2024

### Moderator

Neil Love, MD

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**Co-Moderators**

**Susmitha Apuri, MD**
**Mamta Choksi, MD**
**Sunil Gandhi, MD**
**Lowell L Hart, MD**
**Maen Hussein, MD**
**Zanetta S Lamar, MD**
**Vikas Malhotra, MD**

# Overview

## Saturday, March 23rd

**Module 1: 7:30 AM – 9:10 AM —** Hodgkin and Non-Hodgkin Lymphoma

**Module 2: 9:30 AM – 10:20 AM —** Gynecologic Cancers

**Module 3: 10:20 AM – 11:10 AM —** Localized Breast Cancer; SABCS 2023 Review

**Module 4: 11:10 AM – 12:00 PM —** Metastatic HER2-Positive and Triple-Negative Breast Cancer; SABCS 2023 Review

**Module 5: 12:30 PM – 1:20 PM —** Prostate Cancer

**Module 6: 1:20 PM – 2:10 PM —** Urothelial Bladder Cancer

**Module 7: 2:10 PM – 3:00 PM —** Renal Cell Carcinoma

# Overview

**Module 8: 3:20 PM – 4:10 PM —** Targeted Therapy for Non-Small Cell Lung Cancer

**Module 9: 4:10 PM – 5:00 PM —** Nontargeted Treatments for Lung Cancer

**Sunday, March 24th**

**Module 10: 7:30 AM – 8:20 AM —** Multiple Myeloma

**Module 11: 8:20 AM – 9:10 AM —** Gastroesophageal Cancers

**Module 12: 9:30 AM – 10:20 AM —** Hepatobiliary Cancers

**Module 13: 10:20 AM – 11:10 AM —** Colorectal Cancer

**Module 14: 11:10 AM – 12:00 PM —** Pancreatic Cancer

# Disclosures for Moderator Neil Love, MD

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI Biopharma, a Sobi company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Grail Inc, GSK, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Kronos Bio Inc, Legend Biotech, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc, and Zymeworks Inc.

## Commercial Support

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## Research To Practice CME Planning Committee Members, Staff and Reviewers

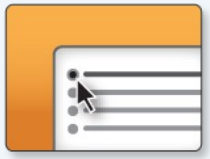
Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

**This program will contain discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.**

# Clinicians in the Meeting Room

**Networked iPads are available.**

**Review Program Slides:** Tap the Program Slides button to review speaker presentations and other program content.



**Answer Survey Questions:** Complete the premeeting survey.


**Ask a Question:** Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

***For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.***

# Clinicians Attending via Zoom

**Review Program Slides:** A link to the program slides will be posted in the chat room at the start of the program.

**Answer Survey Questions:** Complete the pre- and postmeeting surveys.

**Ask a Question:** Submit a challenging case or question for discussion using the Zoom chat room.

**Get CE Credit:** A CE credit link will be provided in the chat room at the conclusion of the program.

***For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.***

# About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from this weekend will be edited and developed into an enduring web-based video/PowerPoint program. An email will be sent to all attendees when the activity is available.

- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

# Overview

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# Third Annual National General Medical Oncology Summit

# Agenda

**Module 1: Follicular Lymphoma (FL) —** Dr Zelenetz

**Module 2: Mantle Cell Lymphoma (MCL) —** Dr Lunning

**Module 3: Hodgkin Lymphoma (HL) —** Dr LaCasce

**Module 4: Diffuse Large B-Cell Lymphoma (DLBCL) —** Dr Maddocks

# Agenda

**Module 1: Follicular Lymphoma (FL) —** Dr Zelenetz

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# Immunotherapy for R/R Follicular Lymphoma

**Andrew D. Zelenetz, M.D., Ph.D.**
Attending Physician, Lymphoma Service
Professor of Medicine, Weill-Cornell Medical College
Chair, NCCN NHL Guideline Panel

# Disclosures

| | |
|---|---|
| **Consulting Agreements** | AbbVie Inc, Adaptive Biotechnologies Corporation, Amgen Inc, AstraZeneca Pharmaceuticals LP, Celgene Corporation, Genentech, a member of the Roche Group, Gilead Sciences Inc, Janssen Biotech Inc, MEI Pharma Inc, MorphoSys, Novartis |
| **Contracted Research** | BeiGene Ltd, Genentech, a member of the Roche Group, MEI Pharma Inc |
| **Data and Safety Monitoring Boards/Committees** | BeiGene Ltd (DMC chair), Bristol Myers Squibb, Celgene Corporation, Juno Therapeutics, a Celgene Company |

# 76-year old man with multiply recurrent follicular lymphoma

- 09/2012: Presented with a sigmoid mass at 28 cm, biopsy demonstrated FL, grade 1-2 ("classical follicular lymphoma"), stage IE (sigmoid)
- 10/24-11/13/2012: Rituximab weekly x 4 with CR
- 10/2015: CT with progressive abdominal nodes, biopsy recurrent FL, active surveillance
- 11/2016: Progressive abdominal pain, PET with area of high grade FDG avid disease, biopsy DLBCL
- 12/19/2016-03/30/2017: R-CHOP x 6 with PET CR
- 08/2019: CT with progressive mesenteric and retroperitoneal nodes, biopsy FL, grade 1-2
- 09/2019-01/2020: Rituximab lenalidomide x 4, < PR
- 01/2020-06/2020: Obinutuzumab-bendamustine with PET CR
- 09/2022: PET with POD, biopsy FL, grade 1-2, low tumor burden active surveillance
- 12/2022: Short interval can with POD
- 02/2023-01/2024: Mosunetuzumab, PR after 8 cycles, EOT POD
- 02/2023: Refer for CAR T-cell

# 76-year old man with multiply recurrent follicular lymphoma

- **Was the sequencing of immunotherapy appropriate with bispecific then CAR T-cells?**

- **Should CAR T-cells have been used first?**

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# Management of Relapsed FL

# Options for Treatment at Relapse

## Established

- Rituximab (R)
- Chemoimmunotherapy not used in 1L ± maintenance
- High dose therapy/autologous stem cell rescue or allogeneic stem cell transplant
- R/G+lenalidomide
- Tazemetostat
- G-zanubrutinib
- Tisagenlecleucel
- Axicabtagene maraleucel
- Mosunetuzumab

## Investigational (very partial list)

- Antibody drug conjugates
- $BH_3$ mimetics
- CelMODs
- Degraders
- CAR T-cells
  - Lisocabtagene maraleucel
- Bispecific antibodies
  - Ondronexamab
  - Epcoritamab
  - Glofitamab

Consider clinical trials prior to development of refractory disease

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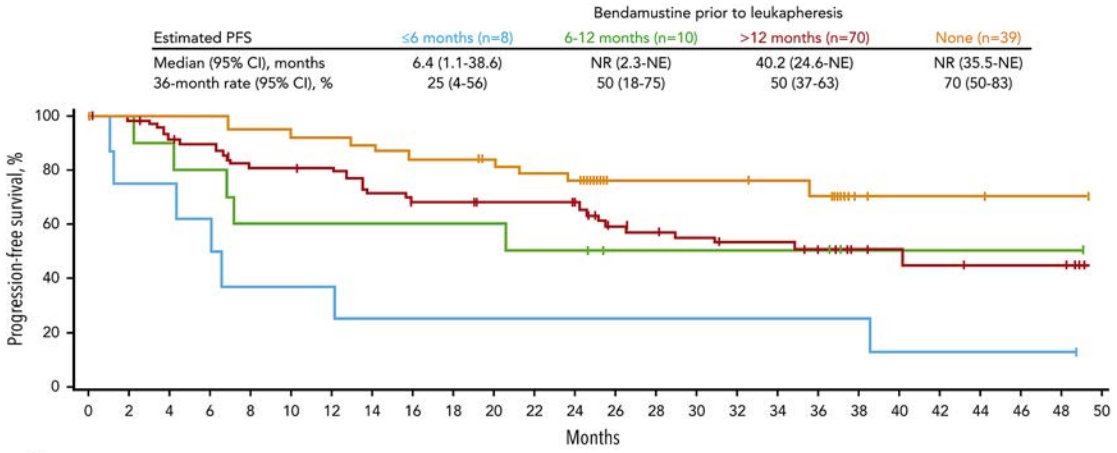
# T-cell Engager and CAR T-cells Relapsed/Refractory Disease

# Comparison of CAR-T therapy data in Follicular Lymphoma

| Brand name (generic) | Axicabtagene ciloleucel[1] | | Tisagenlecleucel[2] |
|---|---|---|---|
| Study population | R/R iNHL after ≥2 prior therapies | | R/R FL after ≥2 prior therapies or post HDT/ASCR |
| Histology | FL | MZL | FL grade 1-3A |
| Median prior therapies (IQR)[b,c] | 3 (1–10) | 3 (2-8) | 4 (2–13) |
| Sample size for efficacy | n=127 | MZL n=31 | n=97 |
| Median follow-up, mo (IQR) | 41.7 | MZL 31.8 | 28.9 |
| ORR (95% CI) | 94% | MZL 77% | 86.2% |
| CRR | 79% | MZL 65% | 68.1% |
| mPFS | 40.2 m | Not reached | NR (8.7–NE) [24-mo PFS 57.4% (46.2-67)] |
| AEs of special interest (% of patients)[b,c] | CRS (all grades, 78%; grade 3+, 7%); neurologic AE (all grades, 56%; grade 3+, 15%) | | CRS (all grades, 47%; grade 3+, 0%), serious neurological AE (all grades, 10.3%; grade 3+, 2.0%) |




**Axicabtagene ciloleucel and Tisagenlecleucel both approved for FL 3L+**
**Not approved for MZL (NCCN listed)**


1. Neelapu et al. Blood (2024) 143:496-506 2.Dreyling et al. Blood (2024) 143:online before publication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# Bispecifics CD3 x CD20 in patients with R/R iNHL

| | Mosunetuzumab[1] (RG7828) | Odronextamab[2] (REGN1979) | Glofitamab[3]* (RG6026) | Epcoritamab[4] (GEN3013) |
|---|---|---|---|---|
| Patients | 90 | 96 | 75 | 128 |
| ORR | 80% | 81% | 81% | 82% |
| CR | 60% | 75% | 69% | 63% |
| PFS | 17.9 m | 20.2 m | Not reported | 15.4 m |

*Indolent NHL

**Mosunetuzumab approved for FL 3L+**
**Epcoritamab approval expected 2024**

1. Budde, Lancet Oncol 2022 23:1055-65; 2. Kim et al. ASH 2022; 3. Dickinson M. et al. ASH 2021 . 4. Linton et al. ASH 2023.

# Epcoritamab, subcutaneous for R/R FL: Evaluation of efficacy and safety

## TRIAL DESIGN: PIVOTAL EPCORE™ NHL-1 STUDY

**Dose escalation**

**B-NHL:**

- ✓ No DLTs
- ✓ MTD not reached
- ✓ RP2D identified
- ✓ Manageable safety profile
- ✓ Encouraging antitumor activity

**Dose expansion**

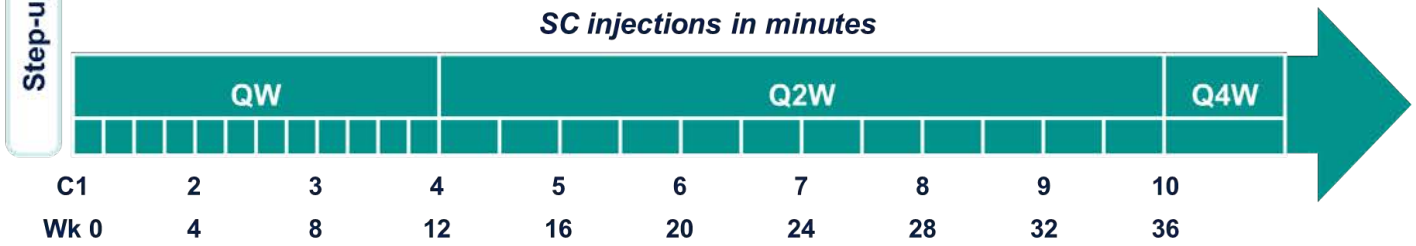
**Key inclusion criteria:**

- R/R CD20+ mature B-cell neoplasm
- ECOG PS 0–2
- ≥2 prior lines of antineoplastic therapy, including ≥1 anti-CD20 mAb
- Prior treatment with an alkylating agent or lenalidomide
- Measurable disease by PET/CT
- Prior CAR T allowed

**Data cutoff: April 21, 2023**
**Median follow-up: 17.4 mo**

**Step-up dosing[a]**

**Epcoritamab SC RP2D 48 mg**
**Treatment until PD[b] or unacceptable toxicity**
**R/R FL 1-3A expansion cohort, N=128**




- **Primary endpoint:** ORR by independent review committee (IRC)
- **Key secondary endpoints:** MRD[c], DOR, TTR, PFS, OS, CR rate, and safety/tolerability

Linton et al. ASH 2023 Abstract 1655

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# Patient characteristics and treatment history

| Demographics | N=128 |
|---|---|
| Median age, y (range) | 65 (39–84) |
| Male, n (%) | 79 (62) |
| Ann Arbor stage, n (%) | |
| I–II | 19 (15) |
| III | 32 (25) |
| IV | 77 (60) |
| FLIPI, n (%)[a] | |
| 0–1 | 17 (13) |
| 2 | 31 (24) |
| 3–5 | 78 (61) |
| Beta-2 microglobulin, n (%)[b] | |
| High | 79 (62) |
| Normal | 45 (35) |

[a]FLIPI was unknown for 1 patient and not applicable for 1 patient. FLIPI was prior to first dose on study. [b]Beta-2 microglobulin was missing for 4 patients.

| Treatment History | N=128 |
|---|---|
| Median time from diagnosis to first dose, y (range) | 6.2 (0.2–35) |
| Median time from end of last line of therapy to first dose, mo (range) | 5.2 (1–105) |
| Median number of prior lines of therapy (range) | 3 (2–9) |
| ≥3 prior lines, n (%) | 81 (32) |
| ≥4 prior lines, n (%) | 40 (31) |
| POD24 – 1L CIT,[a] n (%) | 54 (42) |
| POD24 – any 1L,[b] n (%) | 67 (52) |
| Primary refractory,[c] n (%) | 69 (54) |
| Refractory[c] to last prior systemic therapy, n (%) | 88 (69) |
| Double refractory,[c,d] n (%) | 90 (70) |

[a]Progression within 2 y of initiating first-line treatment that included chemoimmunotherapy. [b]Progression within 2 y of initiating any first-line treatment. [c]Refractory: No response or relapse within 6 mo after therapy. [d]Double refractory: Refractory to both anti-CD20 and an alkylating agent, regardless of 2 treatments being in the same or different treatment lines.

- Most patients had grade 2 (55%) or 3A (32%) FL
- All patients had prior treatment with an anti-CD20 mAb and an alkylating agent
  - Other prior systemic treatments included anthracyclines (77%), nucleotides (48%), topoisomerase inhibitors (36%), iMiDs (31%), PI3K inhibitors (23%), and CAR T-cell therapy (5%)

Linton et al. ASH 2023 Abstract 1655

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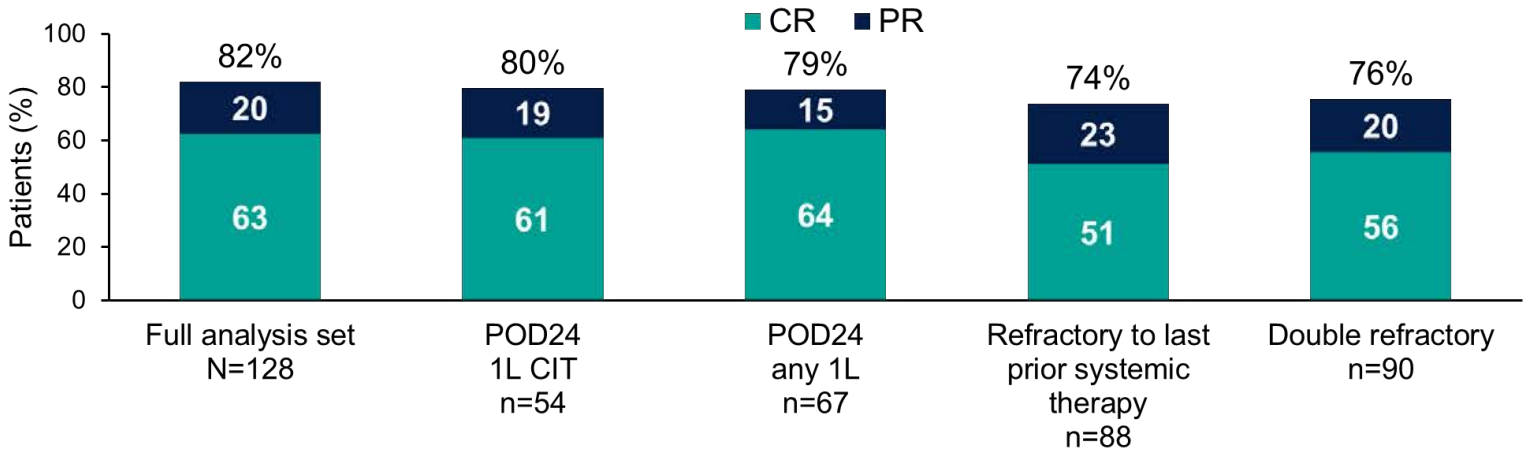
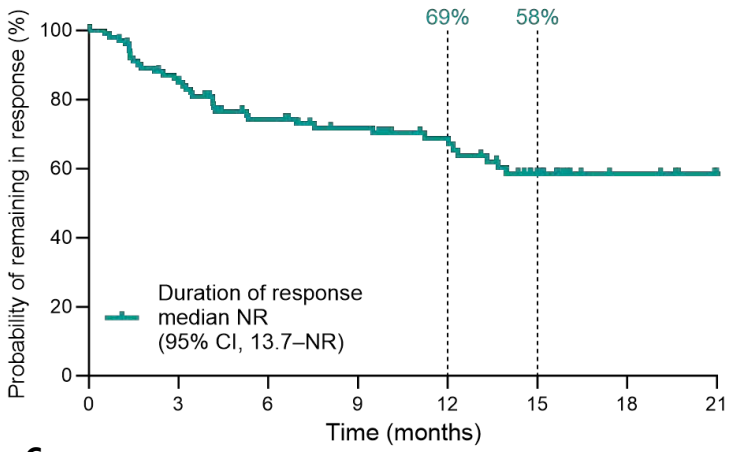
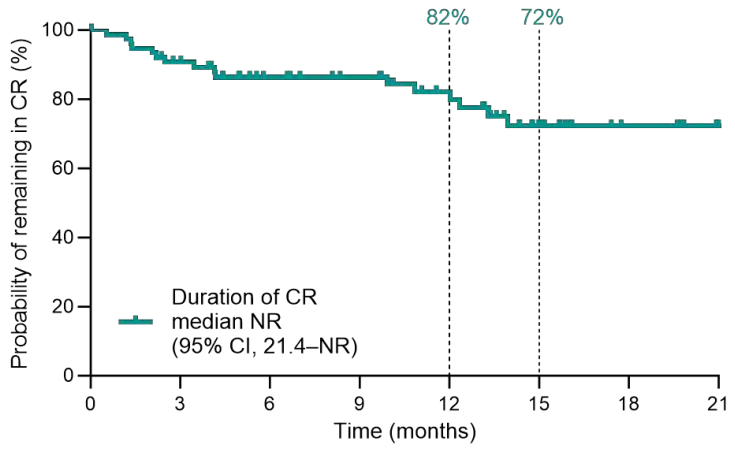
# Epcoritamab for R/R FL: Efficacy




- Median time to response was 1.4 mo (range, 1.0–3.0)
- Median time to complete response was 1.5 mo (range, 1.2–11.1)
- Median time to next antilymphoma therapy was NR (range, 0.2+ to 30.0+)

**Responses Were Deep and Durable**

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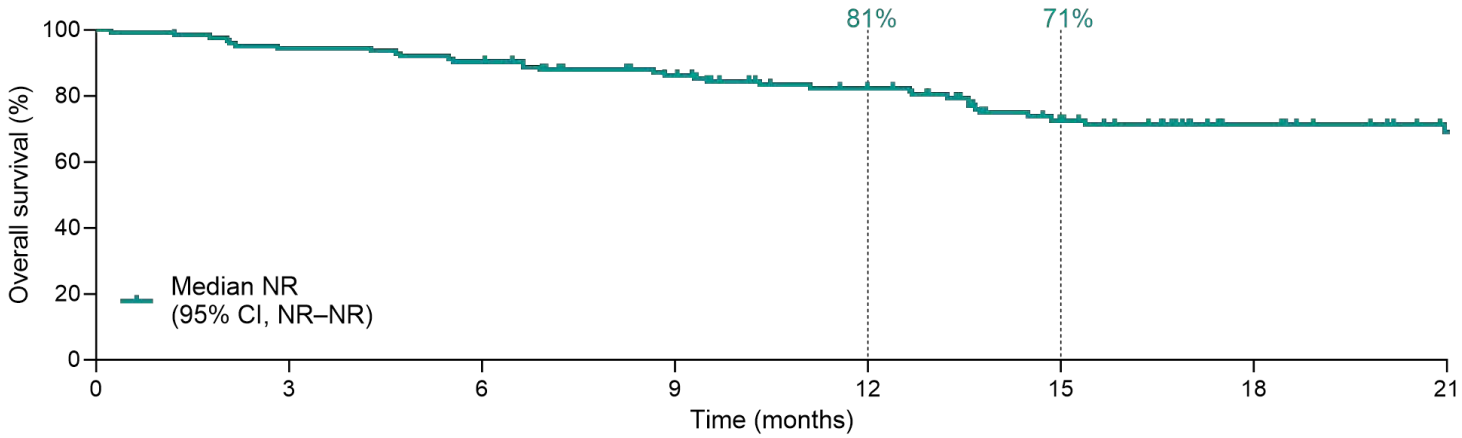
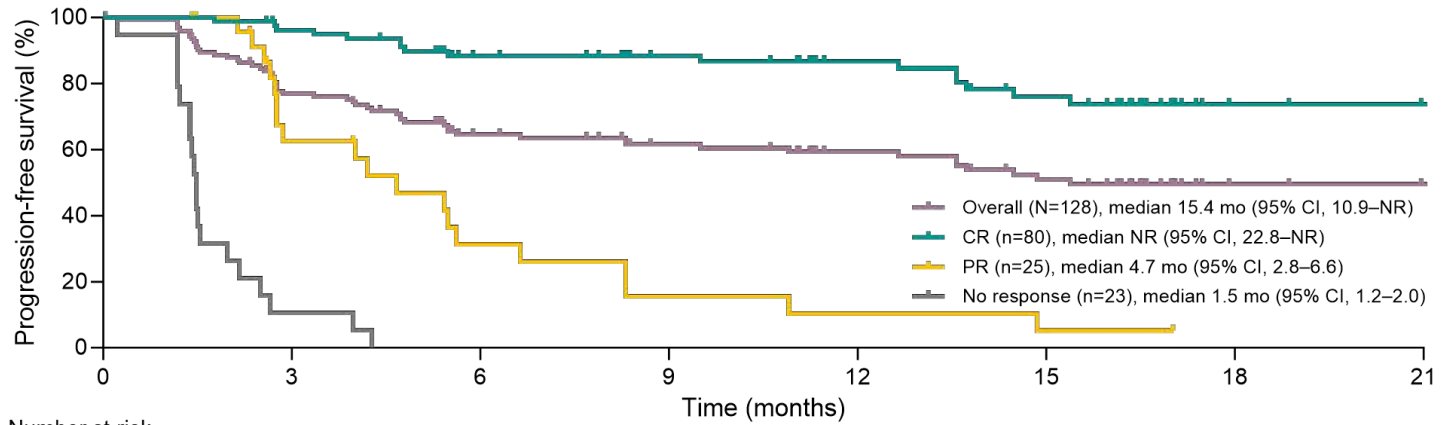
# Epcoritamab for R/R FL: PFS and OS

## Overall Survival




## Progression-Free Survival Median NR in Complete Responders




Number at risk

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 128 | 90 | 67 | 57 | 43 | 35 | 14 | 12 |
| 80 | 75 | 61 | 54 | 41 | 34 | 14 | 12 |
| 25 | 13 | 6 | 3 | 2 | 1 | 0 | 0 |
| 23 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |

Of 100 MRD-evaluable patients, uMRD was achieved in 68 patients and correlated with improved PFS and OS

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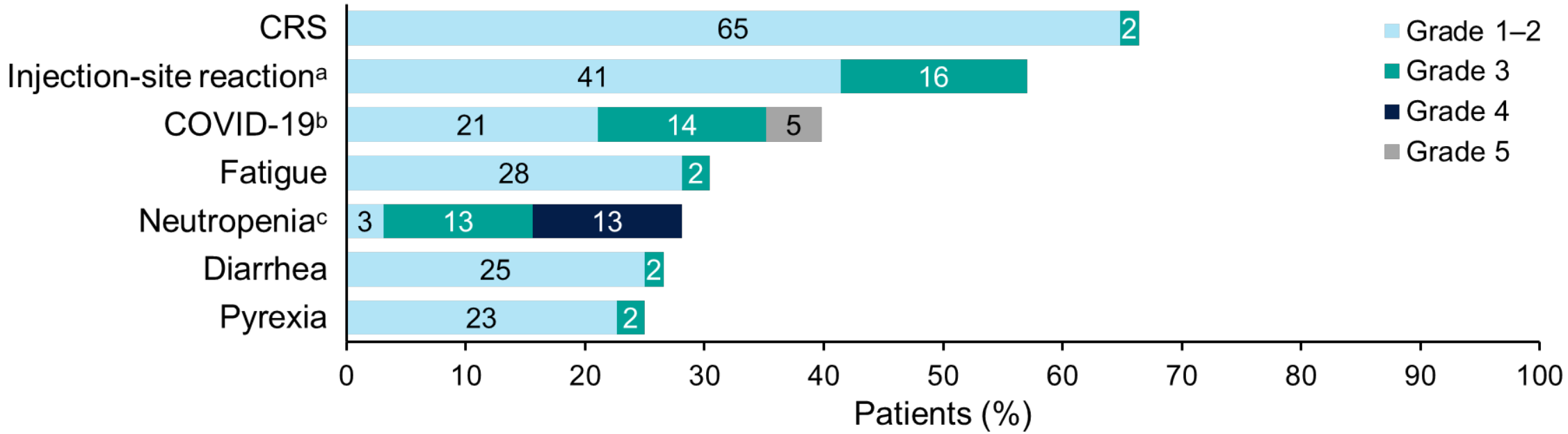
# Epcoritamab for R/R FL: Safety

## Common (>20%) Treatment-Emergent Adverse Events




[a]Combined term includes injection-site reaction, erythema, inflammation, nodule, pain, pruritus, rash, and swelling. [b]Combined term includes COVID-19 and COVID-19 pneumonia. [c]Combined term includes neutropenia and neutrophil count decreased; 4 patients (3%) had febrile neutropenia (all grade 3).

- Safety profile consistent with previous reports
- TEAEs, grade ≥3, occurred in 69% of patients, 38% of pts experience grade ≥3 related to Epcoritamab
- TEAEs led to discontinuation in 19% of patients
- **13 patients have fatal TEAEs**

**Linton et al. ASH 2023 Abstract 1655**

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# Epcoritamab for R/R FL: Cycle 1 Optimization Reduced Risk and Severity of CRS

| | Pivotal Cohort N=128 | C1 Optimization Cohort[b] N=50 |
|---|---|---|
| CRS, n (%)[a] | 85 (66) | 24 (48) |
| Grade 1 | 51 (40) | 20 (40) |
| Grade 2 | 32 (25) | 4 (8) |
| Grade 3 | 2 (2) | 0 |
| Median time to onset after first full dose, h (range) | 15 (1–130) | 60 (3–110) |
| Treated with tocilizumab, n (%) | 31 (24) | 5 (21) |
| **Leading to epcoritamab SC discontinuation, n (%)** | **0** | **0** |
| CRS resolution, n/n (%) | 85/85 (100) | 24/24 (100) |
| Median time to resolution, d (range) | 2 (1–54) | 3 (1–14) |

[a]Graded by Lee et al 2019 criteria.[13] [b]Data cutoff: September 21, 2023. Median follow-up: 3.8 mo (range, 1.9–8.7).

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# Epcoritamab for R/R FL: Safety

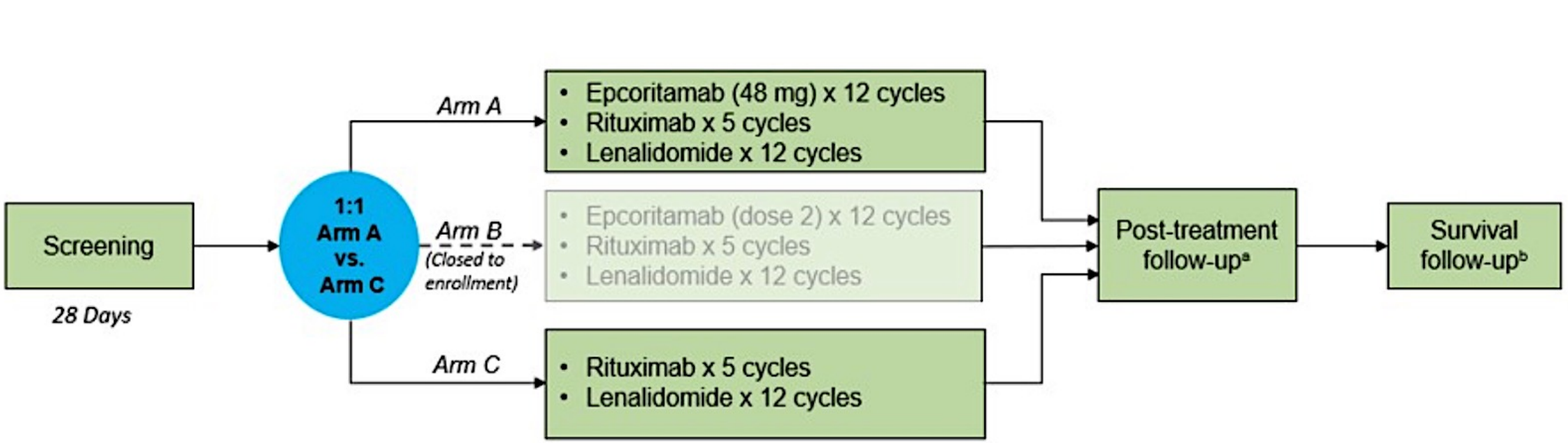
- Safety profile was manageable in the pivotal cohort; further substantial reduction in risk and severity of CRS was observed with C1 optimization and compares favorably to other CD3 x CD20 bispecific antibodies in FL
- In both cohorts, CRS was most common following the first full dose in C1
- Comparable efficacy was observed with C1 optimization

**ICANS, TLS, COVID-19**

- No cases of ICANS with C1 optimization
- In the pivotal cohort, ICANS occurred in 8 pts, all grade 1-2 and resolved with no treatment discontinuation
- No clinical TLS
- COVID-19 impacted the trials with increased incidence of all grades of COVID-19 infection leading to higher-than-expected treatment discontinuations
  - 50% of treatment discontinuations and 46% of fatal TEAEs were due to COVID-19

Linton et al. ASH 2023 Abstract 1655

# EPCORE FL-1: Ongoing Phase III Trial of Epcoritamab with Rituximab and Lenalidomide ($R^2$) versus $R^2$ Alone in R/R FL



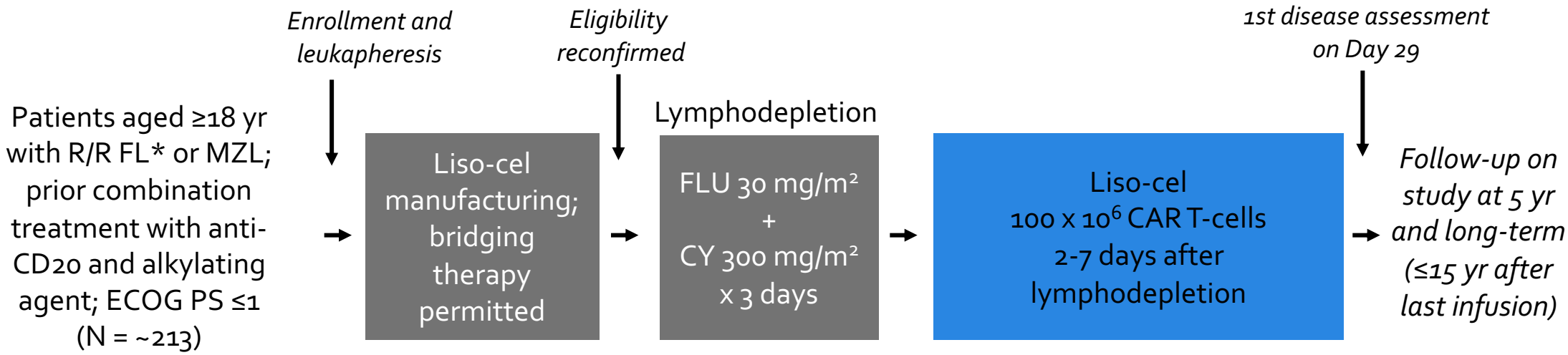

After initial step-up dosing during cycle 1, epcoritamab will be administered weekly in cycles 2-3, then Q4W in cycles 4-12.

[a]Patients who complete treatment or discontinue treatment for reasons other than disease progression will proceed to post-treatment follow-up.
[b]Patients who have confirmed disease progression, initiate another line of treatment for FL, or refuse post-treatment follow-up visits will proceed to survival follow-up.
Q4W, every 4 weeks.

Falchi L et al. ASH 2023;Abstract 3053.

# TRANSCEND FL: Study Design

- Multicenter, open-label, single-arm, phase II trial; data cutoff January 27, 2023




*High-risk features required for 2L patients: POD24 (progression ≤24 mo of diagnosis and after anti-CD20/alkylating agent therapy within 6 mo) or ≥1 mGELF criteria (FL-related symptoms, threatened end-organ function, cytopenia that is secondary to lymphoma or bulky disease, splenomegaly, or stable progression over ≥6 mo).

**Primary endpoint**: IRC-assessed ORR via PET/CT (Lugano 2014 criteria)

**Key secondary endpoints**: CRR, DoR, CR DoR, PFS, OS, safety

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**Morschhauser et al. ASH 2023, Abstract 602**

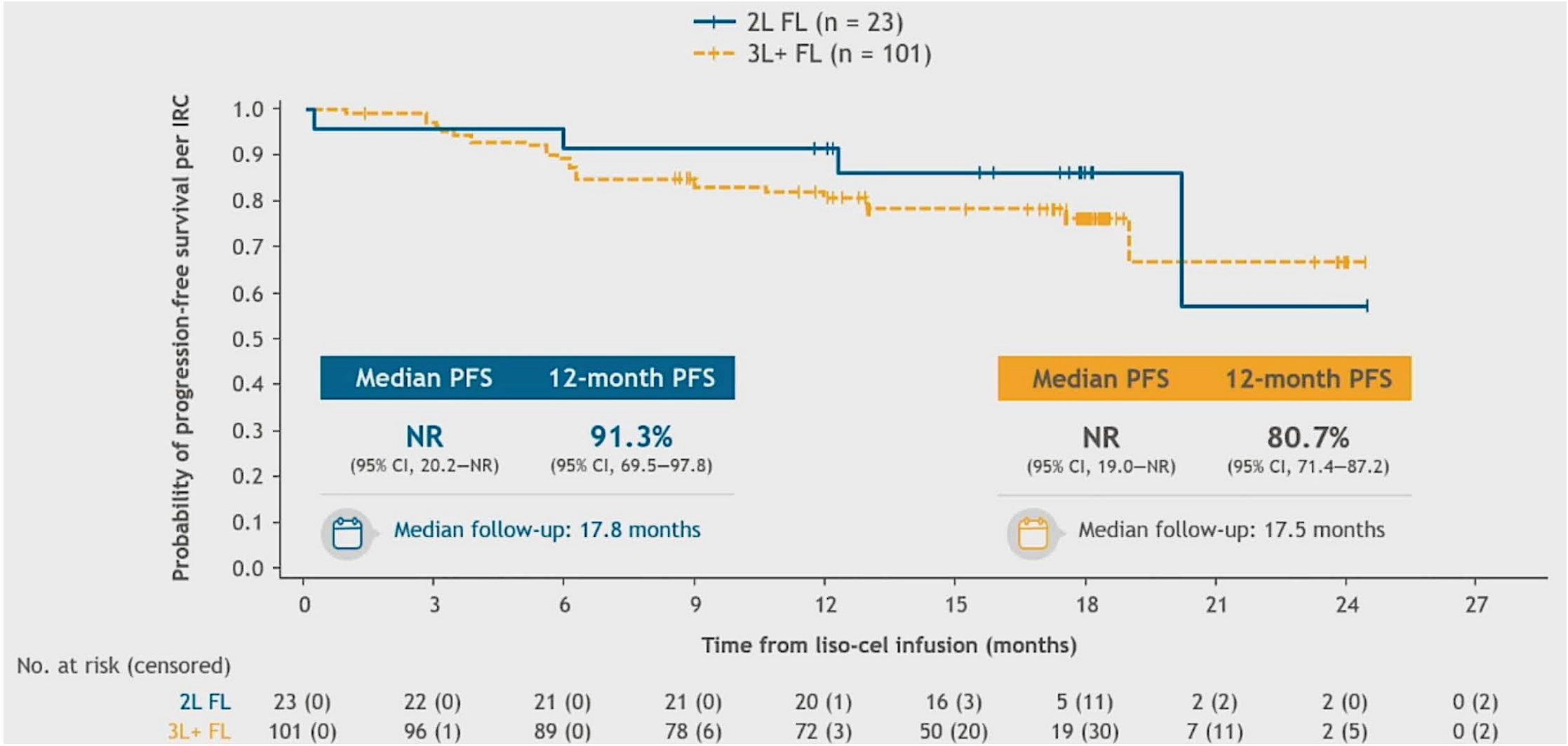
# TRANSCEND FL: Patient characteristics

| | 2L FL (n = 23) | 3L+ FL (n = 107) |
|---|---|---|
| Median (range) age, y | 53 (34–69) | 62 (23–80) |
| Male, n (%) | 17 (74) | 66 (62) |
| FL grade 1 or 2 / 3a at screening,[a] n (%) | 17 (74) / 6 (26) | 81 (76) / 25 (23) |
| Ann Arbor stage at screening, n (%) | | |
| Stage I/II | 6 (26) | 12 (11) |
| Stage III/IV | 17 (74) | 95 (89) |
| FL International Prognostic Index at screening, n (%) | | |
| Low risk (0–1) / intermediate risk (2) | 11 (48) / 4 (17) | 12 (11) / 34 (32) |
| High risk (3–5) | 8 (35) | 61 (57) |
| LDH > ULN before lymphodepletion, n (%) | 6 (26) | 47 (44) |
| Met mGELF criteria at most recent relapse, n (%) | 16 (70) | 57 (53) |
| Symptoms attributable to FL | 6 (26) | 13 (12) |
| Threatened end-organ function/cytopenia secondary to lymphoma/bulky disease | 7 (30) | 24 (22) |
| Splenomegaly | 0 | 4 (4) |
| Steady progression over at least 6 months | 3 (13) | 16 (15) |
| Median (range) prior lines of systemic therapy | 1 (1–1) | 3 (2–10) |
| Prior HSCT, n (%) | 0 | 33 (31) |
| Received prior rituximab and lenalidomide, n (%) | 0 | 23 (21) |
| Refractory to last systemic therapy,[b] n (%) | 15 (65) | 72 (67) |
| Double refractory (anti-CD20 and alkylator),[c] n (%) | 11 (48) | 69 (64) |
| POD24 from initial immunochemotherapy, n (%) | 15 (65) | 58 (54) |
| POD24 from diagnosis, n (%) | 12 (52) | 46 (43) |
| Received bridging therapy, n (%) | 5 (22) | 44 (41) |

Morschhauser et al. ASH 2023, Abstract 602

Memorial Sloan Kettering Cancer Center

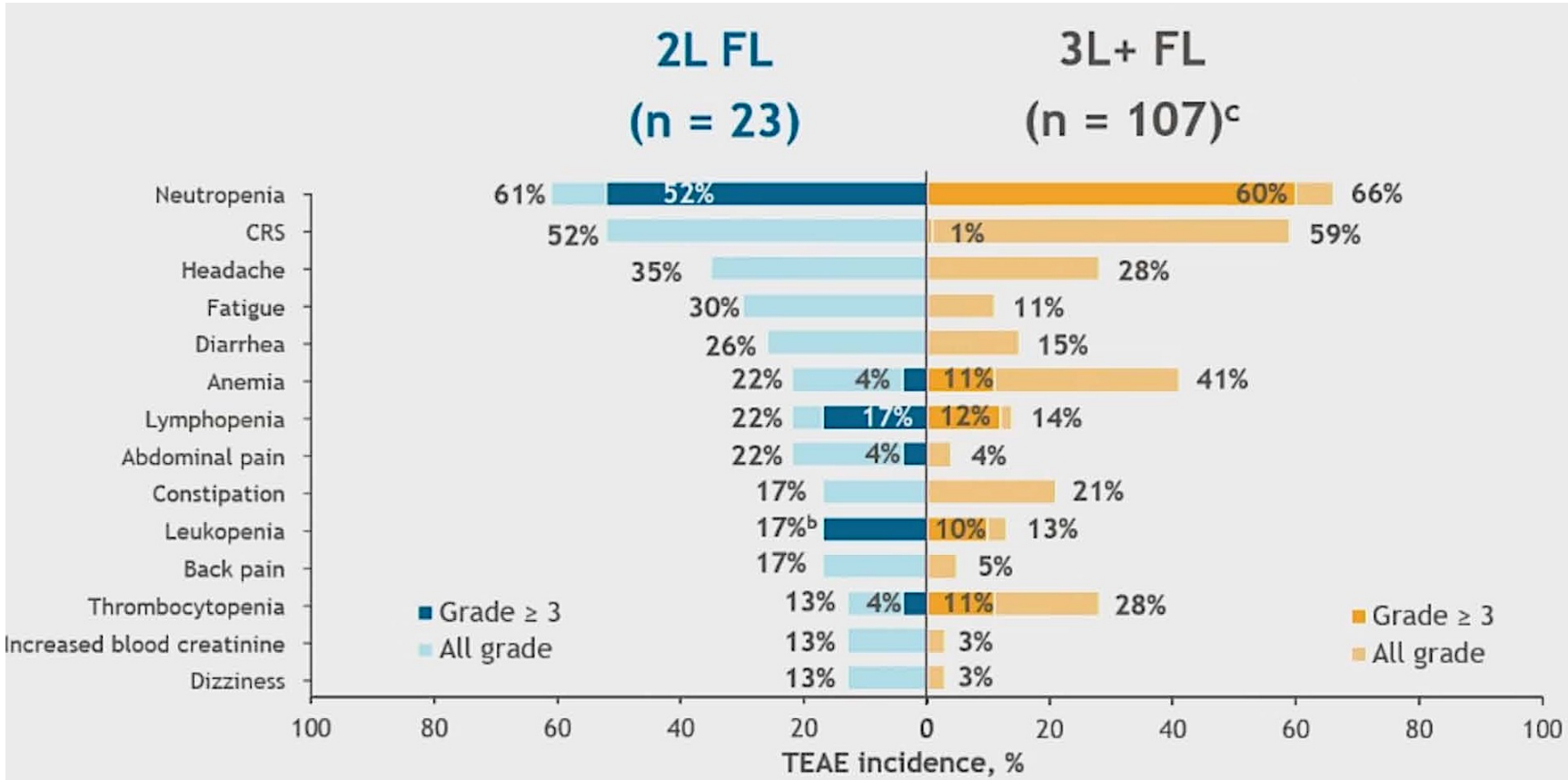
# TRANSCEND FL: Progression-free survival per IRC in efficacy set




Morschhauser et al. ASH 2023, Abstract 602

Memorial Sloan Kettering Cancer Center

# TRANSCEND FL: Most common TEAEs (>10%) in liso-cel-treated set




**TEAEs in 2L vs 3L+ FL**

- 61% vs 78% with grade ≥ 3 TEAEs
- 17% vs 26% with serious TEAEs
- Most common grade ≥ 3 TEAE was neutropenia (52% vs 60%)
  - 1 (4%) vs 5 (5%) with febrile neutropenia
- There was no grade ≥ 3 CRS in 2L FL

[a]TEAE period was defined as the time from initiation of liso-cel administration through and including study Day 90; [b]All cases of leukopenia in 2L FL were grade ≥ 3; [c]Only TEAEs that occurred in ≥ 10% of patients with 2L FL are shown for 3L+ FL.
CRS, cytokine release syndrome; TEAE, treatment-emergent adverse event.

Morschhauser et al. ASH 2023, Abstract 602

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# TRANSCEND FL: Summary

- This is the first report of outcomes in patients with 2L high-risk R/R FL who received CD19-directed CAR T cell therapy
- Although population size was small, a single administration of liso-cel achieved very high CR rate with follow-up ongoing
  - Primary and key secondary endpoints were met with an ORR of 96% and CR rate of 96%, respectively
  - On-study median follow-up was 18.9 months; median was not reached for DOR, PFS, and OS
  - 12-month estimates for DOR, PFS, and OS were 90%, 91%, and 96%, respectively
- Lisocabtagene maraleucel demonstrated a manageable safety profile in patients with 2L R/R FL, with no grade ≥3 CRS or infections and low rates of NEs and prolonged cytopenia
- These data support lisocabtagene maraleucel as a potential new treatment option in patients with 2L R/R FL at high risk for treatment failure

**Morschhauser et al. ASH 2023, Abstract 602**

Memorial Sloan Kettering Cancer Center

# FDA Grants Accelerated Approval to Zanubrutinib for Relapsed or Refractory Follicular Lymphoma

## Press Release: March 7, 2024

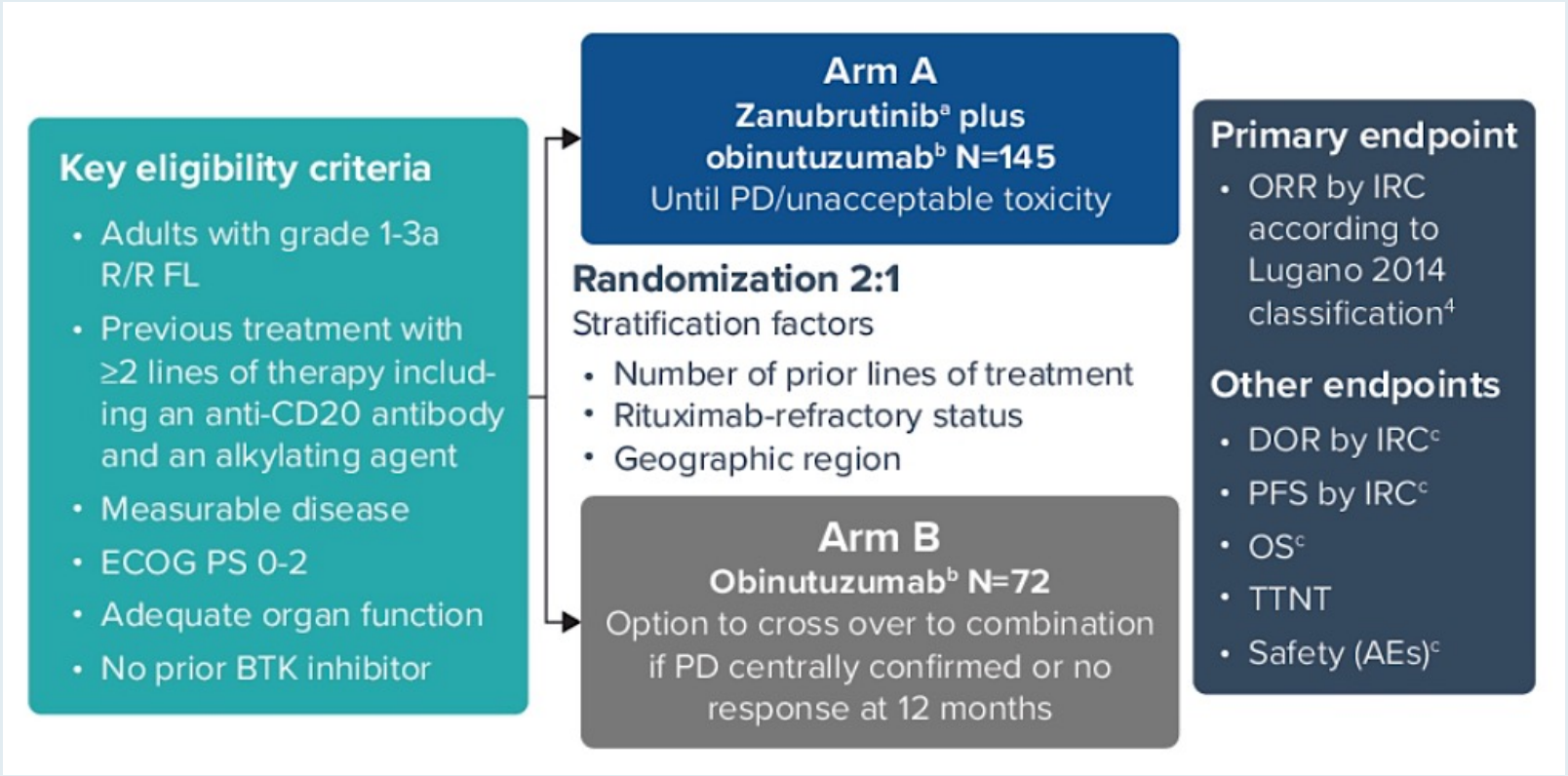
"On March 7, 2024, the Food and Drug Administration granted accelerated approval to zanubrutinib with obinutuzumab for relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy. The regimen was evaluated in Study BGB-3111-212 (ROSEWOOD; NCT03332017), an open-label, multicenter, randomized trial that enrolled 217 adult patients with relapsed or refractory FL after at least 2 prior systemic treatments.

Patients were randomized (2:1) to receive either zanubrutinib 160 mg orally twice daily until disease progression or unacceptable toxicity plus obinutuzumab (ZO), or obinutuzumab alone. The median number of prior lines of therapy was 3 (range 2-11).

ORR was 69% (95% CI: 61, 76) in the ZO arm and 46% (95% CI: 34, 58) in the obinutuzumab arm (two-sided p-value, 0.0012). With a median follow-up of 19.0 months, the median DOR was not reached in the ZO arm (95% CI: 25.3 months, NE) and was 14.0 months (95% CI: 9.2, 25.1) for those patients receiving obinutuzumab monotherapy."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-zanubrutinib-relapsed-or-refractory-follicular-lymphoma

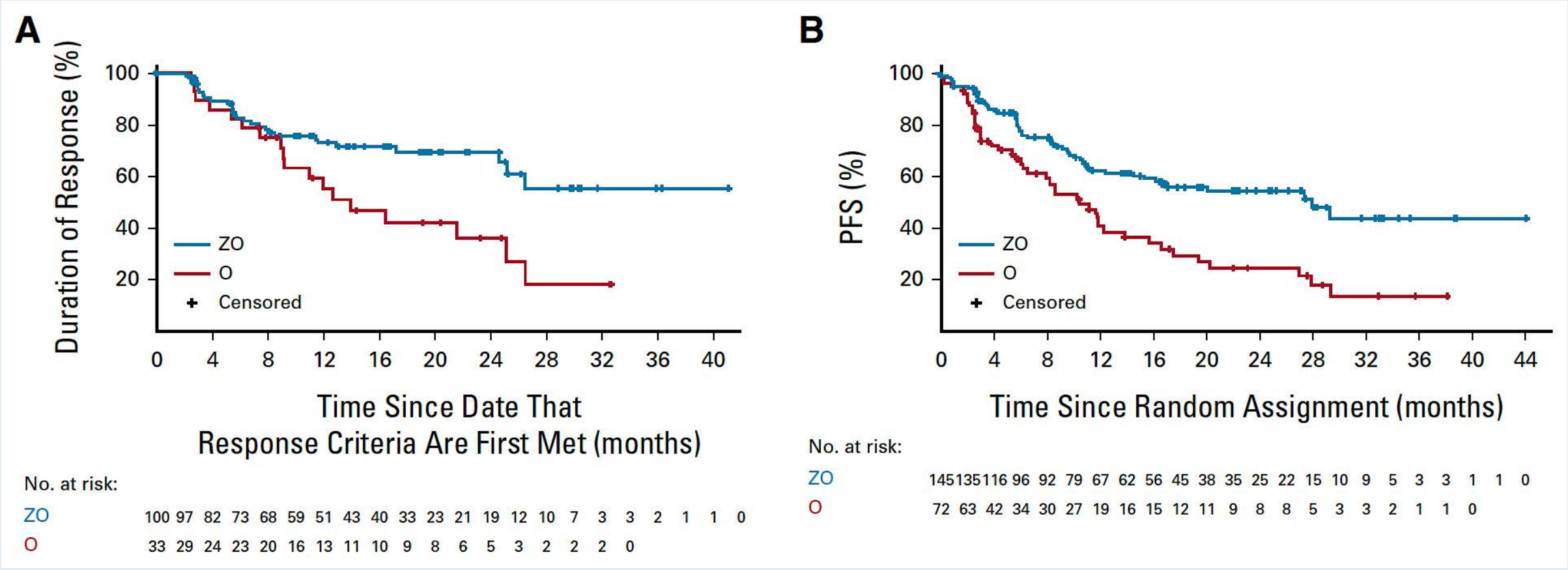
# ROSEWOOD: Phase II Randomized Study of Zanubrutinib plus Obinutuzumab versus Obinutuzumab Monotherapy




| End Point | ZO (n = 145) | O (n = 72) | HR (95% CI) | Two-Sided *P* Value |
|---|---|---|---|---|
| ORR by ICR, % (95% CI) | 69 (61 to 76) | 46 (34 to 58) | — | .001 |
| CR, No. (%) | 57 (39) | 14 (19) | — | .004 |
| PR, No. (%) | 43 (30) | 19 (26) | — | — |

Zinzani PL et al. *J Clin Oncol* 2023;41(33):5107-17.

# ROSEWOOD: DOR and PFS




| End Point | ZO (n = 145) | O (n = 72) | HR (95% CI) | Two-Sided *P* Value |
|---|---|---|---|---|
| DOR by ICR, months, median (95% CI) | NE (25.3 to NE) | 14.0 (9.2 to 25.1) | — | — |
| 18-month rate, % | 69 (58 to 78) | 42 (23 to 60) | — | — |
| Duration of CR by ICR, months, median (95% CI) | NE (26.5 to NE) | 26.5 (2.7 to NE) | — | — |
| 18-month rate, % (95% CI) | 87 (74 to 94) | 51 (21 to 75) | — | — |
| PFS by ICR, months, median (95% CI) | 28.0 (16.1 to NE) | 10.4 (6.5 to 13.8) | 0.50 (0.33 to 0.75) | <.001 |

Zinzani PL et al. *J Clin Oncol* 2023;41(33):5107-17.

RTP RESEARCH TO PRACTICE

# ROSEWOOD: Safety

**TABLE 3.** Any Grade (>10% of patients) and Grade ≥3 (>5% of patients) TEAEs in the Safety Population

| | ZO (n = 143) | | O (n = 71) | |
|---|---|---|---|---|
| Adverse Event | Any Grade, No. (%) | Grade ≥3, No. (%) | Any Grade, No. (%) | Grade ≥3, No. (%) |
| ≥1 TEAE | 135 (94) | 90 (63) | 64 (90) | 34 (48) |
| Thrombocytopenia[a] | 51 (36) | 22 (15) | 17 (24) | 5 (7) |
| Neutropenia[b] | 42 (29) | 35 (24) | 20 (28) | 16 (23) |
| Diarrhea | 26 (18) | 4 (3) | 12 (17) | 1 (1) |
| Fatigue | 22 (15) | 0 (0) | 10 (14) | 1 (1) |
| Constipation | 19 (13) | 0 (0) | 6 (8) | 0 (0) |
| Pyrexia | 19 (13) | 0 (0) | 14 (20) | 0 (0) |
| Cough | 18 (13) | 0 (0) | 9 (13) | 0 (0) |
| Pneumonia | 17 (12) | 14 (10) | 5 (7) | 3 (4) |
| Asthenia | 17 (12) | 1 (1) | 6 (8) | 0 (0) |
| Dyspnea | 16 (11) | 3 (2) | 7 (10) | 0 (0) |
| Back pain | 15 (10) | 1 (1) | 4 (6) | 1 (1) |
| Anemia | 16 (11) | 7 (5) | 7 (10) | 4 (6) |
| COVID-19 | 14 (10) | 8 (6) | 7 (10) | 2 (3) |

Zinzani PL et al. *J Clin Oncol* 2023;41(33):5107-17.

# Agenda

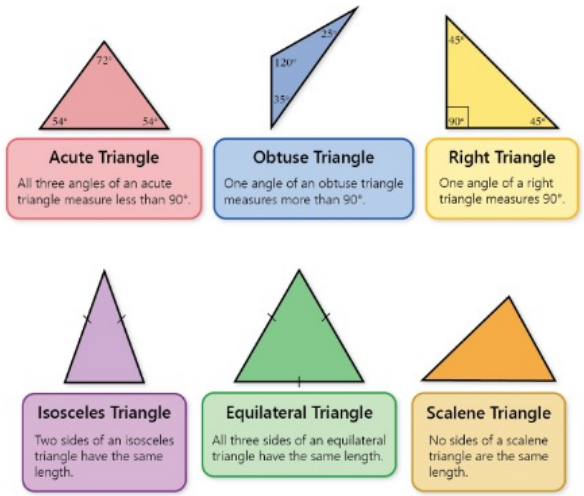
**Module 1: Follicular Lymphoma (FL)** — Dr Zelenetz

**Module 2: Mantle Cell Lymphoma (MCL)** — Dr Lunning

**Module 3: Hodgkin Lymphoma (HL)** — Dr LaCasce

**Module 4: Diffuse Large B-Cell Lymphoma (DLBCL)** — Dr Maddocks

# Mantle Cell Lymphoma: Many Different Triangles




Matthew Lunning D.O. FACP
Associate Professor
University of Nebraska Medical Center

# Disclosures

| | |
|---|---|
| **Consulting Agreements** | AbbVie Inc, AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, Caribou Biosciences Inc, Daiichi Sankyo Inc, Fate Therapeutics, Genentech, a member of the Roche Group, Genmab US Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Kite, A Gilead Company, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Nurix Therapeutics Inc, Recordati, Regeneron Pharmaceuticals Inc, Seagen Inc, Takeda Pharmaceuticals USA Inc |
| **Research Support** | Bristol Myers Squibb, Fate Therapeutics, Sana Biotechnology |

# Case

A 61-year-old man presented with fatigue and a possible non-reducible inguinal hernia making it difficult during calving season

**PMH:** Hypertension, DM2, and HLP

**PE:** ECOG 1.  Left inguinal solid immobile mass measuring 3 X 3 cm; scattered adenopathy in cervical and axillary regions measuring 1-2 cm

**Labs:** CBC with normocytic anemia, CMP normal, LDH elevated

**Excisional Biopsy of mass:** Atypical lymphoid population with areas of blastoid features

- IHC: CD20+, CD5+, cyclin D1+, Sox-11+, Ki67 50%

**FISH:** Translocations involving t(11:14); del(17p) NOT seen

**Molecular:** Positive for TP53 mutation

**PET-CT:** Multiple enlarged in mesenteric and retroperitoneal nodes, largest 5.3 x 3.1 cm

**Bone marrow biopsy:** Hypercellular (50%) with 20% involved with atypical lymphoid aggregates expressing CD20, CD5

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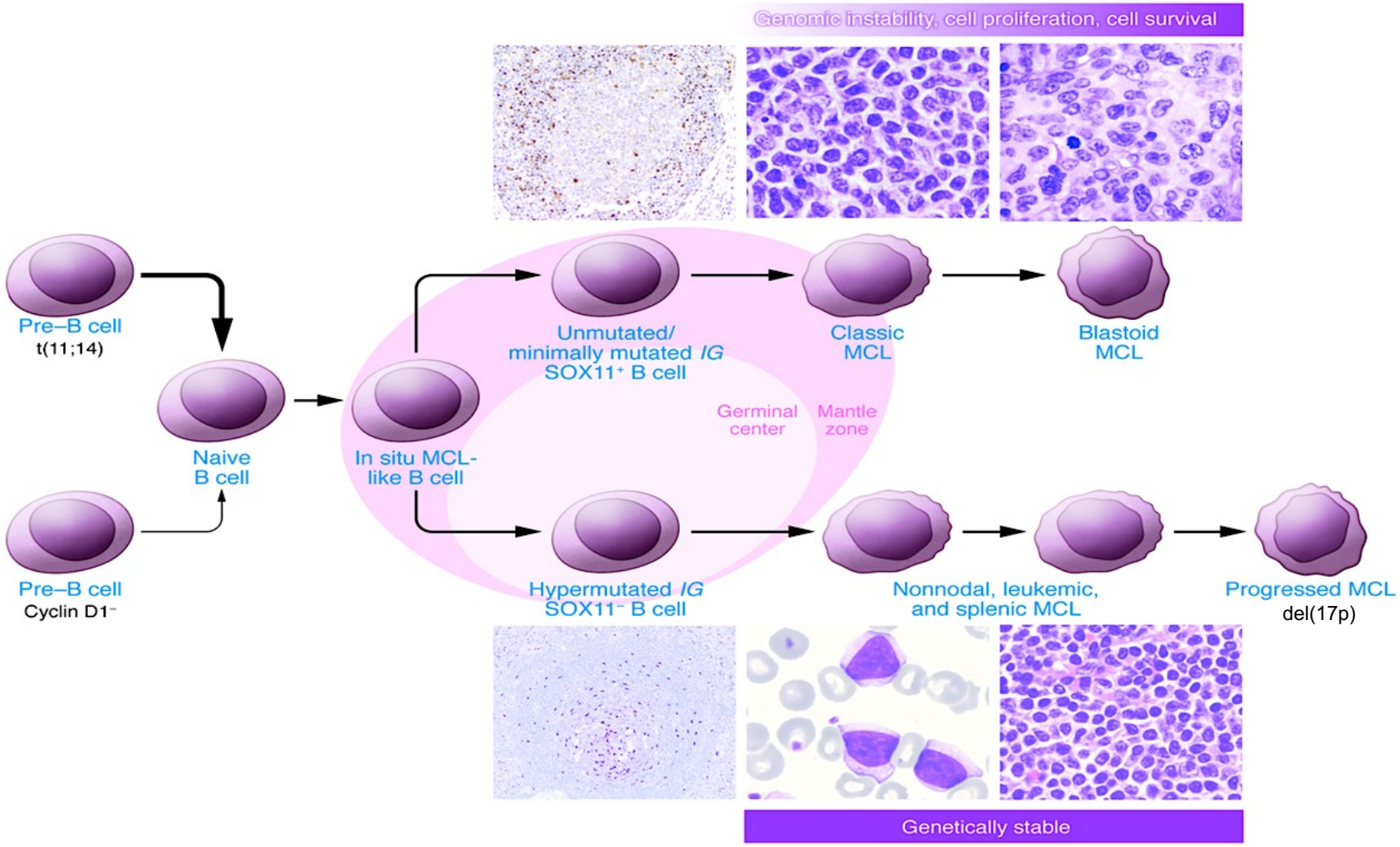
**Bone marrow biopsy:** 20% involved with atypical lymphoid aggregates expressing CD20, CD5

**Impression: Stage IVA (TP53 mutated) Mantle Cell lymphoma, bMIPI High risk**

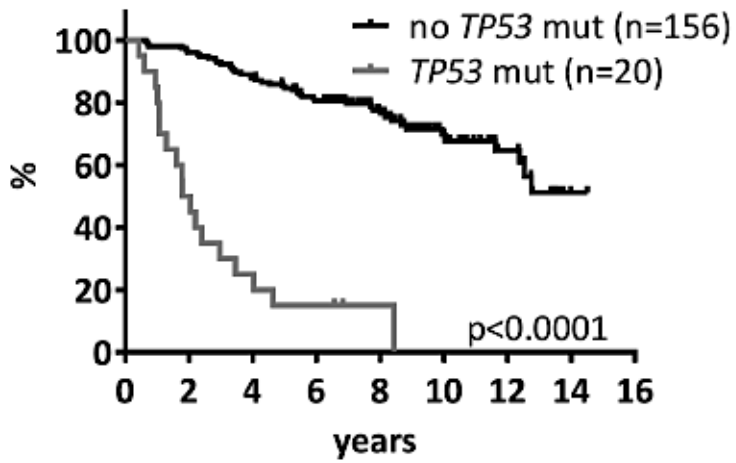
# MCL Pathogenesis



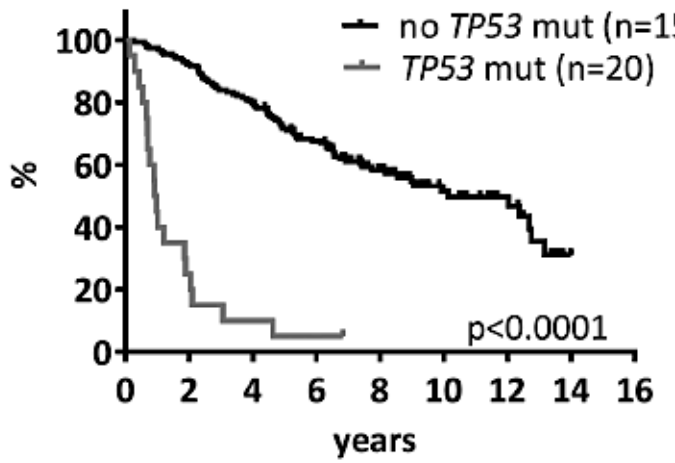

Jares et al. J Clin Invest 2012

# TP53 Mutated MCL = BAD

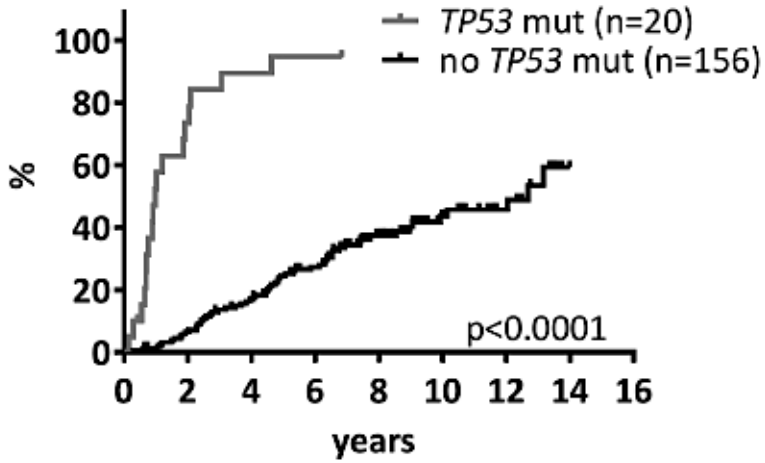
OS




PFS




CIR



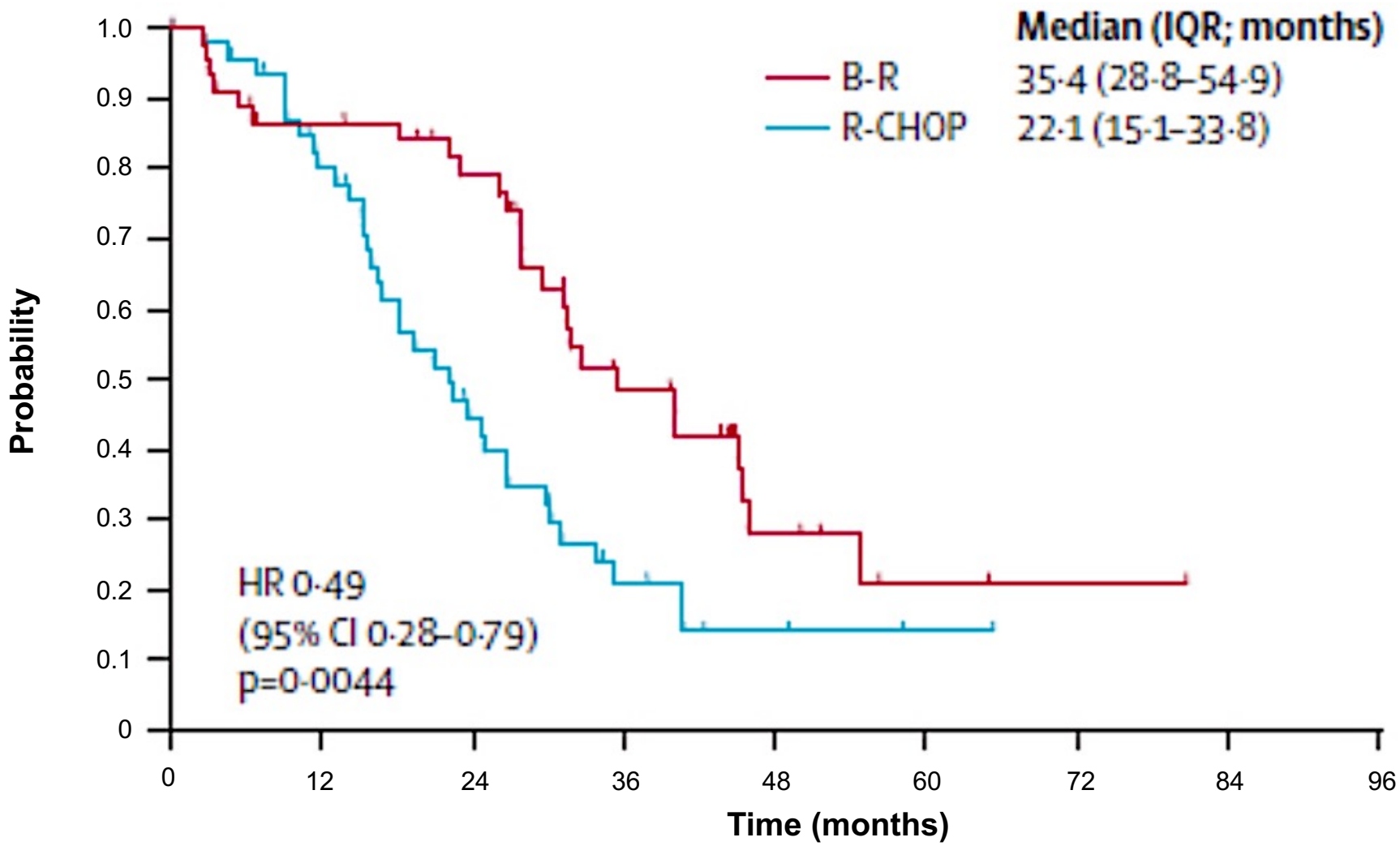

Median PFS = 1.8 years

= 0.9 years

Median OS

Eskelund et al. Blood 2017

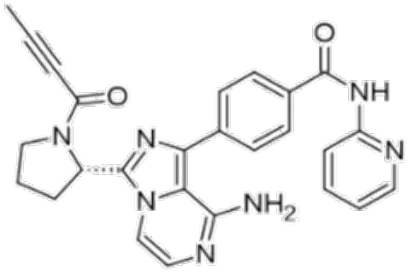
# Most Give BR



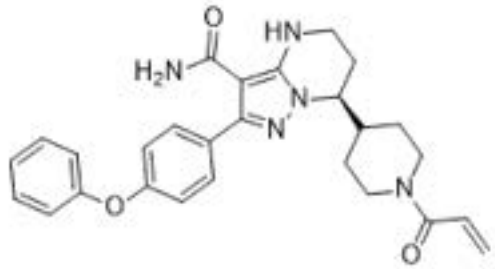

Rummel et al. JCO 2013

# 2nd Generation BTKi

**Acalabrutinib**

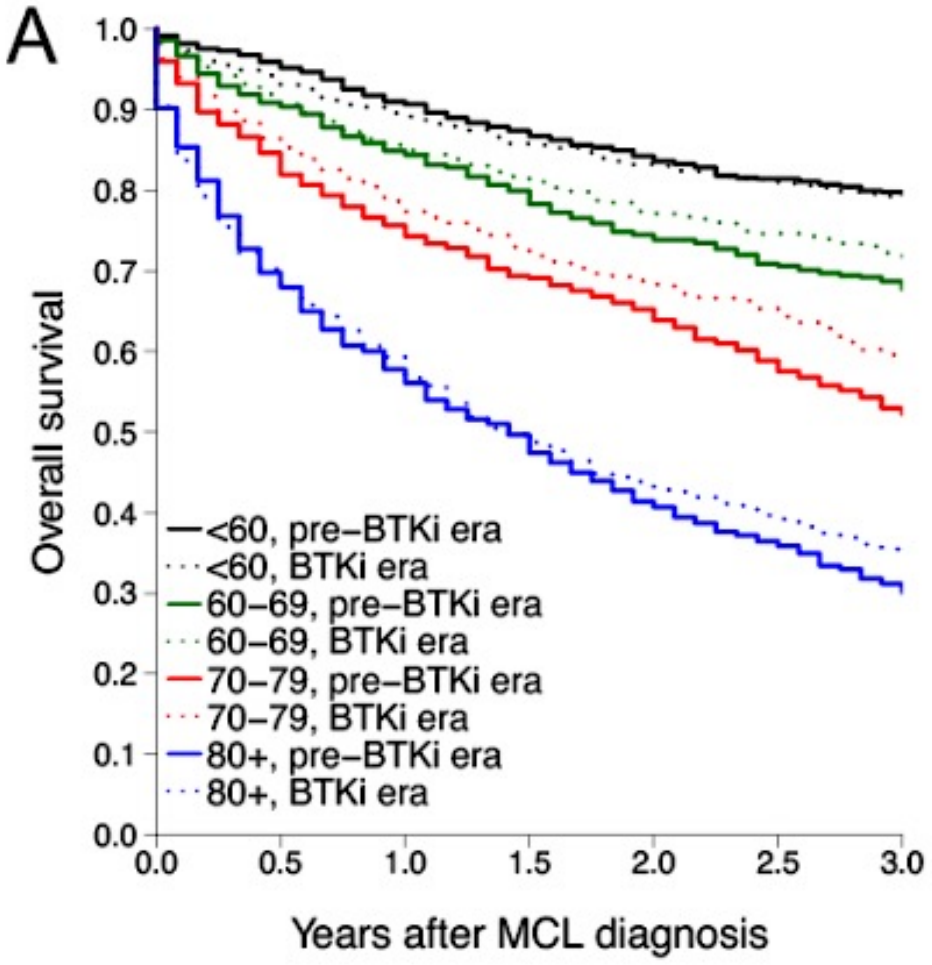



**Zanubrutinib**



# Survival of MCL

| | 3-year all-cause mortality | | 3-year mortality from MCL | |
|---|---|---|---|---|
| | Rate, % | HR (95% CI) | Rate, % | Sub-HR (95% CI) |
| Overall | 39.8 | | 27.3 | |
| <60, pre-BTKi era | 20.5 | 1.00 | 17.3 | 1.00 |
| <60, BTKi era | 21.0 | 1.04 (0.82, 1.31) | 14.3 | 0.80 (0.62, 1.04) |
| 60-69, pre-BTKi era | 32.3 | 1.00 | 24.0 | 1.00 |
| 60-69, BTKi era | 28.4 | **0.85 (0.72, 1.00)** | 19.5 | **0.78 (0.64, 0.94)** |
| 70-79, pre-BTKi era | 47.8 | 1.00 | 33.9 | 1.00 |
| 70-79, BTKi era | 40.4 | **0.80 (0.70, 0.92)** | 27.5 | **0.76 (0.65, 0.90)** |
| >=80, pre-BTKi era | 69.9 | 1.00 | 46.5 | 1.00 |
| >=80, BTKi era | 65.8 | 0.91 (0.80, 1.04) | 42.2 | 0.87 (0.75, 1.02) |




Di et al. ASH 2021 Abs # 182

# Emerging Trials: Front Line

## ECHO

**Clinical trial identifier: NCT02972840**

- ≥65 years of age
- MCL with documentation of a chromosome translocation (11;14)(q13;q32) and/or overexpression of cyclin D1 in association with other relevant markers (eg, CD5, CD19, CD20, PAX5)
- No prior systemic therapy

→ Acalabrutinib + bendamustine + rituximab

→ Bendamustine + rituximab + placebo

**Primary endpoint: PFS**

## MANGROVE

**Clinical trial identifier: NCT04002297**

- ≥70 years OR ≥60 and <70 years ineligible for transplant
- No prior systemic treatment for MCL
- ECOG PS 0-2
- Adequate marrow and organ function

→ Zanubrutinib + rituximab

→ Bendamustine + rituximab

**Primary endpoint: PFS**

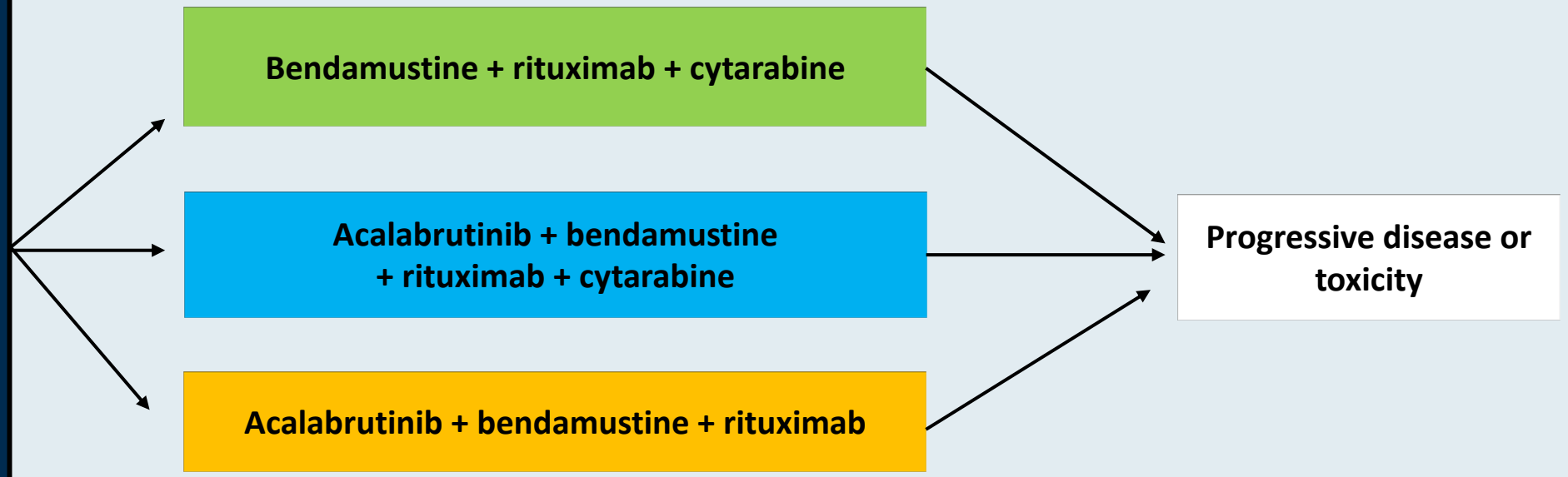
www.clinicaltrials.gov. NCT02972840. Accessed March 2024.
www.clinicaltrials.gov. NCT04002297. Accessed March 2024.

# Emerging Trials: Front Line (Continued)

## ECOG-4181

**Clinical trial identifier: NCT04115631**

- ECOG PS 0-2
- MIPI score must be calculated/reported
- Previously untreated MCL with cyclin D1 (Bcl-1) expression by IHC and/or t(11;14) by cytogenetics or FISH

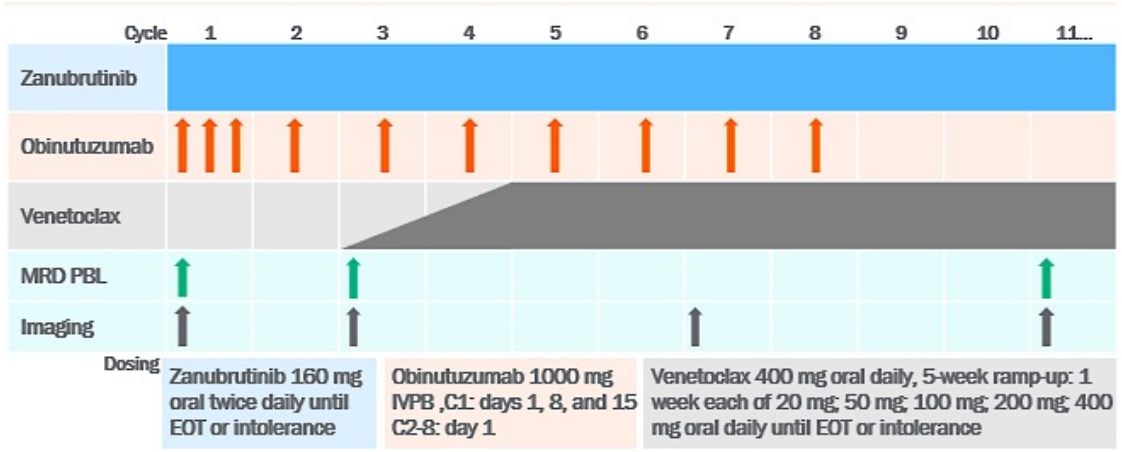


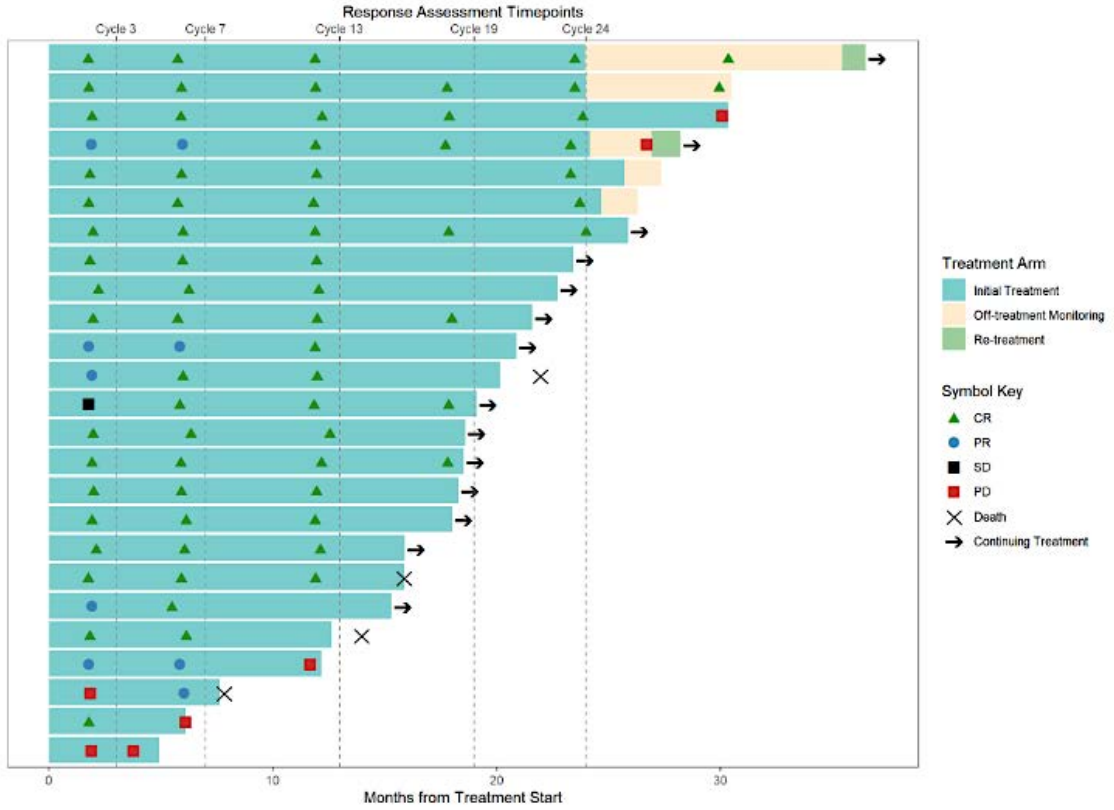

**Primary endpoint: Composite complete response by PET/CT and minimal residual disease negativity rate in peripheral blood**

www.clinicaltrials.gov. NCT04115631. Accessed March 2024.

RTP RESEARCH TO PRACTICE

# BOVen: TP53 Mutated MCL

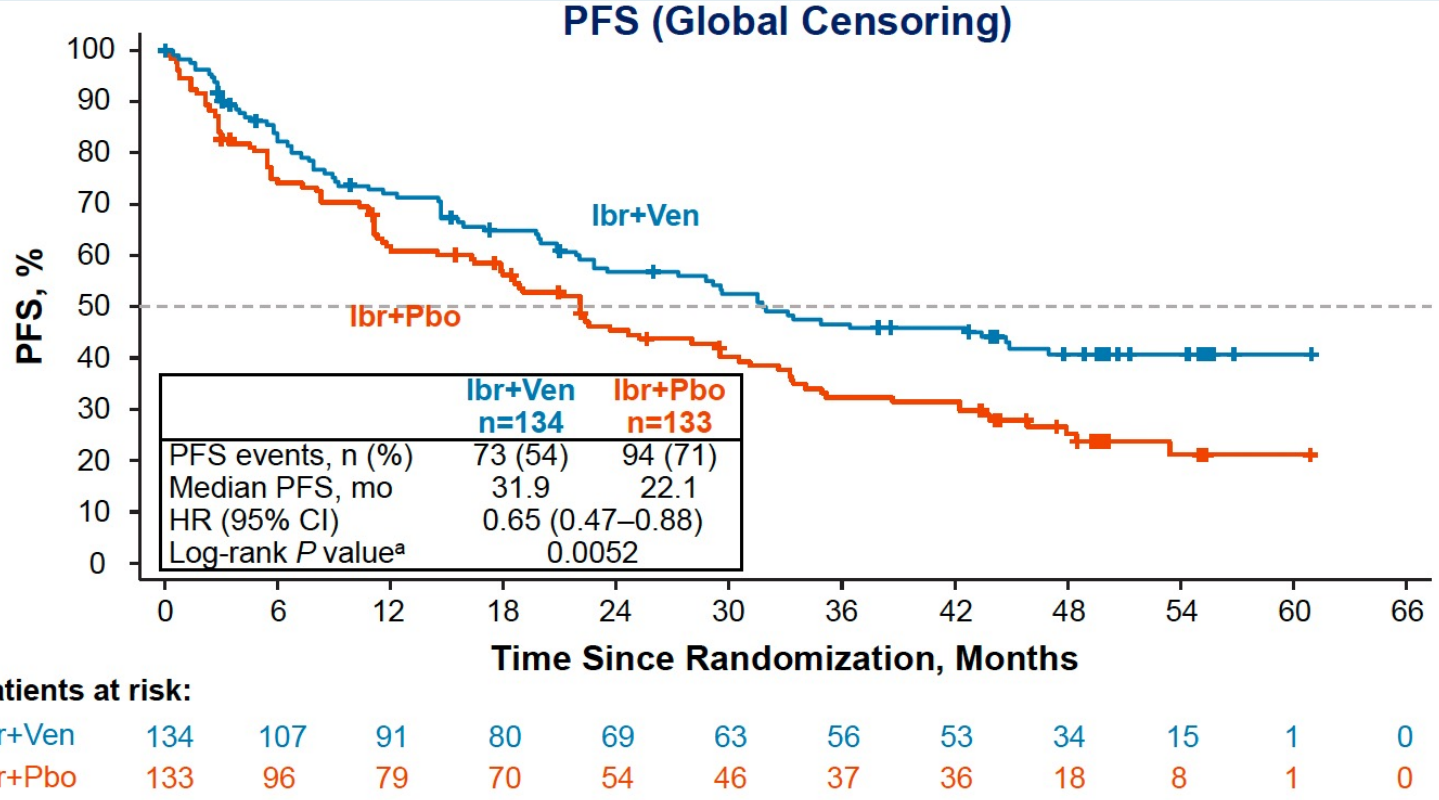



Kumar et al. ASH 2023 Abs # 738

# Phase III SYMPATICO Trial: Ibrutinib + Venetoclax for Relapsed/Refractory MCL

- CR rate and TTNT were also significantly improved with Ibr + Ven
- OS was numerically improved



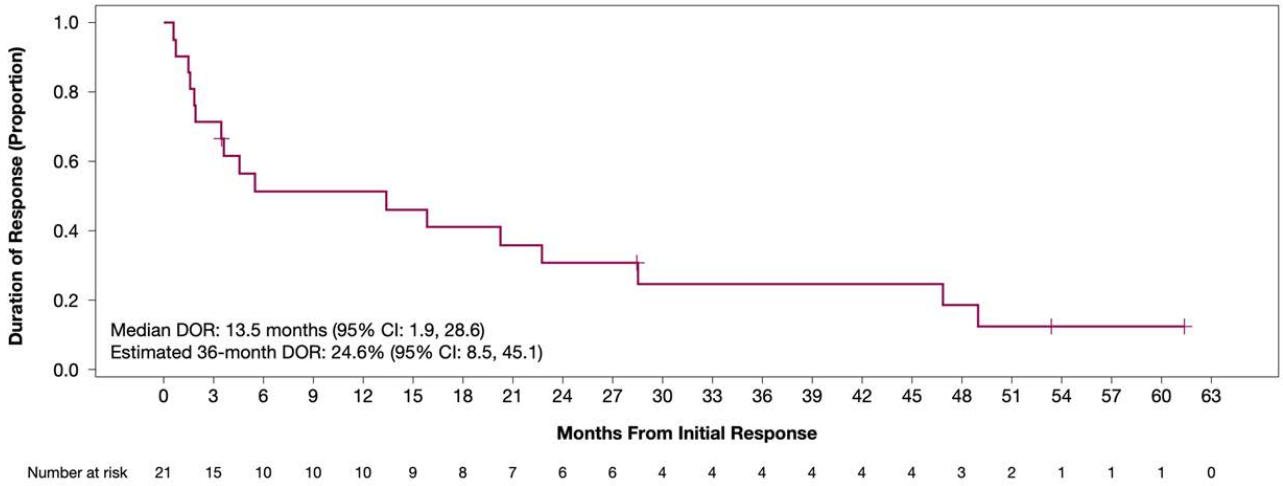

| Median PFS, mo | Global Censoring[b] | | | | US FDA Censoring[c] | | | |
|---|---|---|---|---|---|---|---|---|
| | Ibr+Ven n=134 | Ibr+Pbo n=133 | HR (95% CI) | Log-rank *P* value[a] | Ibr+Ven n=134 | Ibr+Pbo n=133 | HR (95% CI) | Log-rank *P* value[a] |
| **Investigator assessment** | 31.9 | 22.1 | 0.65 (0.47–0.88) | 0.0052 | 42.6 | 22.1 | 0.60 (0.44–0.83) | 0.0021 |
| **IRC assessment** | 31.8 | 20.9 | 0.67 (0.49–0.91) | 0.0108 | 43.5 | 22.1 | 0.63 (0.45–0.87) | 0.0057 |

CR = complete response; TTNT = time to next treatment; OS = overall survival; IRC = independent review committee

Wang M et al. ASH 2023;Abstract LBA-2.

# Rel/Ref MCL: Acala

| | Blastoid/ Pleomorphic MCL (n=26) | All Pts (N=124) |
|---|---|---|
| ORR (CR + PR), % | 81 | 81 |
| CR, % | 39 | 48 |
| Median DOR, mo | 13.5 | 29 |
| Median PFS, mo | 15.2 | 22 |
| Median OS, mo | 36.3 | 59 |




A Fib

- Any grade, n=3 (2.4%)
- Grade 3/4, n=0

Hypertension

- Any grade, n=5 (4.0%)
- Grade 3/4, n=2 (1.6%)

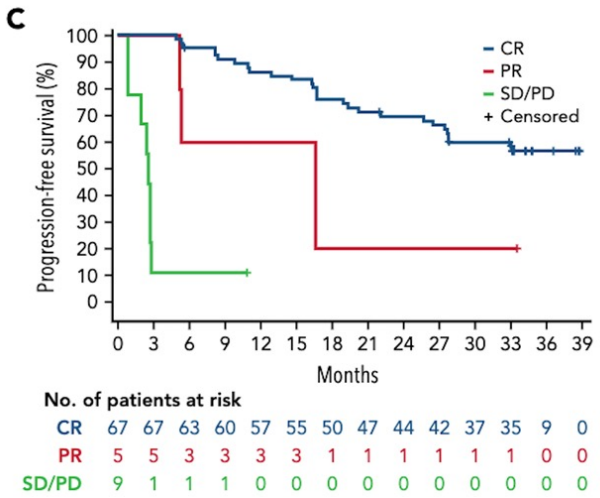
Hemorrhage

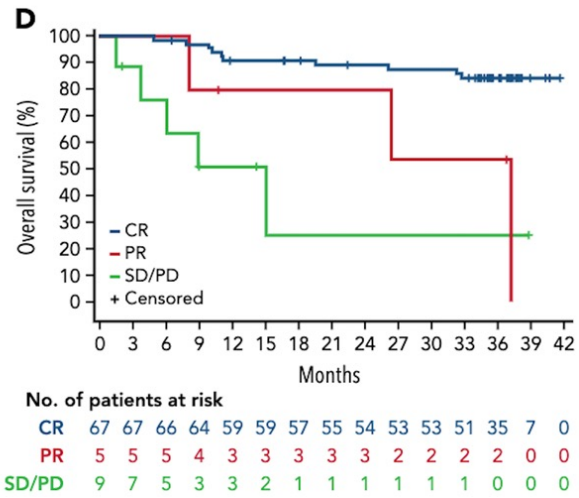
- Any grade, n=46 (37.1%)
- Grade 3/4, n=5 (4.0%)

Le Gouill, et al. EHA 2022. Abs # P1131

# Rel/Ref MCL: Zanu

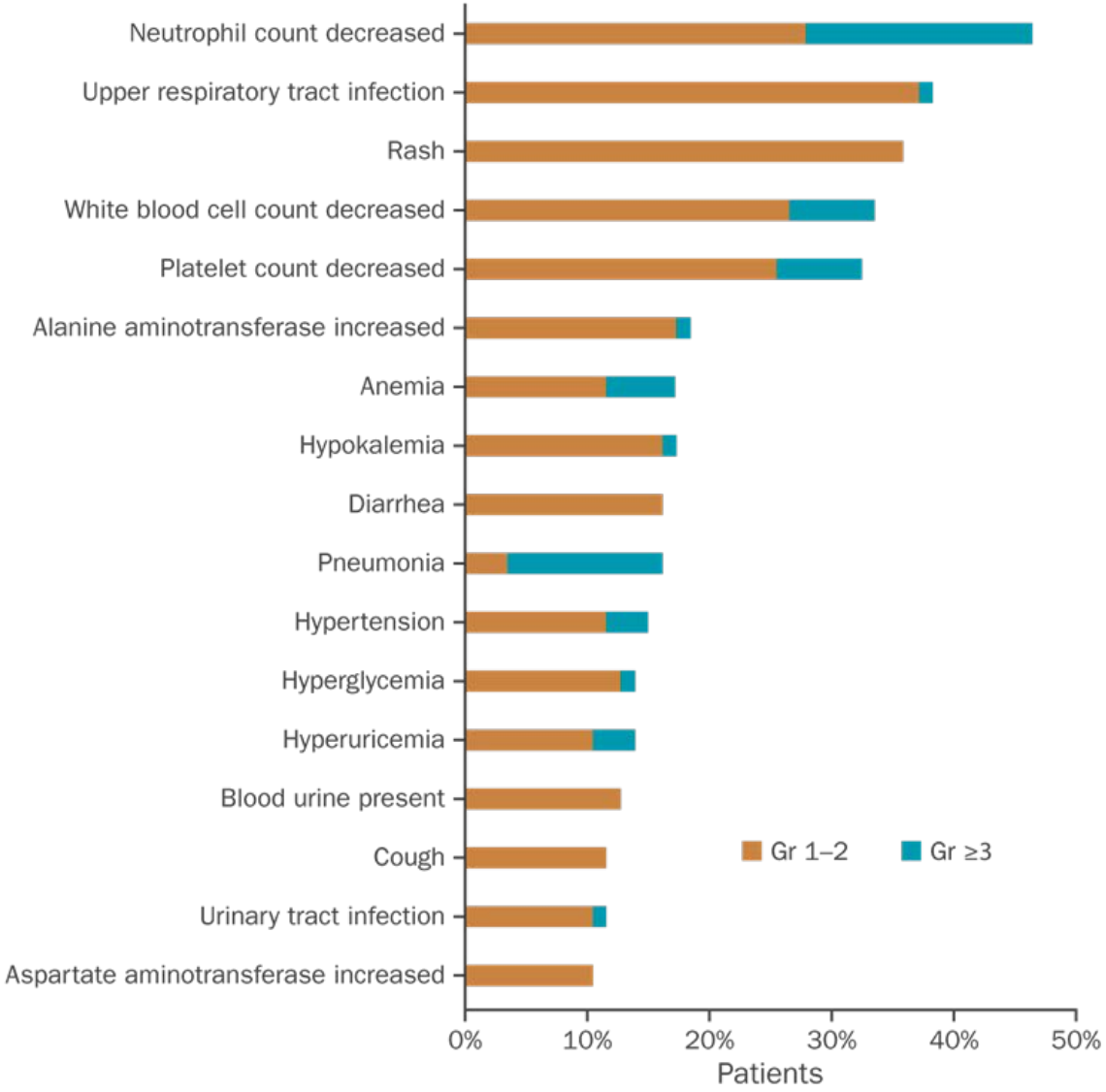
| | N=86 |
|---|---|
| ORR (CR+PR), % (95% CI) | 83.7 (74.2-90.8) |
| Best response, n (%) | |
| CR | 67 (77.9) |
| PR | 5 (5.8) |
| Median follow-up, mo | 30.6 |
| Median DOR, mo (95% CI) | NR (24.9-NE) |
| Median PFS, mo (95% CI) | 33.0 (19.4-NE) |
| 36-month PFS, % (95% CI) | 47.6 (36.2-58.1) |
| 36-month OS, % (95% CI) | 74.8 (63.7-83.0) |



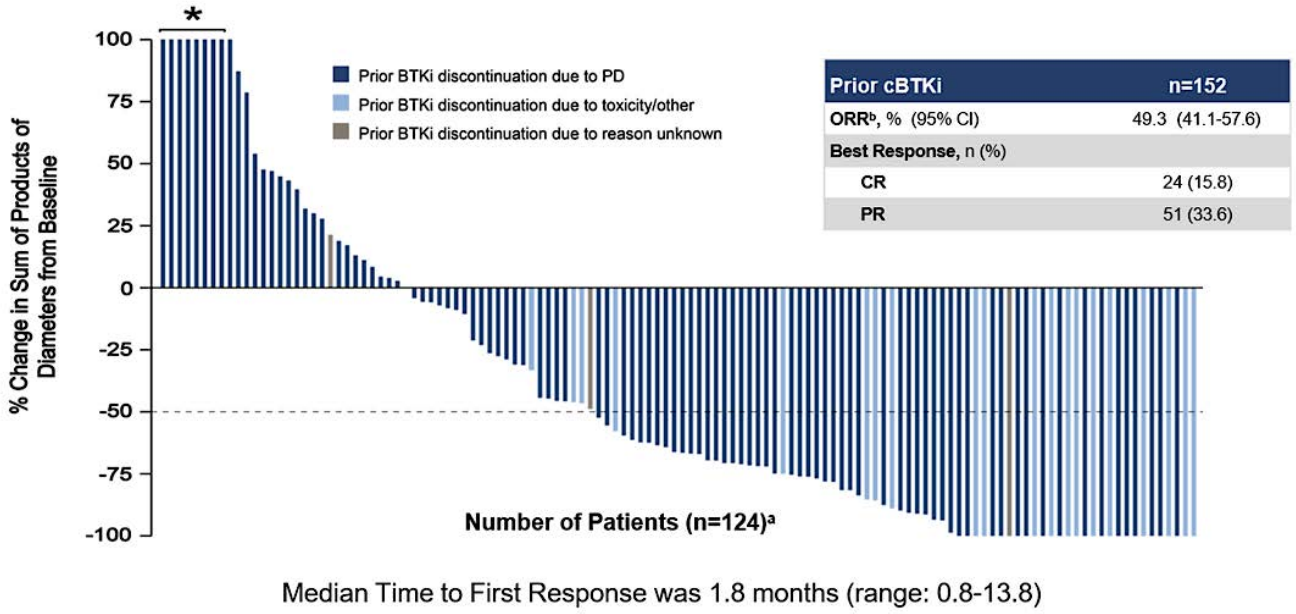

Song et al. Blood. 2022

# Rel/Ref MCL: Zanu



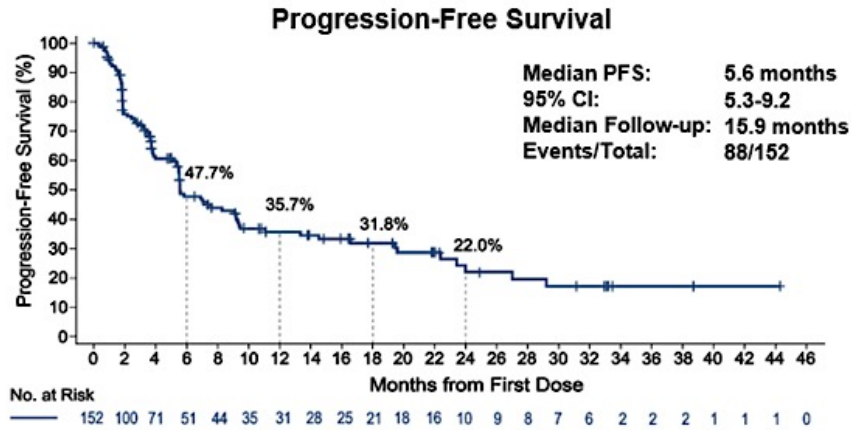

Song et al. Blood. 2022

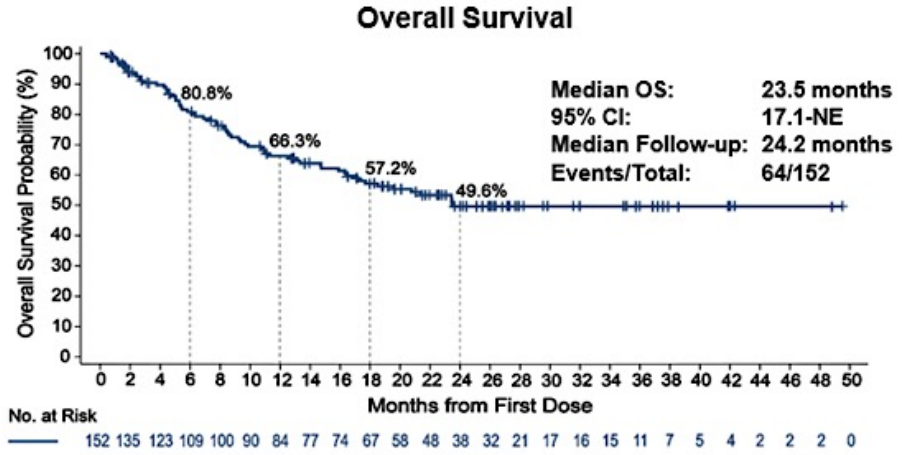
# Rel/Ref MCL: Pirtobrutinib in Pts with Prior cBTKi




| Prior cBTKi | n=152 |
|---|---|
| ORR[b], % (95% CI) | 49.3 (41.1-57.6) |
| **Best Response**, n (%) | |
| CR | 24 (15.8) |
| PR | 51 (33.6) |

Median Time to First Response was 1.8 months (range: 0.8-13.8)

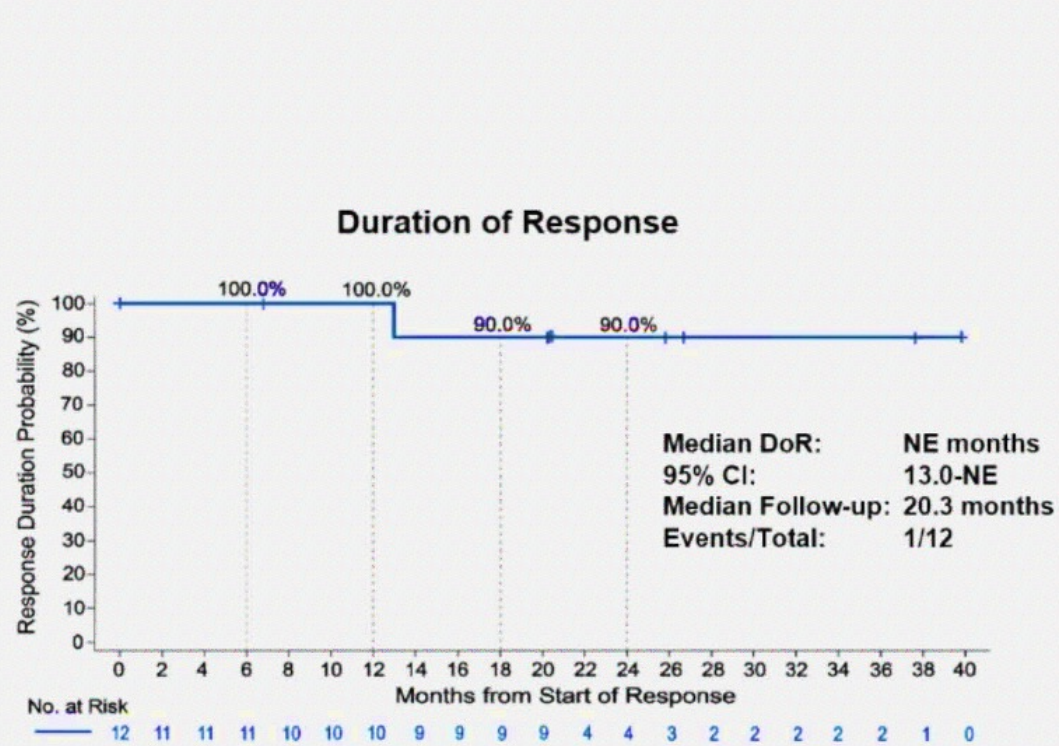


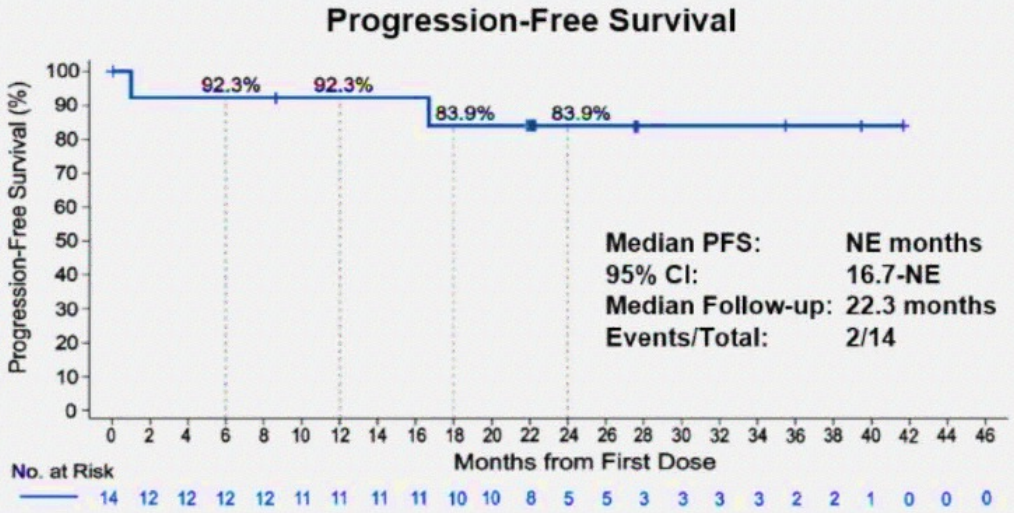



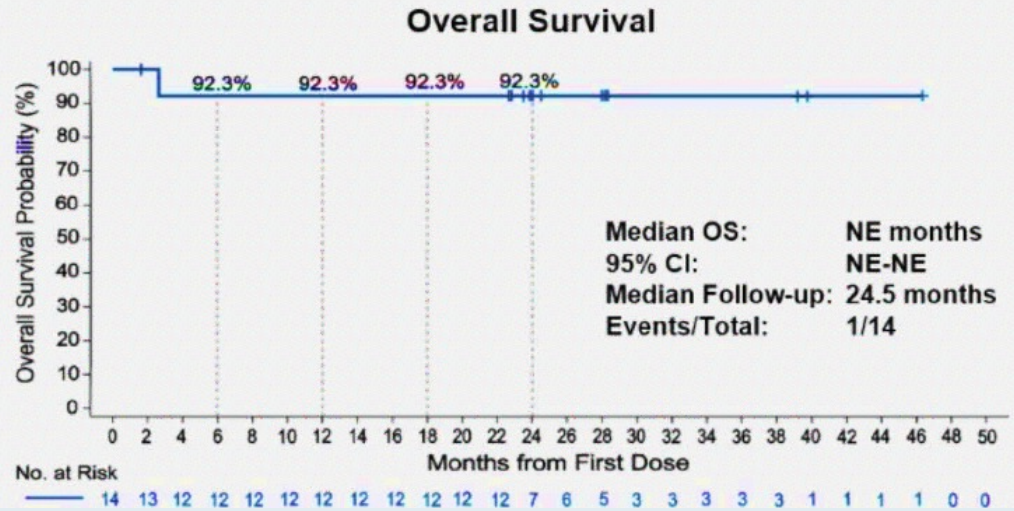

- Pirtobrutinib also demonstrated anti-tumor activity in patients with prior cBTKi and high-risk molecular features including high Ki-67 expression and TP53 mutations.

Cohen et al. ASH 2023 Abs 981

# Pirtobrutinib for Patients with R/R cBTKi-Naïve MCL




cBTKi Naive Cohort:

- The ORR[a] was 85.7% (95% CI: 57.2-98.2)
  - 6 CR (42.9%) and 6 PR (42.9%)

R/R = relapsed/refractory; cBTKi = covalent Bruton tyrosine kinase inhibitor; ORR = overall response rate

Cohen JB et al. ASH 2023;Abstract 981.

# Relapsed/Refractory MCL: Pirtobrutinib – Safety

| | Treatment-Emergent AEs in Patients with MCL (n=166) | | | |
|---|---|---|---|---|
| | All Cause AEs, (≥15%), % | | Treatment-Related AEs, % | |
| **Adverse Event** | **Any Grade** | **Grade ≥3** | **Any Grade** | **Grade ≥3** |
| Fatigue | 31.9 | 3.0 | 21.1 | 2.4 |
| Diarrhea | 22.3 | 0.0 | 12.7 | 0.0 |
| Dyspnea | 17.5 | 1.2 | 9.0 | 0.6 |
| Anemia | 16.9 | 7.8 | 7.2 | 2.4 |
| Platelet Count Decreased | 15.1 | 7.8 | 7.8 | 3.0 |
| **AEs of Interest[a]** | **Any Grade** | **Grade ≥3** | **Any Grade** | **Grade ≥3** |
| Infections[b] | 42.8 | 19.9 | 15.7 | 3.6 |
| Bruising[c] | 16.3 | 0.0 | 11.4 | 0.0 |
| Rash[d] | 14.5 | 0.6 | 9.0 | 0.0 |
| Arthralgia | 9.0 | 1.2 | 2.4 | 0.0 |
| Hemorrhage[e] | 10.2 | 2.4 | 4.2 | 0.6 |
| Hypertension | 4.2 | 0.6 | 1.8 | 0.0 |
| Atrial Fibrillation/Flutter[f,g] | 3.6 | 1.8 | 0.6 | 0.0 |

**Median time on treatment was 5.5 months for the MCL cohort**

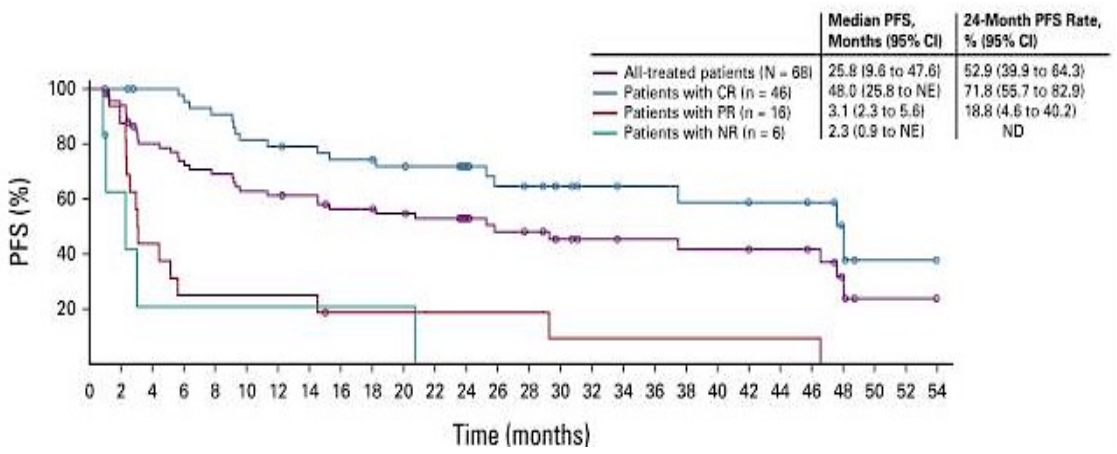
**Discontinuations due to TRAEs occurred in 3% (n=5) of patients with MCL**

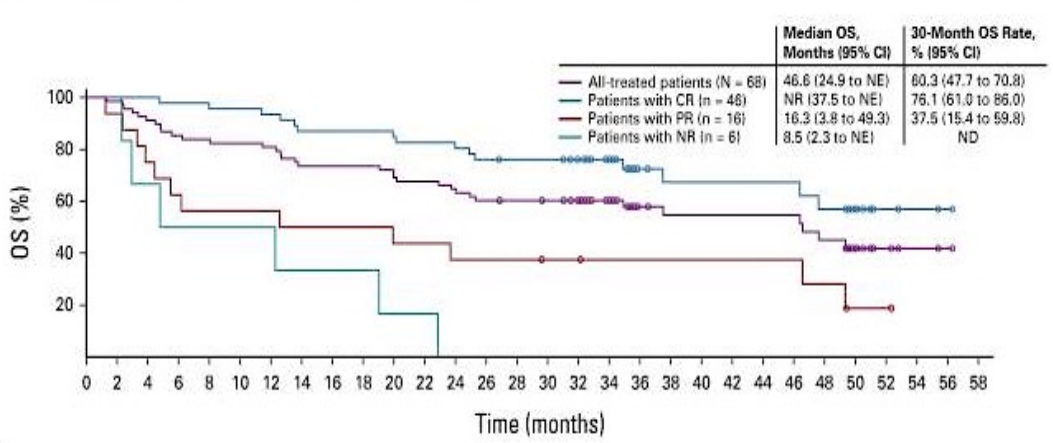
**Dose reductions due to TRAEs occurred in 5% (n=8) of patients with MCL**

Cohen JB et al. ASH 2023;Abstract 981.

# ZUMA-2: Brexu-cel

| | | N=68 |
|---|---|---|
| ORR, n (%) | | 91% |
| Best response, n (%) | CR | 68% |
| | PR | 24% |
| | | |

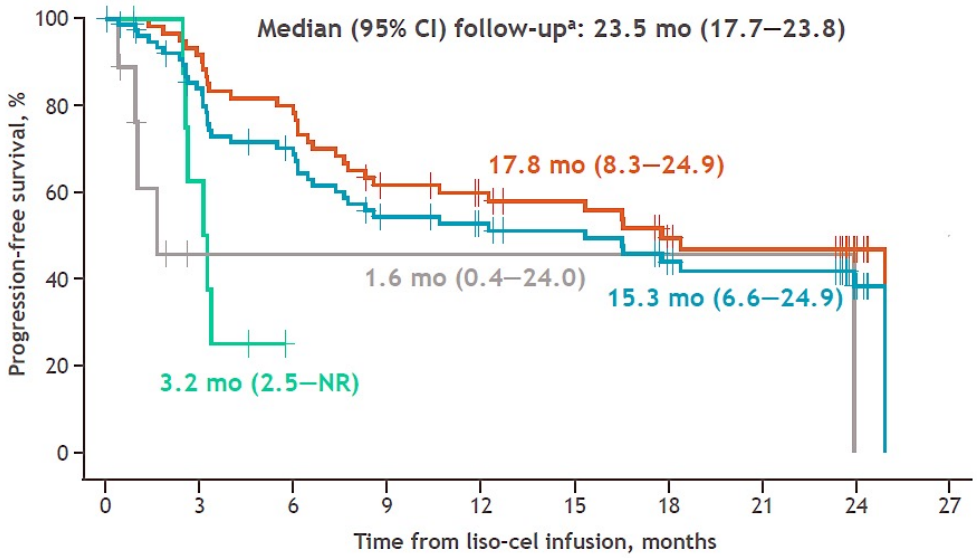


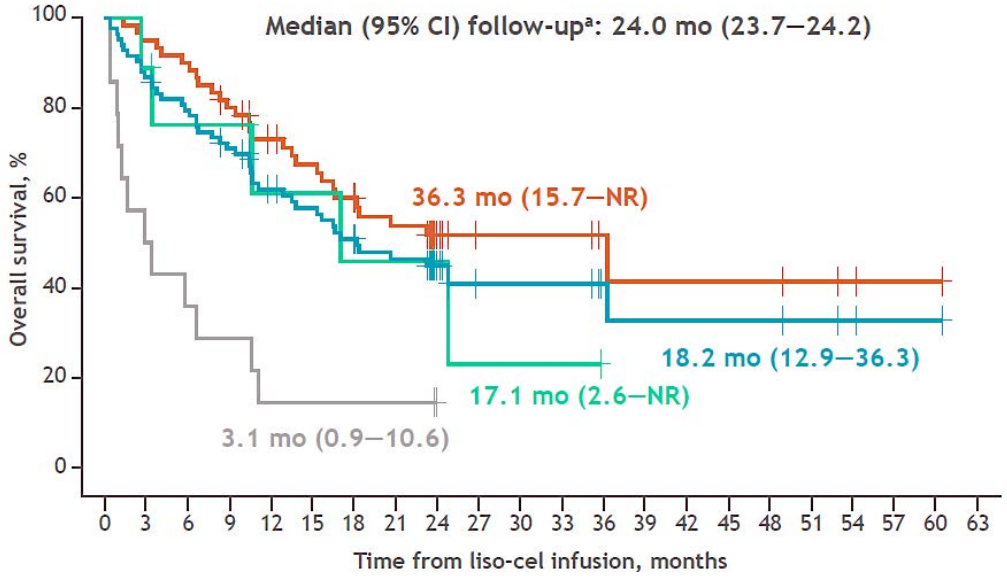




Wang et al. JCO 2023

# TRANSCEND NHL 001: Liso-cel

| | | N=74 |
|---|---|---|
| ORR, n (%) | | 86.5% |
| Best response, n (%) | CR | 74.3% |
| | PR | 12.2% |
| | | |




Wang et al. ICML 2023 Abs LBA3; Wang M, *J Clin Oncol*. Published online December 10, 2023.

# Agenda

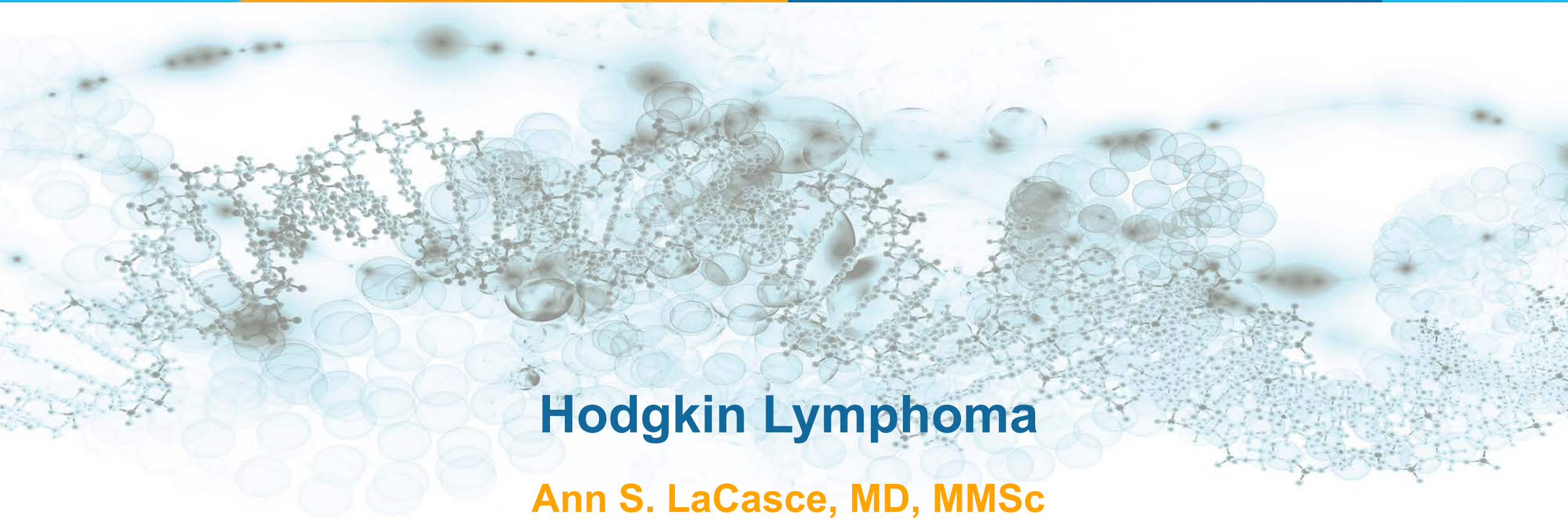
**Module 1: Follicular Lymphoma (FL) —** Dr Zelenetz

**Module 2: Mantle Cell Lymphoma (MCL) —** Dr Lunning

**Module 3: Hodgkin Lymphoma (HL) —** Dr LaCasce

**Module 4: Diffuse Large B-Cell Lymphoma (DLBCL) —** Dr Maddocks

Dana-Farber Cancer Institute



# Hodgkin Lymphoma

Ann S. LaCasce, MD, MMSc

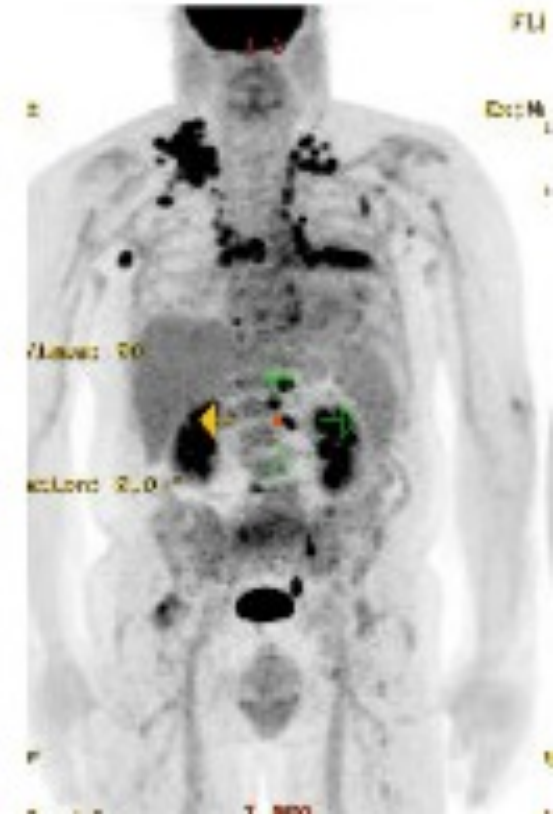
March 23, 2024

# Disclosures

| | |
|---|---|
| **Advisory Committees** | Kite, A Gilead Company, Seagen Inc |
| **Data and Safety Monitoring Board/Committee (Does Not Take Payment)** | Bristol Myers Squibb |

# 59-Year-Old M with Stage IVA cHL

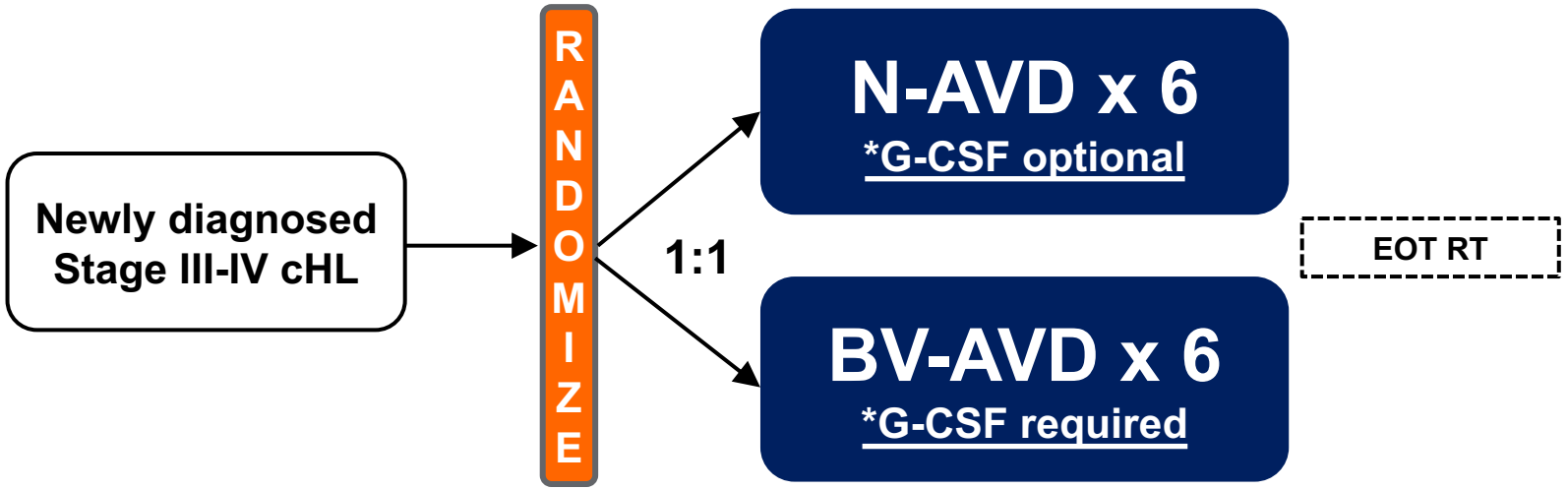
- Noted right neck node on self exam as well as right sided chest pain.
- Chest CT with supraclavicular and mediastinal adenopathy and mild splenomegaly.
- Core need biopsy revealed classic HL, NOS. RS cells CD30 and CD15 positive.
- PET revealed disease in the bilateral supraclavicular and mediastinum. He had uptake in a LUL pulmonary nodule, ribs and spine with soft tissue mass associated with right second rib. He had bilateral effusion and heterogeneous uptake in the axial and appendicular skeleton.
- His IPS was a 3: M, age ≥ 45 and stage IV disease.



# Management of advanced stage HL patients

| Adult oncology US: | Adult oncology Europe: | Pediatric oncology US: |
|---|---|---|
| Brentuximab vedotin + AVD | Escalated BEACOPP (PET adapted) | Brentuximab vedotin + AVEPC +/- RT |
| BV-AVD<br>6 yr PFS: 82% | EscBEACOPP<br>5 yr PFS: 91% | BV-AVEPC + RT<br>3 yr PFS: 92% |
| Neuropathy | Risk of infertility<br>Stem cell damage (MDS/AML) | RT related side effects |
| Connors et al. NEJM 2017 | Borchmann et al. Lancet Onc 2017 | Castellino et al. NEJM 2022 |

# S1826: study design and eligibility criteria




## Key Inclusion

- Age ≥ 12 years old
- HIV+ eligible, if controlled
- Zubrod PS 0-2 (Peds: Lansky)
- LVEF ≥ 50% (or SF ≥ 27%)

## Key Exclusion

- Interstitial lung disease or pneumonitis
- Peripheral neuropathy ≥ Gr2
- Active autoimmune disease

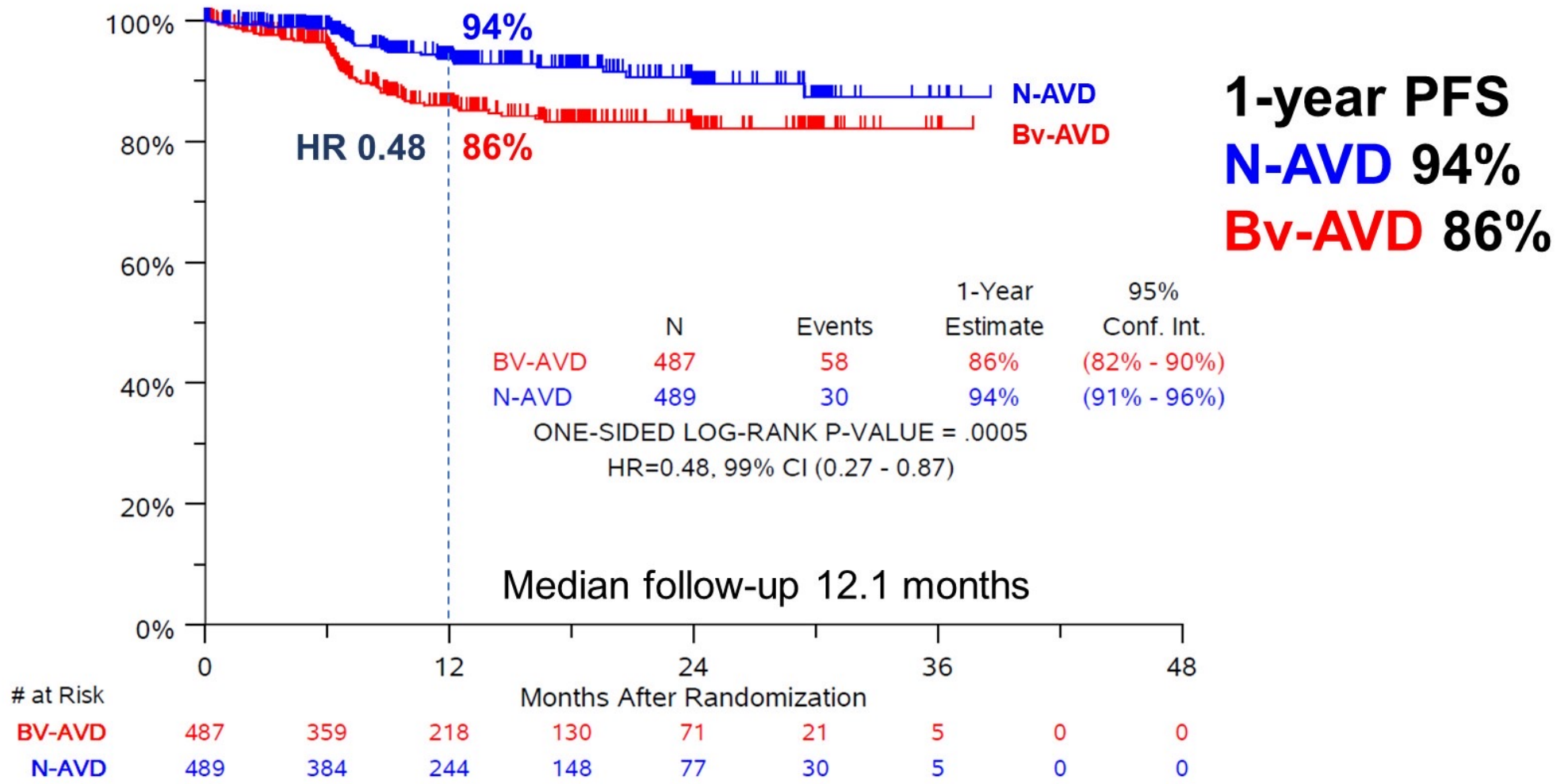
# S1826 Baseline Characteristics

| Baseline characteristics | N-AVD n=489 N (%) | Bv-AVD n=487 N (%) |
|---|---|---|
| Age, median (range) | 27 (12-83) | 26 (12-81) |
| 12-17 years | 120 (25%) | 117 (24%) |
| 18-60 years | 323 (66%) | 323 (66%) |
| ≥ 61 years | 46 (9%) | 47 (10%) |
| Female Sex | 218 (45%) | 213 (44%) |
| Race | | |
| White | 375 (77%) | 364 (75%) |
| Black | 57 (12%) | 56 (11%) |
| Asian | 11 (2%) | 17 (3%) |
| Other/Unknown | 46 (9%) | 50 (10%) |
| Hispanic | 68 (14%) | 59 (12%) |

| Baseline characteristics | N-AVD n=489 N (%) | Bv-AVD n=487 N (%) |
|---|---|---|
| Stage | | |
| III | 187 (38%) | 167 (34%) |
| IV | 301 (62%) | 317 (65%) |
| Not reported | 1 (0.2%) | 3 (1%) |
| B symptoms present | 286 (58%) | 274 (56%) |
| IPS Score | | |
| 0-3 | 331 (68%) | 330 (68%) |
| 4-7 | 158 (32%) | 157 (32%) |
| Bulky disease > 10cm | 155 (32%) | 131 (27%) |
| HIV+ | 10 (2%) | 5 (1%) |

**Representative study, inclusive of high-risk pts**

# S1826 Primary endpoint met: superior PFS of nivolumab-AVD vs BV-AVD




**1-year PFS**
**N-AVD 94%**
**Bv-AVD 86%**



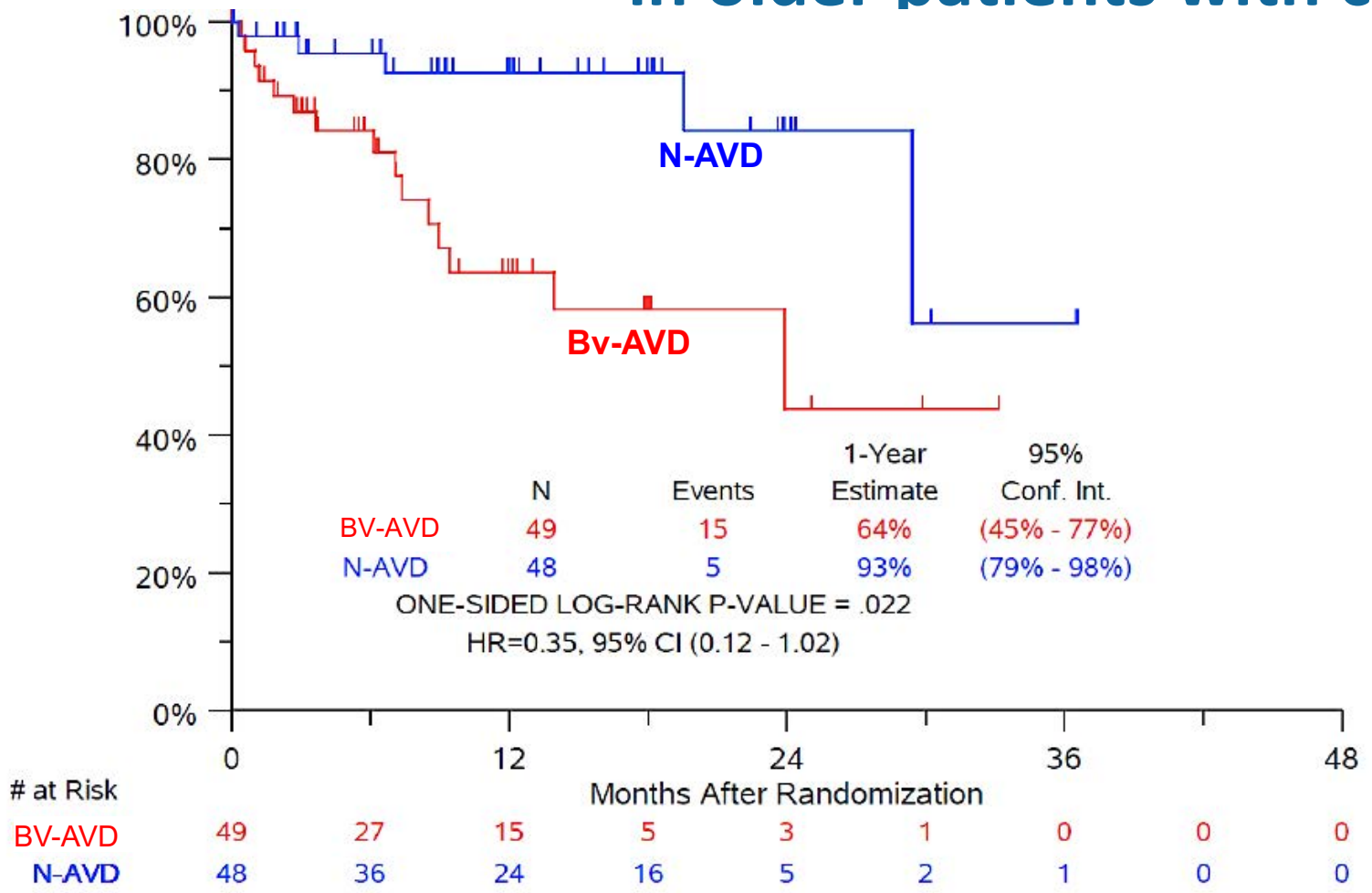
Herrera et al. ASCO 2023

# S1826: Results favor N-AVD with regard to short-term toxicities

| | Received g-csf | Febrile neutropenia | Thyroid dysfunction | ALT increased | Peripheral sensory neuropathy | Peripheral motor neuropathy | Discontinued N or BV |
|---|---|---|---|---|---|---|---|
| N-AVD | 54% | 5% | 10% | 32% | 29% | 4% | 11% |
| BV-AVD* | 95% | 7% | 1% | 41% | 55% | 7% | 22% |

* Growth factor support mandated per protocol

# S1826: N-AVD markedly improves PFS over Bv-AVD in older patients with cHL




**1-year PFS**

**N-AVD 93%**

**Bv-AVD 64%**

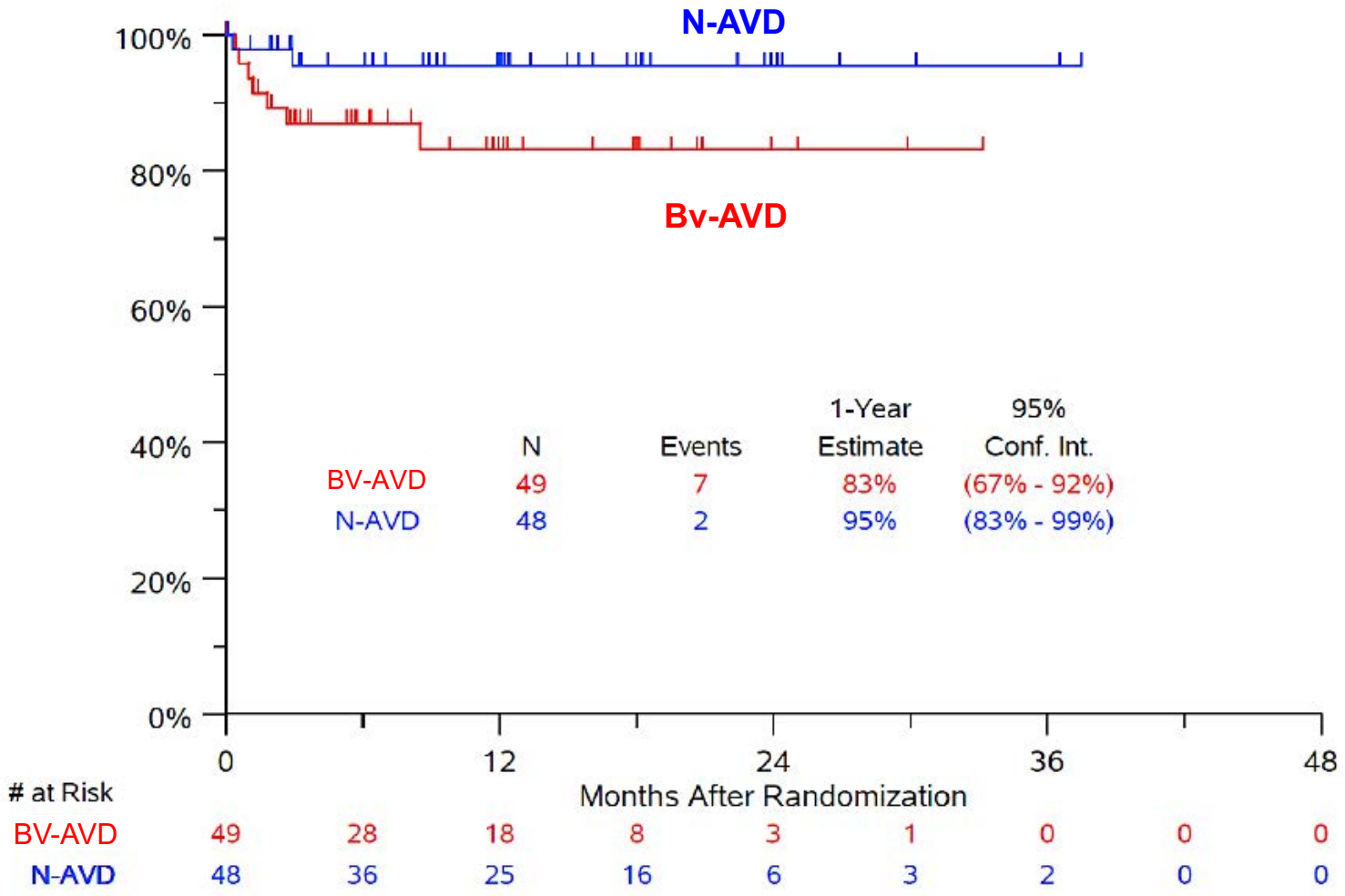
Median follow-up
12.1 months

p-value = 0.022
HR=0.35,
95% CI (0.12-1.02)



Rutherford et al. ASH 2023

# S1826: Fewer deaths occurred on N-AVD vs Bv-AVD




**1-year OS**

**N-AVD 95%**

**Bv-AVD 83%**

Median follow-up
12.1 months

p-value = 0.091
HR=0.35,
95% CI (0.07-1.75)

# S1826: Majority of deaths on Bv-AVD due to infection/sepsis

| Cause of death | N-AVD | Bv-AVD |
|---|---|---|
| Infection | 1 | 3 |
| Sepsis | 1 | 2* |
| Pneumonitis | 0 | 1 |
| Unknown | 0 | 1 |
| **Total OS events** | **2** | **7** |

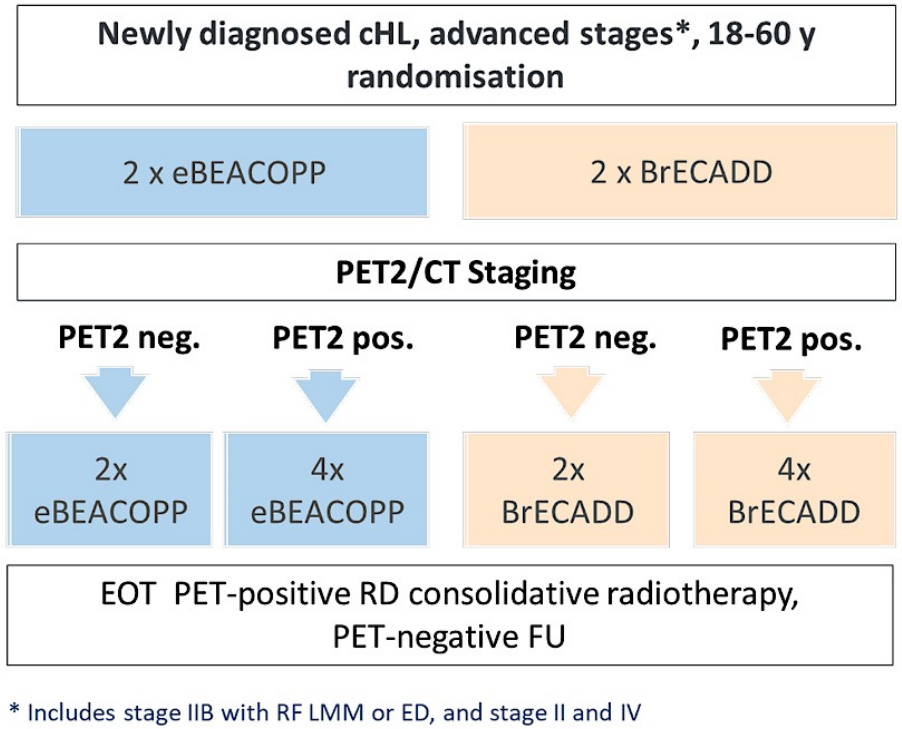
***Non-relapse mortality***
***N-AVD 4% vs Bv-AVD 14%***



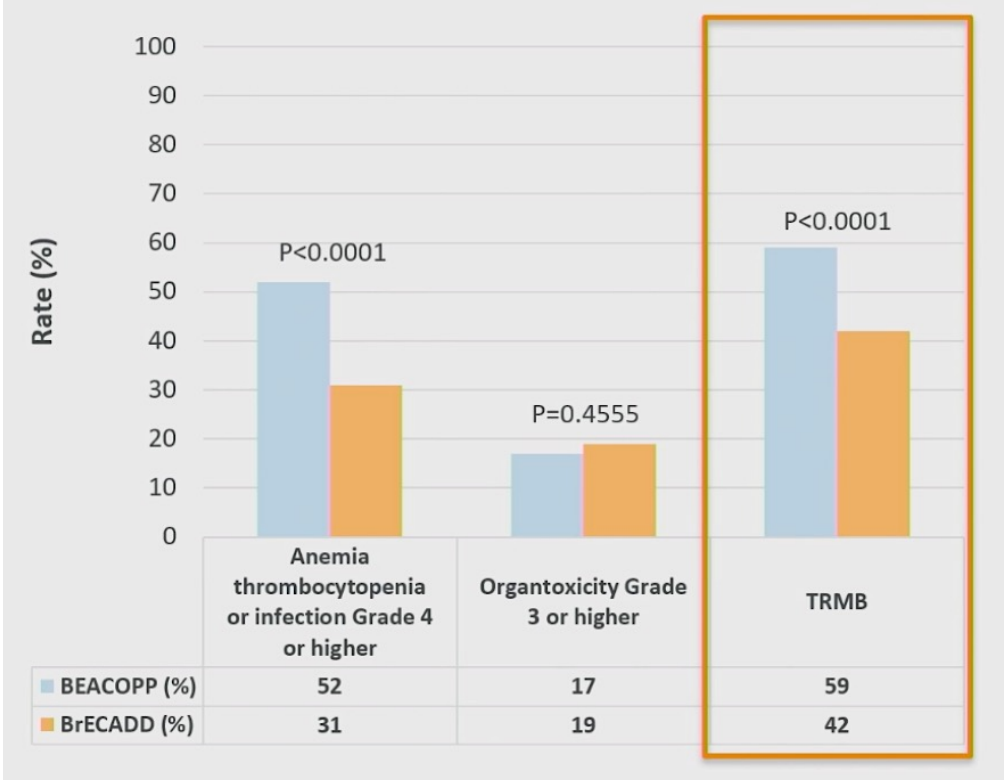
Rutherford et al. ASH 2023

*1 death from COVID-19/sepsis

# HD21:BEACOPP vc BrECADD




* Includes stage IIB with RF LMM or ED, and stage II and IV




**Co-primary endpoints:**

**Superiority for treatment related morbidity**

**Non-inferiority for efficacy**

**BrECADD superior:**

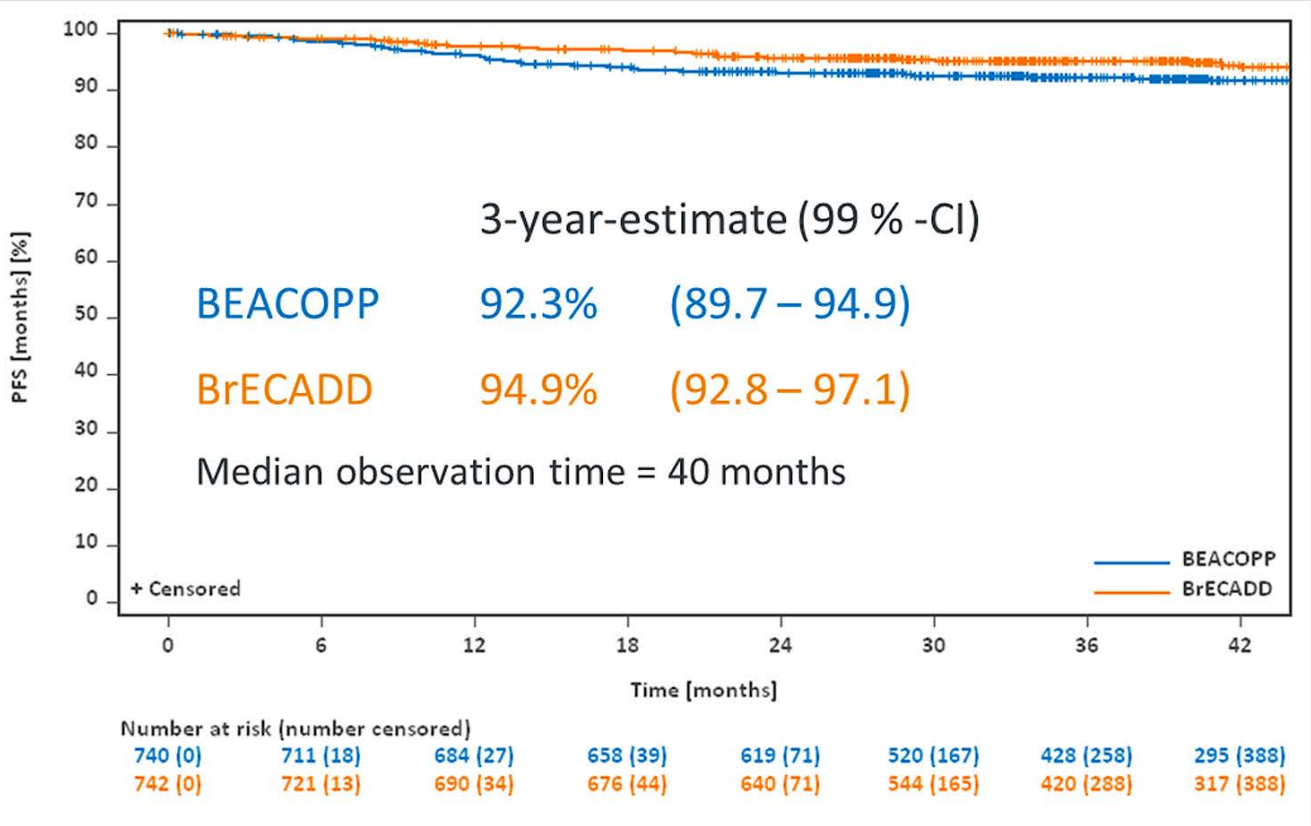
**Lower transfusions**
**Peripheral neuropathy**
**Normalization of FSH**



Borchmann et al. ASH 2022

# BrECADD is non-inferior to eBEACOPP in patients with advanced stage classical Hodgkin Lymphoma: efficacy results of the GHSG phase III HD21 trial.

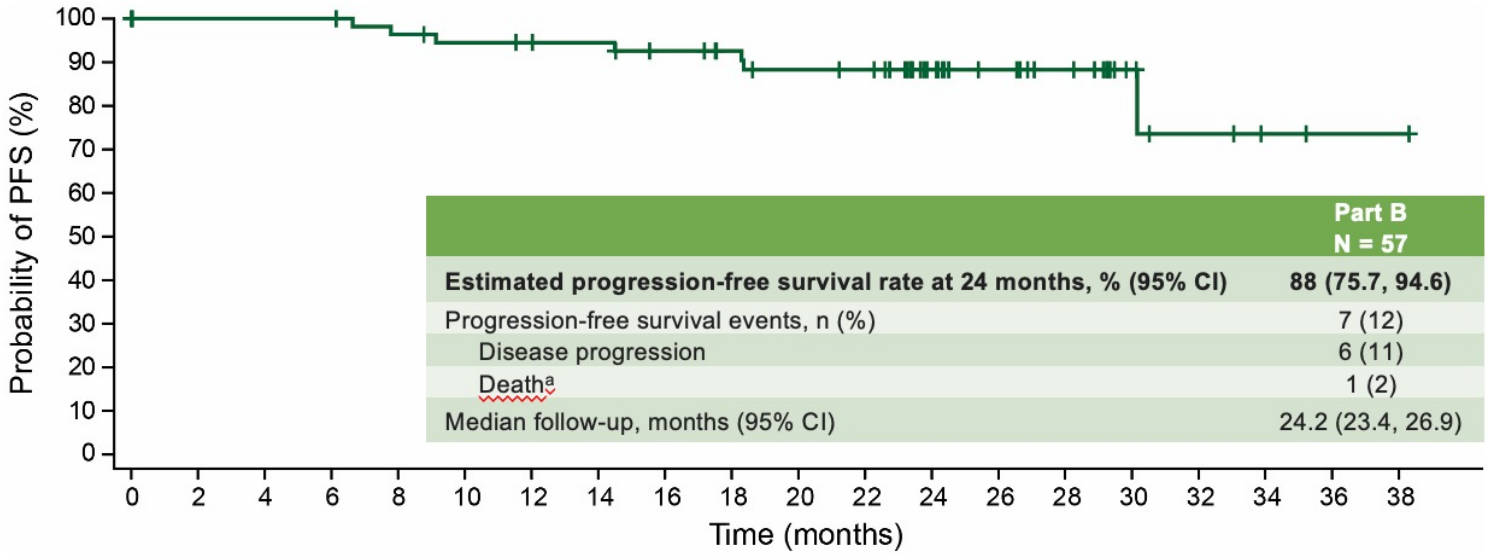
**Borchmann et al.** HD21 PFS – ITT




| | eBEACOPP N=740 | | BrECADD N=742 | |
|---|---|---|---|---|
| | n | % | n | % |
| Progression/Relapse | 55 | **7.4** | 32 | **4.3** |
| Progression | 14 | **1.9** | 5 | **0.7** |
| Early Relapse, FU <= 1 year | 23 | **3.1** | 11 | **1.5** |
| Late Relapse, FU > 1 year | 18 | 2.4 | 16 | 2.2 |
| Death without previous PRO or REL | 6 | 0.9 | 7 | 0.9 |
| **PFS events, total** | **61** | **8.4** | **39** | **5.3** |

# BV+Nivo plus AD in advanced stage HL

88% rate of progression-free survival after 2 years; no patients had subsequent radiation therapy

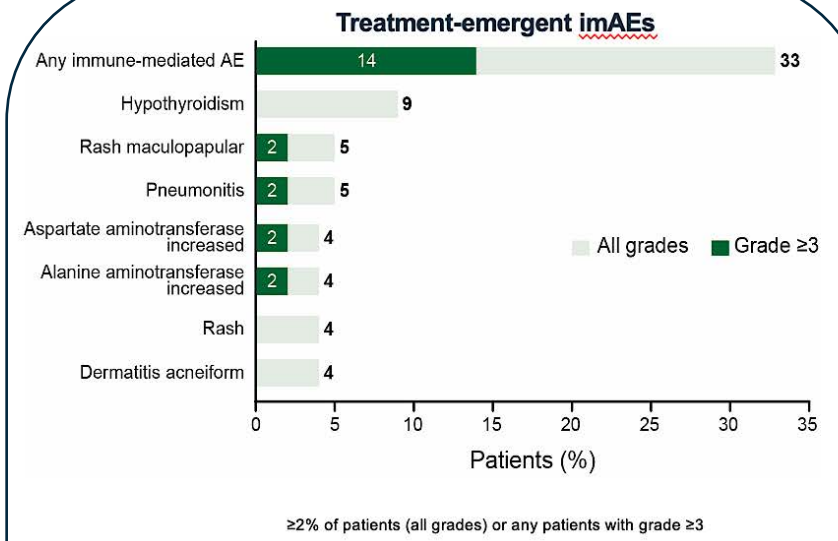



| | Part B N = 57 |
|---|---|
| **Estimated progression-free survival rate at 24 months, % (95% CI)** | **88 (75.7, 94.6)** |
| Progression-free survival events, n (%) | 7 (12) |
| Disease progression | 6 (11) |
| Death[a] | 1 (2) |
| Median follow-up, months (95% CI) | 24.2 (23.4, 26.9) |

N at risk (events)

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Part B | 57(0) | 56(0) | 56(0) | 56(0) | 53(2) | 51(3) | 50(3) | 49(3) | 46(4) | 43(4) | 40(6) | 39(6) | 28(6) | 21(6) | 17(6) | 7(6) | 4(7) | 2(7) | 1(7) | 1(7) |

[a]Patient died due to sepsis approximately 3.5 months following last dose of study drug

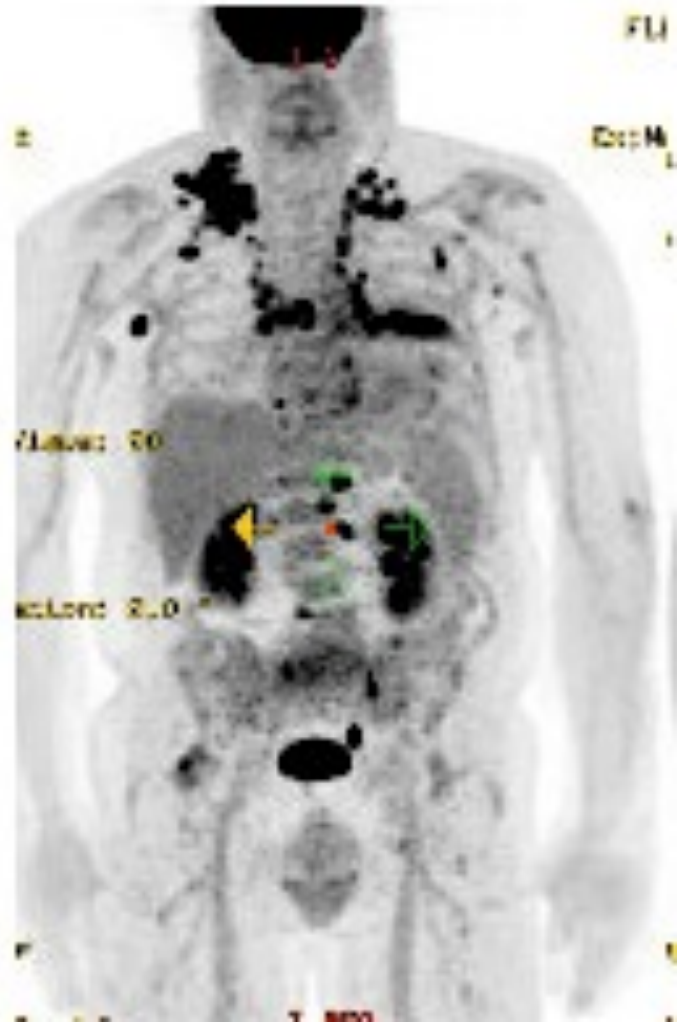



≥2% of patients (all grades) or any patients with grade ≥3

- Immune-mediated adverse events (imAEs) reported were primarily grade 1-2, and were consistent with the safety profile of nivolumab
- 4/57 (7%) had imAEs leading to discontinuation of nivolumab:
  - Colitis (n=1), hypophysitis (n=1), pneumonitis (n=1), Type 1 diabetes (n=1)

# 59-Year-Old M with Stage IVA Disease

- He was treated with BV+AVD
- Course was complicated by peripheral neuropathy and GI toxicity
- Interim and end of treatment PET/CT with Deauville 2
- He remains in remission



# Future directions

## Can we give less chemotherapy?

Some chemo likely required

Add BV to PD-1 inhibitors/optimal regimen

Risk adapt using imaging/ct DNA

PD-1 inhibitors with low CR rates as single agent.

BV-nivo in older patients with mixed results.

Nivo-AVD

BV+nivo + AD

BrECADD

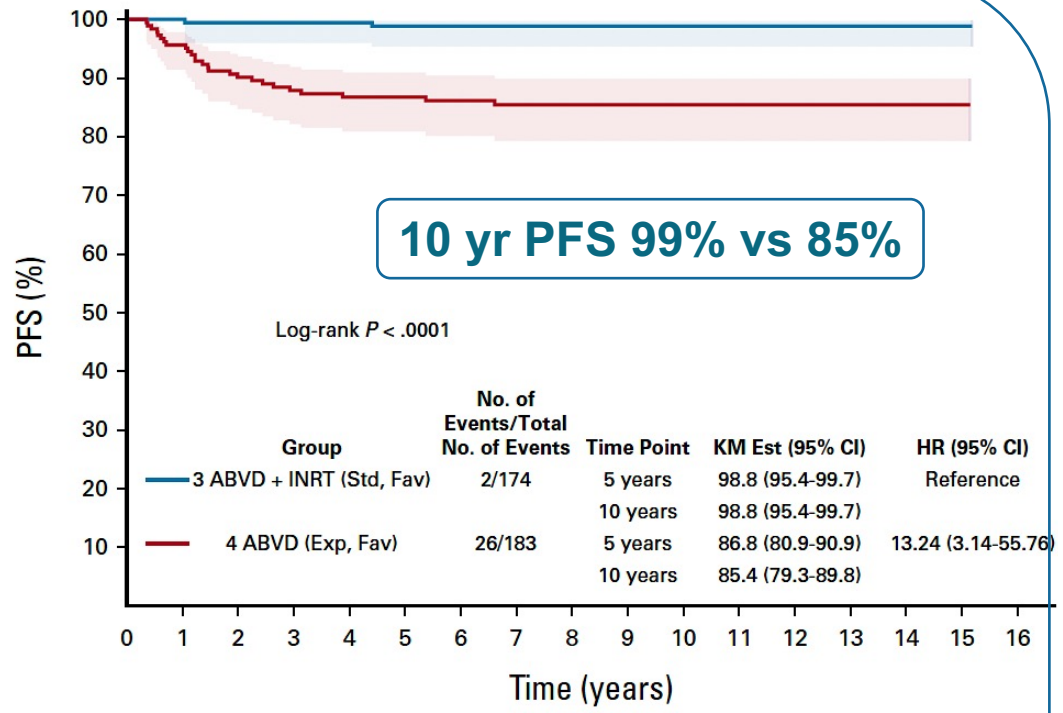
Will require analysis of current data to design de-escalation studies.

# Early stage HL therapy

| Current standard of care | Recent advances | On-going |
|---|---|---|
| ABVD chemotherapy<br><br>PET adapted/individualized use of RT | Many phase 2 studies with encouraging PFS with less RT | Randomized study to assess impact of BV and PD-1 inhibitors |

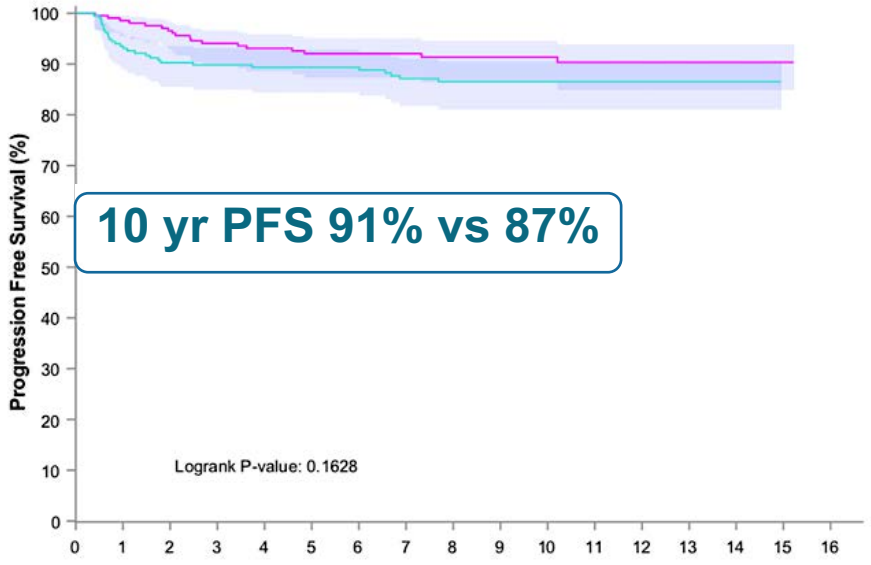
# Long term follow-up of PET 2 negative patients

**Positive PET = Deauville 3-5**
**81% of patients PET2 negative**




No. at risk:

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 3 ABVD + INRT (Std, Fav)- | 174 | 172 | 168 | 132 | 105 | 74 | 32 | 7 | 0 |
| 4 ABVD (Exp, Fav)- | 183 | 163 | 154 | 130 | 107 | 74 | 30 | 3 | 0 |




Patients-at-Risk

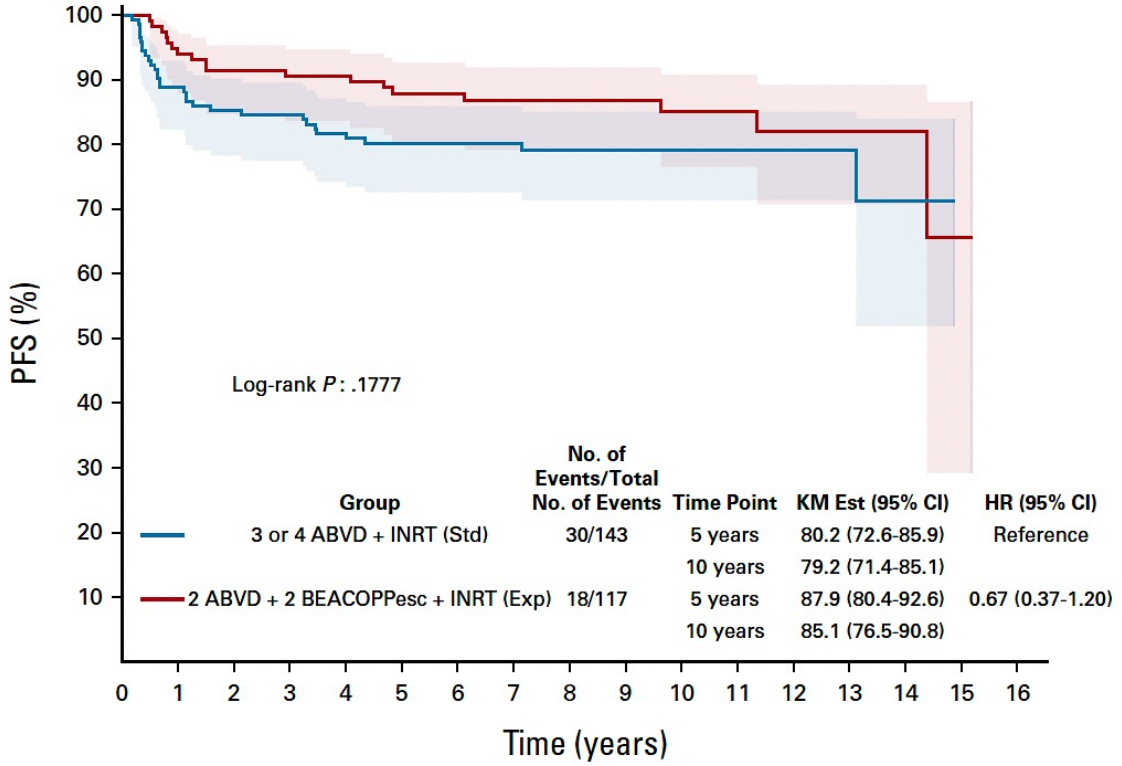
| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 4ABVD+INRT (Std,Unfav)- | 206 | 195 | 185 | 153 | 129 | 96 | 33 | 9 | 0 |
| 6ABVD (Exp,Unfav)- | 216 | 194 | 190 | 169 | 142 | 97 | 44 | 10 | 0 |



Federico et al. JCO 2023

# Long term follow-up of PET 2 positive patients

**Positive PET = Deauville 3-5**
**19% of patients PET2 positive**




No. at risk:

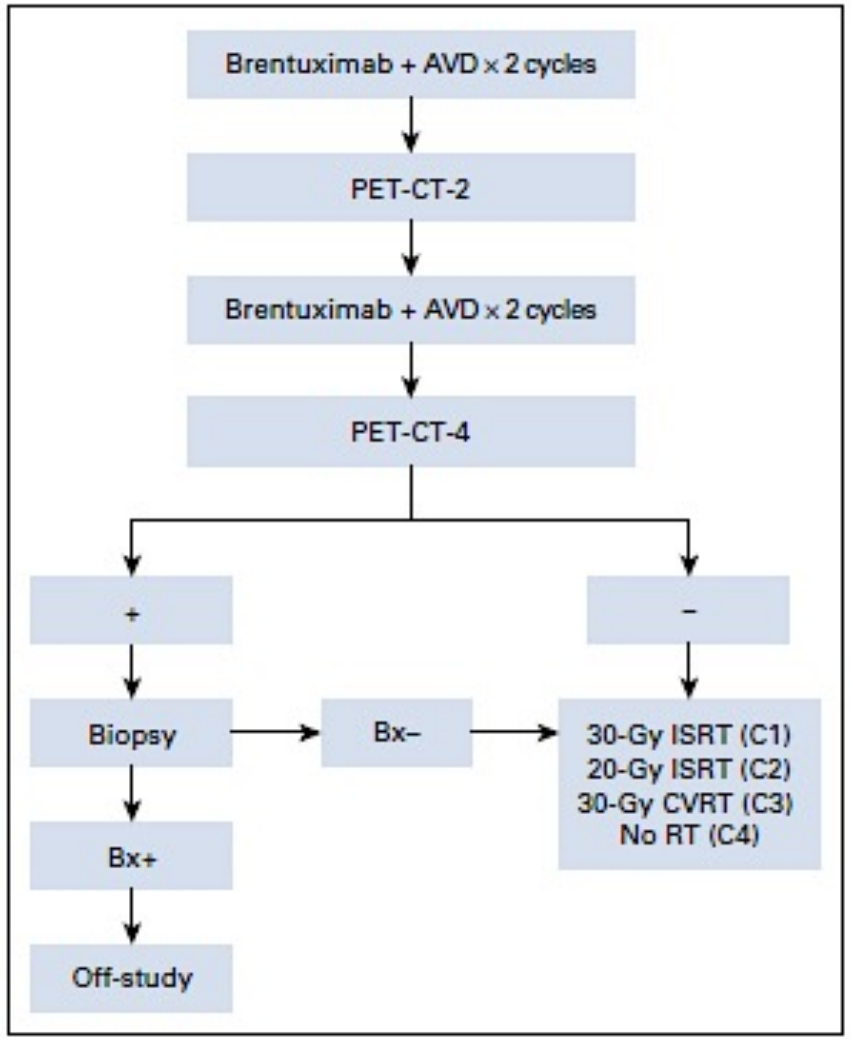
| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 3 or 4 ABVD + INRT (Std)- | 143 | 121 | 112 | 93 | 73 | 51 | 22 | 6 | 0 |
| 2 ABVD + 2 BEACOPPesc + INRT (Exp)- | 117 | 107 | 101 | 87 | 74 | 45 | 21 | 6 | 0 |

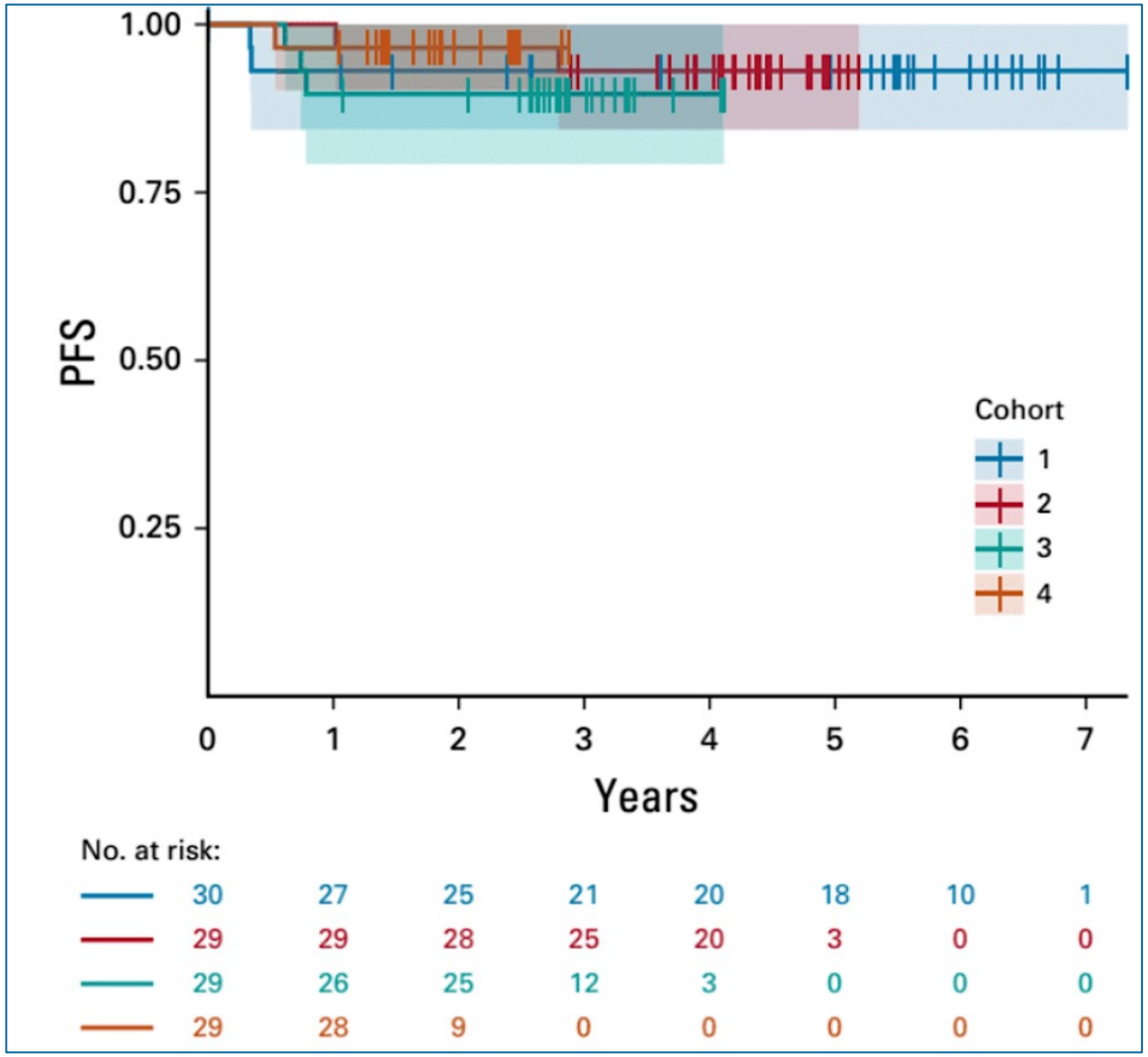
**10 yr PFS 80% vs 85%**



Federico et al. JCO 2023

# BV-AVD +/- RT with excellent outcomes in unfavorable HL



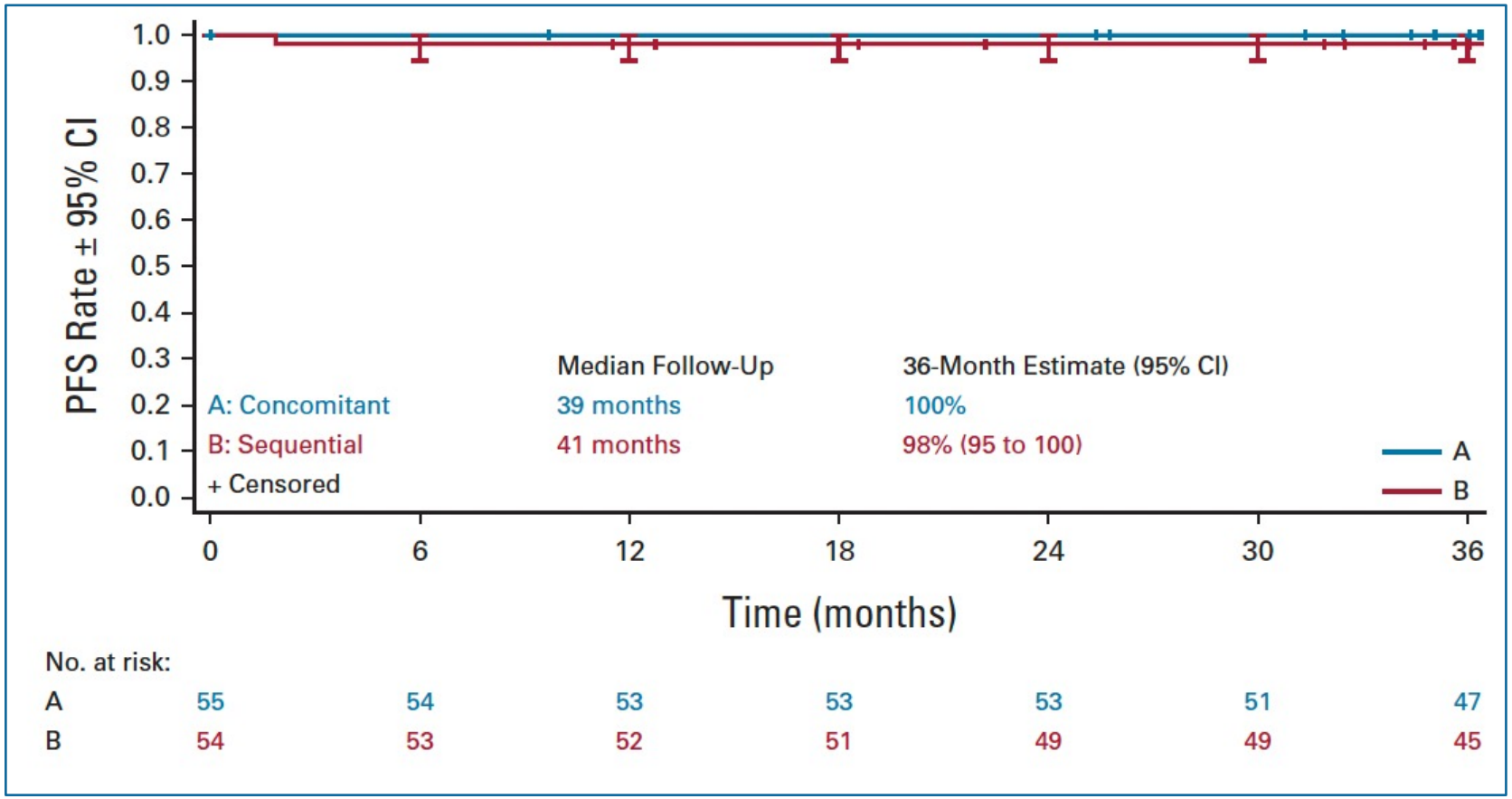



Kumar et al. JCO 2021

# Nivolumab + AVD (concurrent and sequential) in early unfavorable HL very promising though all patients received RT

**Randomized phase 2**
**A: 4 x N-AVD**
**B: 4 x N**
**2 x N-AVD**
**2 x AVD**

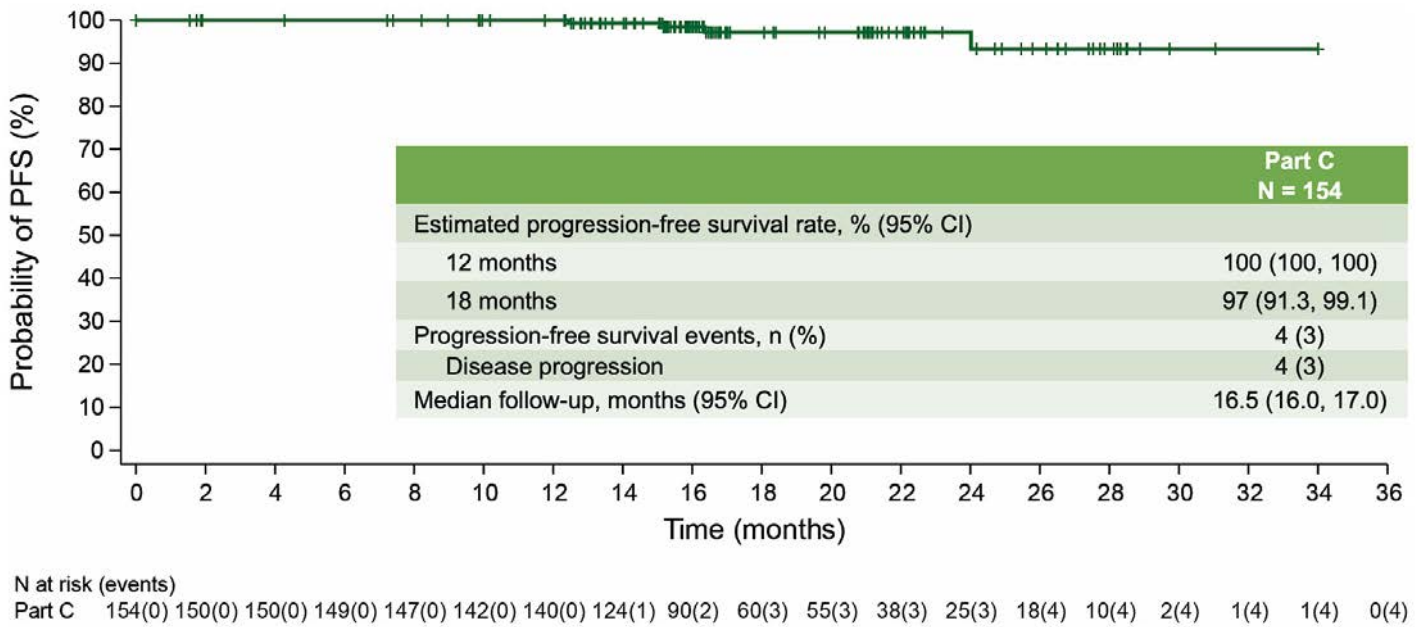
**30 Gy ISRT**






Brocklemann et al. JCO 2022

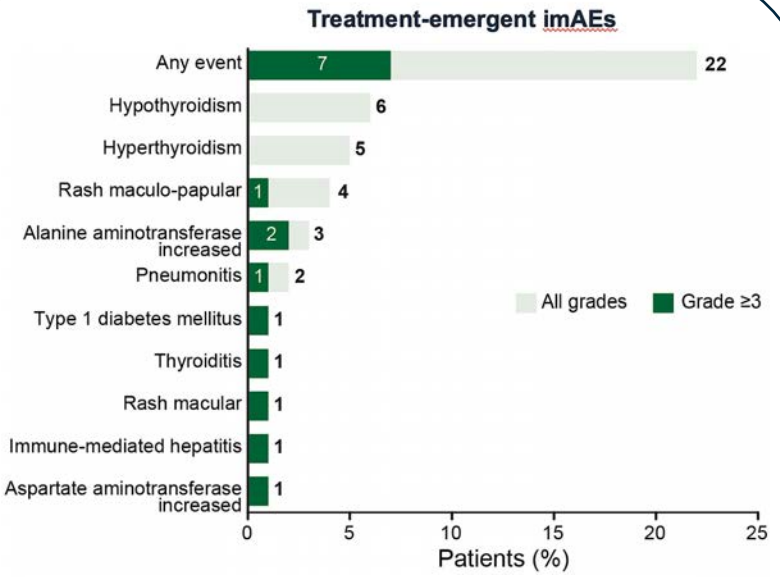
# BV+Nivo plus AD x 4 in non bulky stage I/II HL




| | Part C N = 154 |
|---|---|
| Estimated progression-free survival rate, % (95% CI) | |
| 12 months | 100 (100, 100) |
| 18 months | 97 (91.3, 99.1) |
| Progression-free survival events, n (%) | 4 (3) |
| Disease progression | 4 (3) |
| Median follow-up, months (95% CI) | 16.5 (16.0, 17.0) |

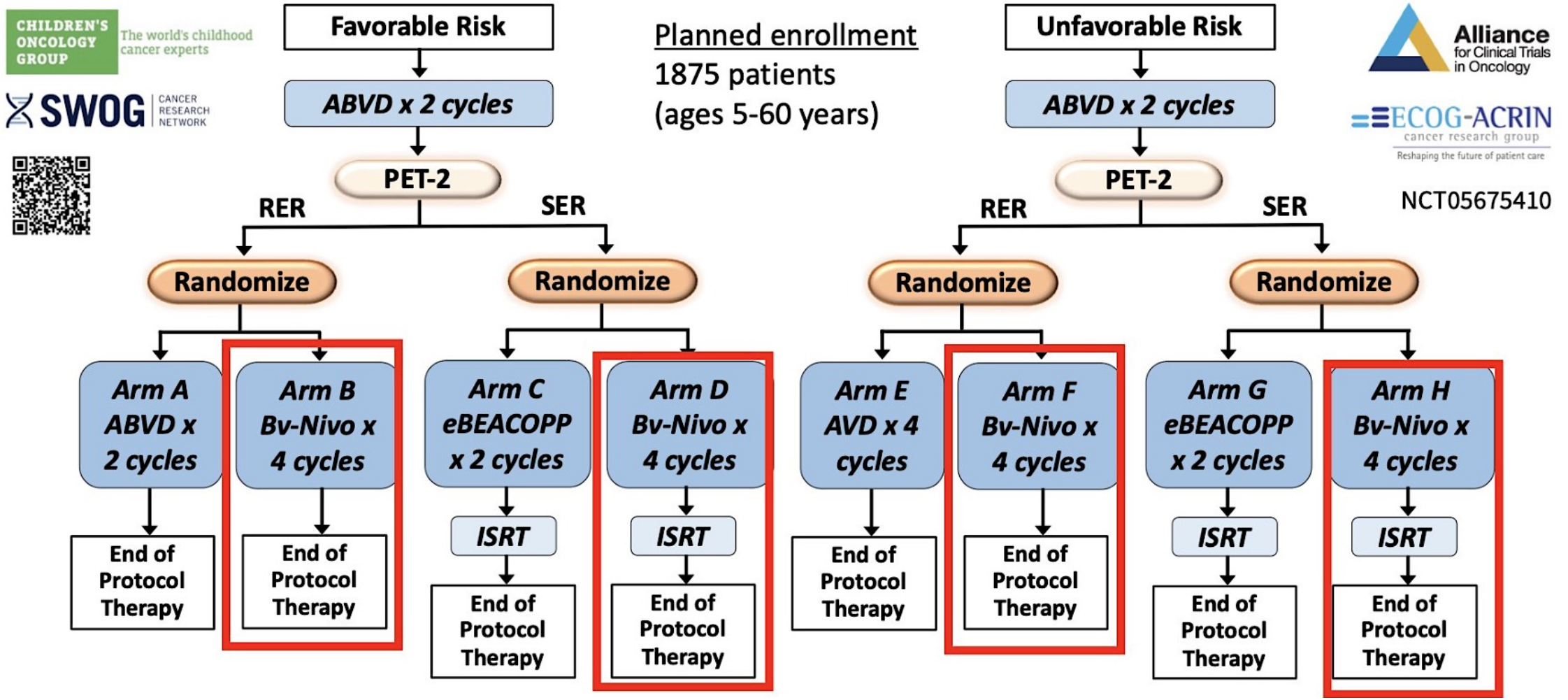
N at risk (events)

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Part C | 154(0) | 150(0) | 150(0) | 149(0) | 147(0) | 142(0) | 140(0) | 124(1) | 90(2) | 60(3) | 55(3) | 38(3) | 25(3) | 18(4) | 10(4) | 2(4) | 1(4) | 1(4) | 0(4) |




- The maximum grades for immune-mediated adverse events (imAEs) reported were primarily grade 1-2, and were consistent with the safety profile of nivolumab
- 4/154 (3%) had imAEs leading to discontinuation of nivolumab:
  - Pneumonitis (n=2), hepatitis (n=1), thyroiditis (n=1)

# Standard therapy vs. immuno-oncology for children and adults with newly diagnosed stage I and II classic HL: AHOD 2131



# Agenda

**Module 1: Follicular Lymphoma (FL) —** Dr Zelenetz

**Module 2: Mantle Cell Lymphoma (MCL) —** Dr Lunning

**Module 3: Hodgkin Lymphoma (HL) —** Dr LaCasce

**Module 4: Diffuse Large B-Cell Lymphoma (DLBCL) —** Dr Maddocks

# Diffuse Large B Cell Lymphoma (DLBCL)

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# Disclosures

| | |
|---|---|
| **Consulting Agreements** | AbbVie Inc, ADC Therapeutics, AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, Genentech, a member of the Roche Group, Genmab US Inc, Incyte Corporation, Janssen Biotech Inc, Kite, A Gilead Company, Lilly, MorphoSys |

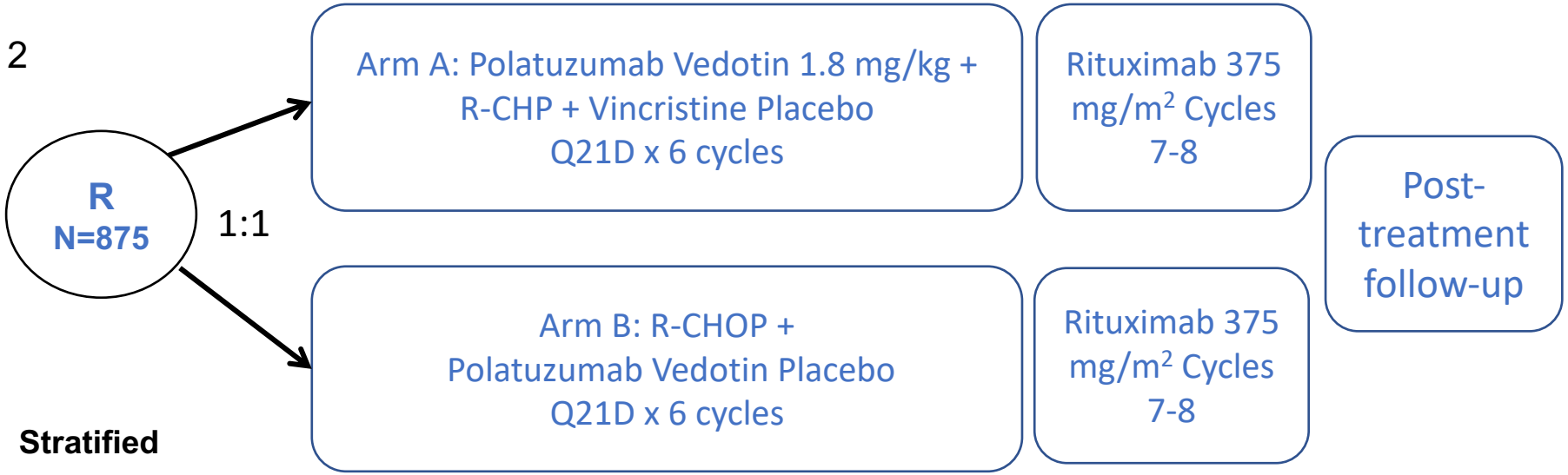
# Patient Case

- 54 yo F with Stage IV Aggressive B Cell Lymphoma with rearrangement of c-myc and bcl-2
- Treated with 6 cycles of DA-REPOCH with IT methotrexate
- End of treatment PET consistent with CMR
- 7 months later presents with symptomatic relapse with inguinal node
- Pulse dex followed by leukapheresis
- Radiation to bulky inguinal disease
- Axi-cel infusion
- Day +30 PR, followed by progression
- Clinical Trial vs. Bispecific Antibody

# POLARIX: R-CHOP vs R-CHP + Polatuzumab

**Key eligibility criteria**

- Previously untreated DLBCL
- Stage II to IV disease
- IPI ≥ 2
- ECOG PS ≤ 2




**Stratified**

- IPI Score (2 vs 3-5)
- Bulky Disease (present vs absent)
- Region

**Primary endpoint:** PFS by INV

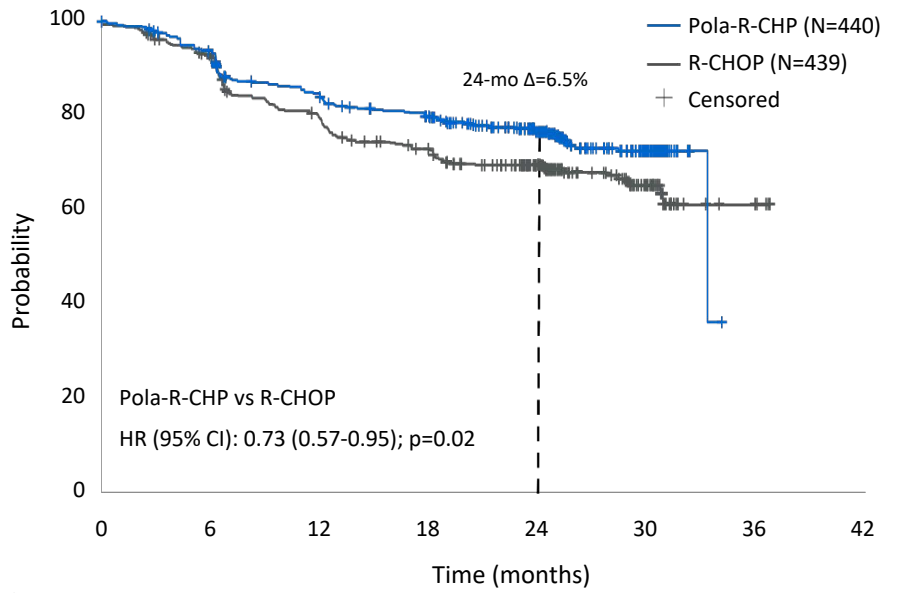
**Key secondary endpoints:** $EFS_{efficacy}$ by INV, PET CR at EOT by BICR, OS, safety

Tilly H, et al. *N Engl J Med.* 2022;386(4):351-363.

# POLARIX: R-CHOP vs R-CHP + Polatuzumab

## 2-yr PFS 76.7 vs 70.2

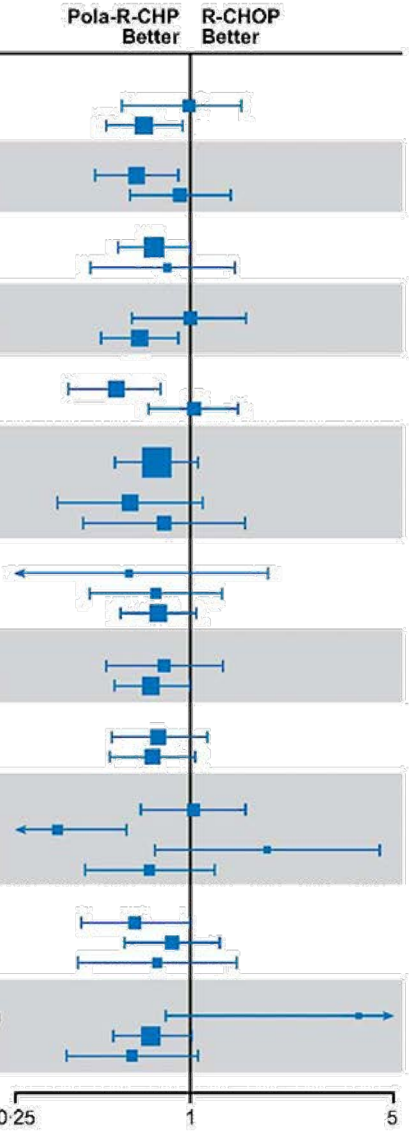
PFS




Number at risk

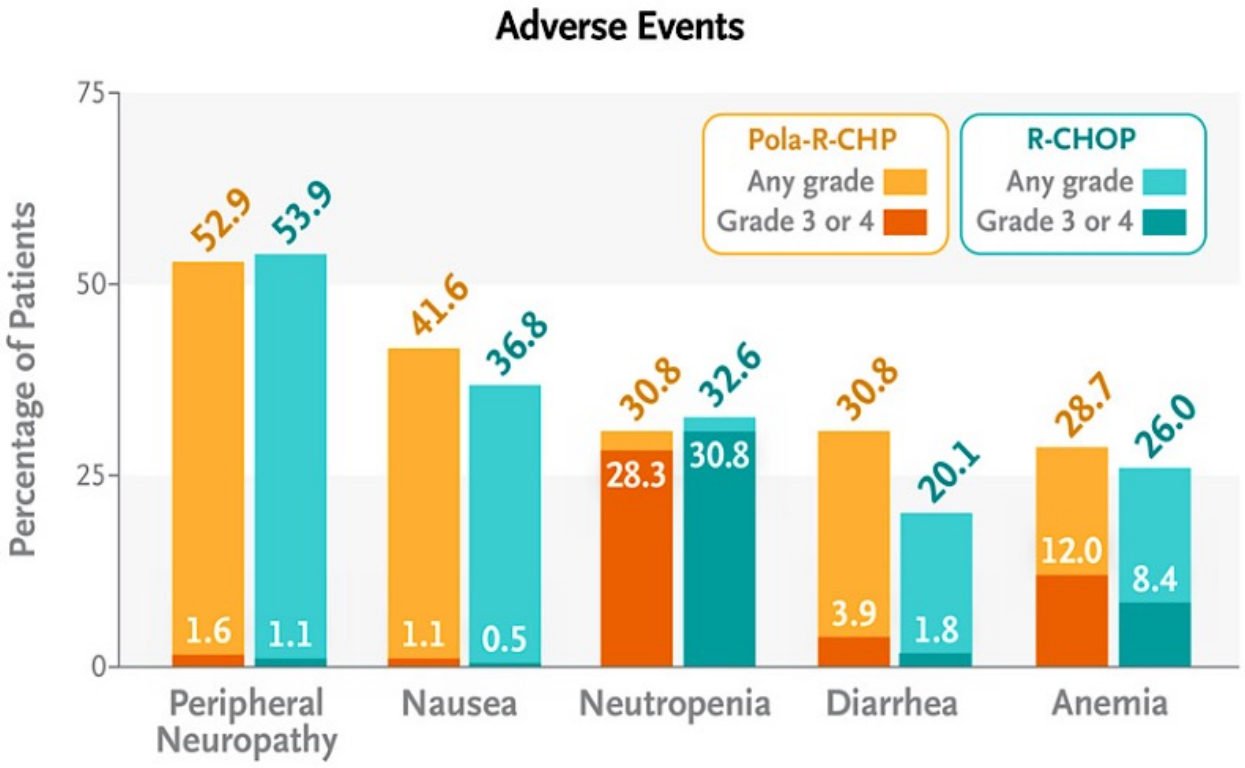
| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Pola-R-CHP | 440 | 404 | 353 | 327 | 246 | 78 | NE | NE |
| R-CHOP | 439 | 389 | 330 | 296 | 220 | 78 | 3 | NE |

| Baseline Risk Factors | Total N | Pola-R-CHP (N=440) n | Pola-R-CHP (N=440) 2-year Rate | R-CHOP (N=439) n | R-CHOP (N=439) 2-year Rate | Hazard Ratio | 95% Wald CI |
|---|---|---|---|---|---|---|---|
| Age group | | | | | | | |
| ≤60 | 271 | 140 | 74·1 | 131 | 71·9 | 0·9 | (0·6 to 1·5) |
| >60 | 608 | 300 | 77·9 | 308 | 69·5 | 0·7 | (0·5 to 0·9) |
| Sex | | | | | | | |
| Male | 473 | 239 | 75·9 | 234 | 65·9 | 0·7 | (0·5 to 0·9) |
| Female | 406 | 201 | 77·7 | 205 | 75·2 | 0·9 | (0·6 to 1·4) |
| ECOG PS | | | | | | | |
| 0–1 | 737 | 374 | 78·4 | 363 | 71·2 | 0·8 | (0·6 to 1·0) |
| 2 | 141 | 66 | 67·2 | 75 | 65·0 | 0·8 | (0·5 to 1·4) |
| IPI score | | | | | | | |
| IPI 2 | 334 | 167 | 79·3 | 167 | 78·5 | 1·0 | (0·6 to 1·6) |
| IPI 3–5 | 545 | 273 | 75·2 | 272 | 65·1 | 0·7 | (0·5 to 0·9) |
| Bulky disease | | | | | | | |
| Absent | 494 | 247 | 82·7 | 247 | 70·7 | 0·6 | (0·4 to 0·8) |
| Present | 385 | 193 | 69·0 | 192 | 69·7 | 1·0 | (0·7 to 1·5) |
| Geographic region | | | | | | | |
| Western Europe, United States, Canada, and Australia | 603 | 302 | 78.6 | 301 | 72.0 | 0.8 | (0·6 to 1·1) |
| Asia | 160 | 81 | 74.3 | 79 | 65.6 | 0.6 | (0·4 to 1·5) |
| Rest of world | 116 | 57 | 70.8 | 59 | 67.3 | 0.9 | (0·6 to 1·5) |
| Ann Arbor stage | | | | | | | |
| I–II | 99 | 47 | 89·1 | 52 | 85·5 | 0·6 | (0·2 to 1·8) |
| III | 232 | 124 | 80·7 | 108 | 73·6 | 0·8 | (0·5 to 1·3) |
| IV | 548 | 269 | 72·6 | 279 | 66·1 | 0·8 | (0·6 to 1·1) |
| Baseline LDH | | | | | | | |
| ≤ULN | 300 | 146 | 78·9 | 154 | 75·6 | 0·8 | (0·5 to 1·3) |
| >ULN | 575 | 291 | 75·4 | 284 | 67·2 | 0·7 | (0·5 to 1·0) |
| No. of extranodal sites | | | | | | | |
| 0–1 | 453 | 227 | 80·2 | 226 | 74·5 | 0·8 | (0·5 to 1·1) |
| ≥2 | 426 | 213 | 73·0 | 213 | 65·8 | 0·7 | (0·5 to 1·0) |
| Cell-of-origin | | | | | | | |
| GCB | 352 | 184 | 75·1 | 168 | 76·9 | 1·0 | (0·7 to 1·5) |
| ABC | 221 | 102 | 83·9 | 119 | 58·8 | 0·4 | (0·2 to 0·6) |
| Unclassified | 95 | 44 | 73·0 | 51 | 86·2 | 1·9 | (0·8 to 4·5) |
| Unknown | 211 | 110 | 73·8 | 101 | 64·3 | 0·7 | (0·4 to 1·2) |
| Double expressor by IHC | | | | | | | |
| DEL | 290 | 139 | 75·5 | 151 | 63·1 | 0·6 | (0·4 to 1·0) |
| Non DEL | 438 | 223 | 77·7 | 215 | 75·7 | 0·9 | (0·6 to 1·3) |
| Unknown | 151 | 78 | 76·0 | 73 | 69·8 | 0·8 | (0·4 to 1·5) |
| Double- or triple-hit lymphoma | | | | | | | |
| Yes | 45 | 26 | 69·0 | 19 | 88·9 | 3·8 | (0·8 to 17·6) |
| No | 620 | 305 | 76·8 | 315 | 70·3 | 0·7 | (0·5 to 1·0) |
| Unknown | 214 | 109 | 78·5 | 105 | 66·4 | 0·6 | (0·4 to 1·1) |




Tilly H, et al. *N Engl J Med.* 2022;386(4):351-363.

# POLARIX: R-CHOP vs R-CHP + Polatuzumab




| 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 cutoff: June 28, 2021; median 28.2 months' follow-up.

| | Any Grade | Grade 3–4 | Any Grade | Grade 3–4 |
|---|---|---|---|---|
| **PN** | 230 (52.9) | 7 (1.6) | 236 (53.9) | 5 (1.1) |
| **FN** | 62 (14.3) | 60 (13.8) | 35 (8.0) | 35 (8.0) |

Tilly H, et al. *N Engl J Med.* 2022;386(4):351-363.

# CAR T-Cell Therapy: Randomized Trials in Second Line for Refractory DLBCL

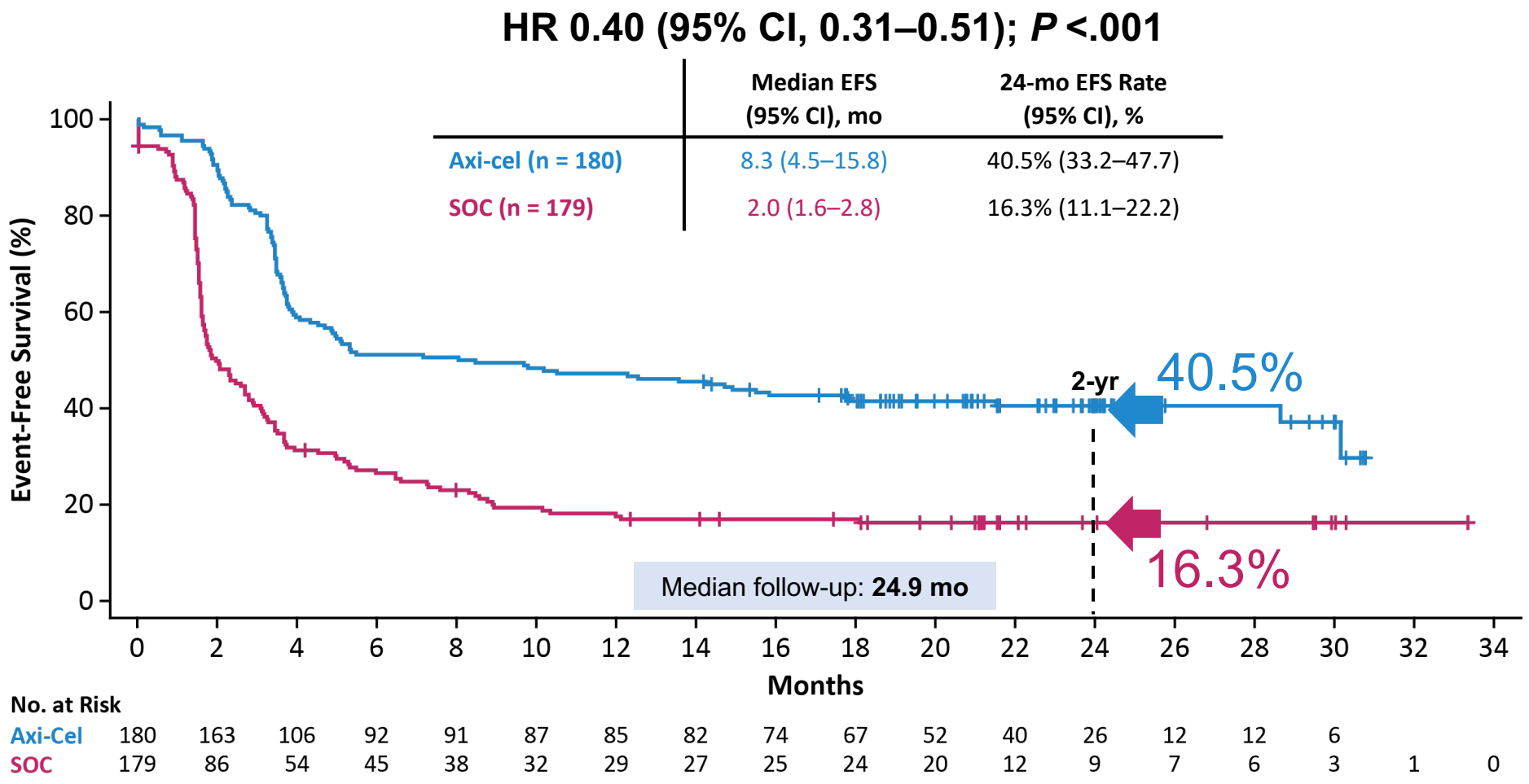
**Patient population: Primary refractory or relapse within 12 mo of therapy**

| | Bridging Allowed* | Bridging, % | CAR T, % | ASCT, % | Crossover Planned† | Crossover, % | Primary Endpoint |
|---|---|---|---|---|---|---|---|
| ZUMA-7<br>N = 180 | No<br>(Steroids) | 0 | 94 | 36 | No | 56 | EFS |
| TRANSFORM<br>N = 92 | Yes<br>(Protocol Defined SOC) | 63 | 97 | 46 | Yes | 51 | EFS |
| BELINDA<br>N = 162 | Yes<br>(PI Choice of 4 Platinum Based Regimens) | 83 | 96 | 33 | Yes | 51 | EFS |

*ZUMA-7 allowed steroids only; †BELINDA permitted crossover only after 2 lines of salvage.

Locke FL, et al. *New Engl J Med.* 2022;386(7):640-654; Kamdar M, et al. ASH 2021. Abstract 91;
Bishop MR, et al. *New Engl J Med.* 2022;386(7):629-639.

# ZUMA-7 (axi-cel): Primary Endpoint



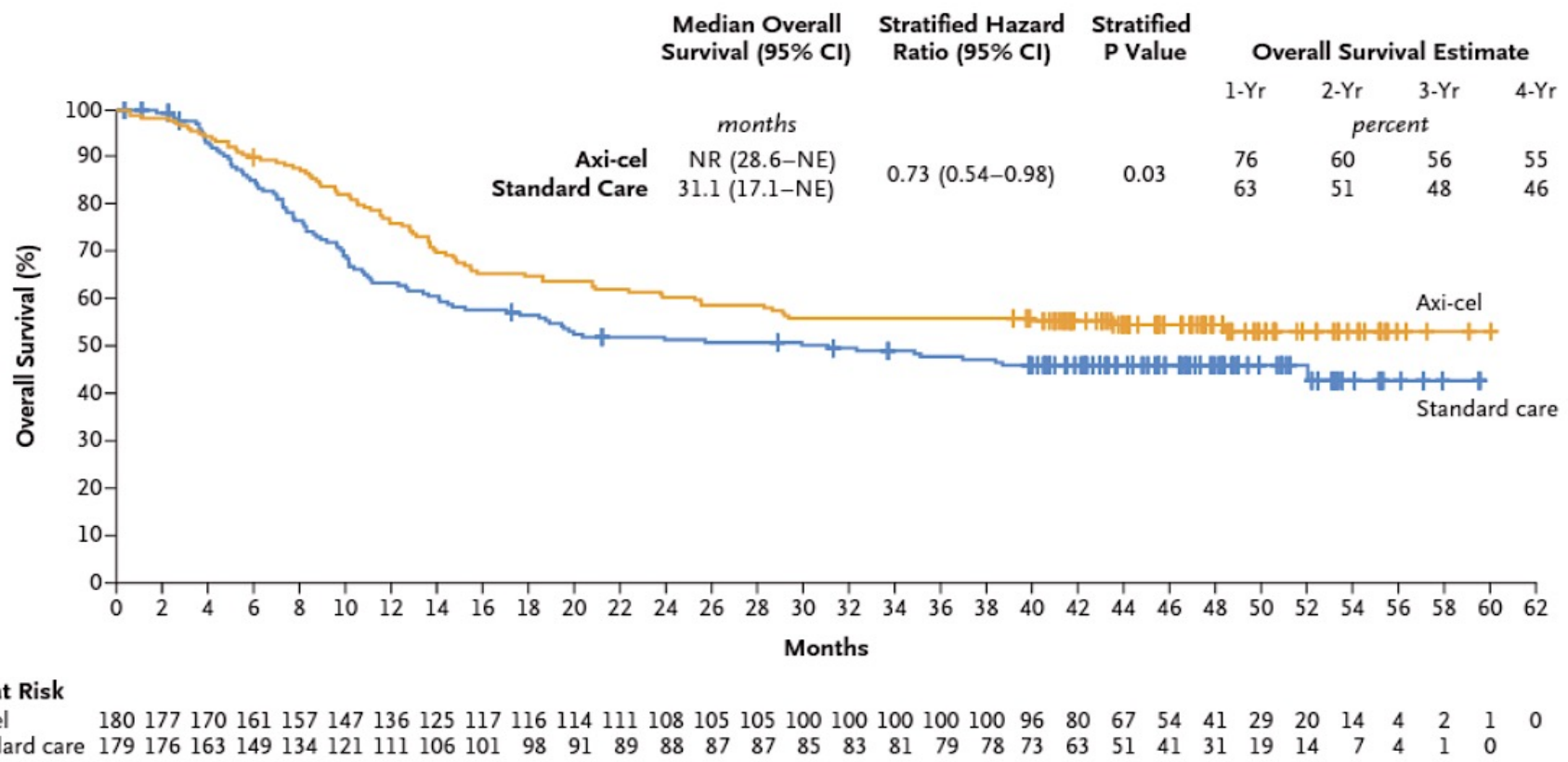

Locke FL, et al. *New Engl J Med.* 2022;386(7):640-654.

# ZUMA-7 (axi-cel)

- **Secondary endpoints (axi-cel vs SOC)**
  - ORR: 83% vs 50%
  - Median OS: NR vs 35.1 mo (HR 0.73)
  - Median PFS: 14.7 vs 3.7 mo (HR 0.49)
- **Safety**
  - Axi-cel–related CRS
    - Any grade: 92%; grade ≥3: 6%
    - Median onset 3 days, median duration 7 days
  - Neurotoxicity
    - Most common: tremor, confusional state, aphasia
    - Any grade: 60% vs 20%; grade ≥3: 21% vs 1%

Locke FL, et al. *New Engl J Med.* 2022;386(7):640-654.

# ZUMA-7 (axi-cel): Overall Survival

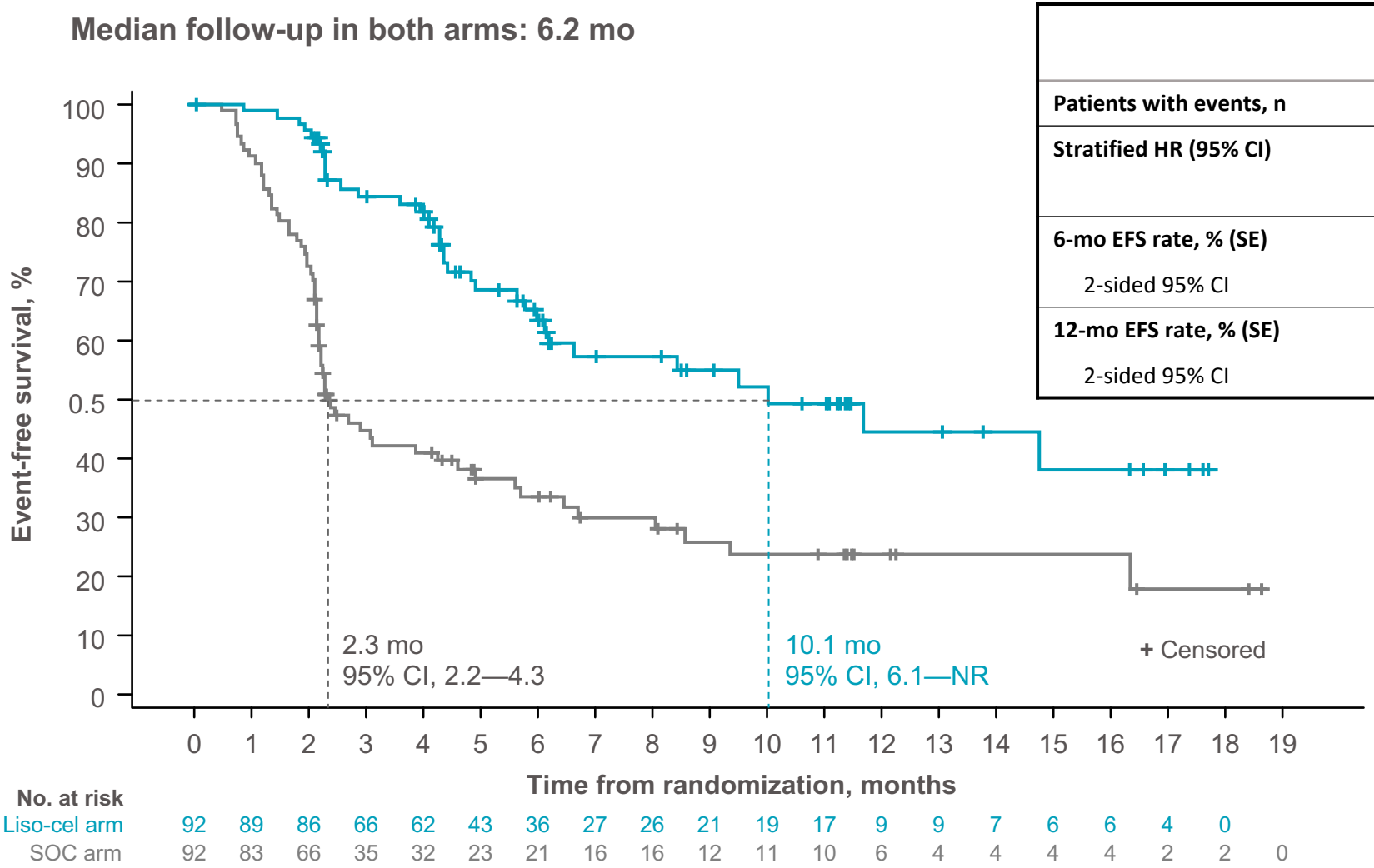



**Median Follow-up**, 47.2 mo

Axi-cel was associated with improved QoL by PRO

Westin JR, et al. N Engl *J Med.* 2023;389:148-157.

# TRANSFORM (liso-cel): Primary Endpoint




| | Liso-cel Arm (n = 92) | SOC Arm (n = 92) |
|---|---|---|
| **Patients with events, n** | 35 | 63 |
| **Stratified HR (95% CI)** | **0.349** (0.229–0.530) *P* <.0001 | |
| **6-mo EFS rate, % (SE)** | 63.3 (5.77) | 33.4 (5.30) |
| 2-sided 95% CI | 52.0–74.7 | 23.0–43.8 |
| **12-mo EFS rate, % (SE)** | 44.5 (7.72) | 23.7 (5.28) |
| 2-sided 95% CI | 29.4–59.6 | 13.4–34.1 |

Kamdar M, et al. ASH 2021. Abstract 91.

# TRANSFORM (liso-cel)

- **Secondary endpoints (liso-cel vs SOC)**
  - ORR: 86% vs 48%
  - Median OS: NR vs 16.4 mo (HR 0.51)
    - NR vs 29.9 months
  - Median PFS: 14.8 vs 5.7 mo (HR 0.41)
- **Safety**
  - Liso-cel–related CRS
    - Any grade: 49%; grade ≥3: 1%
    - Median onset 5 days, median duration 4 days
  - Neurologic events
    - Grade 3 events include encephalopathy, mental status change, aphasia, tremor, muscular weakness
    - Any grade: 12%; grade ≥3: 4%

Kamdar M, et al. ASH 2021. Abstract 91; Abrahmson JS, et al. *Blood.* 2023;141(14):1675-1684.

# EPCORE NHL-1 Phase 2 Study of Epcoritamab in Patients With R/R LBCL: Study Design[1-3]

**Dose escalation**

**Dose expansion data cutoff: November 18, 2022**
**Median follow-up: 20.0 mo**

## Key Inclusion Criteria

- R/R CD20+ mature B-cell neoplasm
- ECOG PS 0-2
- ≥2 prior lines of antineoplastic therapy, including ≥1 anti-CD20 mAb
- FDG PET–avid and measurable disease by CT/MRI
- Prior CAR T-cell therapy allowed

**Step-up dosing[a]**

**Epcoritamab SUBQ RP2D 48 mg**
qw C1-3,
q2w C4-9,
q4w C10+

**Treatment until PD[b,c] or unacceptable toxicity**

**LBCL Cohort N=157**
DLBCL, HGBCL, PMBCL, and FL Gr3B

- To ensure patient safety and better characterize CRS, inpatient monitoring was required at first full dose for 24 h in this part of the study
- **Primary endpoint:** ORR by IRC
- **Key secondary endpoints:** DOR, TTR, PFS, OS, CR rate, safety/tolerability

[a] Step-up dosing (priming 0.16 mg and intermediate 0.8 mg dosing before first full dose) and corticosteroid prophylaxis were used to mitigate CRS. [b] Radiographic disease evaluation was performed every 6 weeks for the first 24 weeks (6, 12, 18, and 24 weeks), then every 12 weeks (36 and 48 weeks), and every 6 months thereafter. [c] Measurable disease with CT or MRI scan with involvement of ≥2 lesions/nodes with a long axis >1.5 cm and short axis >1.0 cm (or 1 lesion/node with a long axis >2.0 cm and short axis ≥1.0 cm) and FDG PET scan that demonstrates positive lesion(s) compatible with CT-defined (or MRI-defined) anatomical tumor sites for FDG-avid lymphomas.

Karimi Y, et al. ASCO 2023. Abstract 7525. 2. Jurczak W, et al. EHA 2023. Abstract P1118. 3. Thieblemont C, et al. EHA 2022. Abstract LB2364.

# EPCORE NHL-1 Phase 2 Study of Epcoritamab in Patients With R/R LBCL: Efficacy

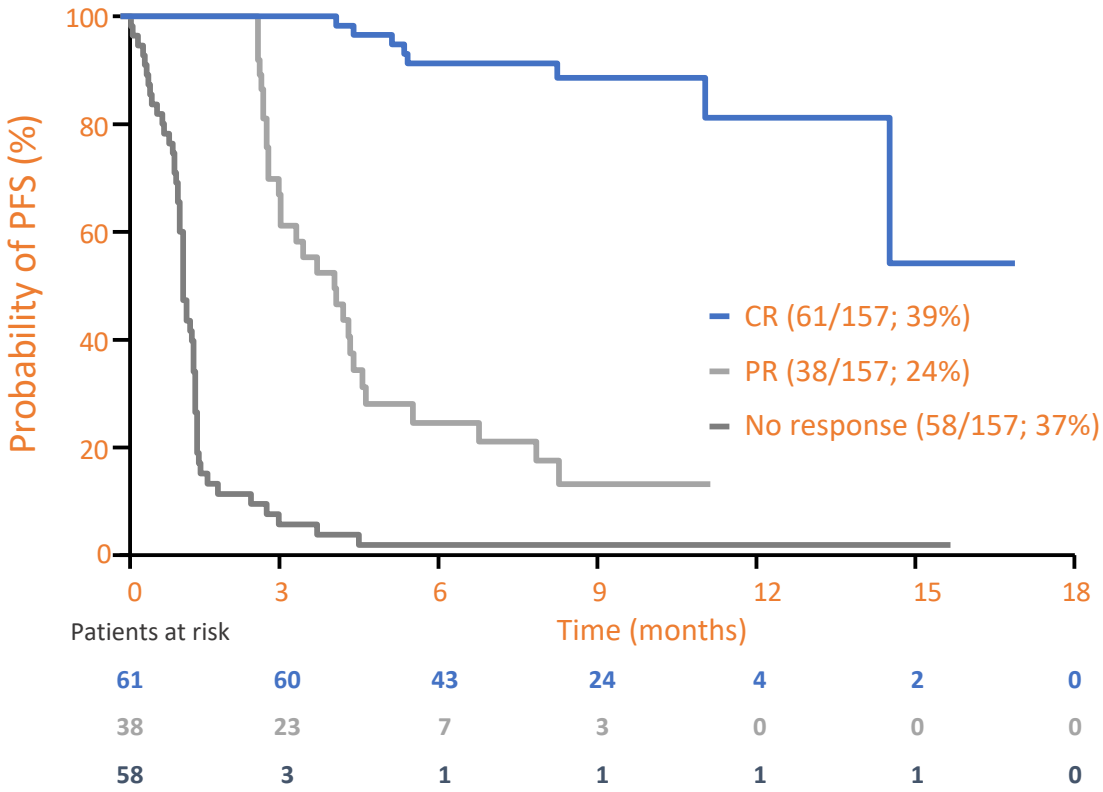
**Best response rates[2]**
- CR: 39.0%
- ORR: 63.0%

**Subgroup CR rate[2]**
- After CAR T cell: 34%
- Refractory: 30%

**Survival**
- Median PFS: 4.4 mo[2]
- OS: 57% at 12 mo[1]
- Median DOR: 12 mo[2]
- Median DOR of CR: NR[2]

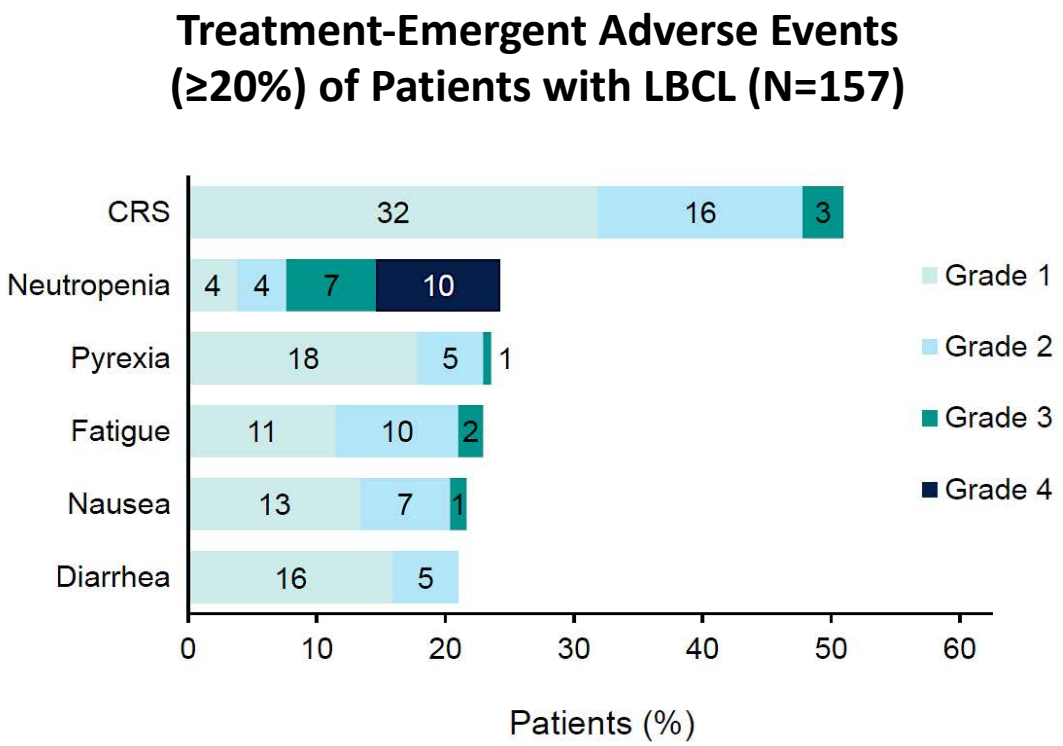
| Kaplan-Meier Estimate | DLBCL (n=55) |
|---|---|
| Median DOR for patients who achieved a CR, mo (95% CI) | 20.8 (17.3-NR) |
| Median PFS for patients who achieved a CR, mo (95% CI) | NR (18.5-NR) |
| Median OS for patients who achieved a CR, mo (95% CI) | NR (NR-NR) |
| Median OS for all patients with DLBCL, mo (95% CI)[c] | 19.4 (11.7-NR) |

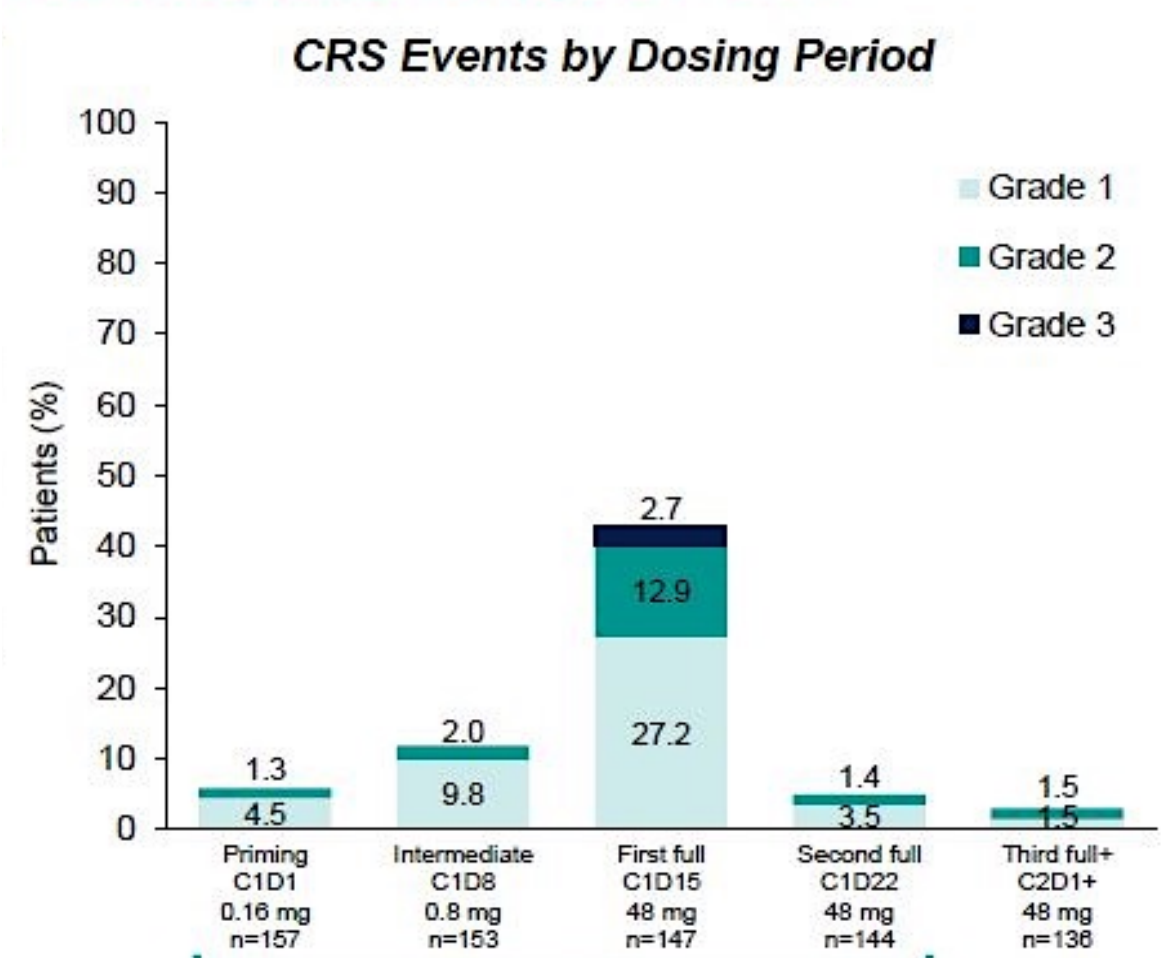
**PFS in Patients with LBCL[2]**




Thieblemont C, et al. EHA 2022. Abstract LB2364; 2. Thieblemont C, et al. *J Clin Oncol.* 2023;41(12):2238-2247.

# EPCORE NHL-1 Phase 2 Study of Epcoritamab in Patients With R/R LBCL: Safety

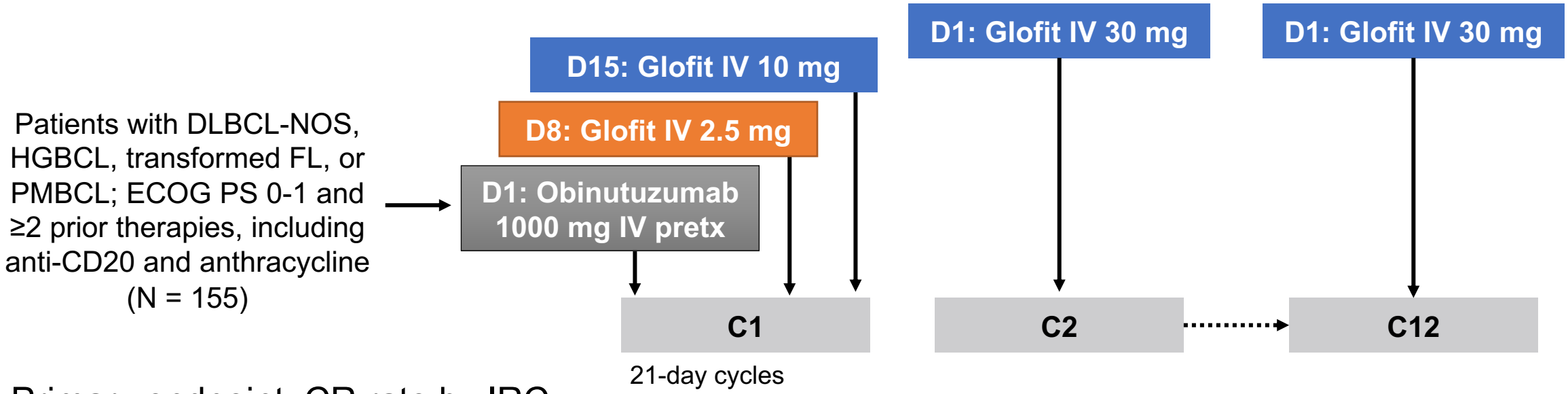



Karimi Y, et al. ASCO 2023. Abstract 7525. 2. Jurczak W, et al. EHA 2023. Abstract P1118. 3. Thieblemont C, et al. EHA 2022. Abstract LB2364.

# Phase II Expansion Study: Glofitamab in R/R DLBCL

- Single-arm phase II expansion trial



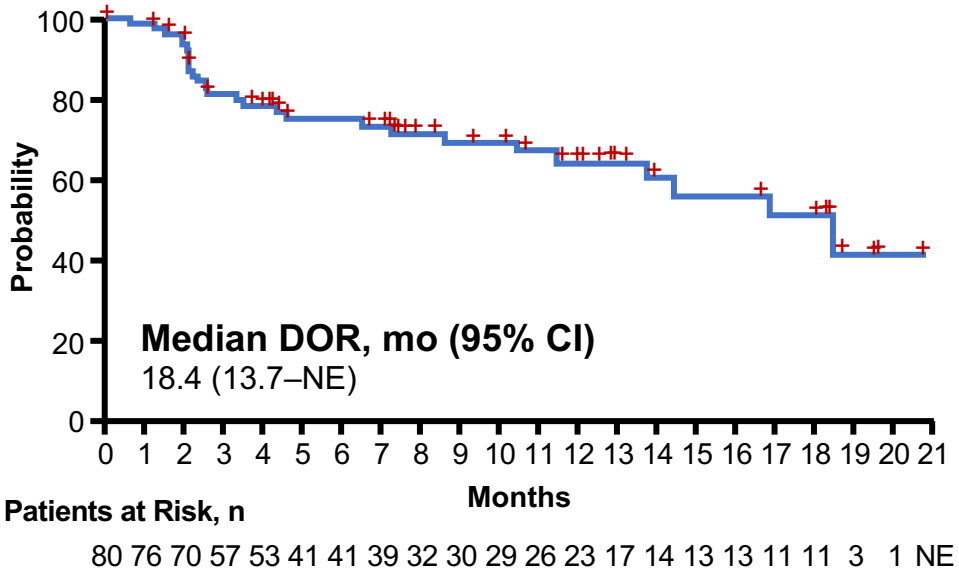

- Primary endpoint: CR rate by IRC
- Key secondary endpoints: ORR rate, DoR, DoCR, PFS, and OS

Dickinson MJ, et al. EHA 2022. Abstract S220; Dickinson MJ, et al. *N Engl J Med.* 2022;387(24):2220-2231.

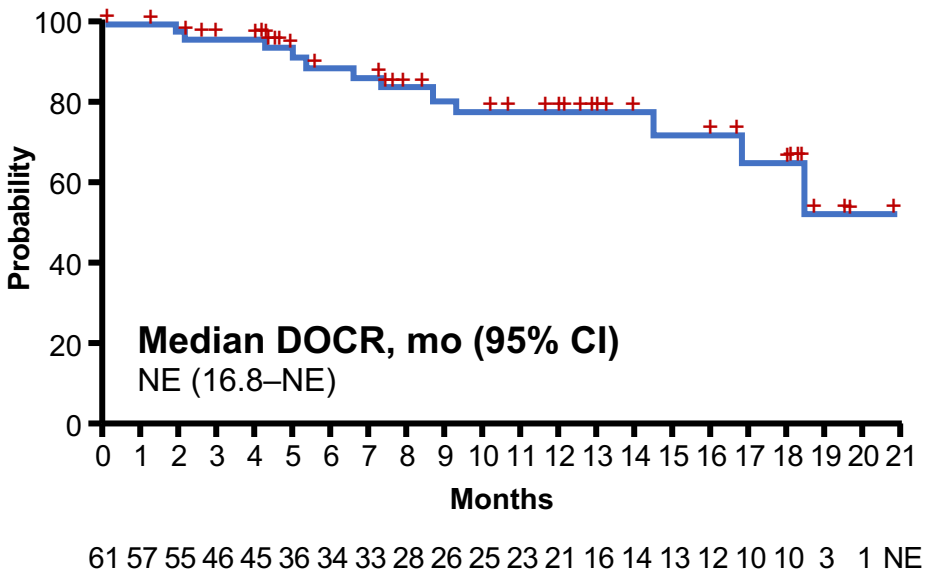
# Phase II Expansion Study of Glofitamab: Efficacy

Median follow-up: 12.6 mo

**Duration of overall response by IRC**




**Duration of complete response by IRC**




| | N = 80 |
|---|---|
| Median DOR follow-up, mo (range) | 10.6 (0–21) |
| 12-mo DOR, % (95% CI) | 63.6 (51.1–76.2) |
| Ongoing response at CCOD, n (%) | 53 (66.3) |

| | n = 61 |
|---|---|
| Median DOCR follow-up, mo (range) | 10.6 (0–21) |
| 12-mo DOCR, % (95% CI) | 77.6 (64.3–90.8) |
| CRs ongoing at CCOD, n (%) | 49 (80.3) |

| Response, % | N = 155 |
|---|---|
| Best response | |
| ▪ ORR | 51.6 |
| ▪ CR | 39.4 |
| Subgroup CR rate | |
| ▪ After CAR T-cell therapy | 35 |
| ▪ Relapsed | 70 |
| ▪ Refractory | 34 |

| Survival, Mo | N = 155 |
|---|---|
| Median PFS | 4.9 |
| Median OS | 11.5 |

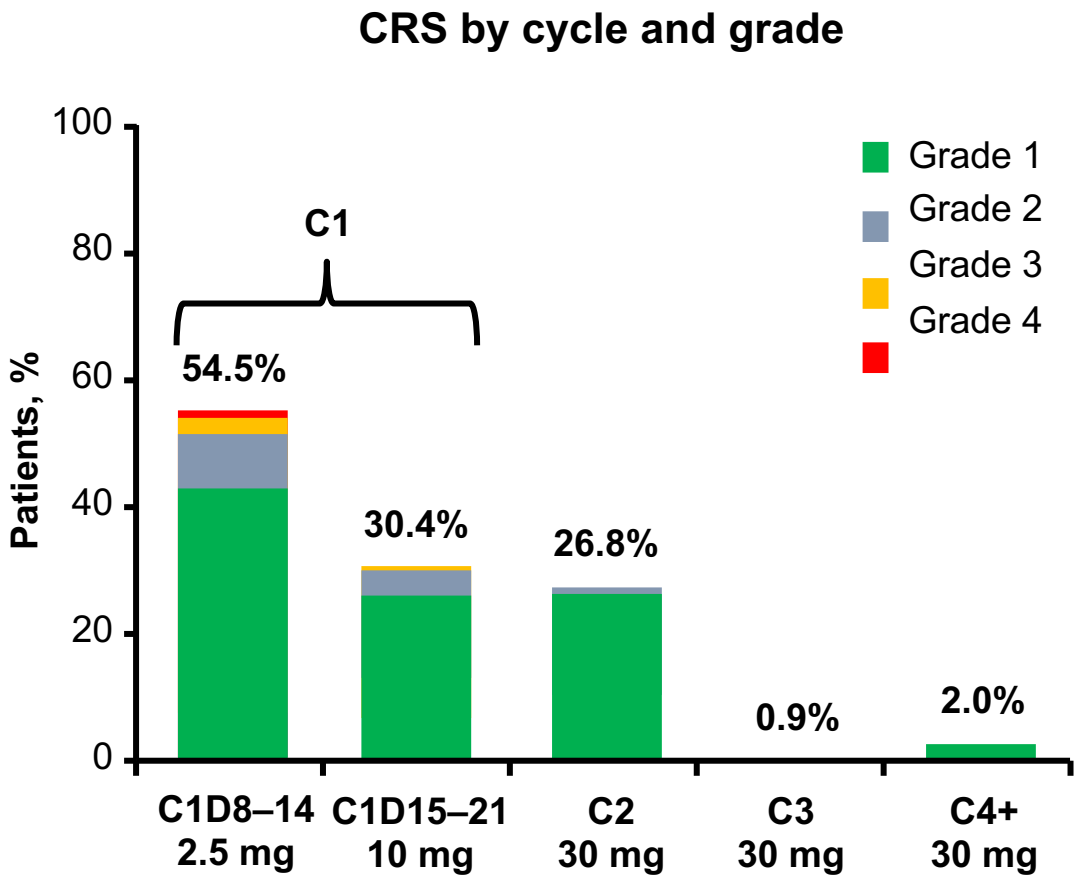
Median F/U 32 mos

Median DOCR 26.9 mo
Median PFS 24 mo
Median OS NE


Dickinson MJ, et al. EHA 2022. Abstract S220; Dickinson MJ, et al. *N Engl J Med.* 2022;387(24):2220-2231.
Hutchings M et al. ASH 2023;Abstract 433

# Phase II Expansion Study of Glofitamab: Safety

| CRS Parameter | Glofitamab (N = 154) |
|---|---|
| Any-grade CRS, n (%)<br>▪ Grade 1<br>▪ Grade 2<br>▪ Grade 3<br>▪ Grade 4 | 97 (63.0)<br>73 (47.4)<br>18 (11.7)<br>4 (2.6)<br>2 (1.3) |
| Median time to CRS onset from C1D8 dose, hr (range) | 13.6 (6.2–51.8) |
| Corticosteroids given, n/N (%) | 27/97 (27.8) |
| Tocilizumab given, n/N (%) | 31/97 (32.0) |
| Any ICANS, n (%)<br>▪ Grade ≥3 | 12 (7.8)<br>4 (2.6) |

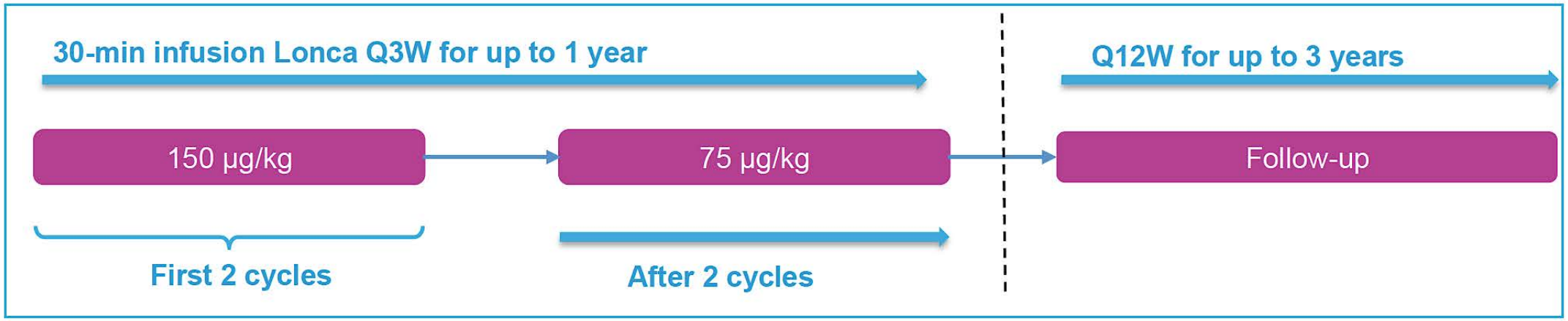



Dickinson MJ, et al. EHA 2022. Abstract S220; Dickinson MJ, et al. *N Engl J Med.* 2022;387(24):2220-2231.

# Loncastuximab Tesirine: LOTIS-2 Trial
# Single-Arm Open-Label Phase II Study in DLBCL

**Patient population:**
**Patients with R/R DLBCL following ≥2 lines of prior systemic therapy**

**Primary objective:**
Evaluate efficacy, **using ORR** (central review), and **safety** of the full Phase 2 study population

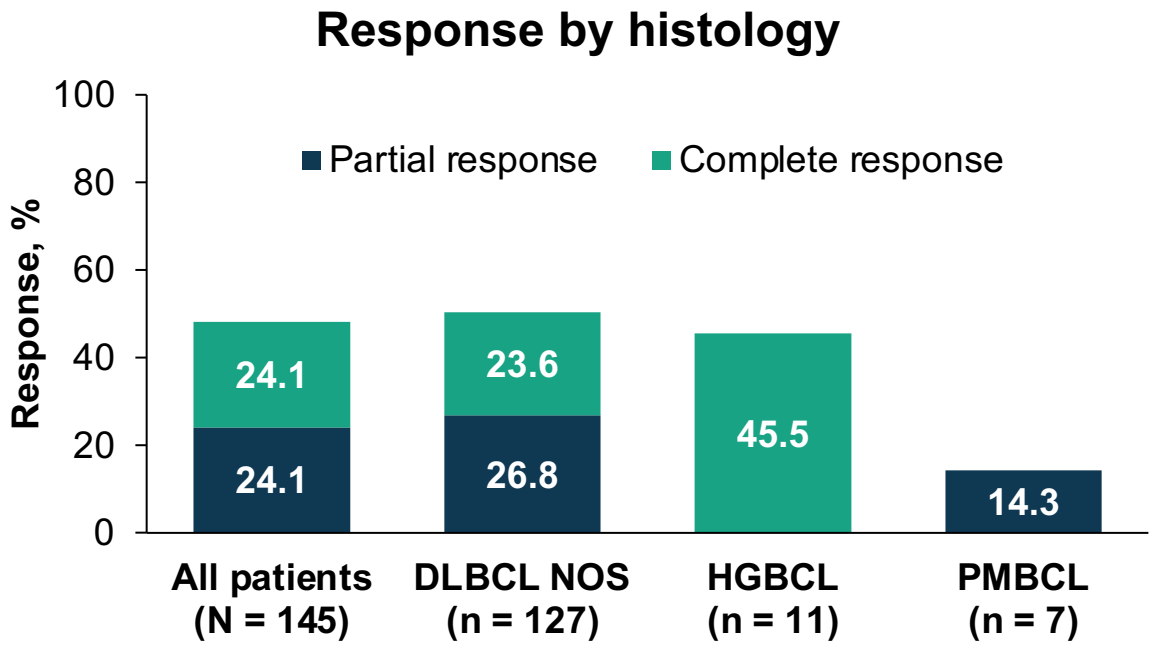



**Key inclusion criteria:** transplant-eligible and -ineligible patients; DLBCL NOS; DLBCL arising from low-grade lymphoma; HGBCL with *MYC* and *BCL2* and/or *BCL6* rearrangements; ECOG PS 0–2; patients with prior CD19-directed therapy if CD19 positive.

Caimi P, et al. *Lancet Oncol.* 2021; 22(6):790-800.

# Loncastuximab Tesirine: CD19 ADC

- Median 3 prior therapies (range, 2–7)
- Primary refractory, n = 29 (20%)
- Double/triple hit, n = 15 (10.3%)
- Prior ASCT, n = 21 (14.5%)

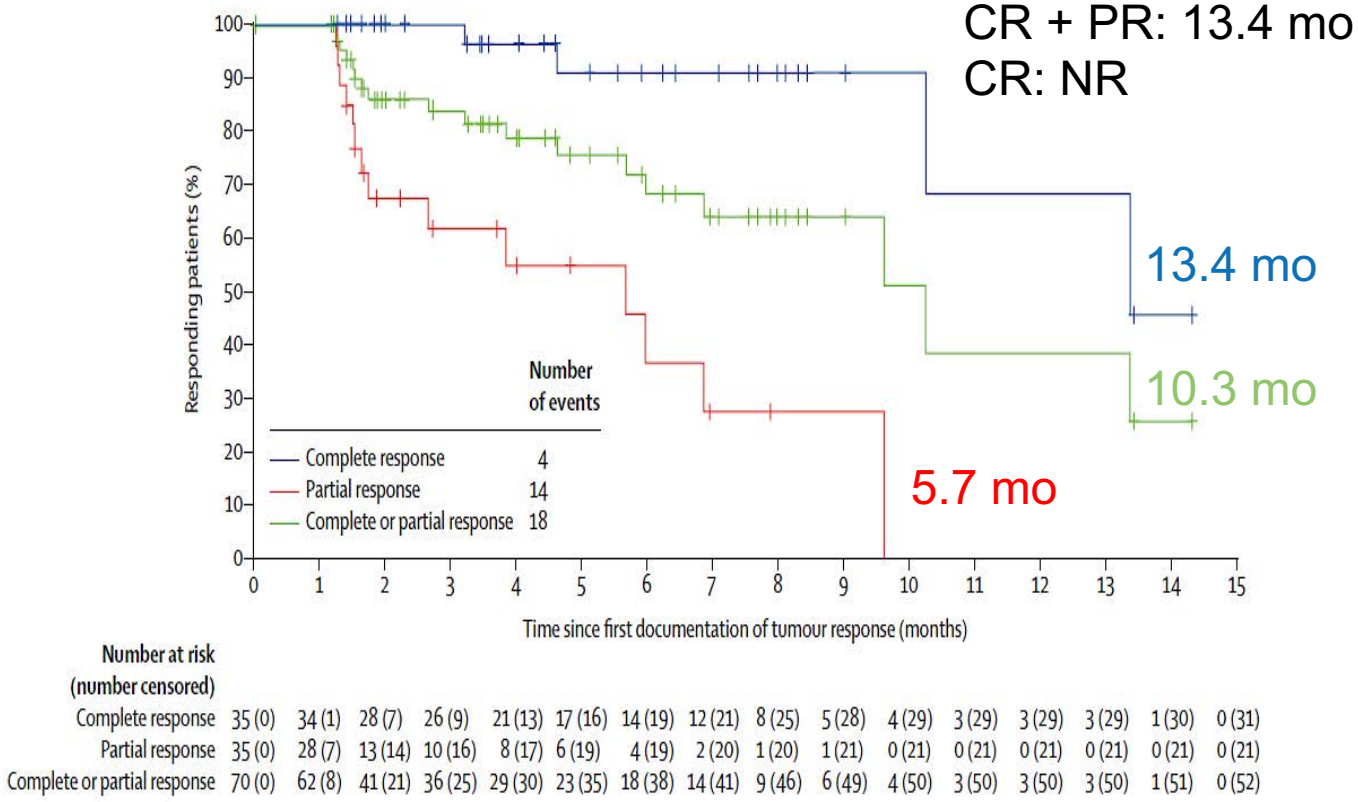



| | N = 145 (%) |
|---|---|
| Overall response rate | 70 (48.3) |
| Complete response | 35 (24.1) |
| Partial response | 35 (24.1) |
| Stable disease | 22 (15) |
| Progressive disease | 53 (37) |
| Median PFS | 4.9 mo |
| Median overall survival | 9.9 mo |
| Median DOR | 10.3 mo |

Activity across high-risk subgroups
Refractory Disease
High Grade B Cell
Prior ASCT
Prior CAR-T

Caimi P, et al. *Lancet Oncol.* 2021; 22(6):790-800.

# LOTIS-2: Duration of Response and Safety




| Adverse Event | Patients, n (%) |
|---|---|
| Any TEAE | 143 (98.6) |
| GGT increased | 59 (40.7) |
| Neutropenia | 57 (39.3) |
| Thrombocytopenia | 48 (33.1) |
| Fatigue | 40 (27.6) |
| Anemia | 38 (26.2) |
| Nausea | 34 (23.4) |
| Cough | 32 (22.1) |
| Alkaline phosphatase increased | 29 (20.0) |
| Peripheral edema | 29 (20.0) |

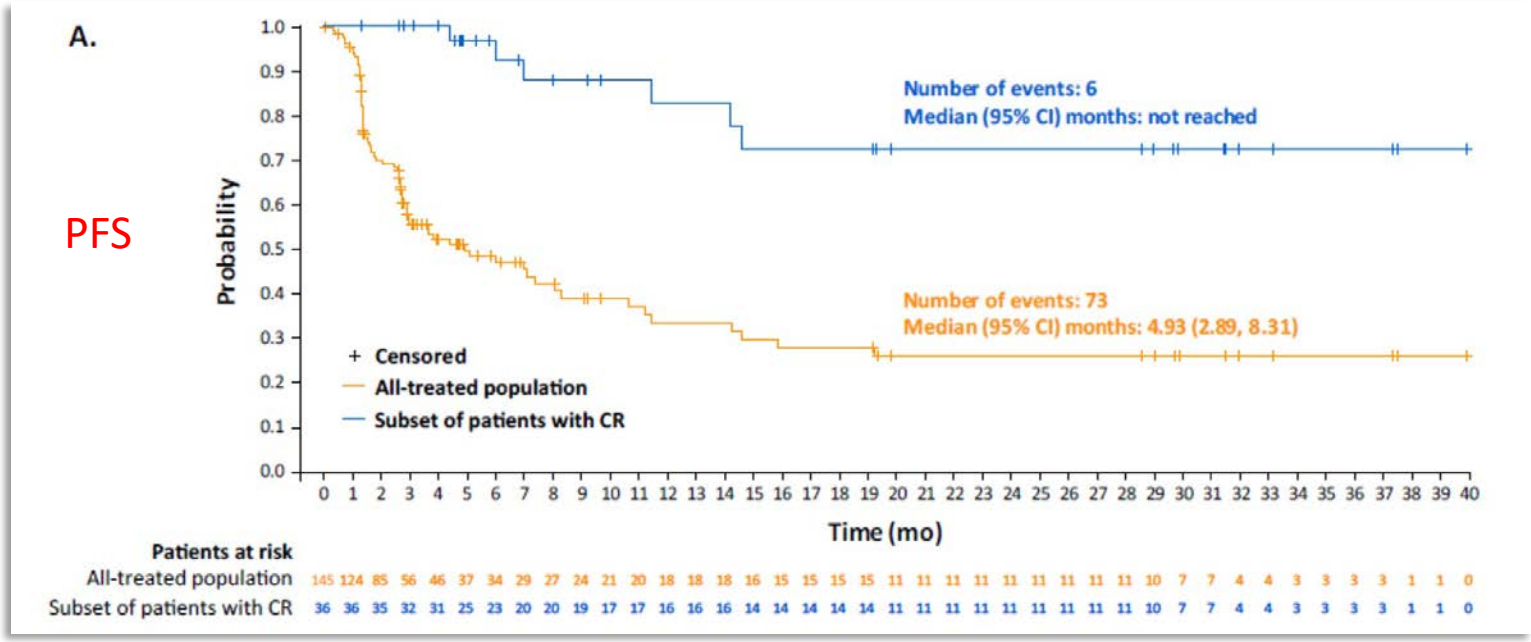
**16 (44%) patients had CRs >1 yr, which were ongoing at the 1-yr follow-up, and 11 (31%) had CRs >2 yr**

- TEAE (related) leading to treatment discontinuation: 27 (18.6%)
- Treatment delays: 62 (42.8%)

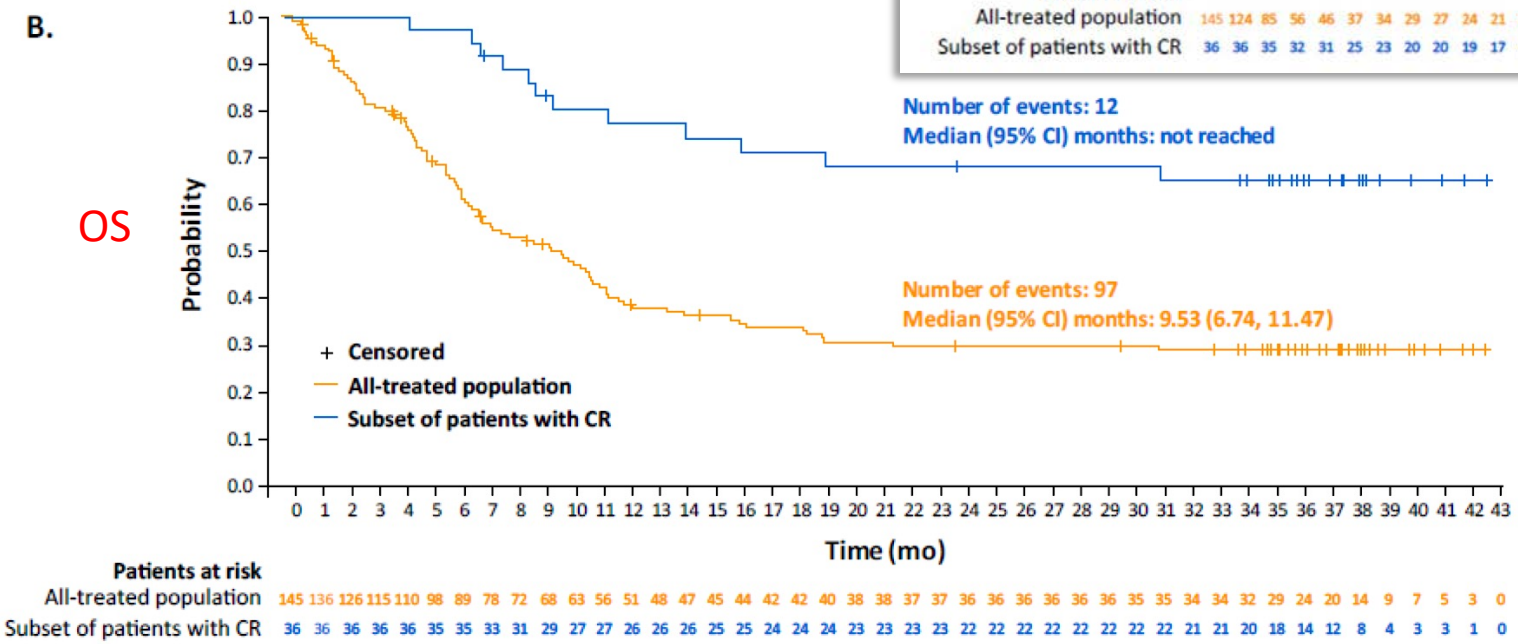
Caimi P, et al. *Lancet Oncol.* 2021; 22(6):790-800; Kahl BS, et al. SOHO 2021. Abstract ABCL-022.

# Loncastuximab Tesirine: Updated Results

PFS



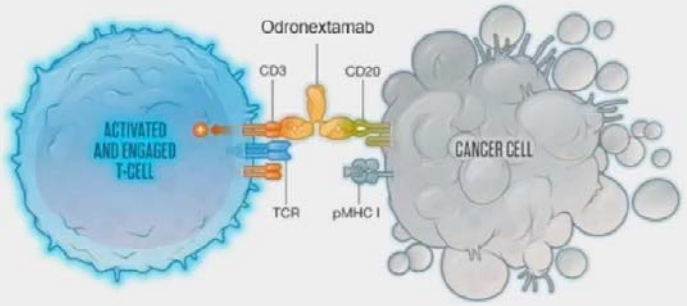

OS




Caimi PF et al. EHA 2023;Abstract P1132.

# ELM-2: Odronextamab for R/R DLBCL

**Odronextamab mechanism of action**
Fc-silenced, human, CD20×CD3 bispecific antibody




Binds CD20 on malignant B cells and CD3 on T cells, to elicit T-cell-mediated cytotoxicity

**Key eligibility criteria**
- DLBCL per WHO 2016 classification[1]
- ECOG PS 0 or 1
- Refractory to or relapsed after ≥2 prior lines of therapy, including an anti-CD20 antibody and an alkylator

**Primary endpoint:** ORR* by ICR

**Secondary endpoints:**
- ORR* by local investigator
- CR*, DOR*, PFS*, and OS
- Safety and tolerability
- Patient-reported outcomes

**Key exploratory endpoint:** MRD

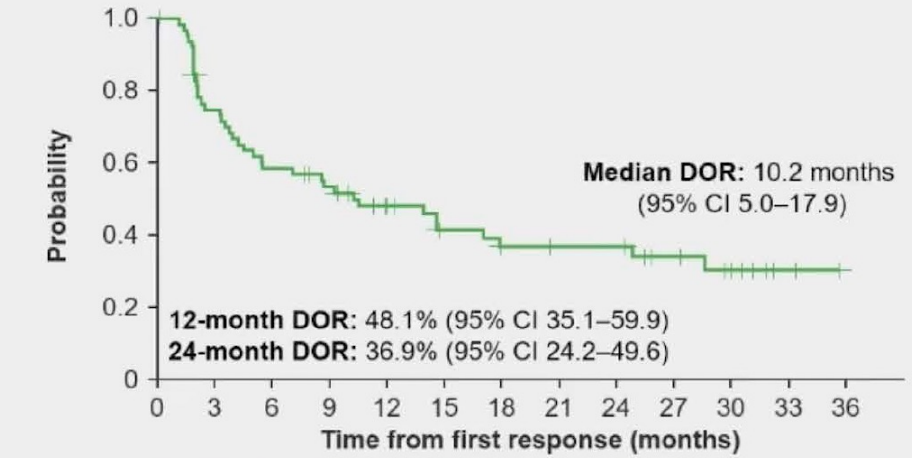
**Odronextamab administration (IV, 21-day cycles)**

| Cycle 1 (step up) | Cycles 2–4 | Cycle 5+ (maintenance) |
|---|---|---|
| D1/2, 8/9, 15/16 | D1, 8, 15 | Q2W → Q4W if durable CR (≥9 mos) |
| 0.7/4/20 mg† | 160 mg | 320 mg |

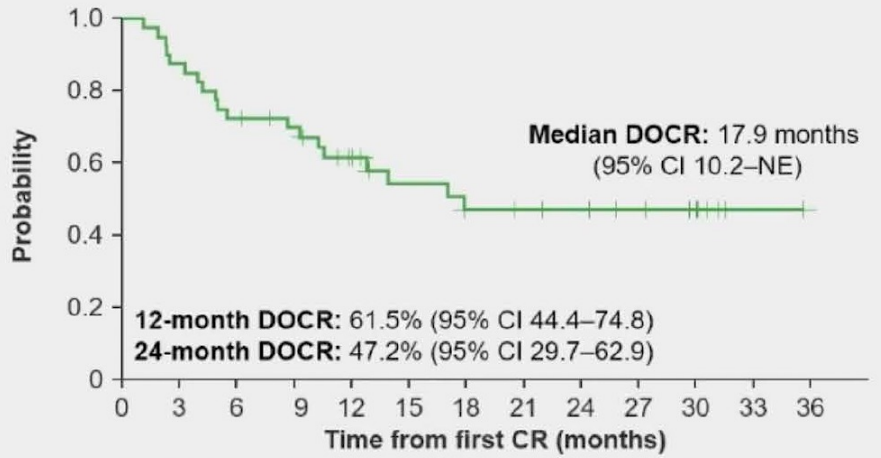
**Cycle 4 Day 15**
First post-baseline response assessment

**ORR = 52.0%; CR = 31.5%**

**DOR**




**DOCR**

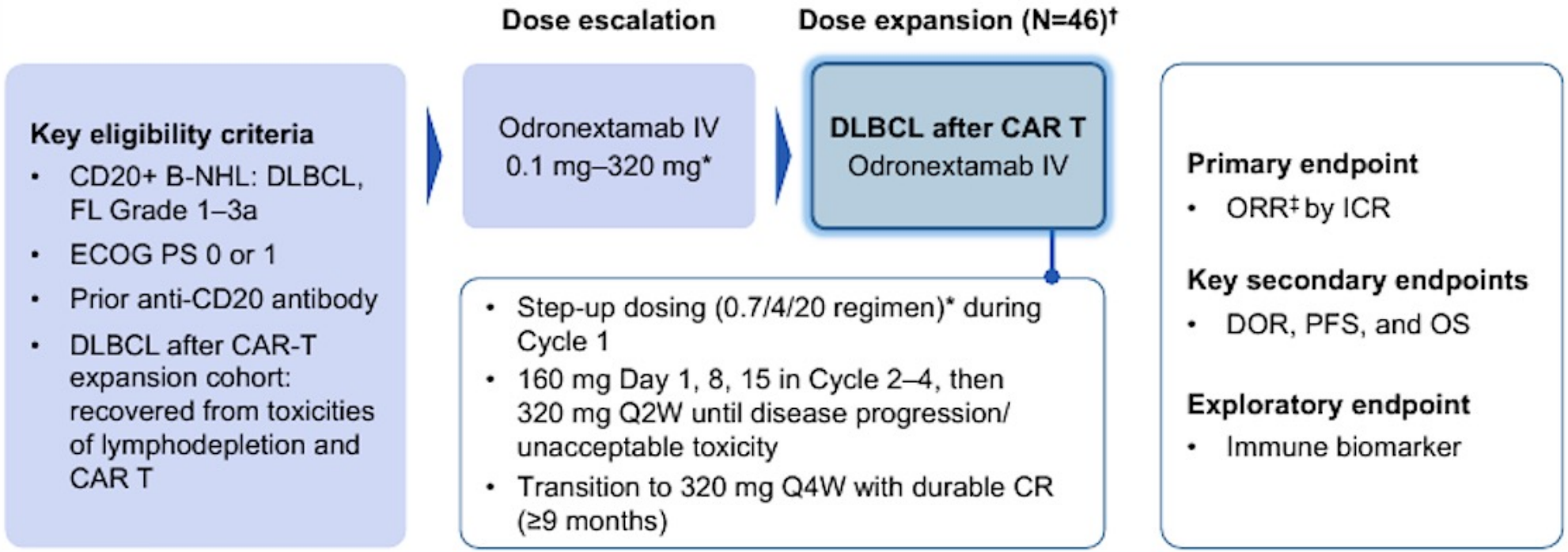



- The most common AE was CRS in 55.1% of patients and was mostly Grade 1-2.

Ayyappan S et al. ASH 2023;Abstract 436.

# ELM-1 Study: Odronextamab

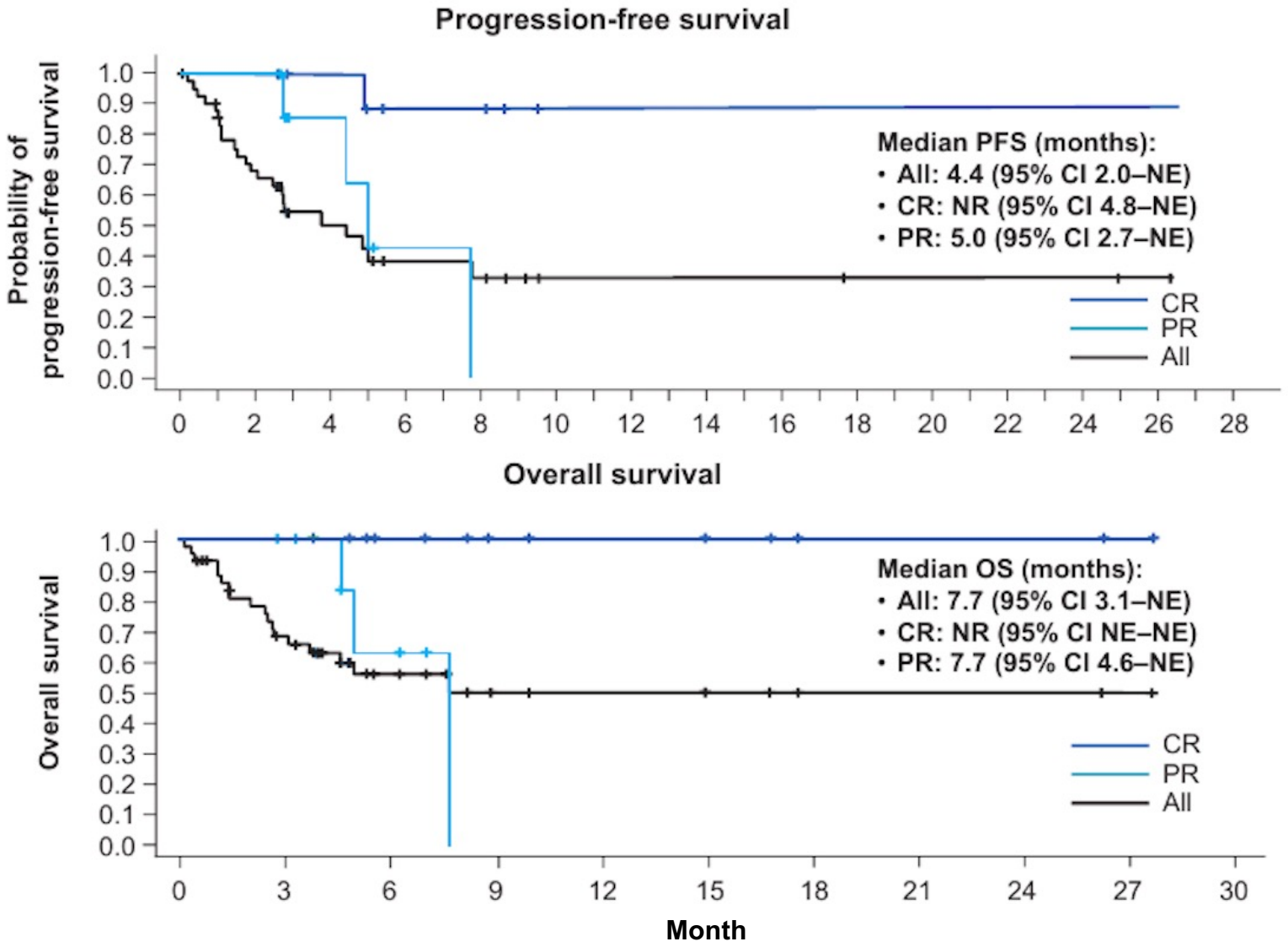
## Figure 1. ELM-1 study design – DLBCL post CAR-T cohort




*Revisions to step-up dosing were reported previously.[4] †FL, DLBCL without prior CAR T, MCL, MZL, and other B-NHL cohorts are not shown. ‡According to Lugano criteria.[6]
B-NHL, B-cell non-Hodgkin lymphoma; CAR, chimeric antigen receptor; CD, cluster of differentiation; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; ICR, independent central review; IV, intravenous; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q2W, once every 2 weeks; Q4W, once every 4 weeks.

Crombie J et al. ASH 2023;Abstract 4461.

# ELM-1: Odronextamab After CAR T-Cell Therapy




| Response data | |
|---|---|
| ORR | 47.7% |
| CR | 29.5% |

- The most common AE was CRS occurring in 52.3% of patients. All events were Grade 1-2 and resolved with a median time to resolution of 2 days.

Crombie J et al. ASH 2023;Abstract 4461.

# The Annual
# National General Medical Oncology Summit

## Saturday, March 23, 2024

### Moderator

Neil Love, MD

### Faculty

Emmanuel S Antonarakis, MD
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Matthew D Galsky, MD
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Joyce O'Shaughnessy, MD
Brian Rini, MD
Jonathan E Rosenberg, MD
Hope S Rugo, MD
Helena Yu, MD
Andrew D Zelenetz, MD, PhD

# *We are taking a short break!*

**The program will resume at 9:30 AM ET**

# *Up Next…*

**Drs Bradley Monk and David O'Malley**
**discuss the management of gynecologic cancers**

RTP
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TO PRACTICE