Understanding the Current Paradigm and New Approaches in the Care of Patients with Cancer

A Complimentary NCPD Hybrid Symposium Series Held During the 50th Annual ONS Congress

Non-Hodgkin Lymphoma

Saturday, April 12, 2025

6:00 PM – 7:30 PM

Faculty

Christopher Flowers, MD, MS
Manali Kamdar, MD, MBBS
Robin Klebig, MSN, APRN, CNP, AOCNP
Caitlin Murphy, DNP, FNP-BC, AOCNP

Moderator

Neil Love, MD

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Faculty

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Nurse Practitioner, Lymphoma Group
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Clinical Director of Lymphoma Services
Morton and Sandra Saffer Endowed Chair in Hematology Research
Division of Hematology, Hematologic Malignancies
University of Colorado Cancer Center
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Dr Flowers — Disclosures

Consulting Agreements	AbbVie Inc, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Celgene Corporation, Denovo Biopharma, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Karyopharm Therapeutics
Contracted Research	4D Pharma PLC, AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Alaunos Therapeutics, Allogene Therapeutics, Amgen Inc, Bayer HealthCare Pharmaceuticals, Celgene Corporation, Cellectis, EMD Serono Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Guardant Health, Iovance Biotherapeutics, Janssen Biotech Inc, Kite, A Gilead Company, MorphoSys, Nektar Therapeutics, Novartis, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Sanofi, Takeda Pharmaceuticals USA Inc, TG Therapeutics Inc, Xencor
Nonrelevant Financial Relationships	Burroughs Wellcome Fund, Cancer Prevention and Research Institute of Texas (CPRIT Scholar in Cancer Research), Eastern Cooperative Oncology Group, Foresight Diagnostics, National Cancer Institute, N-Power Medicine Inc, V Foundation

Dr Kamdar — Disclosures

Consulting Agreements	AbbVie Inc, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Bristol Myers Squibb, Celgene Corporation, Genentech, a member of the Roche Group
Contracted Research	Novartis
Data and Safety Monitoring Boards/Committees	Celgene Corporation, Genentech, a member of the Roche Group

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Ms Klebig — Disclosures

No relevant conflicts of interest to disclose.

Ms Murphy — Disclosures

Advisory Committees	Genmab US Inc, Seagen Inc

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Commercial Support

This activity is supported by educational grants from ADC Therapeutics and AstraZeneca Pharmaceuticals LP.

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

This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

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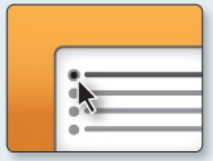
Clinicians in the Meeting Room

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 pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

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.

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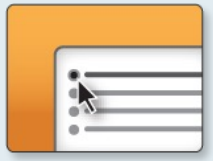
Clinicians Attending via Zoom

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. Survey questions will be discussed throughout the meeting.

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

Get NCPD Credit: An NCPD credit link will be provided in the chat room at the conclusion of the program.

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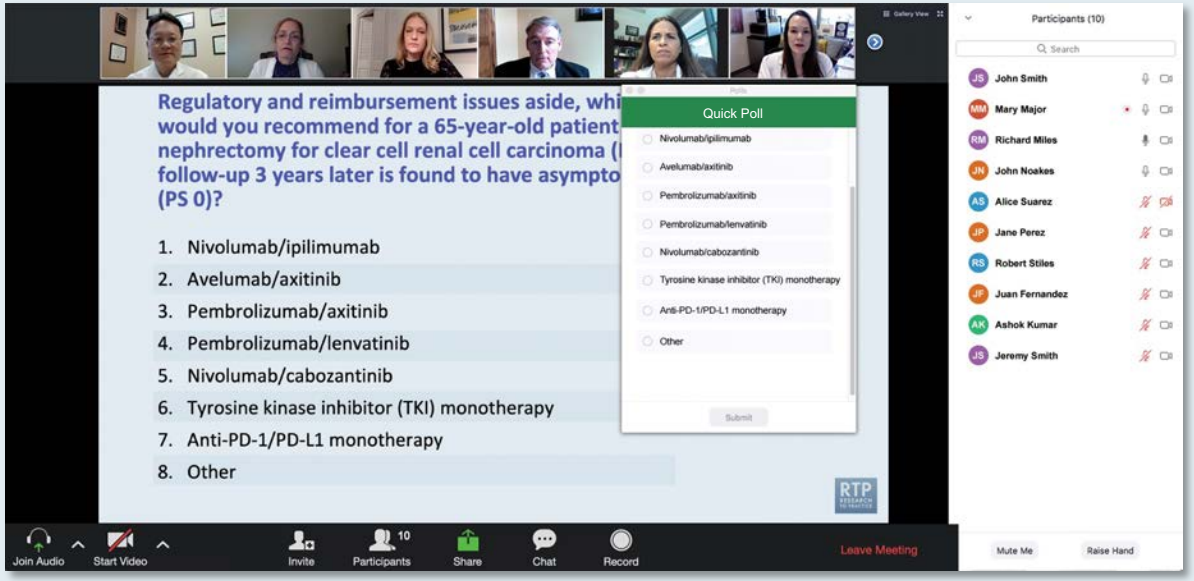
Clinicians, Please Complete the Pre- and Postmeeting Surveys



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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based 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**

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ONCOLOGY NURSING UPDATE

WITH DR NEIL LOVE

Bispecific Antibodies in Lymphoma Part 2 — An Interview with Ms Amy Goodrich for Oncology Nurses

MS AMY GOODRICH

THE SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER

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50TH ANNUAL ONS™ Congress

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Welcome ONS Members!

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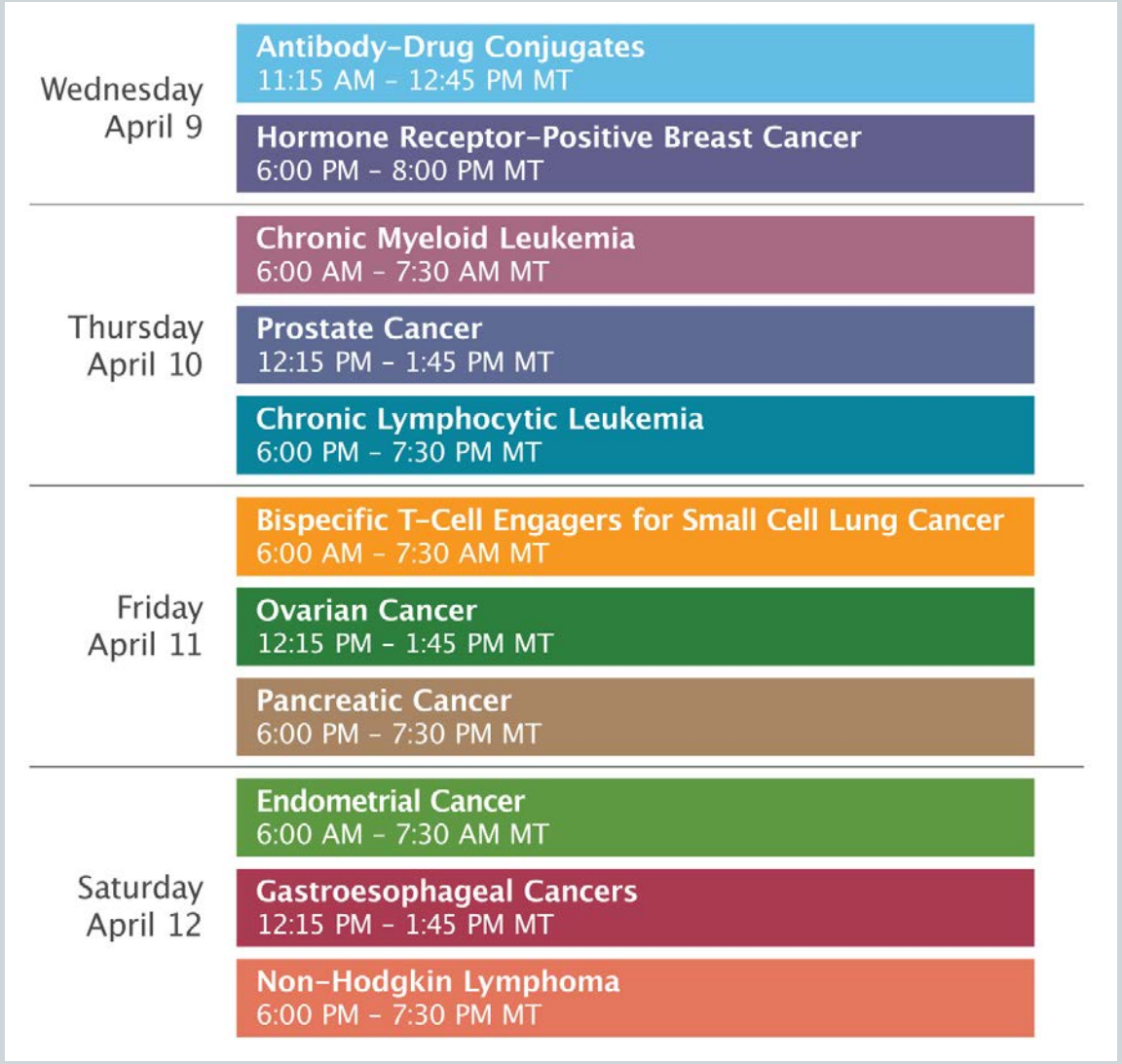
“Understanding the Current Paradigm and New Approaches”
Seventeenth Annual RTP-ONS NCPD Symposium Series



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Understanding the Current Paradigm and New Approaches
RTP Faculty at ONS 2025

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Agenda

Introduction: Overview of Bispecific Antibodies and Chimeric Antigen Receptor T-Cell Therapy for Non-Hodgkin Lymphoma

Module 1: Current and Future Use of Bruton Tyrosine Kinase Inhibitors for Mantle Cell Lymphoma

Module 2: First-Line Therapy for Diffuse Large B-Cell Lymphoma (DLBCL)

Module 3: Role of Loncastuximab Tesirine for Patients with Relapsed/Refractory (R/R) DLBCL

Module 4: Role of Tafasitamab for Patients with R/R DLBCL and Follicular Lymphoma

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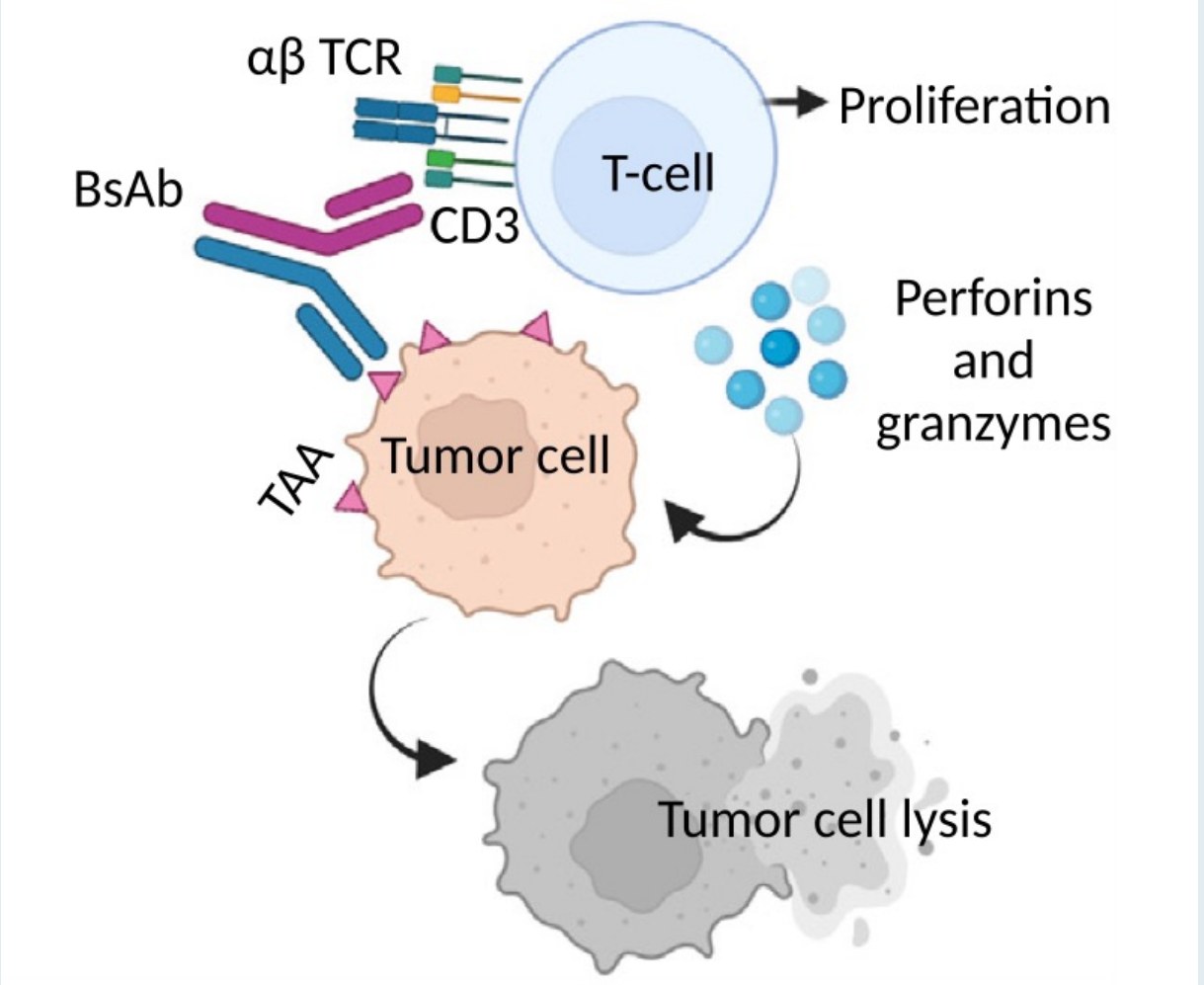
Mechanism of Bispecific Antibodies



Herrera M et al. *Trends Cancer* 2024;10(10):893-919.

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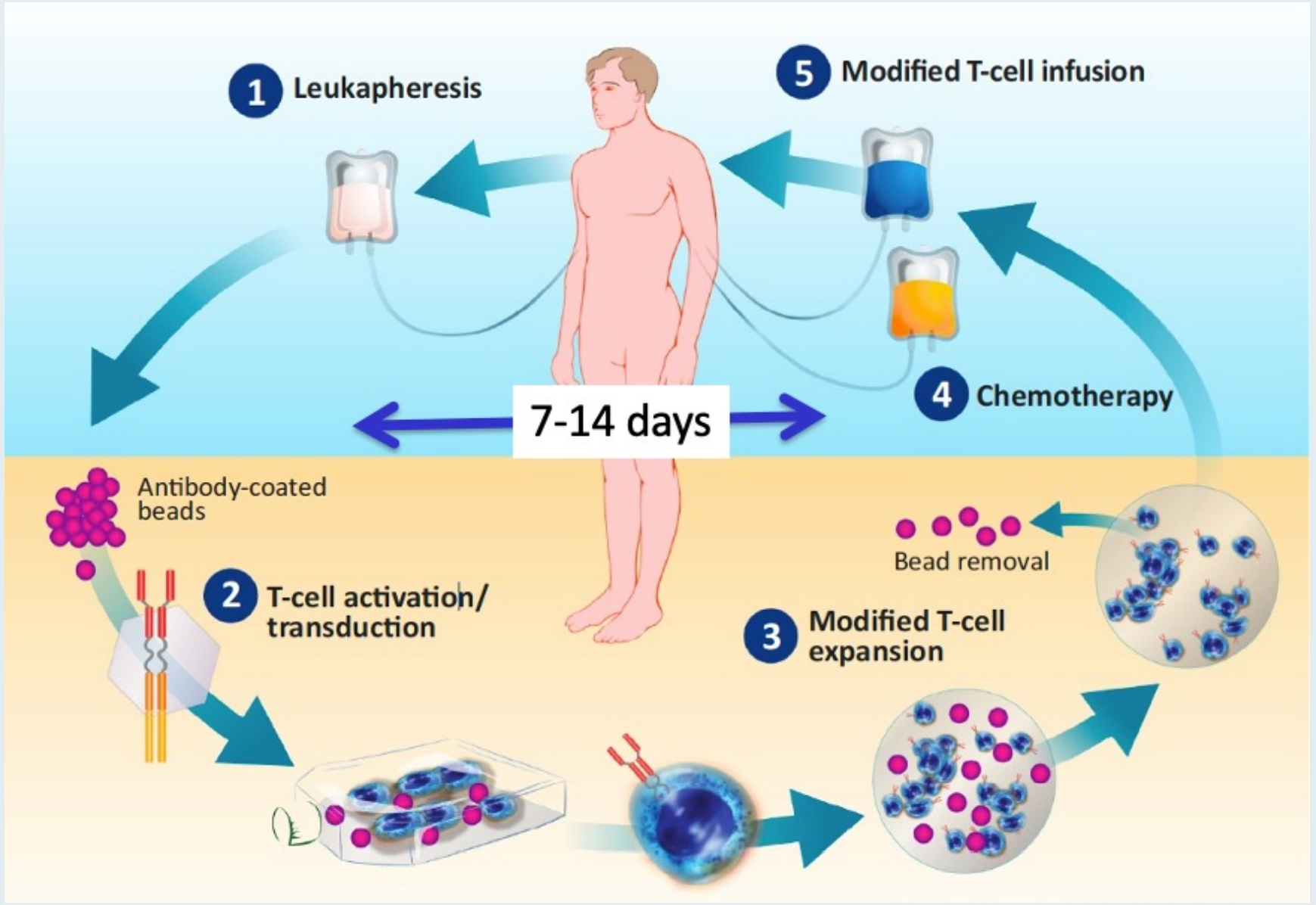
Approved and Investigational Bispecific Antibodies in R/R NHL

Drug Name	Route of Administration	FDA Approval Status
Mosunetuzumab	Intravenous	Approved (FL)
Glofitamab	Intravenous	Approved (DLBCL)
Epcoritamab	Subcutaneous	Approved (DLBCL, FL)
Odronextamab	Intravenous	Investigational (DLBCL, FL)

Respective package inserts. Accessed April 2025.

Overview of CAR T-Cell Therapy



Modification, Courtesy of David Porter, MD

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Approved CAR-T Cell Therapies in R/R NHL

Drug Name	Disease State
Tisagenlecleucel	DLBCL, FL
Axicabtagene ciloleucel	DLBCL, FL
Lisocabtagene maraleucel	DLBCL, FL, MCL
Brexucabtagene autoleucel	MCL

Respective package inserts. Accessed April 2025.

Clinical Management of CRS

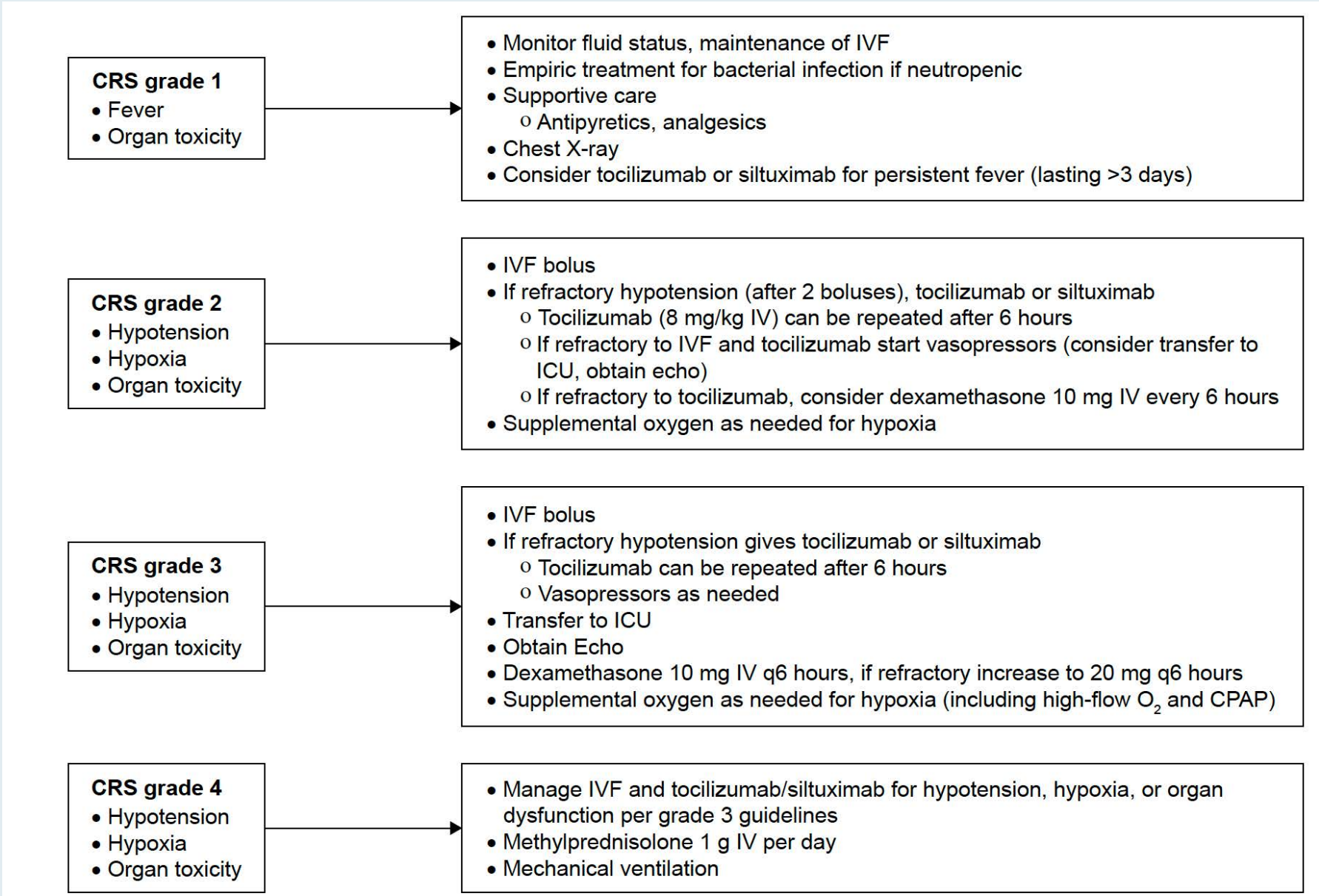

Figure 4 CRS management recommendations by Neelapu et al.[28]

Riegler LL et al. *Ther Clin Risk Manag* 2019;15:323-335.

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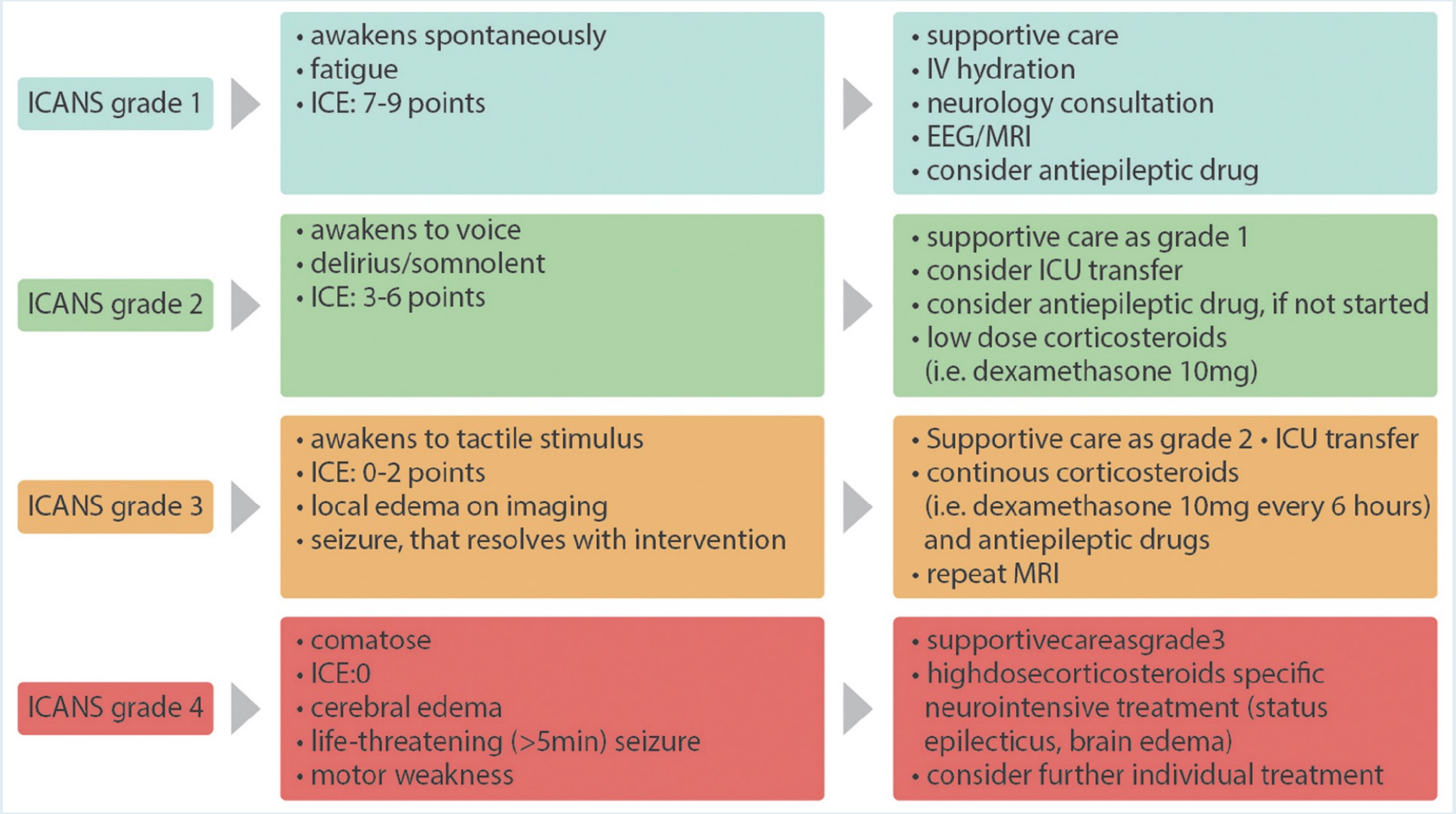
Clinical Management of ICANS



Garcia Borrega J et al. *Hemasphere* 2019;3(2):e191.

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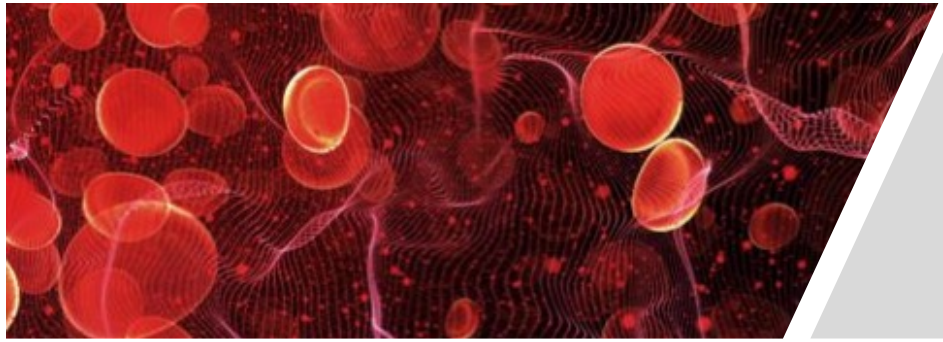
Clinical Scenario

An older patient with newly diagnosed MCL is about to start first-line treatment with acalabrutinib/bendamustine/rituximab



Understanding the Current Paradigm and New Approaches in the Care of Patients with Non-Hodgkin Lymphoma

Manali Kamdar, MD, MBBS
Associate Professor of Medicine, Clinical director of lymphoma services,
Morton and Sandra Saffer Endowed Chair in Hematology Research, Division of Hematology,
University of Colorado

ONS congress, RTP Symposium, 4/12/2025

Current and Future Use of BTK Inhibitors in Mantle Cell Lymphoma

Clinical Case

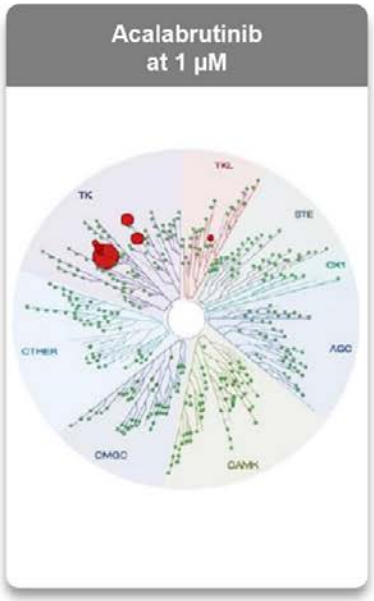
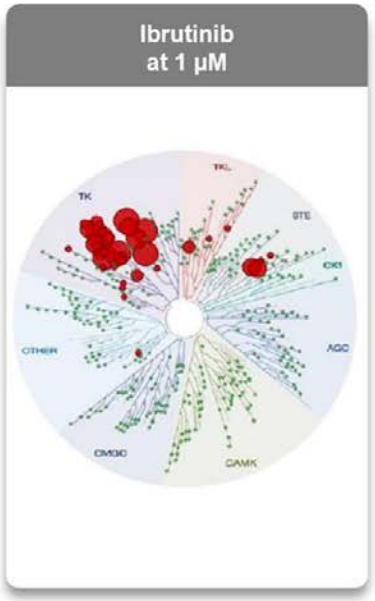
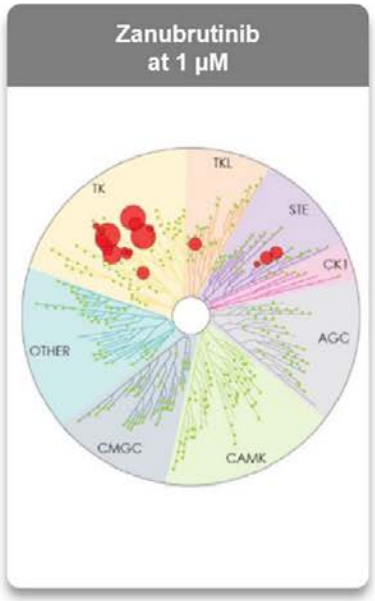
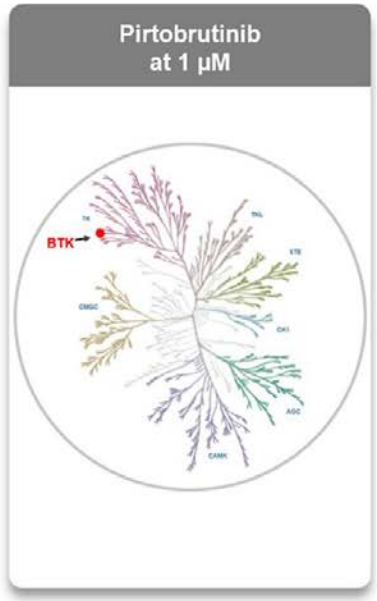
77-year-old male with ECOG 1 with PMH sig for Afib controlled on metoprolol and apixaban, noted gradual onset fatigue and dyspnea over 6 months. Work up including a CT scan revealed adenopathy above and below the diaphragm. Excisional biopsy of the inguinal node was consistent with Mantle cell lymphoma, **blastoid variant, ki67 70%.** Labs revealed mild anemia and thrombocytopenia, **LDH elevated**. Bone marrow biopsy positive for involvement with MCL. FISH and NGS **did not show any TP53 aberration.**

Next steps in the management of High-risk MCL in an older patient?

BTK inhibitors in Mantle Cell Lymphoma

Covalent BTKi

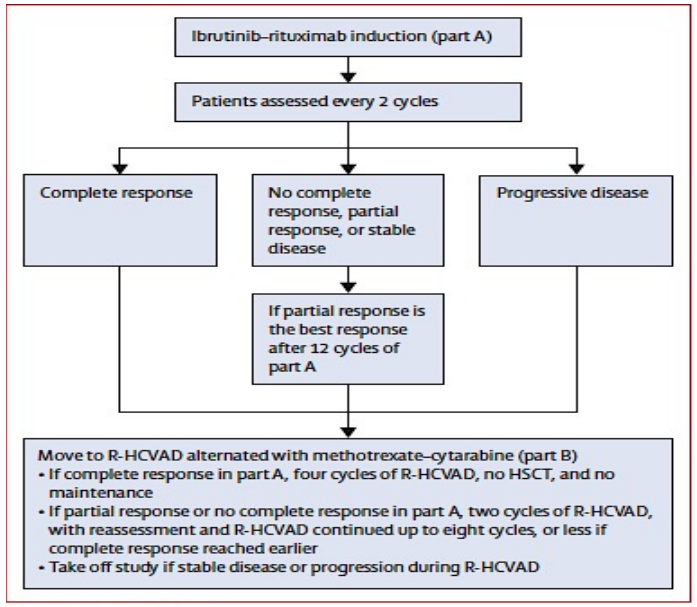
Non-Covalent BTKi

2nd Gen	1st Gen	2nd Gen	
Acalabrutinib at 1 µM	Ibrutinib at 1 µM	Zanubrutinib at 1 µM	Pirtobrutinib at 1 µM
			
Approved 2017	Approved 2013 Indication Withdrawn 2023	Approved 2019	Approved in 2023

Treatment Paradigm in young and fit untreated MCL

- 1993: HD chemo + ASCT
- 1990s: CHOP, FC, CEOP
- 1998: HyperCVAD
- 2005: R-CHOP, R-HyperCVAD
- 2008: Nordic Regimen
- 2016: MCL Younger
- 2017: LYMA (R maintenance)
- 2020: BR/HiDAC

<u>Issues with Cytotoxic Rx</u>
Tolerability
Toxicity (Short and Long term)
Efficacy in high-risk MCL (TP53 +)



WINDOW STUDY

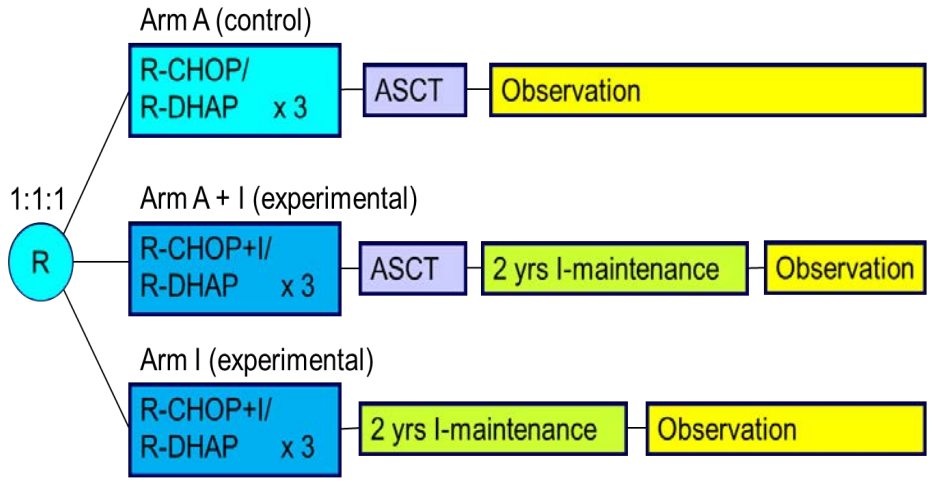
N = 131
ORR : 89%
CR: 77%

5-yr PFS 67%
5-yr OS 95%

Incorporating BTKi upfront Feasible
Chemo-based
TP53-mut CR lower

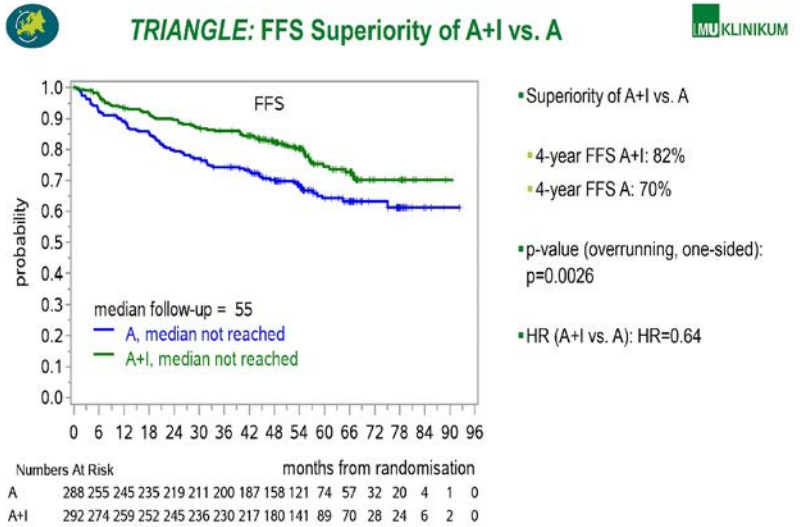
Wang et al. Lancet Oncol. 2022

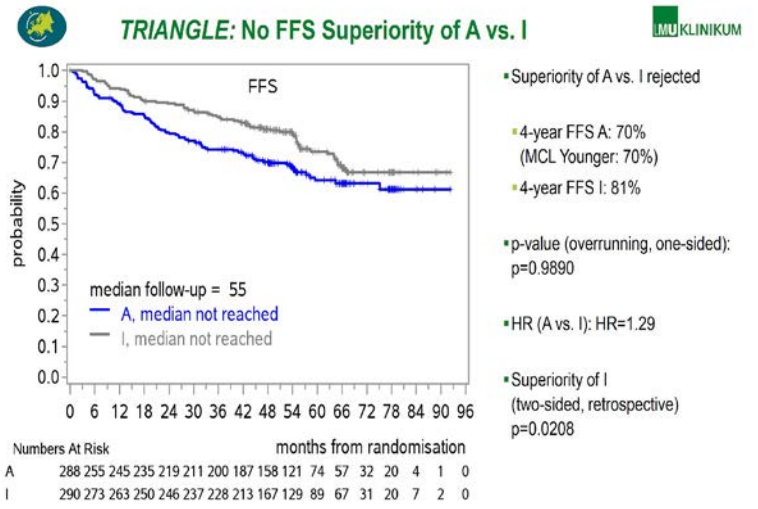
TRIANGLE PHASE III Study: Can Ibrutinib + SOC substitute ASCT in young/fit MCL?



Primary endpoint: FFS
Secondary endpoints: Response rates, PFS, RD, OS, safety

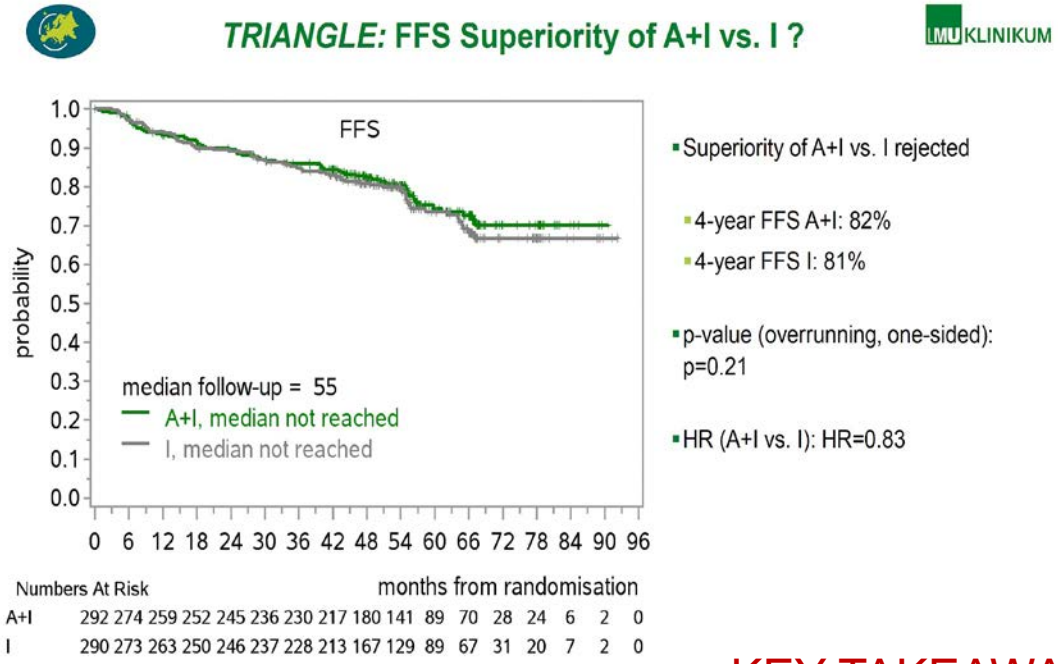
Previously untreated stage II-IV MCL
Age <66 years
Suitable for HA and ASCT
ECOG PS 0-2
Rituximab maintenance (without or with Ibrutinib) was started in
168 (58 %)/165 (57 %)/158 (54 %) of A/A+I/I randomized patients
Median FU 55 months



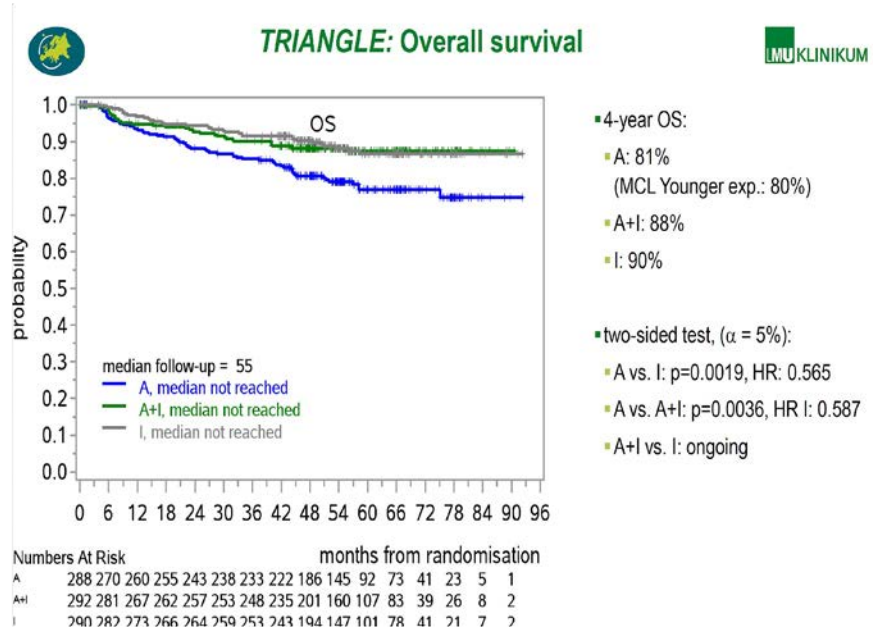


Dreyling M et al. Lancet 2024;403(10441):2293-306.
Dreyling M, et al. ASH 2024;Abstract 240.

TRIANGLE PHASE III Study: Can Ibrutinib + SOC substitute ASCT in young/fit MCL?



- Superiority of A+I vs. I rejected
  - 4-year FFS A+I: 82%
  - 4-year FFS I: 81%
- p-value (overrunning, one-sided): p=0.21
- HR (A+I vs. I): HR=0.83



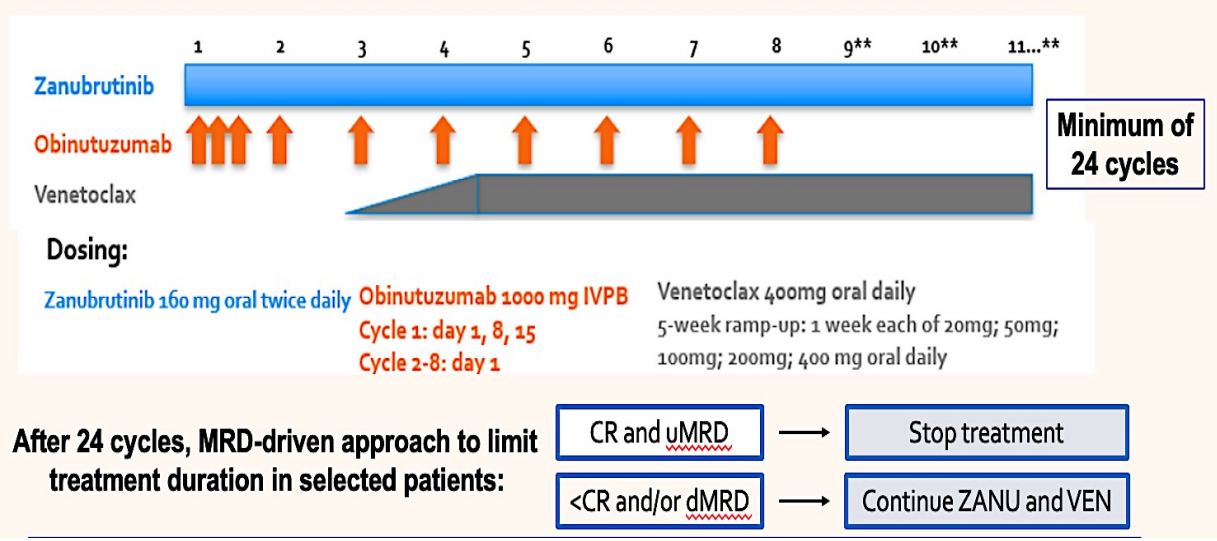
- 4-year OS:
  - A: 81%
    (MCL Younger exp.: 80%)
  - A+I: 88%
  - I: 90%
- two-sided test, (α = 5%):
  - A vs. I: p=0.0019, HR: 0.565
  - A vs. A+I: p=0.0036, HR I: 0.587
  - A+I vs. I: ongoing

KEY TAKEAWAYS

BTKi + Chemo can Substitute ASCT in 1L MCL
No sufficient benefit of ASCT + I vs. I even in high-risk patients (TP53, high Ki67, Blastoid)
TRIANGLE regimen -- new SOC in younger MCL patients
Implications :
Substitution of Ibrutinib with Sec Gen BTKi
Can we do better in High-Risk disease – Chemo in TP53 ?
Treatment at relapse ? Rechallenging with BTKi ? Something else?

Dreyling M, et al. ASH 2024;Abstract 240.

A multicenter, phase 2 trial with zanubrutinib, obinutuzumab, and venetoclax (BOVen) in patients with treatment-naïve, ***TP53*-mutant** MCL



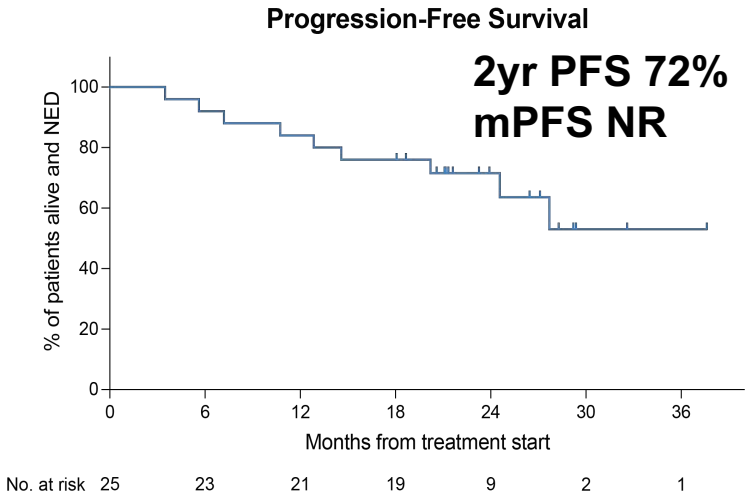
N= 25; mAge 65 (29-82)
Primary Endpoint: PFS at 2y
Median FU 23.3 months

SAFETY

well-tolerated and safe
Most common AEs were diarrhea, COVID19 infection, neutropenia
Grade 3 neutropenia (16%) resolved with GCSF
Diarrhea was predominantly grade 1

RESULTS:

ORR 96%, CR 88%
5 PD, 4 deaths (In response, 2 covid)
11 completed therapy
10 with MRD data – 8/10 uMRD – stopped
2/10- dMRD- continuing Ven plus Zanu



Practice Implications

NCCN – TP53mut
? TRIANGLE
Rx at Relapse?

Kumar et al ASH 2023; Abstract 738

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ASCT ERA

- 2022: WINDOW-1
- 2023: TRIANGLE
- 2024: BOVEN

CHEMO + BTKi ERA

Treatment Paradigm in elderly and unfit untreated MCL

- 1990: CHOP, FC, CEOP
- 2012: R-CHOP with Ritux Maintenance
- 2013: BR
- 2017: RBAC
- 2018: VR-CAP

+ BTKi Trials

The NEW ENGLAND JOURNAL of MEDICINE

www.nejm.org/doi/full/10.1056/NEJMoa2201817

ORIGINAL ARTICLE

Ibrutinib plus Bendamustine and Rituximab in Untreated Mantle-Cell Lymphoma

Michael L. Wang, M.D., Wojciech Jurczak, M.D., Ph.D., Mats Jerkeman, M.D., Ph.D.,

SHINE: A Randomized, Double-Blind, Phase III Study

Patients
- Previously untreated MCL
- ≥ 65 years of age
- Stage II-IV disease
- No planned stem cell transplant

Stratification factor
- Simplified MIPI score (low vs intermediate vs high)

Enrolled between May 2013 and November 2014 at 183 sites

N = 523

R 1:1

BR induction for 6 cycles → if CR or PR → Rituximab maintenance every 8 weeks for 12 cycles

Ibrutinib 560 mg (4 capsules daily) until PD or unacceptable toxicity

BR induction for 6 cycles → if CR or PR → Rituximab maintenance every 8 weeks for 12 cycles

Placebo (4 capsules daily) until PD or unacceptable toxicity

Primary end point: PFS (investigator-assessed) in the ITT population

Key secondary end points: response rate, time to next treatment, overall survival, safety

Induction: Bendamustine 90 mg/m2 Days 1 and 2, Rituximab 375 mg/m2 Day 1, Q4W. A cycle is defined as 28 days.

CR, complete response; ITT, intent-to-treat; MIPI, Mantle Cell Lymphoma International Prognostic Index; PD, progressive disease; PFS, progression-free survival; PR, partial response.

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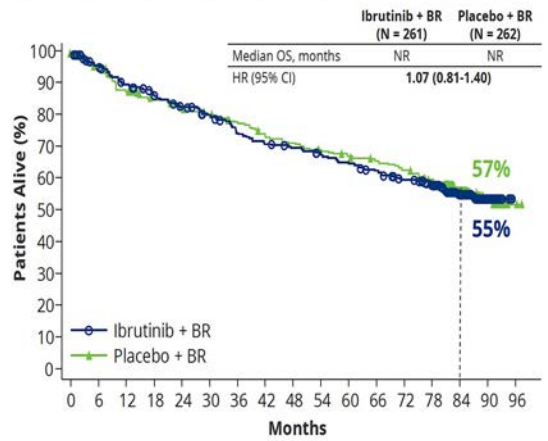


Cause of death	Ibrutinib + BR (N = 261)	Placebo + BR (N = 262)
Death due to PD and TEAE	58 (22.2%)	70 (26.7%)
Death due to PD	30 (11.5%)	54 (20.6%)
Death due to TEAEs*	28 (10.7%)	16 (6.1%)
Death during post-treatment follow-up excluding PD and TEAEs	46 (17.6%)	37 (14.1%)
Total deaths	104 (39.8%)	107 (40.8%)

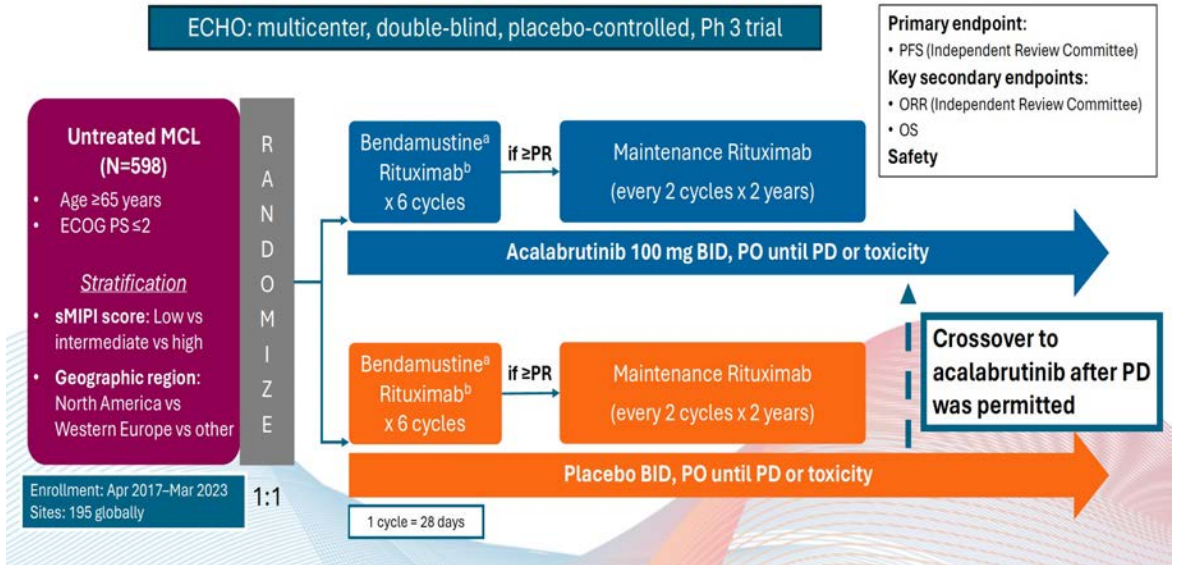
- Death due to Covid-19: 3 patients in the ibrutinib arm during the TEAE period and 2 patients in the placebo arm after the TEAE period
- Exploratory analysis of cause-specific survival including only deaths due to PD or TEAEs showed an HR of 0.88

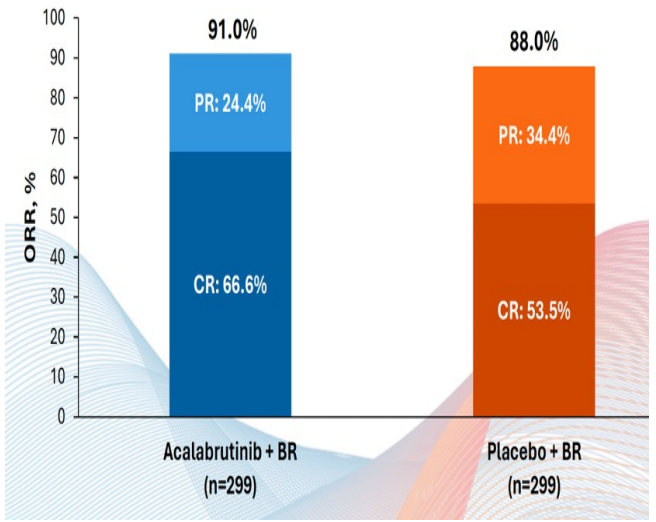
*The most common grade 5 TEAE was infections in the ibrutinib and placebo arms: 9 versus 5 patients. Grade 5 TEAE of cardiac disorders occurred in 3 versus 5 patients, respectively.

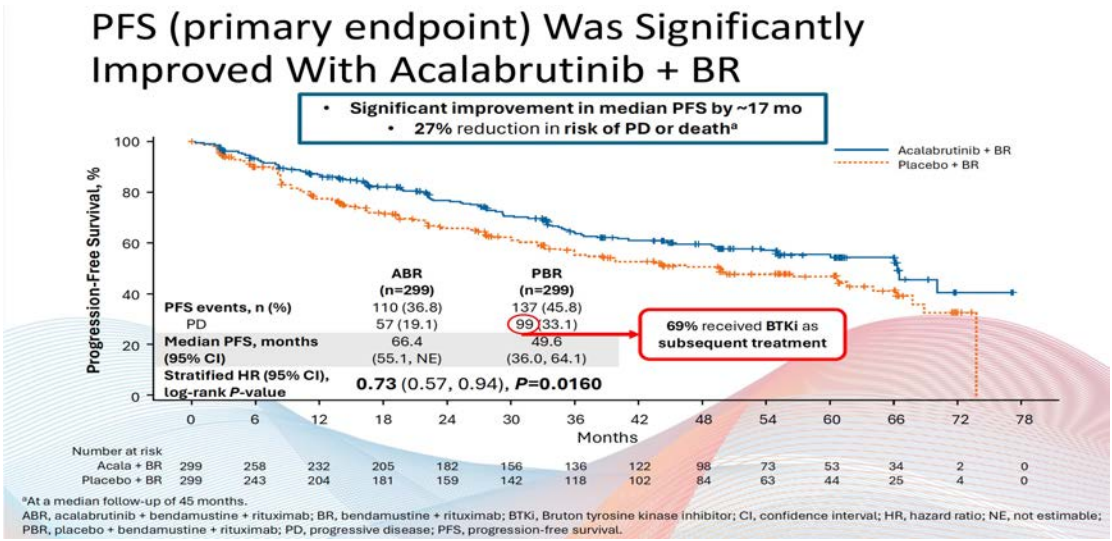
CI, confidence interval; HR, hazard ratio; NR, not reached; PD, progressive disease; TEAE, treatment-emergent adverse event.

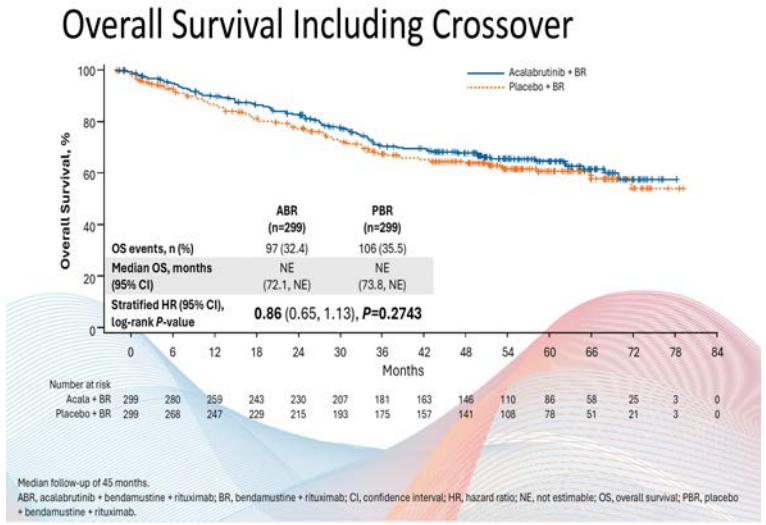
15

Acalabrutinib plus bendamustine and rituximab in untreated MCL: Results from the phase 3, double-blind, placebo-controlled ECHO trial









Wang et al. EHA 2024;Abstract LBA 3439

Toxicity

	Acalabrutinib + BR (n=297)		Placebo + BR (n=297)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Event, n (%)				
Atrial fibrillation	18 (6.1)	11 (3.7)	13 (4.4)	5 (1.7)
Hypertension	36 (12.1)	16 (5.4)	47 (15.8)	25 (8.4)
Major bleeding[a]	7 (2.4)	6 (2.0)	16 (5.4)	10 (3.4)
Infections[b]	232 (78.1)	122 (41.1)	211 (71.0)	101 (34.0)
Second primary malignancies (excluding non-melanoma skin)[b]	29 (9.8)	16 (5.4)	32 (10.8)	20 (6.7)

	COVID-19–related AEs	
n (%)	Acalabrutinib + BR (n=297)	Placebo + BR (n=297)
Any AE	121 (40.7)	88 (29.6)
Grade ≥3	60 (20.2)	50 (16.8)
Grade 5	28 (9.4)	20 (6.7)
SAEs	60 (20.2)	52 (17.5)
Grade ≥3	58 (19.5)	48 (16.2)
AE leading to acalabrutinib/ placebo discontinuation	31 (10.4)	19 (6.4)

Treatment Paradigm in elderly and unfit untreated MCL

- 1990: CHOP, FC, CEOP
- 2012: R-CHOP with Ritux Maintenance
- 2013: BR
- 2017: RBAC
- 2018: VR-CAP

CHEMO ERA

- 2022: SHINE
- 2024: BOVEN
- 2024: ECHO

CHEMO + BTKi ERA

Clinical Case

77-year-old male with ECOG 1 with PMH sig for Afib controlled on metoprolol and apixaban, noted gradual onset fatigue and dyspnea over 6 months. Exam revealed axillary and cervical adenopathy. Work up including a CT scan revealed adenopathy above and below the diaphragm. Excisional biopsy of the inguinal node was consistent with Mantle cell lymphoma, **blastoid variant, ki67 70%.** Labs revealed mild anemia and thrombocytopenia, **LDH elevated**. Bone marrow biopsy positive for involvement with MCL. FISH and NGS **did not show any TP53 aberration.**

In Jan 2025 – BR plus Acalabrutinib

C1– headaches, diarrhea – Continued Acalabrutinib – supportive care

C2– Complicated by nose bleeds --- temporary interruption of Acalabrutinib and apixaban

C3 – going well thus far + symptoms have resolved + on exam no evidence of adenopathy

Next steps – If in a CR at EOT – Acalabrutinib until progression?
MRD driven approach? Durability?

Management of MCL in 2025

Practice Impact

- Essential to check TP53 aberration status at diagnosis
- ASCT no longer required for young/fit patients
- Upfront treatment with 2nd generation BTKi's (BOVEN or TRIANGLE) new SOC in young/fit patients
- Upfront treatment with 2nd generation BTKi's MAY be incorporated in old/unfit patients

Lingering questions

- Treatment at relapse ? – BTKi retreatment? CAR-T ?
- High-risk (esp TP53 mutation +) MCL needs novel DURABLE approaches
- CUREs still elusive – need long-term follow up, clinical trials.

Roundtable Discussion

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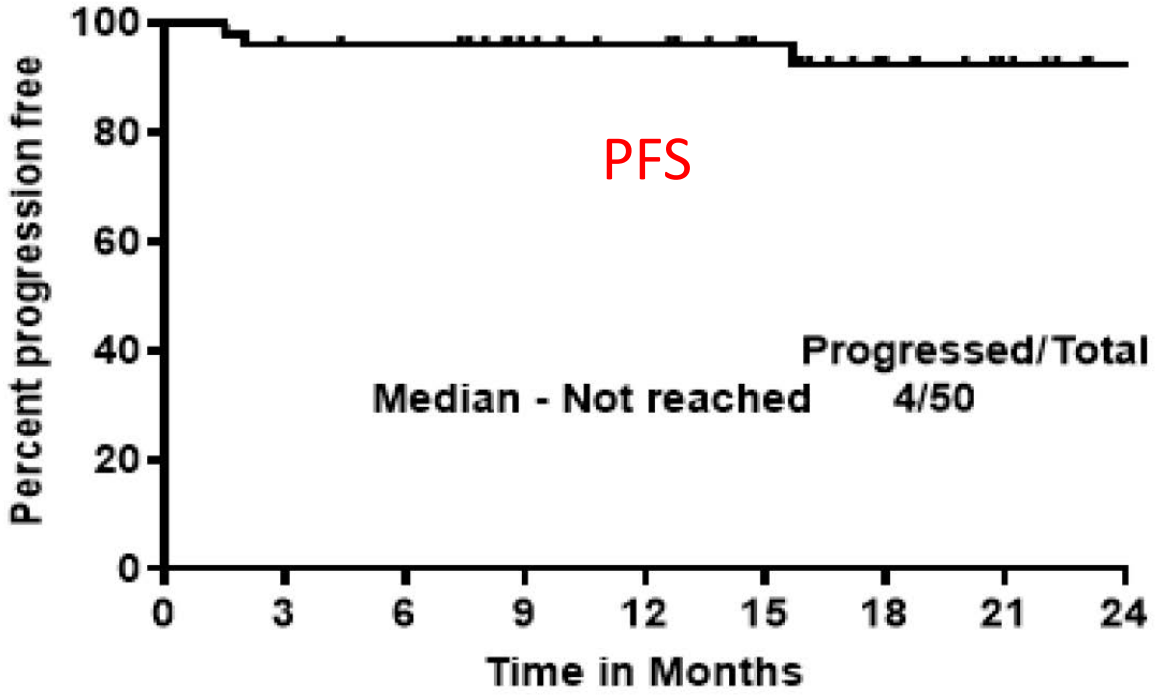
Phase II Study of Acalabrutinib with Rituximab as First-Line Therapy for Older Patients with MCL

Frontline AR in elderly MCL-Responses

Response (ITT)	All patients
Week 12 Best response#	N (%)
Evaluable patients*	49
ORR	46/50 (92)
CR	37/50 (74)
PR	9/50 (18)
Best response$	
Evaluable patients	49
ORR	46/50 (92)
CR	46/50 (92)
MRD at LFU (n=32)##	19/32 (60%) MRD negative
Median number of AR cycles to reach CR (range)	3(2-7)



With median follow-up of 28 months,
median PFS and OS were not reached.

2-year PFS: 94%
2-year OS: 96%

Jain P et al. ASH 2024;Abstract 3038.

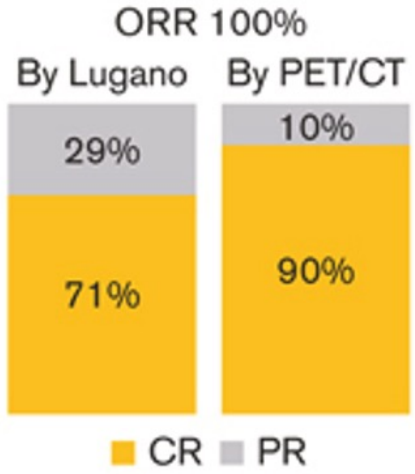
A Phase I Study of Acalabrutinib + Venetoclax + Rituximab in MCL

Patients
Treatment-naive
MCL (N = 21)

Acalabrutinib: From cycle 1, day 1: 100 mg BID until PD or treatment discontinuation

Venetoclax: From cycle 2, day 1 after ramp-up: 400 mg daily, through cycle 25

Rituximab: 375 mg/m^2 (day 1, 6 cycles); maintenance every other cycle for pts with CR or PR through cycle 24



With median follow-up of 27.8 months, median PFS and OS were not reached.

1-year PFS: 90.5% (95% CI, 67.0-97.5)
2-year PFS: 63.2% (95% CI, 34.7-82.0)

1-year OS: 95.2% (95% CI, 70.7-99.3)
2-year OS: 75.2% (95% CI, 50.3-88.9)

RTP RESEARCH TO PRACTICE

Wang M et al. *Blood Adv* 2024;8(17):4539-4548.

ONS 2025 NHL

Robin Klebig, APRN, CNP, AOCNP

April 12, 2025

Scenario 4: An older patient with newly diagnosed mantle cell lymphoma (MCL) is about to start first-line treatment with acalabrutinib/BR

- ***What side effects can occur with ibrutinib, acalabrutinib, zanubrutinib and pirtobrutinib? What do you tell your patients about to start one of these agents about potential toxicities? How does this vary according to the specific agent?***
- Bleeding/bruising (all – but more common with **ibrutinib**)
    - Avoid NSAIDS due to increased risk of bleeding
- Atrial fibrillation (more common with **ibrutinib**)
- Hypertension (more common with **ibrutinib**)
- Ventricular arrhythmias, heart failure
- Arthralgia (more common with **ibrutinib)**
- Headache (**acalabrutinib**)
- Diarrhea
- Low blood counts (neutropenia, anemia, thrombocytopenia)
- Infection
- Fatigue
- Rash
- Nail changes (**ibrutinib**)

Nursing Considerations for Patients Receiving a BTK Inhibitor — Ms Klebig

- ***How do you monitor for and manage common toxicities associated with BTK inhibitors?***
- Bleeding/bruising – assess pt for bleeding/bruising; educate on risk; avoid NSAIDs; hold BTK inhibitor prior to and after surgical/invasive procedures (3-7 days depending on procedure)
- A fib/HTN – Monitor blood pressure and symptoms of A fib (lightheadedness, palpitations, irregular or fast heart rate)
- Arthralgias – remain active, acetaminophen, warmth, topical analgesics, avoid NSAIDs
- Headache – acetaminophen & caffeine, hydration; reassure typically resolves after first month
- Diarrhea – dietary modification, loperamide; reassure typically resolves after a few months
- Cytopenias – monitor and educate pts on neutropenic precautions, monitoring for infection, bleeding risk, etc
- Fatigue – encourage activity to maintain conditioning, balance with rest periods, prioritize activities
- Nail changes – may try cuticle oil to nail bed, Biotin (2.5 mg daily)

An older patient w/ newly diagnosed mantle cell lymphoma starting first-line treatment with acalabrutinib/BR

- 63 yo male
- PMH:
  - Gout
- SH: Married, 2 children, ammunition specialist, enjoys fishing and golfing
- Lives 1-1/2 hrs from Mayo Clinic

Presentation – 2020

- Palpated right inguinal node
  - had been present x 2 years before reporting

- Bx: Mantle cell lymphoma
- Bone marrow: 5% involvement

- Elected to observe as asymptomatic, indolent, COVID

Progression 9/2021

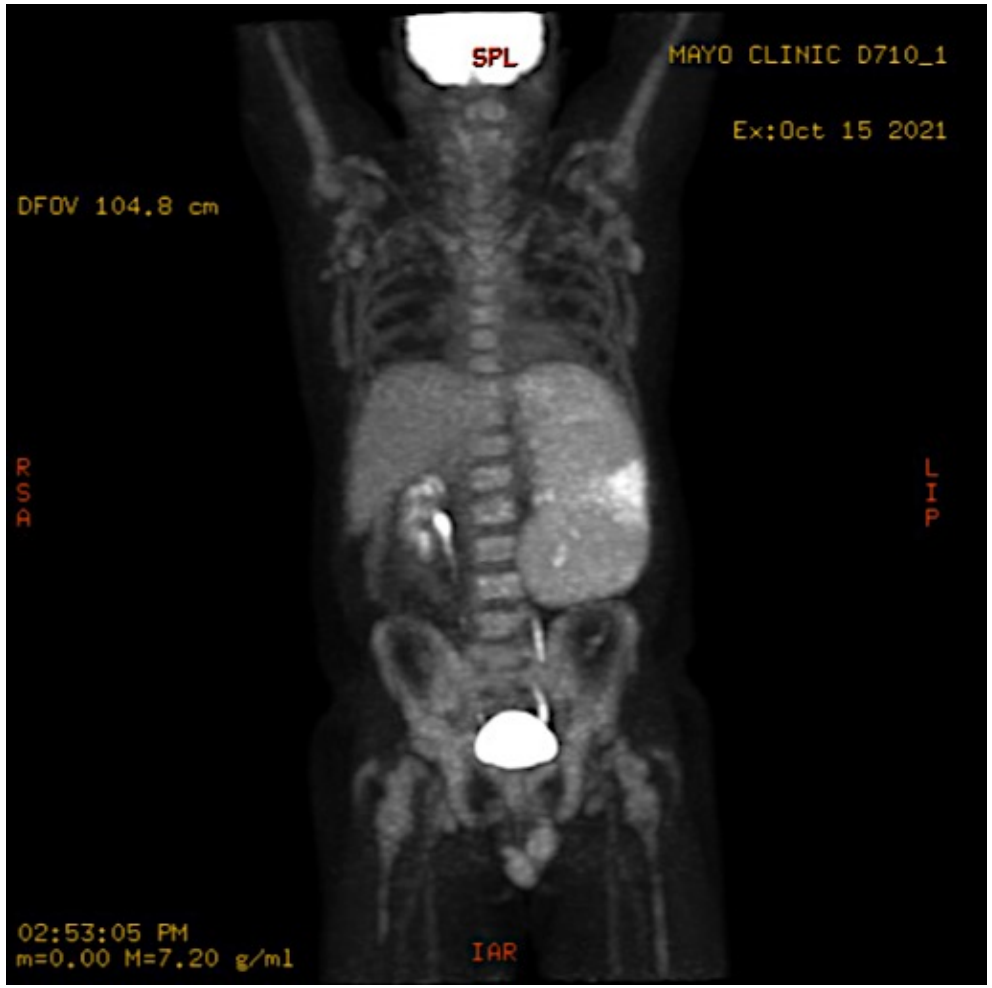
- Presented to ED w/ LUQ pain radiating to Left shoulder
- CT showed splenomegaly with splenic infarct

- Bone marrow: 60% involvement by MCL

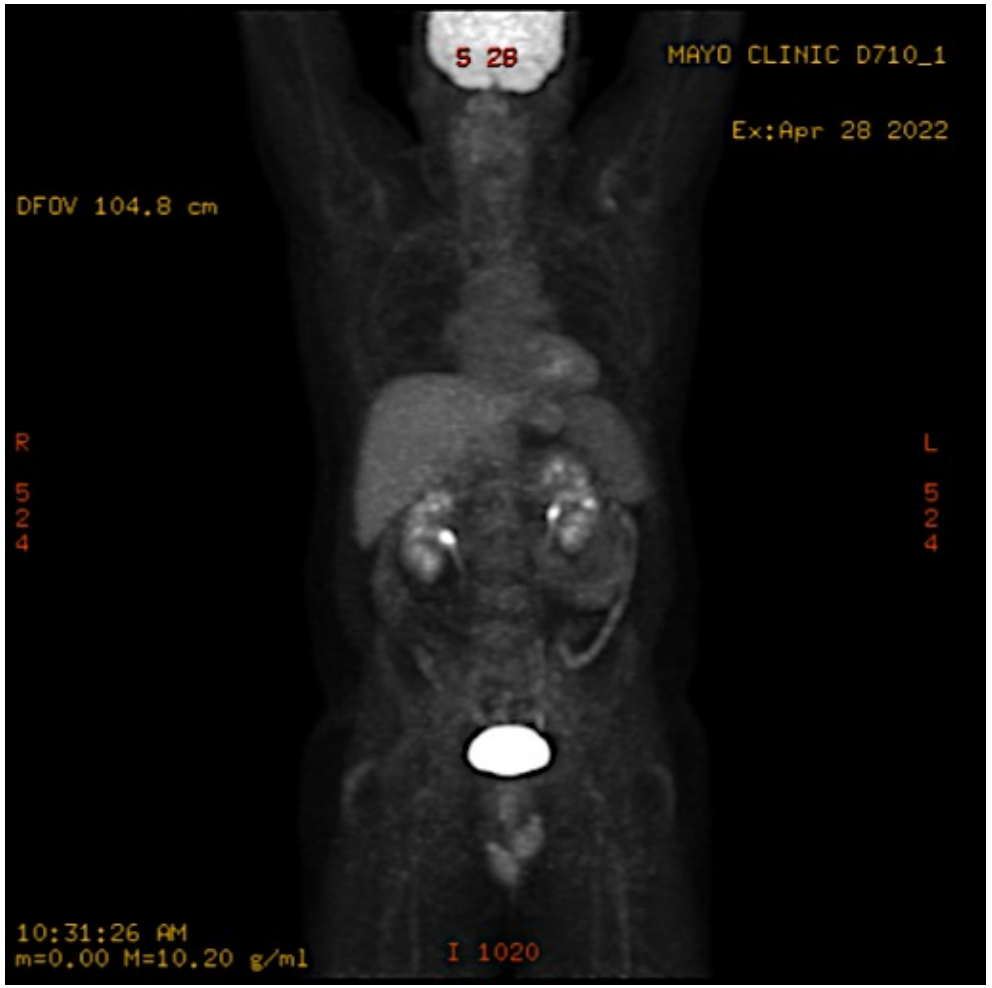
- Initiated rituximab, bendamustine, acalabrutinib per EA4181

Response

Baseline



After 6 cycles – Deauville 1



Response

- Bone marrow – negative

- MRD negative

Discussion & Plan

- Options
  - Observation
  - Auto SCT
  - Maintenance rituximab
  - Consideration of clinical trial EA4151
    - If MRD (-) would randomize to rituximab maintenance or SCT f/b maintenance

- *They were building their dream house on a lake – wanted to enjoy the summer – timing wasn't right to consider SCT*

- *Elected maintenance rituximab*

He will complete rituximab maintenance in May 2025

Then they are off to Italy for a vacation with their family (including the grandbabies!) for their 40th wedding anniversary

Roundtable Discussion

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Agenda

Introduction: Overview of Bispecific Antibodies and Chimeric Antigen Receptor T-Cell Therapy for Non-Hodgkin Lymphoma

Module 1: Current and Future Use of Bruton Tyrosine Kinase Inhibitors for Mantle Cell Lymphoma

Module 2: First-Line Therapy for Diffuse Large B-Cell Lymphoma (DLBCL)

Module 3: Role of Loncastuximab Tesirine for Patients with Relapsed/Refractory (R/R) DLBCL

Module 4: Role of Tafasitamab for Patients with R/R DLBCL and Follicular Lymphoma

Clinical Scenario

A patient with newly diagnosed DLBCL is about to start first-line treatment with polatuzumab vedotin/R-CHP

Advances in the First-line Treatment of Diffuse Large B-Cell Lymphoma

Christopher Flowers, MD, MS, FASCO

Division Head
Chair, Professor

Division of Cancer Medicine
Department of Lymphoma/Myeloma

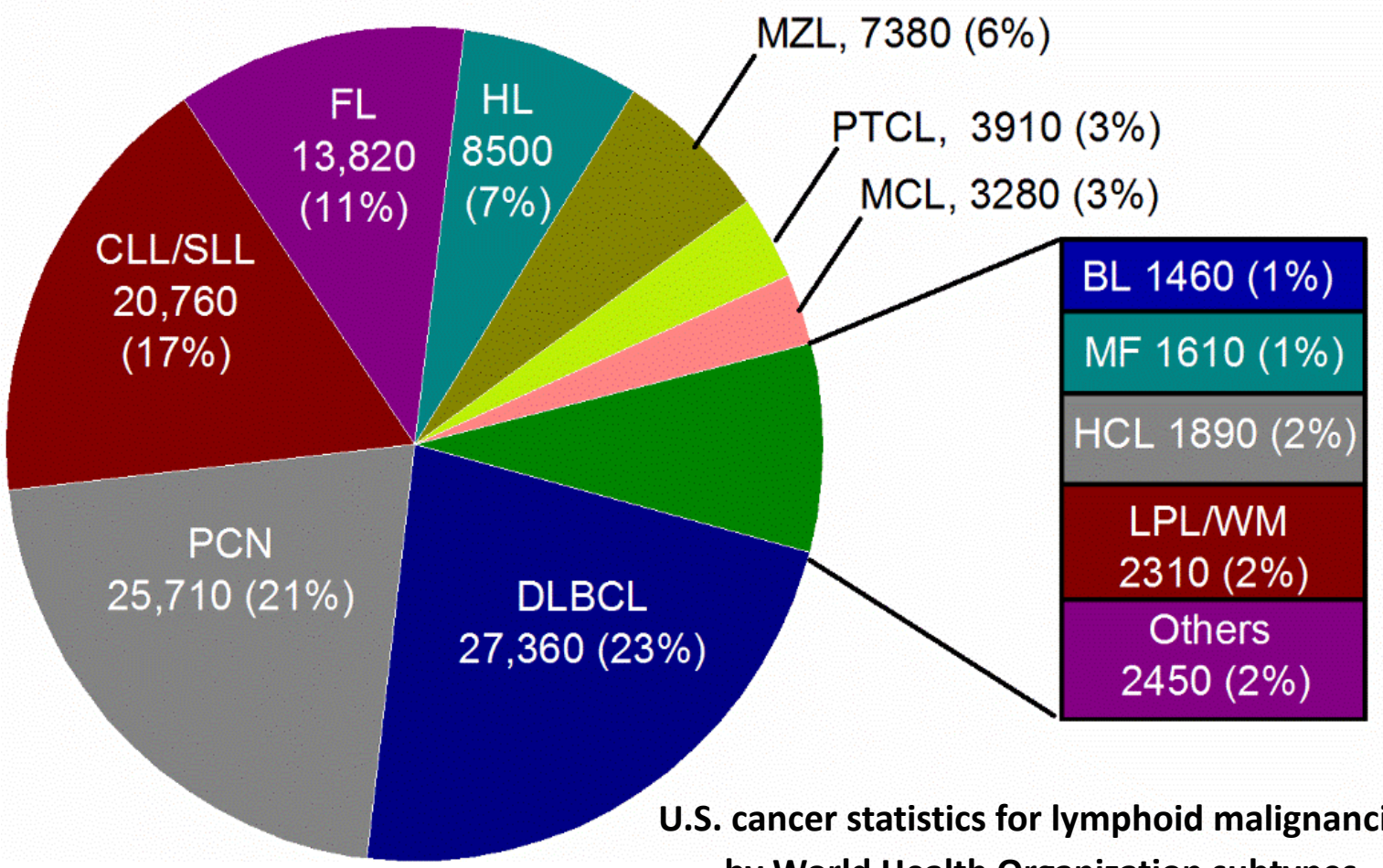
THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Case: 63 yo woman with DLBCL

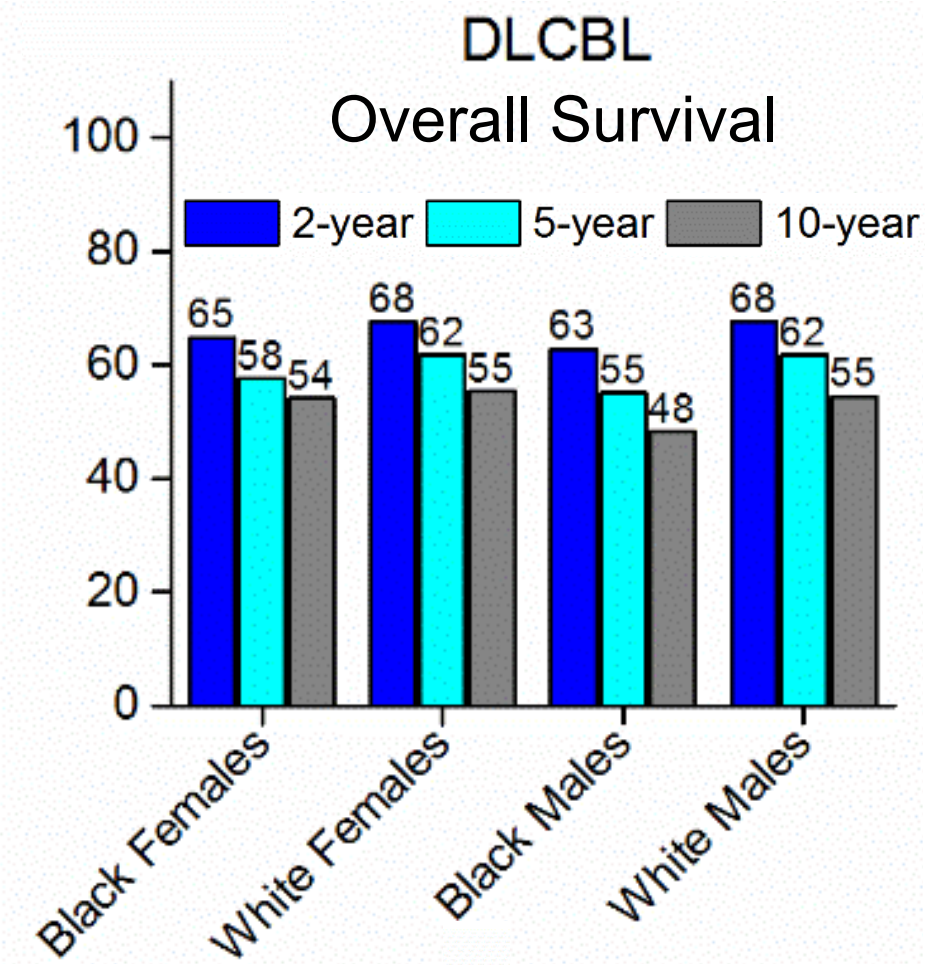
Initially admitted with epidural DLBCL with compression fracture

- IR Biopsy showed ABC subtype
- PET/CT Stage IV disease with BM involvement by PET
- LDH > ULN
- LP negative

Annual Incidence of Lymphoid Cancers in the United States



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

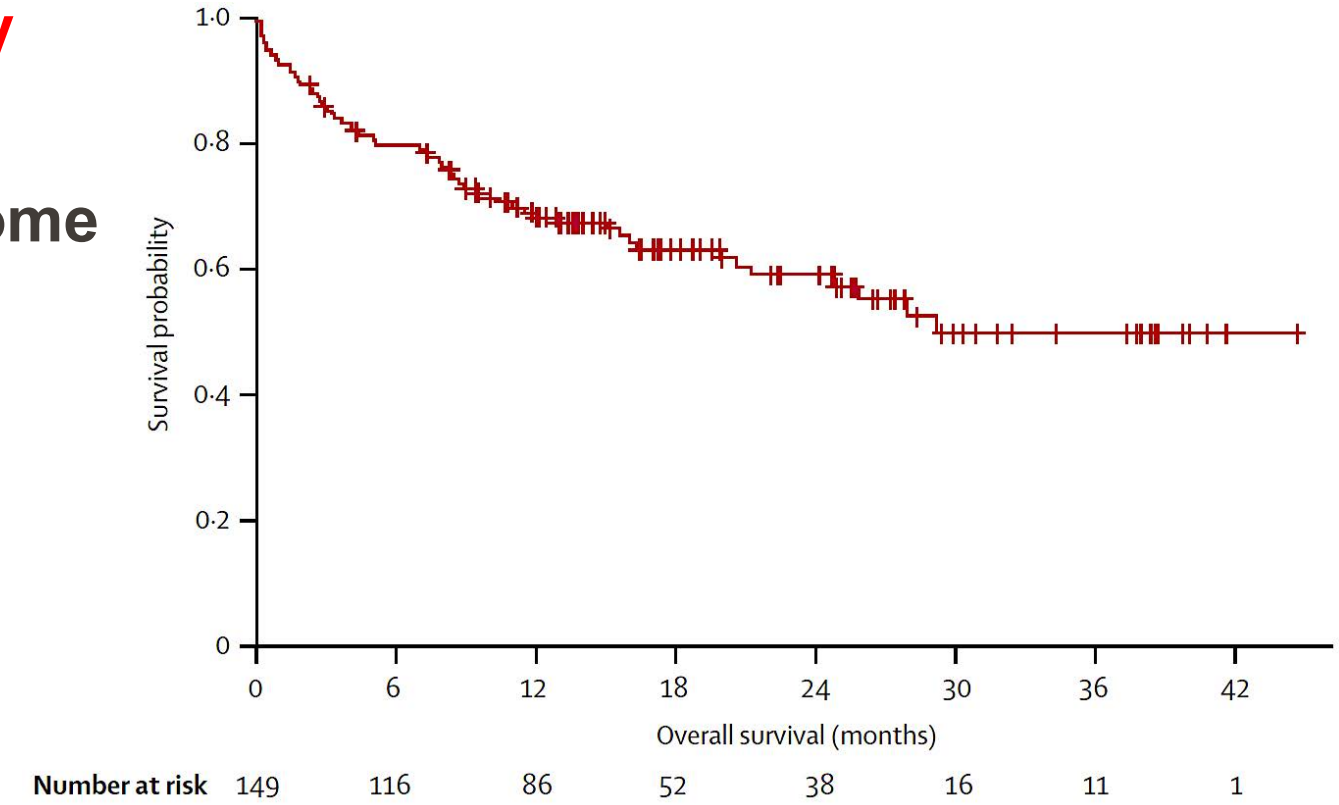


Teras LR, DeSantis CE, Morton LM, Cerhan JR, Jemal A, Flowers CR
CA Cancer J Clin. 2016

There is unmet need for older patients

- PFS from R- mini-CHOP is not adequate: 2-yr 47%
- Only 72% received the full intended 6 cycles
- 12 deaths, 8% grade 5 toxicity

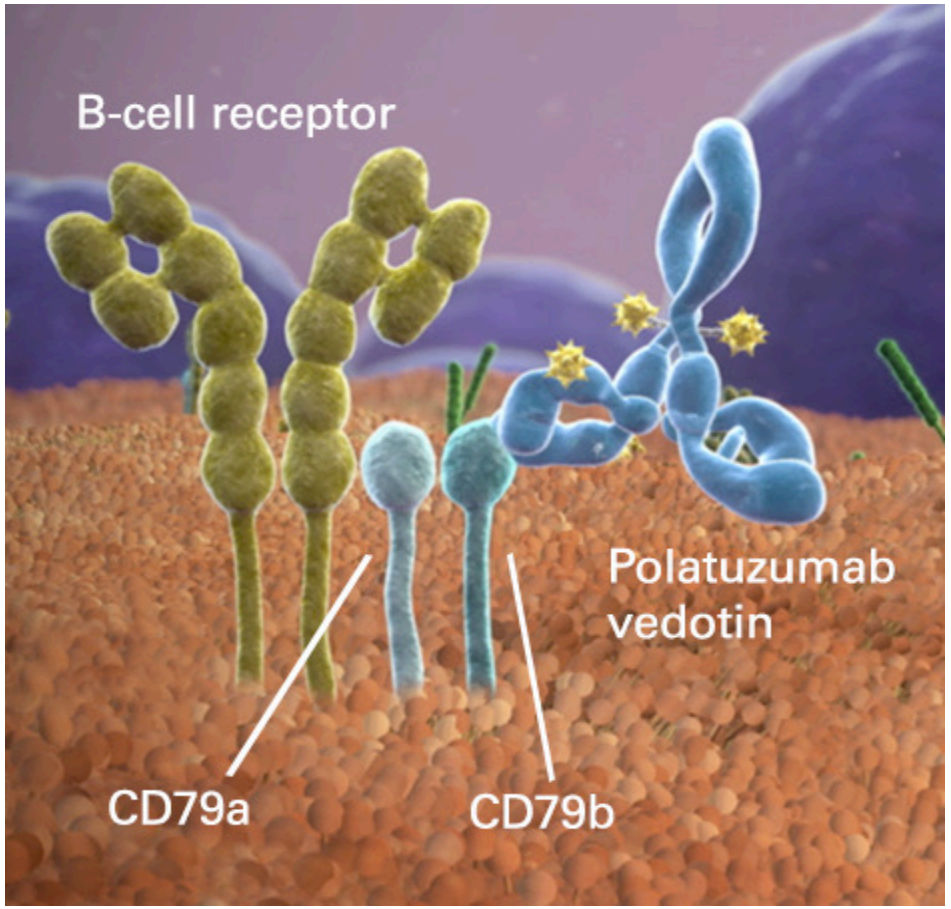
- Unmet need to improve outcome
  - ?

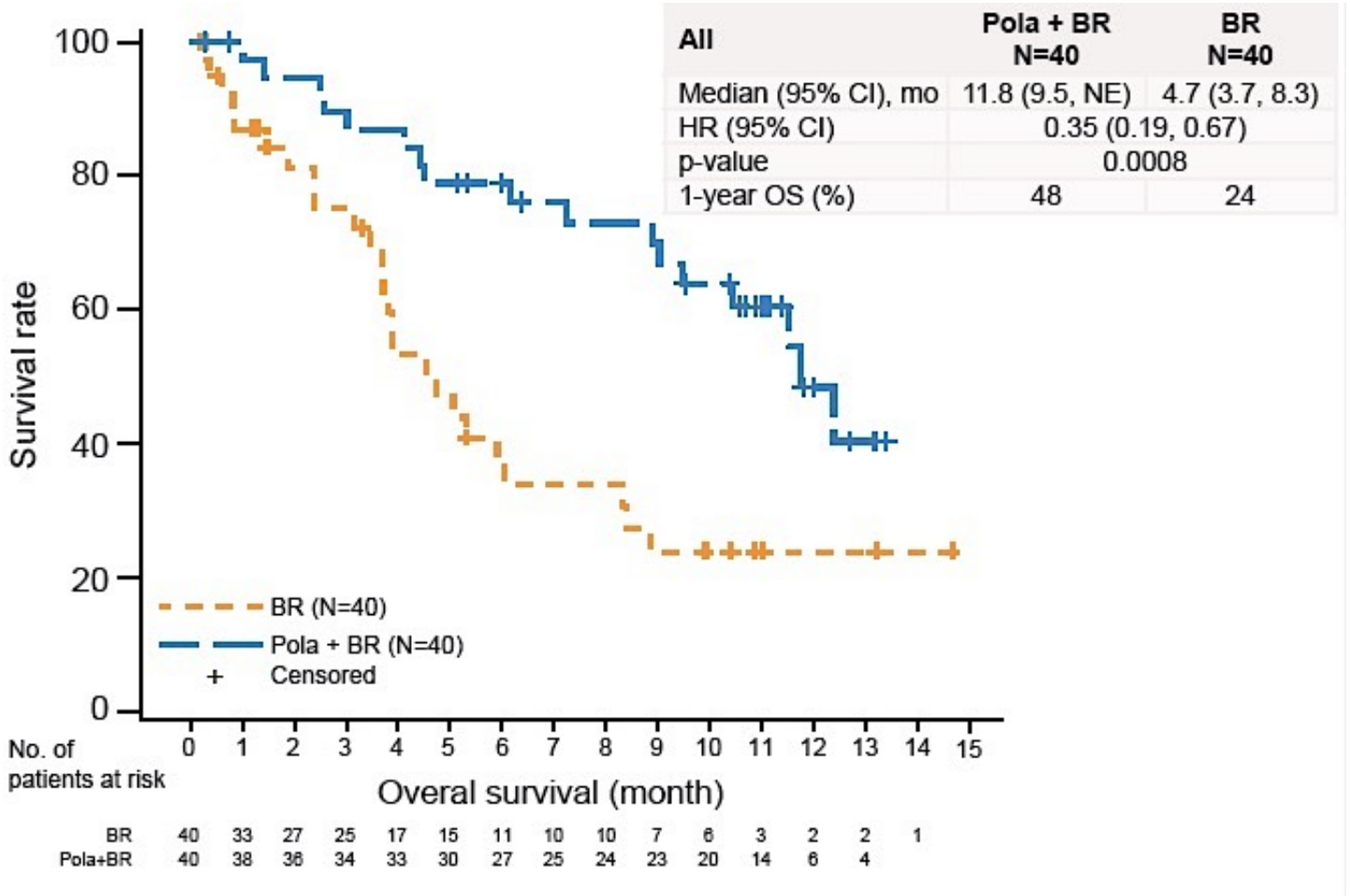


Peyrade F et al. *Lancet Oncol*. 2011; 12(5):460-8

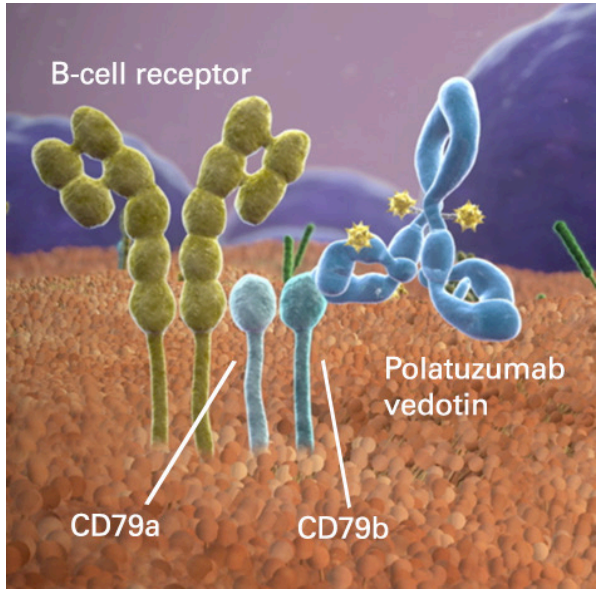
Polatuzumab Vedotin in Relapsed or Refractory Diffuse Large B-Cell Lymphoma *J Clin Oncol.* 2020

Laurie H Sehn, Alex F Herrera, Christopher R Flowers, Manali Kamdar, Andrew McMillan, Mark Hertzberg, Sarit Assouline, Tae Min Kim, Won Seog Kim, Muhit Ozcan, Jamie Hirata, Elicia Penuel, Elicia Penuel, Ji Cheng, Joseph N. Paulson, Grace Ku, Matthew Matasar





POLARIX: 1L DLBCL Phase 3



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Polatuzumab Vedotin in Previously Untreated Diffuse Large B-Cell Lymphoma

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

Patients

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

Stratification factors

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

R 1:1

Pola-R-CHP

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

R-CHOP

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

Cycles 1–6
(1 cycle=21 days)

Rituximab
375mg/m^2

Cycles 7 & 8

Primary endpoint

Progression-free survival (Investigator-assessed)

Secondary endpoints

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

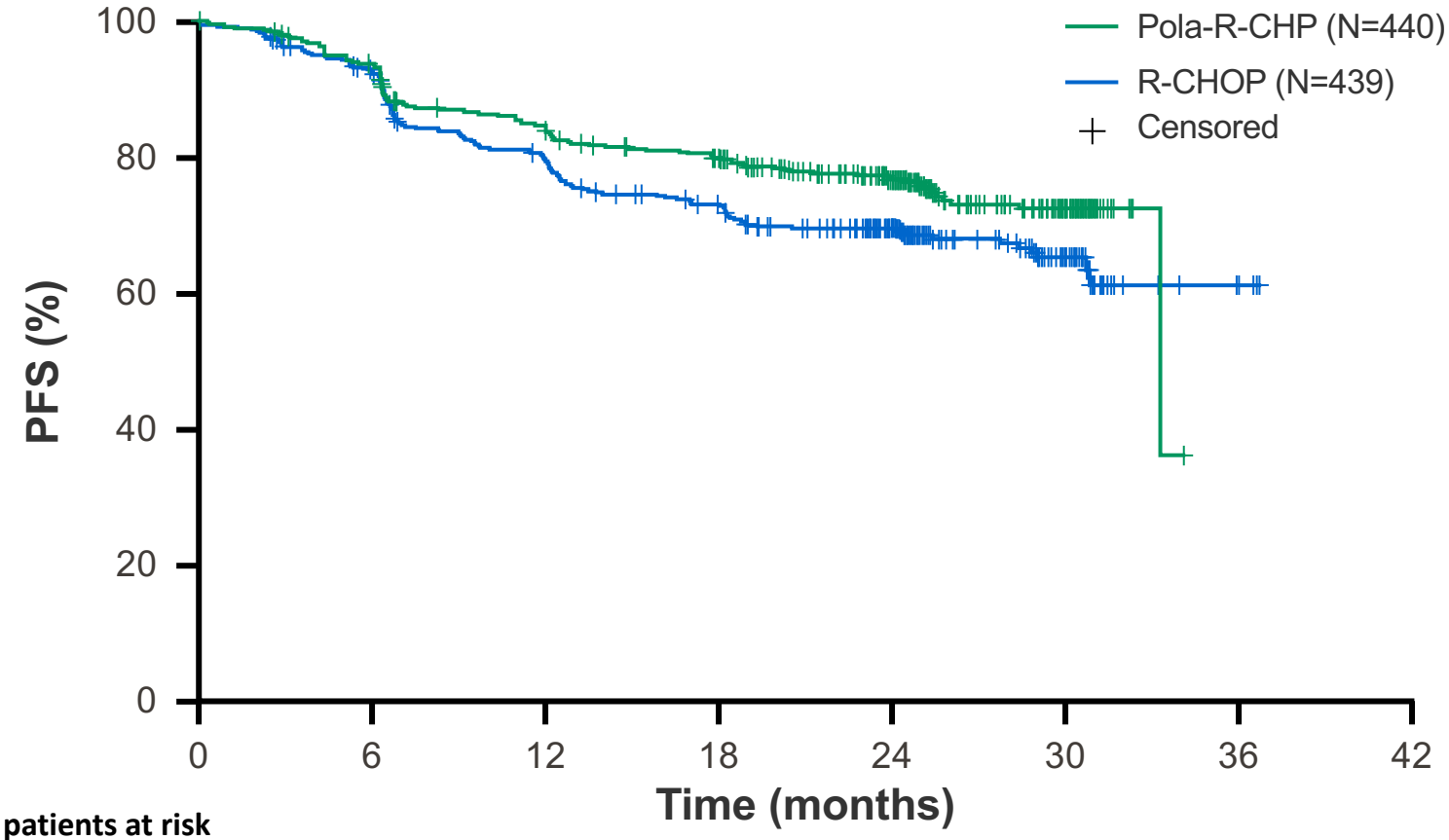
Safety endpoints

Incidence, nature, and severity of adverse events

Tilly et al. *NEJM* 2021

Primary endpoint: Progression-free survival

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



No. of patients at risk

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

HR 0.73 **(P=0.02)**

95% CI: 0.57, 0.95

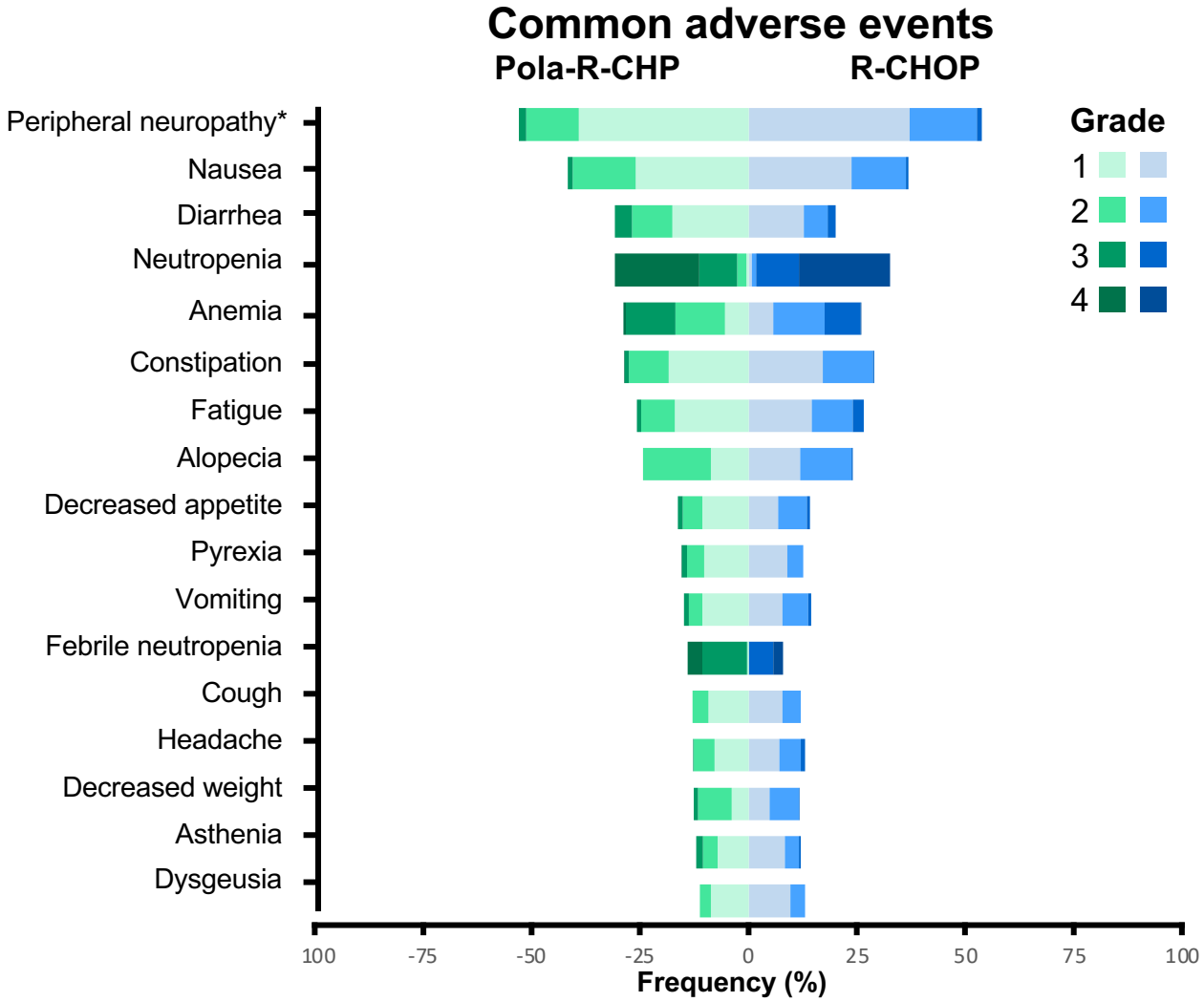
- Pola-R-CHP demonstrated a **27% reduction in the relative risk of disease progression, relapse, or death** vs R-CHOP
- **24-month PFS:** 76.7% with Pola-R-CHP vs 70.2% with R-CHOP (Δ**=6.5%**)
- **5-year PFS:** 63.1% with Pola-R-CHP vs 59.1% with R-CHOP

Tilly et al. *NEJM* 2021
Salles ASH 2024

Safety summary

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

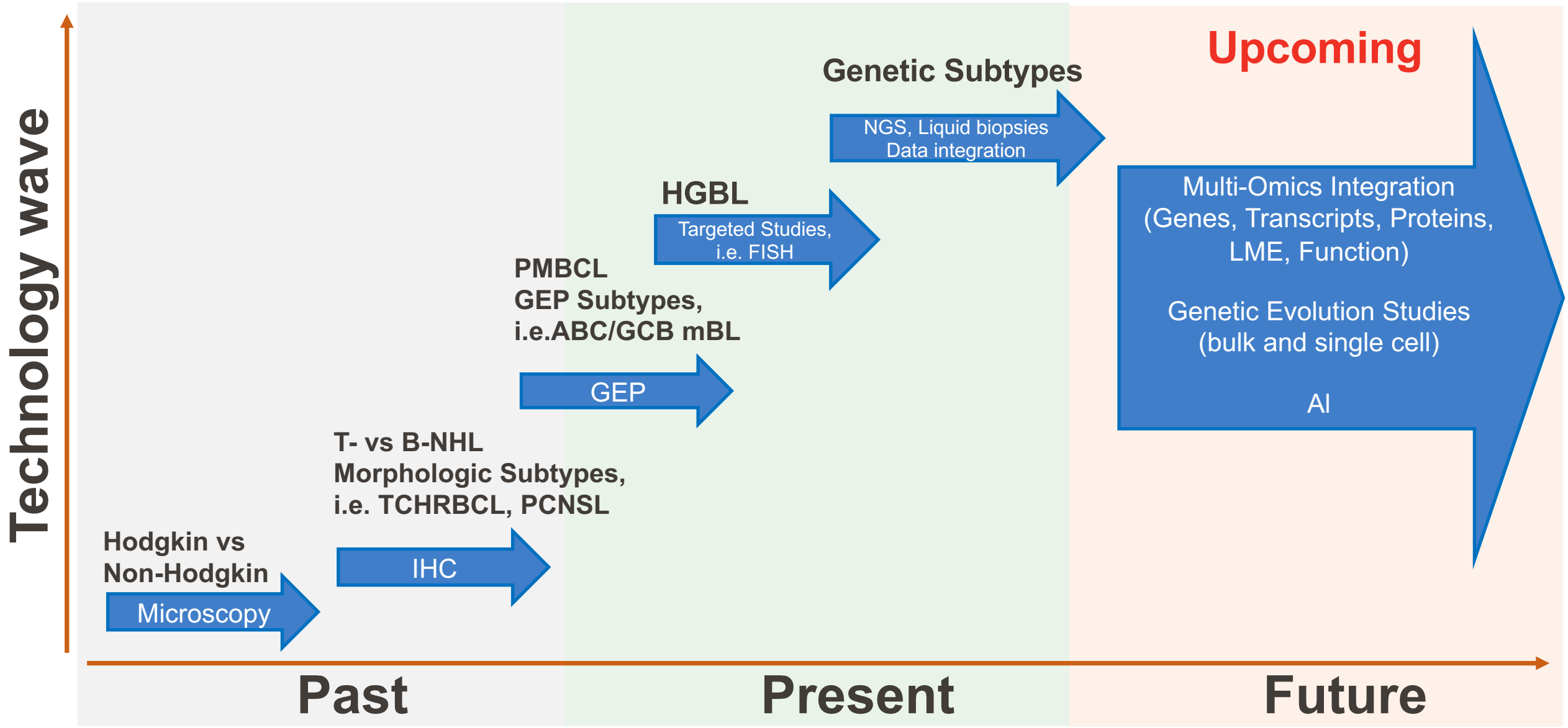
n (%)	Pola-R-CHP (N=435)	R-CHOP (N=438)
Any-grade adverse events	426 (97.9)	431 (98.4)
Grade 3–4	251 (57.7)	252 (57.5)
Grade 5	13 (3.0)	10 (2.3)
Serious adverse events	148 (34.0)	134 (30.6)
Adverse events leading to:		
Discontinuation of any study drug	27 (6.2)	29 (6.6)
Polatuzumab vedotin / vincristine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



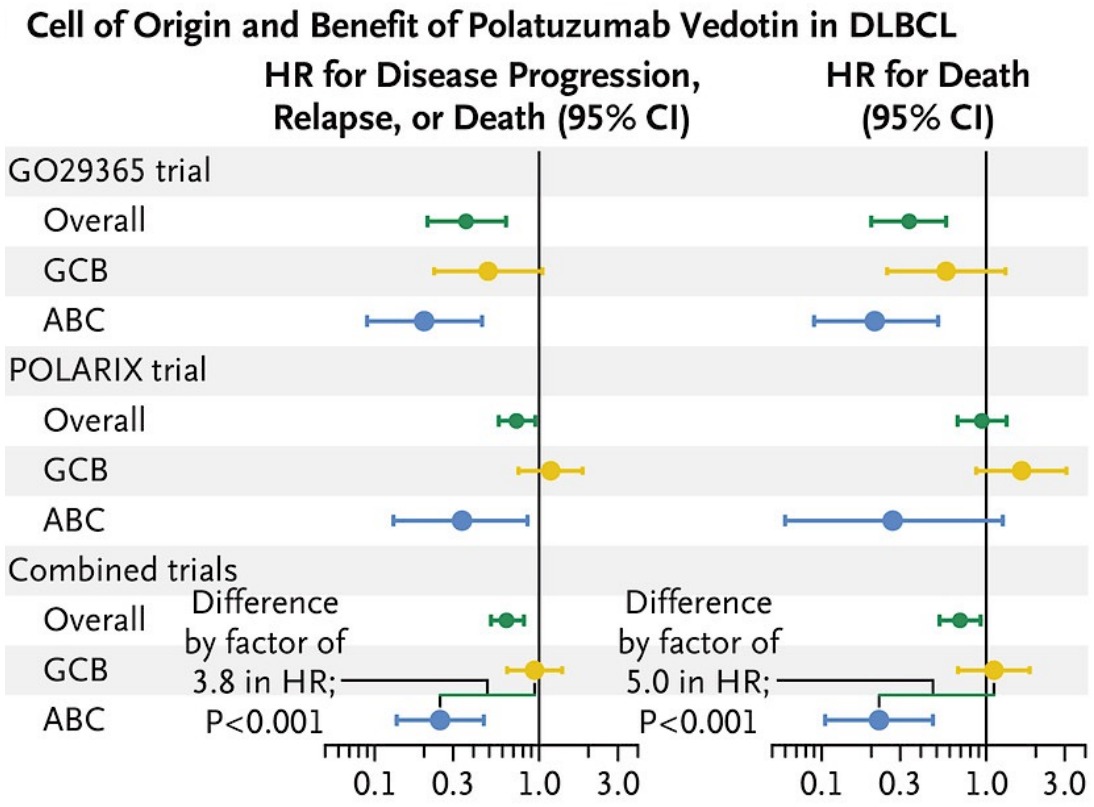
- ITT population. Data cut-off: June 28, 2021; median 28.2 months' follow-up.
  CI, confidence interval; HR, hazard ratio; NE, not evaluable; PFS, progression-free survival.

Tilly et al. *NEJM* 2021

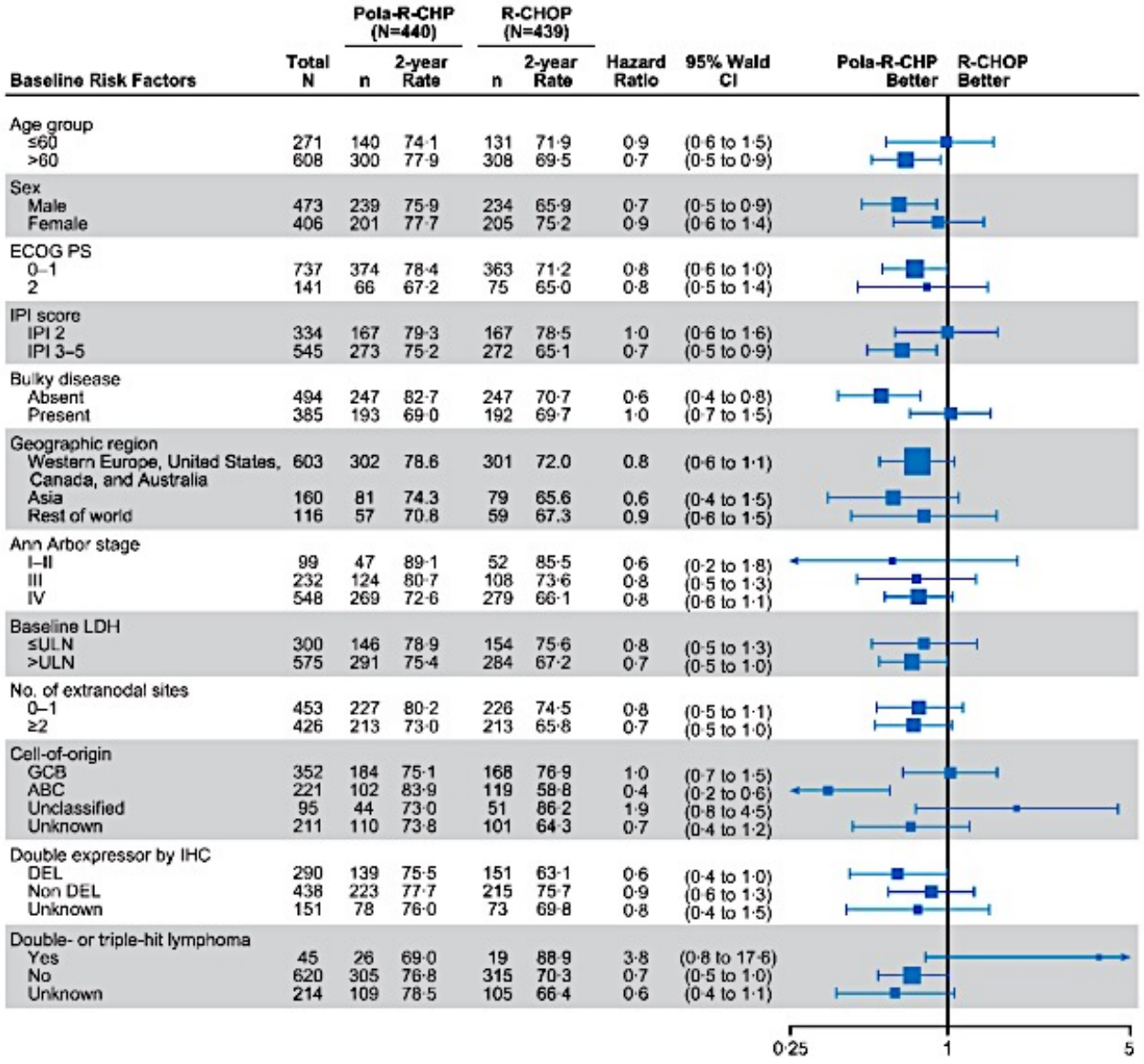
Evolving Molecular Classification with Technology



Polatuzumab Vedotin Efficacy in DLBCL Subtypes by COO



Palmer et al. *NEJM* 2023



Tilly et al. *NEJM* 2022

Take Home Points & Future Directions

- Pola-R-CHP provides a novel 1L therapy with ↑ PFS
- Molecularly targeted therapy for DLBCL
  - Needs new testing approaches
  - Need to consider all factors that influence outcomes

Roundtable Discussion

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Nursing Considerations for Patients Receiving Polatuzumab Vedotin

Caitlin Murphy DNP, FNP-BC, AOCNP

1st Line Treatment: Diffuse Large B Cell Lymphoma

- **R-CHOP**
  - Rituximab (CD-20 mab)
  - Cyclophosphamide (Alkylating Agent)
  - Doxorubicin (Anthracycline)
  - Vincristine (Vinca alkaloid)
  - Prednisone (Steroid)
- **R-Pola-CHP**
  - Rituximab (CD-20 mab)
  - Cyclophosphamide (Alkylating Agent)
  - Doxorubicin (Anthracycline)
  - **Polatuzumab vedotin** (CD-79 monoclonal ab)
  - Prednisone (Steroid)

Adverse Effects/Common Toxicities

- Monitor for HSR reaction
- Peripheral Neuropathy—may occur with first cycle and it is cumulative!
  - Monitor this over time with each cycle
    - ADLs (texting/typing on phone, signature, buttons on clothing, jewelry)
- Febrile Neutropenia
- Infection—URIs
  - Vaccinate prior to initiation of treatment if feasible
- Hematological AEs
  - Most notable: lymphopenia followed by anemia, neutropenia & thrombocytopenia
- GI--low rates of diarrhea but more notable than in R-CHOP arm
- Fatigue
  - Exercise!

Supportive Care

- Premedicate patients with an antihistamine and antipyretic at least 30 to 60 minutes prior to infusion to help mitigate infusion-related reactions
- Prophylaxis with granulocyte colony-stimulating factor (G-CSF)
- *Pneumocystis jiroveci pneumonia* and herpesvirus prophylaxis throughout treatment
- Tumor lysis prophylaxis
- DDI interactions
  - CYP3A Inhibitors---monitor for signs of toxicity
  - CYP3A Inducers---may decrease unconjugated MMAE AUC

Polatuzumab vedotin package insert.

Dosing Schedule

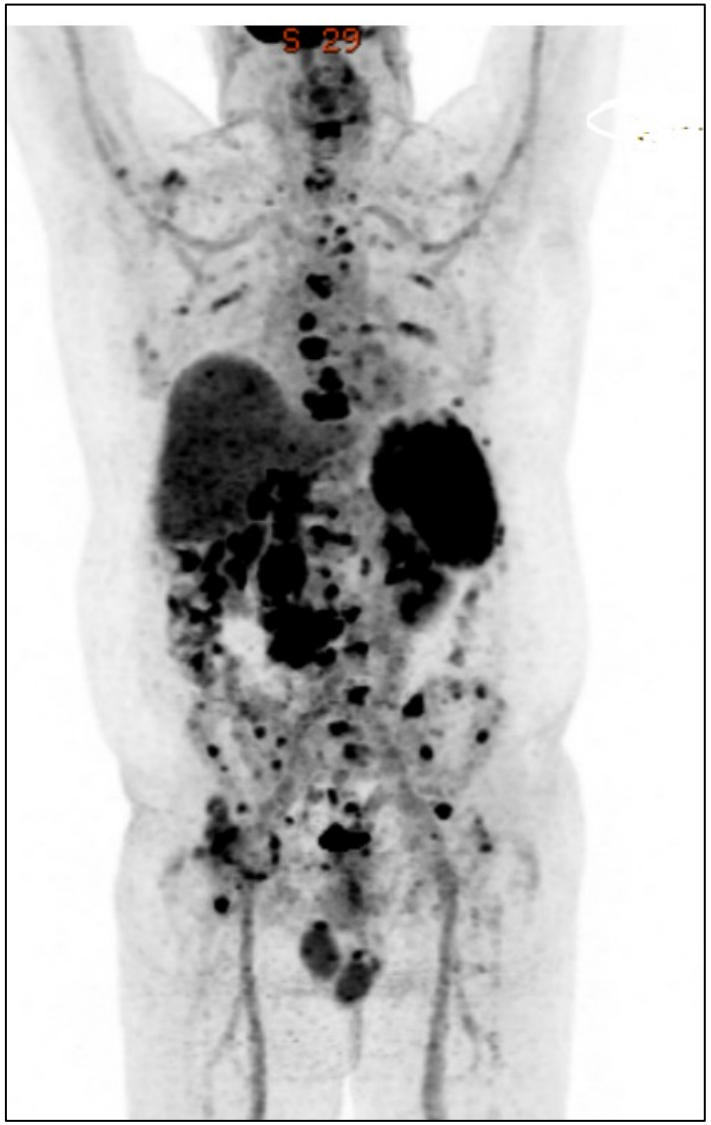
- 21-day cycle x 6 cycles

- Polatuzumab vedotin
  - Cycle 1: Infused over 90 minutes with 90-minute post infusion monitoring
  - If tolerated, increase rate to 30 minutes with 30-minute post infusion monitoring

Polatuzumab vedotin package insert.

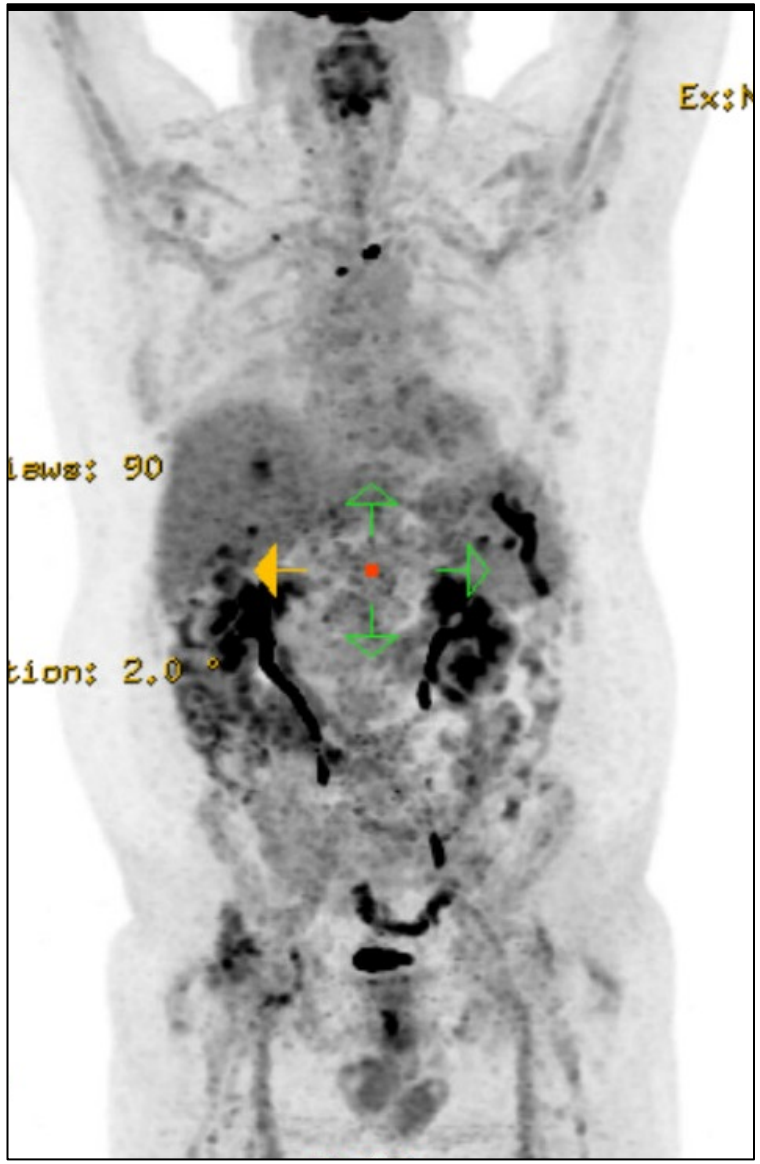
Meet the patient

- 64 y/o male presents to local PCP with persistent right hip pain concerning for labral tear, arthritis
- Core needle biopsy of RP node which demonstrates diffuse large B-cell lymphoma (non GCB subtype)
- LDH elevated at 313
- Renal function preserved with creatinine 0.91 on baseline labs



Interim PET

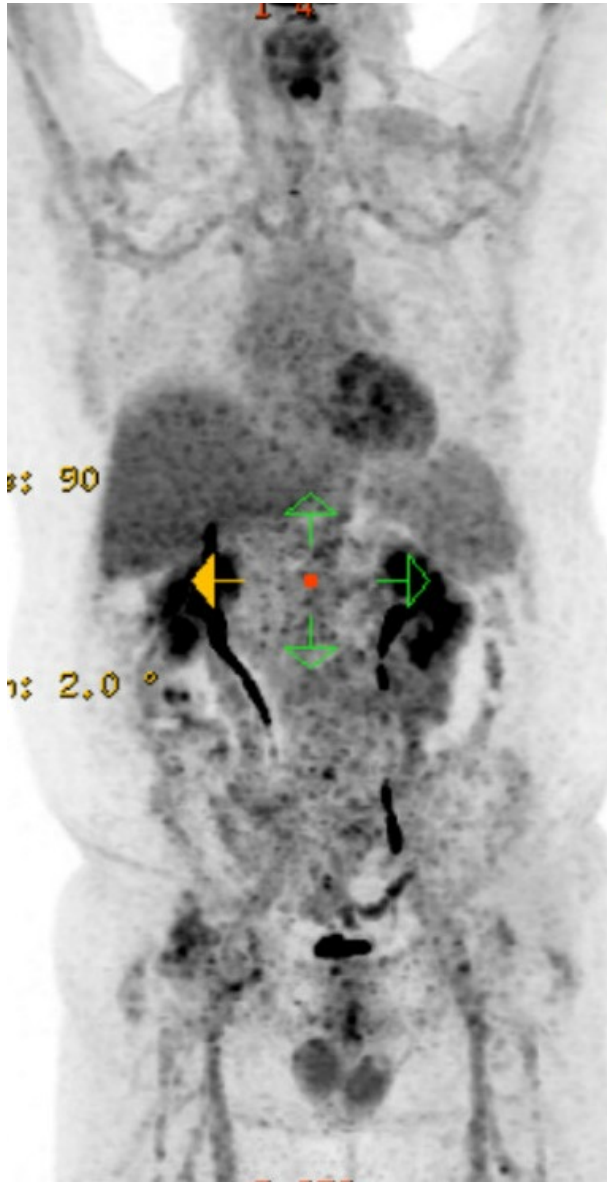
- Patient reports
  - Fatigue
  - Mild nausea controlled with anti-emetic regimen
    - Aprepitant
    - Palonosetron
    - Olanzapine
  - Grade 1-2 neuropathy in fingertips



EOT PET

Treatment related symptoms:

- Improvement in fatigue
- Gradual improvement in neuropathy (numbness, tingling)



Roundtable Discussion

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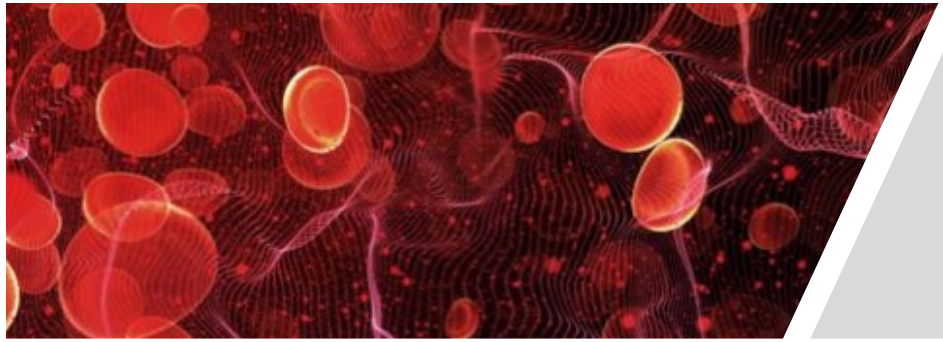
Module 4: Role of Tafasitamab for Patients with R/R DLBCL and Follicular Lymphoma

Clinical Scenario

A patient with R/R DLBCL is about to start treatment with loncastuximab tesirine



Understanding the Current Paradigm and New Approaches in the Care of Patients with Non-Hodgkin Lymphoma

Manali Kamdar, MD, MBBS
Associate Professor of Medicine, Clinical director of lymphoma services,
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University of Colorado

ONS congress, RTP Symposium, 4/12/2025

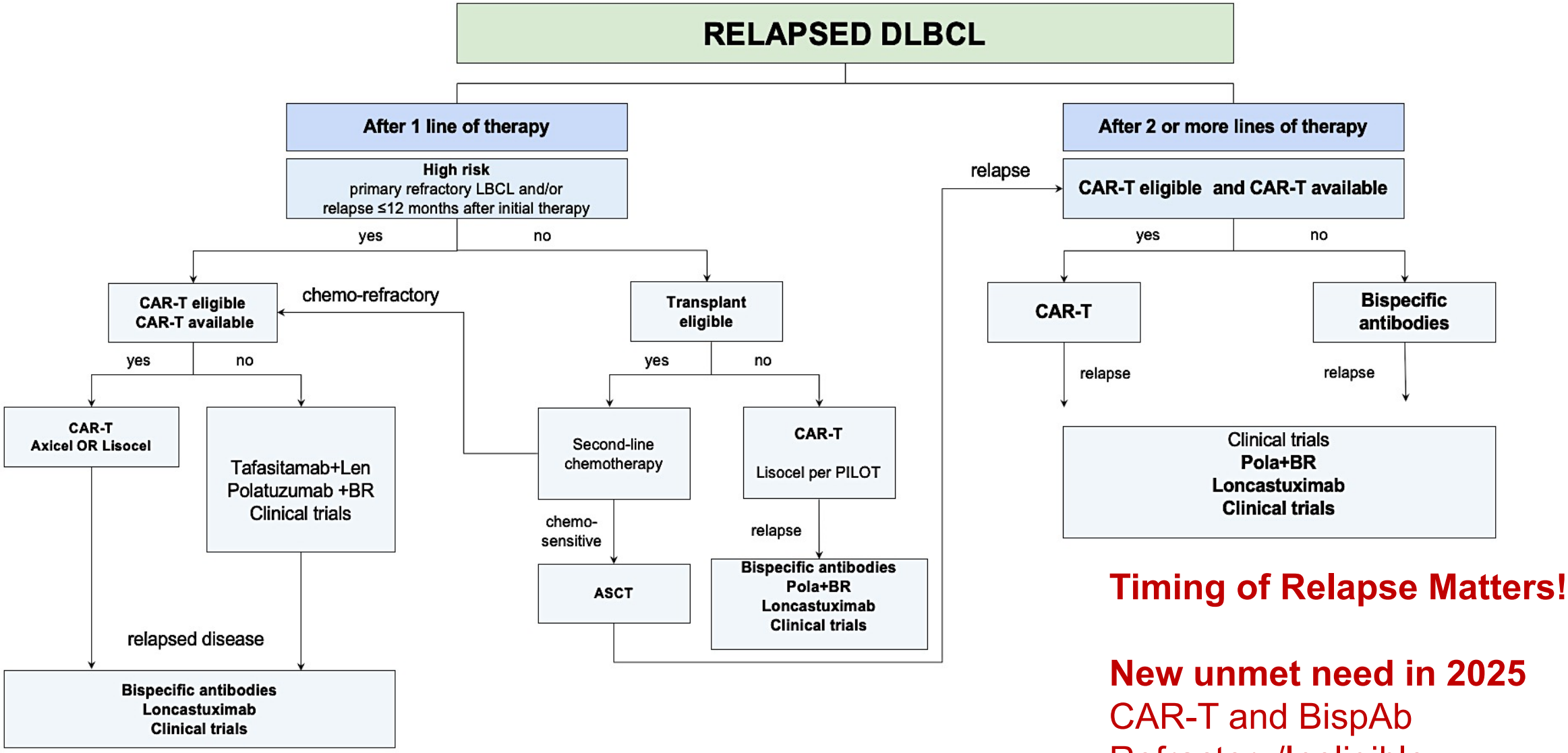
Role of Loncastuximab Tesirine for Patients with R/R DLBCL

Clinical Case

- 65 yo male with ECOG 1 with PMH sig for CAD (stent in 2009) on aspirin, HTN, DM on insulin, Neuropathy grade 2 on gabapentin. Diagnosed in 2023 with Stage III DLBCL, GC subtype, FISH normal treated from 4/2023-8/2023 achieved a CR. Unfortunately, relapsed in 6/2024 with biopsy proven Stage III DLBCL. Underwent Apheresis, bridging therapy with R-Gem-Ox and then received CAR-T cell therapy with Lisocel in 8/2024. Course complicated by Grade 2 CRS from which he fully recovered. D90 PET CT in 11/2024 showed a CR.
- PET CT at the 6-month mark post-CAR in 2/2025 showed disease progression.
- Biopsy confirms Localized DLBCL- CD19 +ve, CD20 -ve.
- ECOG 1, Counts normal.

- Next steps --- ?

Treatment Algorithm for R/R DLBCL in 2025



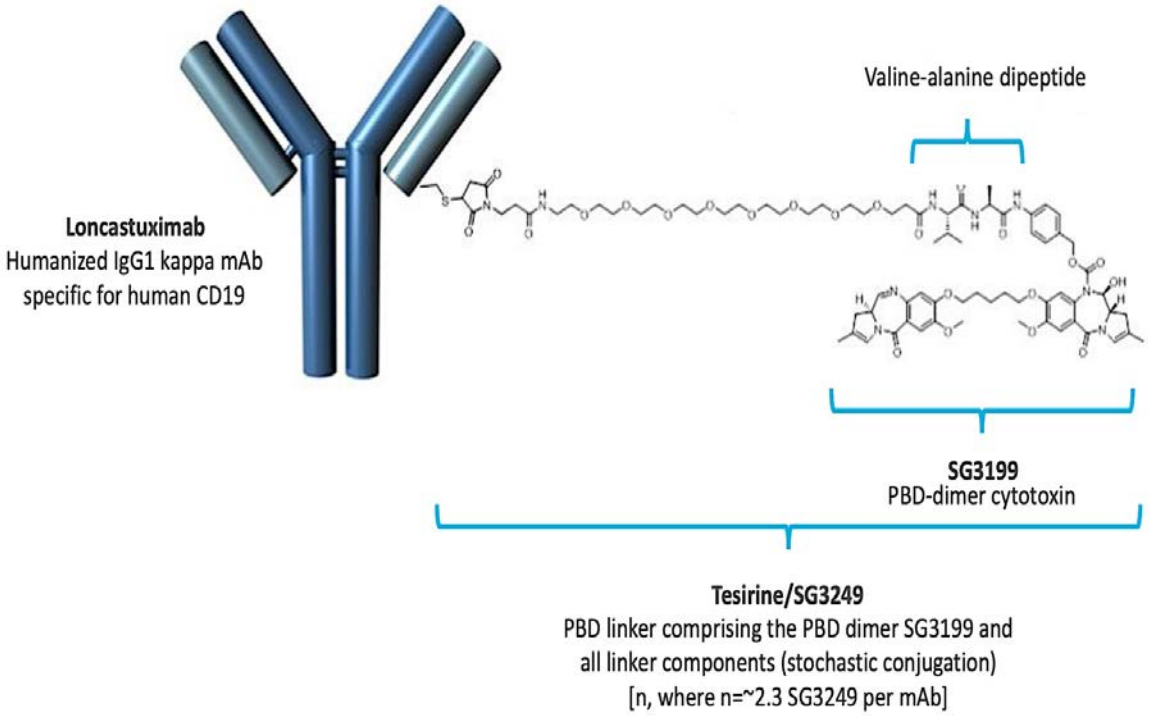
Timing of Relapse Matters!

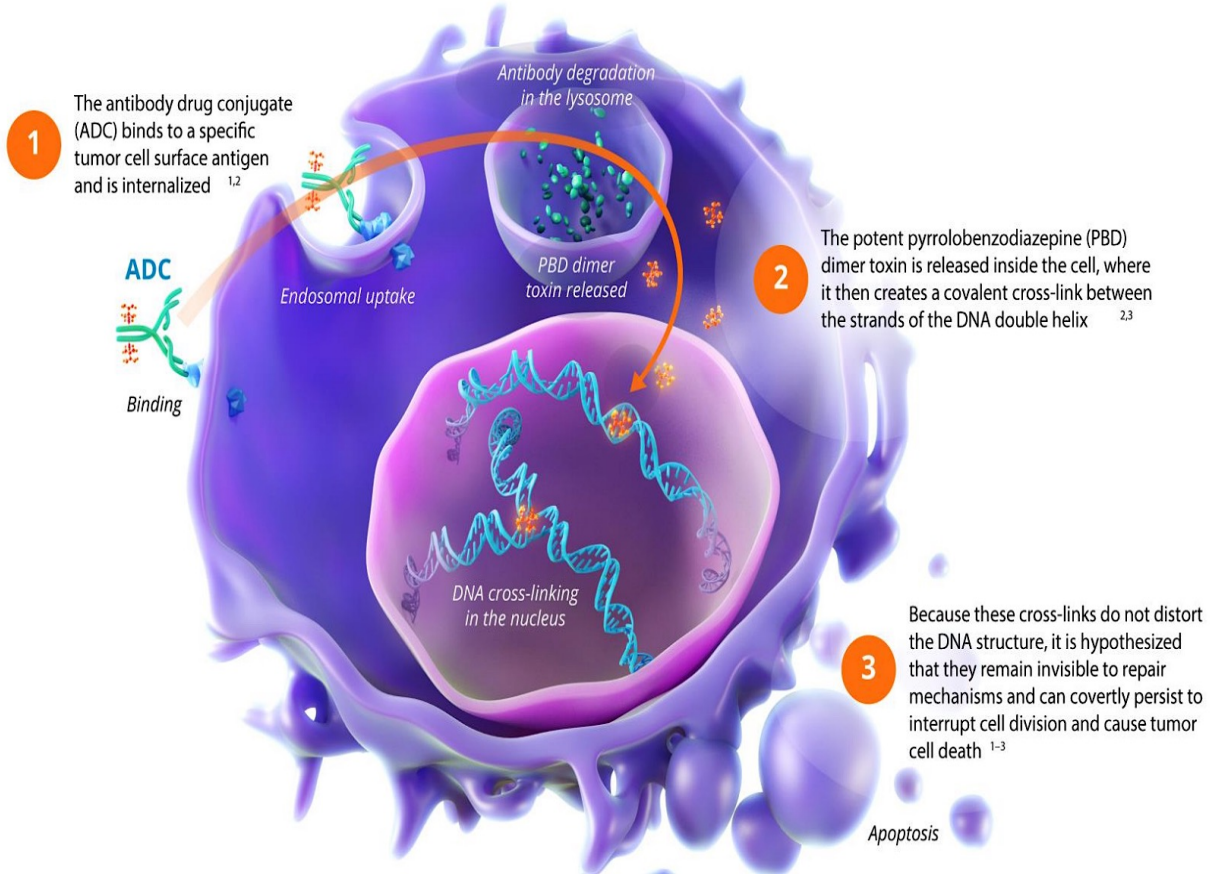
New unmet need in 2025
CAR-T and BispAb
Refractory/Ineligible

Kamdar et al ASH Education book 2023

Mechanism of Action of Loncastuximab Tesirine

Antibody drug conjugate
ADCT-402





Target- CD19, Cytotoxin- PBD

LOTIS-2: The Pivotal Phase 2 Open-Label Study

Primary Endpoint: Overall response rate (ORR) by IRC

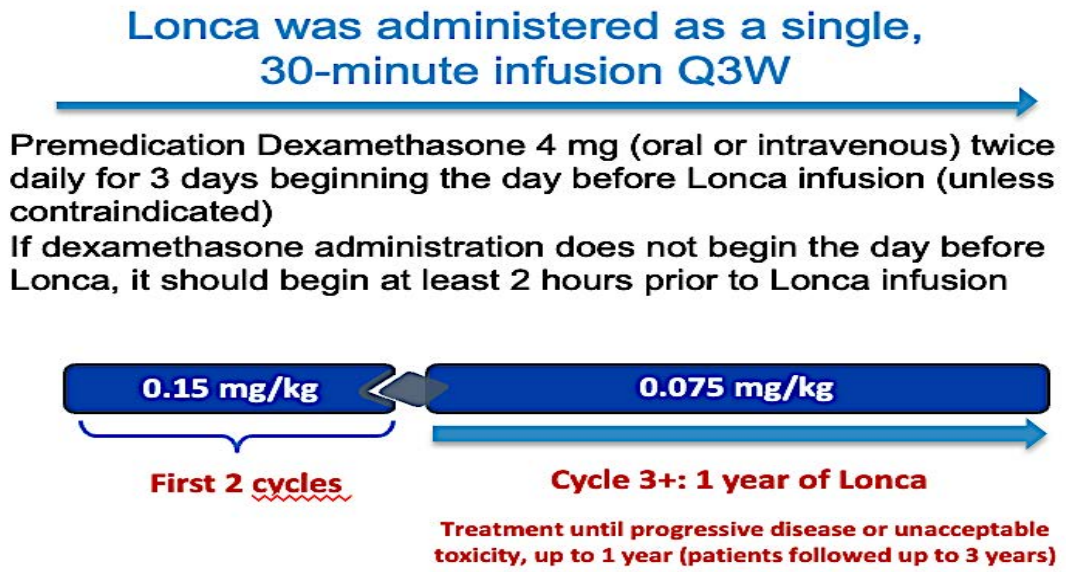
N=145,

R/R DLBCL (including Transformed lymphoma) after ≥2 prior LOT,

Median age 66 (23-94), mLOT 3 (2-7),

Primary Refractory – 20%; Refractory to last rx 60%,

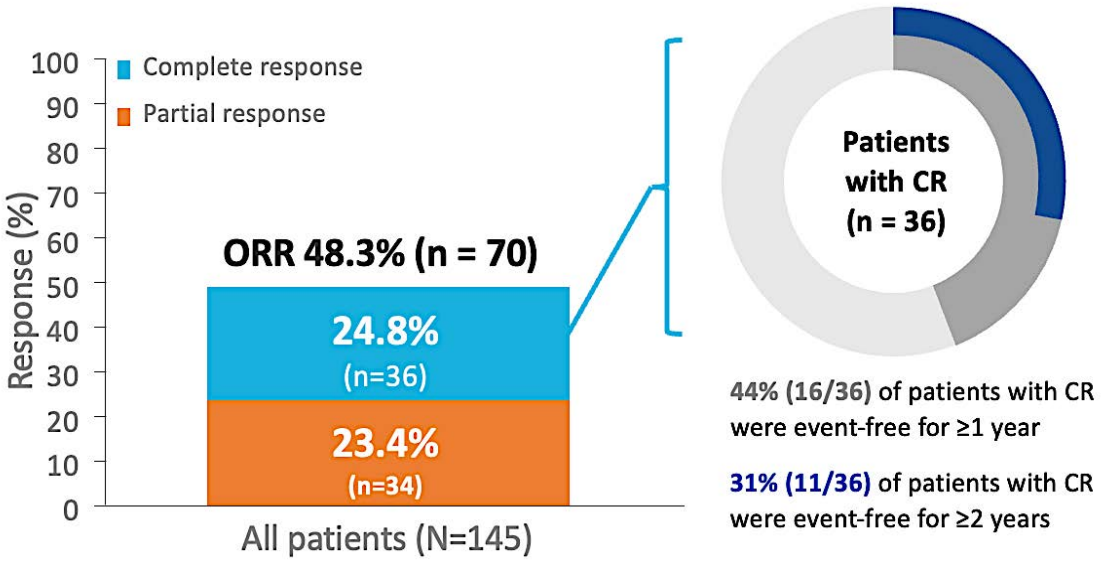
Prior CD19-CAR- 10% (n=14- all had CD19 expression)



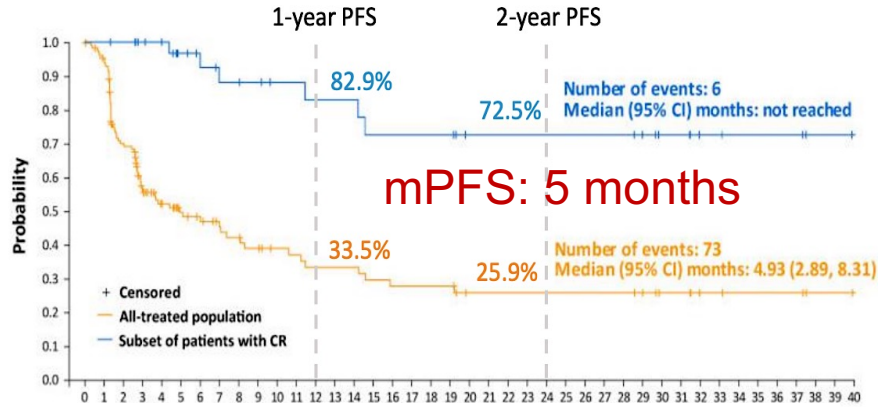
Caimi et al., Hematologica 2024

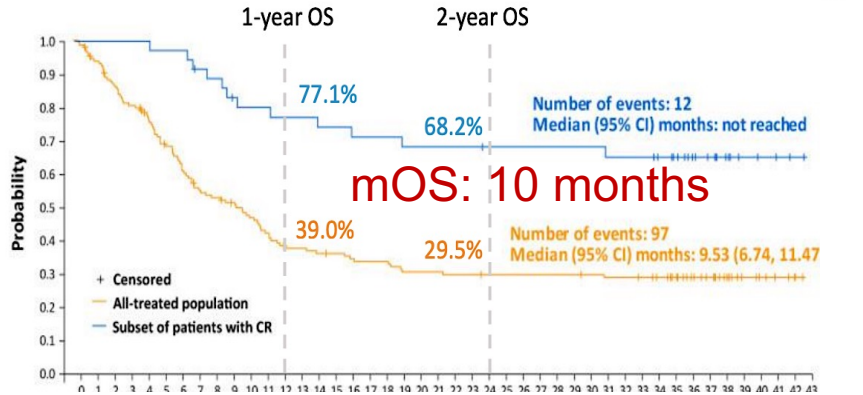
LOTIS-2: Final Efficacy Results (N=145)

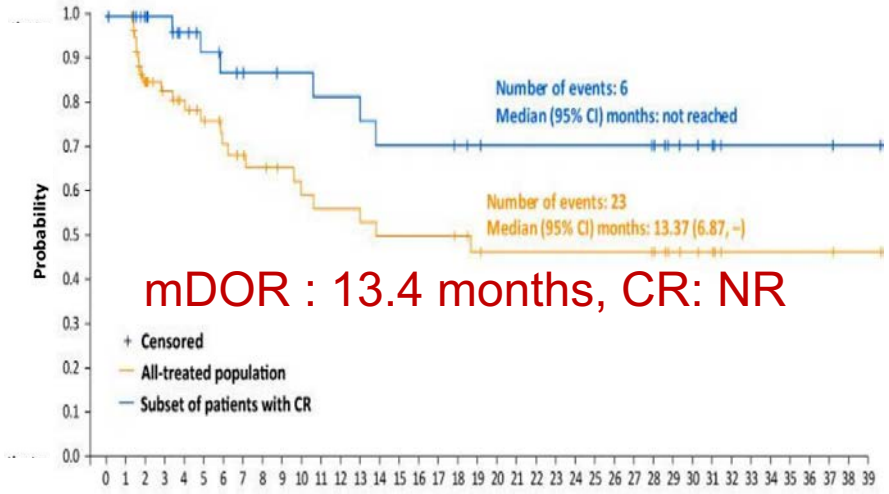
Median FU 7.8 months (0.3 - 42m)



Median Lonca cycles: 3.0 (1-26)
Median Lonca cycles for CR: 8.0 (1-26);
Median Time to Response: 41 days (35-247)







Safety

	All-treated Population (N = 145)			All-treated Population (N = 145)	
	All grades, n (%)	Grade ≥3, n (%)		All grades, n (%)	Grade ≥3, n (%)
Any TEAE	143 (98.6)	107 (73.8)	Increased ALT	22 (15.2)	4 (2.8)
Increased GGT	61 (42.1)	25 (17.2)	Decreased appetite	22 (15.2)	-
Neutropenia	58 (40.0)	38 (26.2)	Leukopenia	21 (14.5)	13 (9.0)
Thrombocytopenia	48 (33.1)	26 (17.9)	Hypomagnesemia	20 (13.8)	1 (0.7)
Fatigue	40 (27.6)	2 (1.4)	Pruritus	19 (13.1)	-
Anemia	38 (26.2)	15 (10.3)	Rash	19 (13.1)	1 (0.7)
Nausea	34 (23.4)	-	Vomiting	19 (13.1)	-
Cough	33 (22.8)	1 (0.7)	Abdominal pain	17 (11.7)	4 (2.8)
Increased blood ALP	29 (20.0)	1 (0.7)	Constipation	17 (11.7)	-
Peripheral edema	29 (20.0)	2 (1.4)	Dyspnea	17 (11.7)	2 (1.4)
Pyrexia	28 (19.3)	2 (1.4)	Insomnia	16 (11.0)	-
Diarrhea	25 (17.2)	3 (2.1)	Pleural effusion	16 (11.0)	3 (2.1)
Increased AST	23 (15.9)	1 (0.7)	Erythema	15 (10.3)	1 (0.7)
Hypokalemia	23 (15.9)	6 (4.1)	Headache	15 (10.3)	1 (0.7)
Hypophosphatemia	23 (15.9)	8 (5.5)	Photosensitivity reaction	15 (10.3)	3 (2.1)

Rx Discontinuation – 19%
Dose Interruption – 50%
Dose Reduction – 8%

Management Pearls

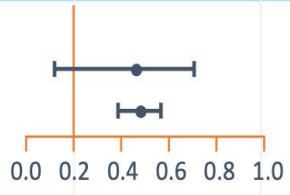
Sun Protectants
Euvolemia- Diuretics
Dexamethasone

Sequencing with CD19- CAR-T cell therapies

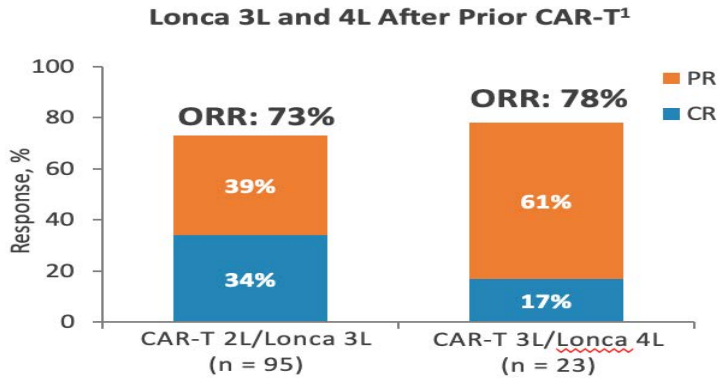
CD19 CAR → Lonca-T

1) Subgroup Analysis LOTIS-2
N=14, CR=3, PR=3

Subgroup	Patients (n/N)	ORR	ORR (95% CI)
Prior CAR-T therapy			
Yes	6/14		42.9 (17.7, 71.1)
No	64/131		48.9 (40.0, 57.7)



2) Multicenter Retrospective Study[1]



Duration of Response	Lonca in 3L (n = 95)	Lonca in 4L (n = 23)
Median DOR (95% CI)	NR (8, NR)	7.6 (6.0, 8.9)
12-month DOR, %	68	22

Lonca-T → CD19-CAR-T

1) Retrospective analysis- LOTIS-2

N=14, 10/14 CD19+, 4 UK

CR= 6/14 (43%), PR= 1/14

2) CIBMTR Registry Study[2]

Best Response to CAR-T Therapy, %	Lonca Therapy Type		
	Last LOT n = 5	BT n = 11	N =16
Complete remission	60	36	44
Partial remission	0	27	19
No response/stable disease	20	18	19
Progressive disease	20	18	19

1.Epperla, et al. Tandem 2024/*Blood Cancer J* 2024
2.Hamadani, et al. Tandem 2024/*eJHaem* 2024

Clinical Case

- 65 yo male with ECOG 1 with PMH sig for CAD (stent in 2009) on aspirin, HTN, DM on insulin, Neuropathy grade 2 on gabapentin. Diagnosed in 2023 with Stage III DLBCL, GC subtype, FISH normal treated from 4/2023-8/2023 achieved a CR. Unfortunately, relapsed in 6/2024 with biopsy proven Stage III DLBCL. Underwent Apheresis, bridging therapy with R-Gem-Ox and then received CAR-T cell therapy with Lisocel in 8/2024. Course complicated by Grade 2 CRS from which he fully recovered. D90 PET CT in 11/2024 showed a CR.
- PET CT at the 6-month mark post-CAR in 2/2025 showed disease progression.
- Biopsy confirms Localized DLBCL- CD19 +ve, CD20 -ve.
- ECOG 1, Counts normal.

- Next steps --- Initiated Single Agent Lonca-T in February 2025
- March 2025 – Isolated adenopathy clinically smaller
- Next questions – Is in CR --- Allo SCT ?? Or continue Lonca-T ??

Roundtable Discussion

RTP
RESEARCH
TO PRACTICE

ONS 2025 NHL

Robin Klebig, APRN, CNP, AOCNP

April 12, 2025

Scenario 2: A patient with R/R DLBCL is about to start treatment with loncastuximab tesirine

- ***What do you tell your patients about to start treatment with loncastuximab tesirine about how it works and why they are receiving it?***
- Your lymphoma has not responded to prior traditional chemotherapy – this drug is indicated for relapsed/refractory DLBCL after 2 or more lines of systemic therapy
- Clinical studies have shown 48% overall response rate and 24% CR in patients with relapsed/refractory DLBCL
- Antibody-drug conjugate (monoclonal antibody and chemotherapy drug)
  - Monoclonal antibody targets CD19 on surface of the lymphoma cells
  - Once bound to the cell, the drug is internalized by the cell and chemotherapy component is released inside the cancer cell, causing DNA damage that leads to the cancer cell death
- The drug is given intravenously over 30 minutes every 3 weeks
  - 0.15 mg/kg for first 2 cycles
  - smaller dose (0.075 mg/kg) for subsequent cycles
- Treatment will continue until disease progression or unacceptable toxicity

Scenario 2: A patient with R/R DLBCL is about to start treatment with loncastuximab tesirine

- ***What side effects can occur with loncastuximab tesirine? What do you tell your patients about to start loncastuximab tesirine about potential toxicities?***

- Common side effects include
  - Nausea
  - Fatigue
  - Cytopenias (anemia, neutropenia, thrombocytopenia)
  - Liver enzyme abnormalities (GGT)
  - Edema
  - Effusions
  - Shortness of breath
  - Severe cutaneous reactions/photosensitivity

- **You will be premedicated with dexamethasone to reduce risk of side effects (fluid retention)**
  - Dexamethasone 4 mg twice daily x 3 days – <u>beginning day before loncastuximab infusion</u>
    - If dexamethasone does not begin day before loncastuximab, should begin at least 2 hours prior to infusion
- **Avoid sun exposure, wear protective clothing, use sunscreen**

Nursing Considerations for Patients Receiving Loncastuximab Tesirine — Ms Klebig

- ***How do you monitor for and manage common toxicities associated with loncastuximab tesirine?***
  - Premedicate with antiemetic
  - Monitor labs (CBC)
    - Hold if ANC <1.0, consider G-CSF
      - education on neutropenic precautions and infection monitoring
    - Hold if plts <50,000
      - education on s/s bleeding/bruising
  - Monitor LFTs (GGT)
    - Hold if grade 3 (>5.0-20.0 ULN)
  - Potential for pleural/pericardial effusions
    - Monitor for swelling, weight gain, respiratory symptoms
    - May require dose delay or modification if Grade 2 or higher edema/effusion
    - Diuretics may be required
  - **Dexamethasone education/administration**
  - Extravasation may cause irritation, swelling, pain, and/or tissue damage
  - Monitor phosphorus
    - May require replacement

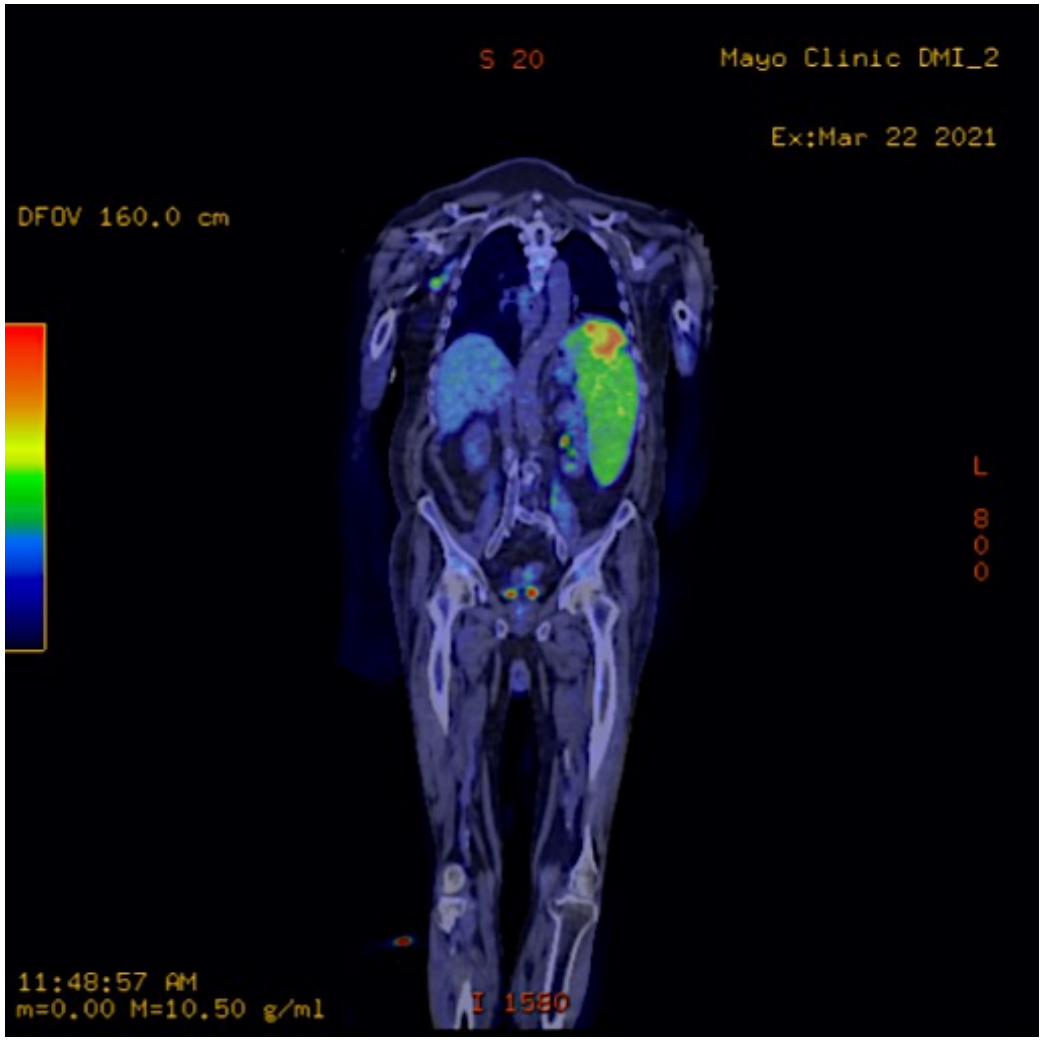
A patient who received loncastuximab for R/R DLBCL

- 74 yo male
- PMH:
  - Chronic ischemic heart disease, CAD s/p LAD stent, ICD, unstable angina
  - DVT/PE w/ Factor V Leiden on clopidogrel, warfarin, ASA s/p IVC filter
  - DM2
  - COPD
  - Parkinson's disease
  - Splenic marginal zone NHL s/p 6 doses of rituximab 15 mos prior
- SH: Widowed, 2 children, retired factory worker, enjoys fishing and gambling
- Lives 1-1/2 hrs from Mayo Clinic

DLBCL presentation

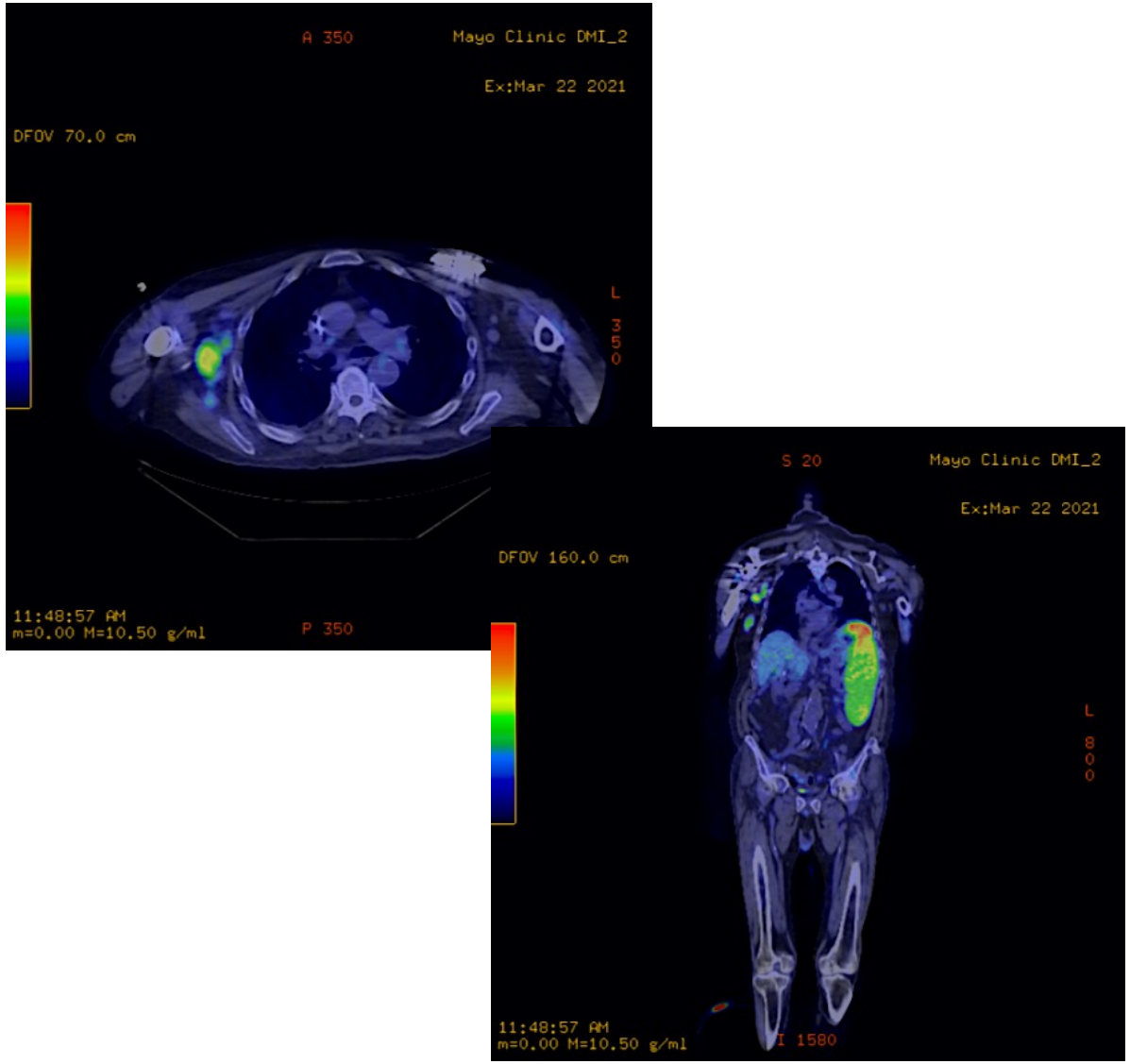
- Presented to local ED with abdominal pain, SOB
- PE: Splenomegaly
- Labs:
  - Hgb 9.0, plts 49K, ANC 1.23
- CT: splenic infarct, external iliac lymphadenopathy

- Transferred to Mayo Clinic
- Rough hospital course, splenectomy planned but respiratory failure >> ICU



Thankfully, another “hot spot” to biopsy

- Lymph node, Right axillary, core bx: Diffuse large B-cell lymphoma
- COMMENT: CD5 expression on the tumor suggests transformation from previously diagnosed CD5-positive low-grade B-cell lymphoma
- Non-GCB, double-expressor of MYC and BCL2
- FISH negative for MYC, BCL2 and BCL6 rearrangements



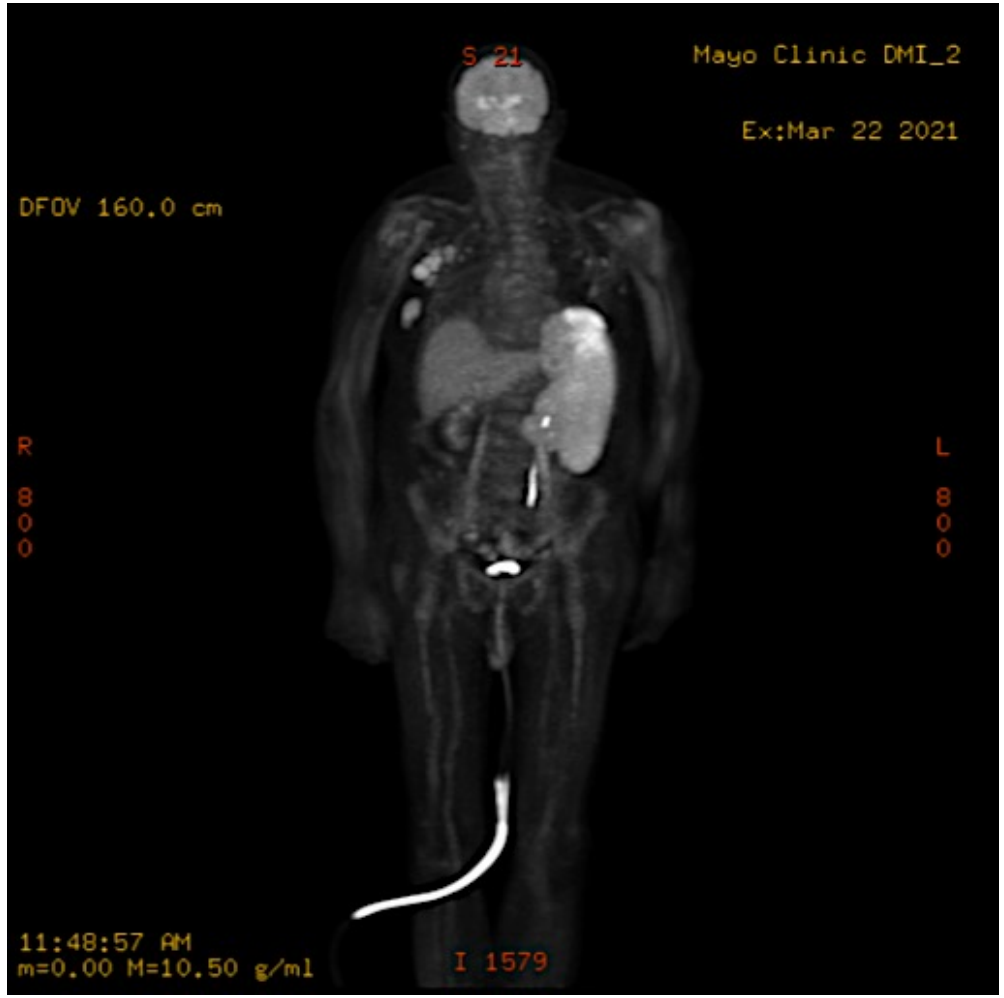
Treatment course

- Rituximab and methylprednisolone
  - While awaiting biopsy results

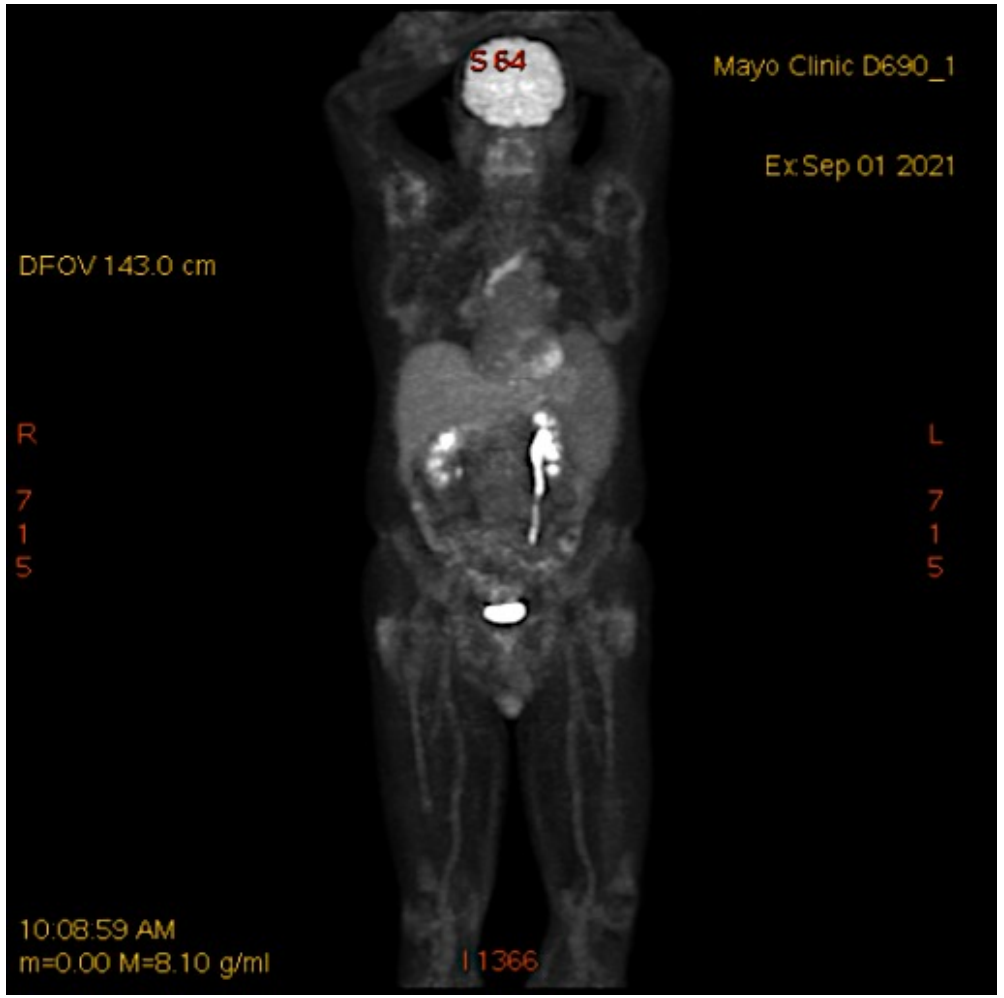
- R-CEOP x 6 cycles
  - Anthracyclines avoided due to significant cardiac history
  - Rituximab, cyclophosphamide, etoposide, vincristine, prednisone

Response

Baseline



After 6 cycles R-CEOP – Deauville 2



Response

Baseline

- Bone marrow: 60% involved by mixed small B cell and large B cell lymphoma

After 6 cycles R-CEOP

- Bone marrow: Minimal involvement by B-cell lymphoma (less than 5%), similar to previously described with large B cell lymphoma involvement

Refractory DLBCL

- Options discussed
  - Polatuzumab/BR
  - Tafasitamab/lenalidomide
  - Loncastuximab
  - Selinexor
  - Not a candidate for clinical trial due to cardiac disease

- Selected loncastuximab due to schedule (1 day every 3 weeks)

Loncastuximab course

- Tolerated well
- Bone marrow repeated after 6 cycles – negative

- Elected to hold/discontinue treatment since CR and had multiple other comorbidities
  - GI bleed due to AVMs, ulcers, anticoagulation
  - COPD
  - Cardiac issues

- Expired 6 months later due to COPD exacerbation, heart failure

Roundtable Discussion

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction: Overview of Bispecific Antibodies and Chimeric Antigen Receptor T-Cell Therapy for Non-Hodgkin Lymphoma

Module 1: Current and Future Use of Bruton Tyrosine Kinase Inhibitors for Mantle Cell Lymphoma

Module 2: First-Line Therapy for Diffuse Large B-Cell Lymphoma (DLBCL)

Module 3: Role of Loncastuximab Tesirine for Patients with Relapsed/Refractory (R/R) DLBCL

Module 4: Role of Tafasitamab for Patients with R/R DLBCL and Follicular Lymphoma

RTP RESEARCH TO PRACTICE

Clinical Scenario

A patient with R/R DLBCL is about to start treatment with tafasitamab/lenalidomide

Relapsed/Refractory Diffuse Large B-Cell Lymphoma

Christopher Flowers, MD, MS, FASCO

Division Head
Chair, Professor

Division of Cancer Medicine
Department of Lymphoma/Myeloma

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Case: 72 yo man with DLBCL

- Initially diagnosed with DLBCL at age 66 with extensive retroperitoneal disease treated on protocol with R-CHOP + X. Tolerated therapy well with the exception of being admitted twice for neutropenic fever. Improved on empiric antibiotics, Cultures negative.

- Experienced relapse at 28 months and received autologous SCT with PD on EOT scan and then received CAR T cell therapy

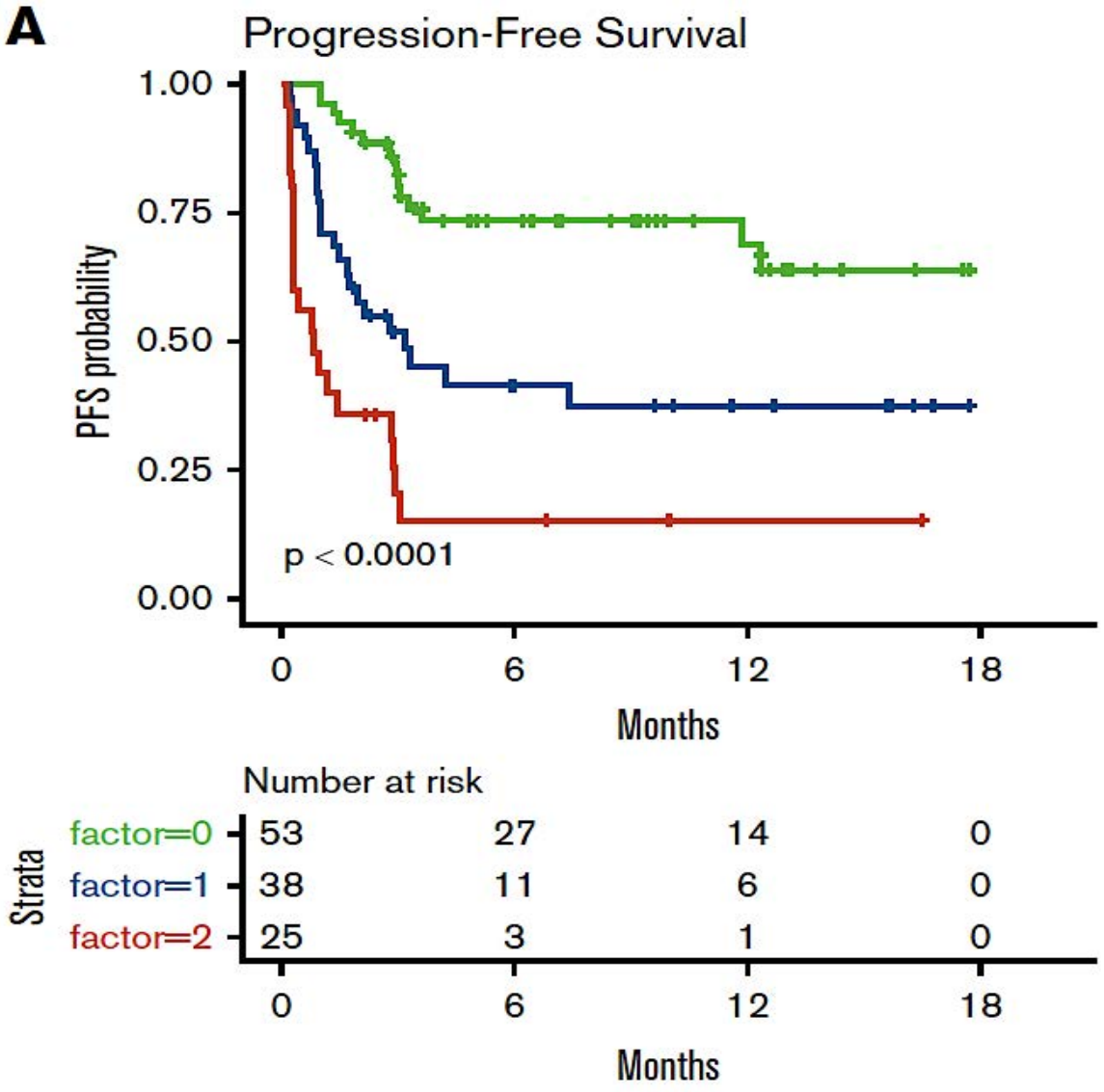
- Now returns 3 years later with a new inguinal LN biopsy proven to be relapsed DLBCL with ABC subtype and here for initiation of next line of therapy

Who are “old” patients?

- Definition
  - 65: American Society of Clinical Oncology
  - 70: International Society of Geriatric Oncology
- Importance of assessment of functional status
  - Chronological age is less important
  - Geriatric assessment
    - **Not standardized**
      - Provides challenge in interpreting trial or research results
- SEER-Medicare study
  - 57% of patients age >85 only received palliative care or no treatment

Diamond A et al. *ASH*. 2022

Not Everyone Will Benefit from CAR-T



Predictive factors associated with poor outcome following CAR T-cell therapy:

- ≥ 2 extranodal sites
- TMTV > 80 mL
- Elevated LDH

Vercellino L et al. *Blood Adv.* 2020;4(22):5607-5615.

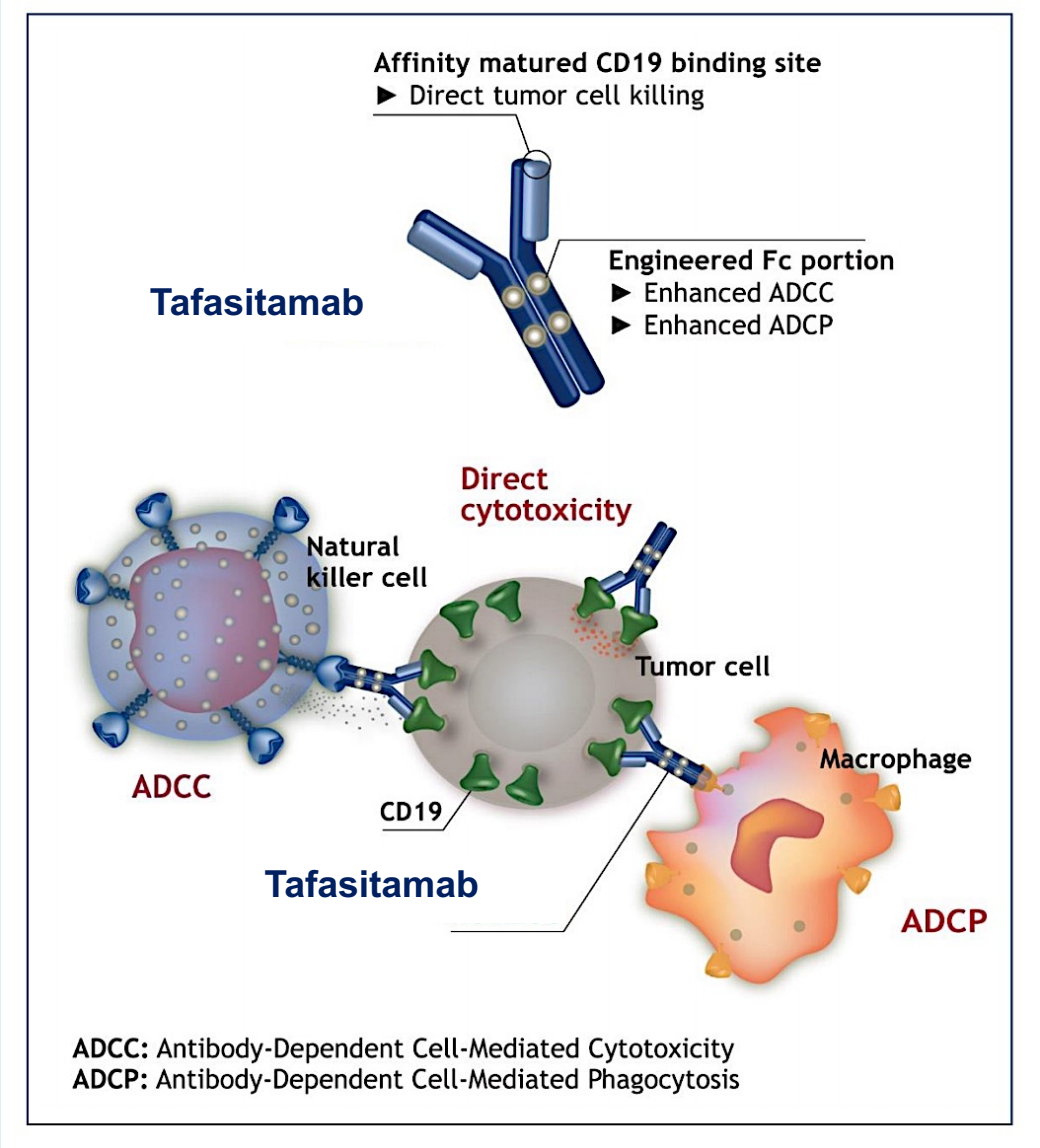
Selected Therapies Approved in R/R DLBCL

	Pola-BR	Selinexor	Tafasitamab/Lenalidomide	Loncastuximab Tesirine
MOA	Anti-CD79b ADC	XPO-1 inhibitor	Anti-CD19 mAb/Immunomodulator	Anti-CD19 ADC
ORR	45%	28%	58%	48%
CR rate	40%	10%	40%	24%
PFS	9.2 m	2.6 m	11.6 m	4.9 m
DOR	12.6 m	9.3 m	43.9 m	10.3 m
OS	12.4 m	NR	33.5 m	9.9 m

Novel salvage regimens may improve outcomes with ASCT

Sehn LH et al. *Blood Adv*. 2022;6(2):533-543.
Kalakonda N et al. *Lancet Haematol.* 2020;7(7):e511-e522.
Duell J et al. *Haematologica*. 2021;106(9):2417-2426.
Caimi PF et al. *Lancet Oncol.* 2021;22(6):790-800.

Tafasitamab Mechanism of Action

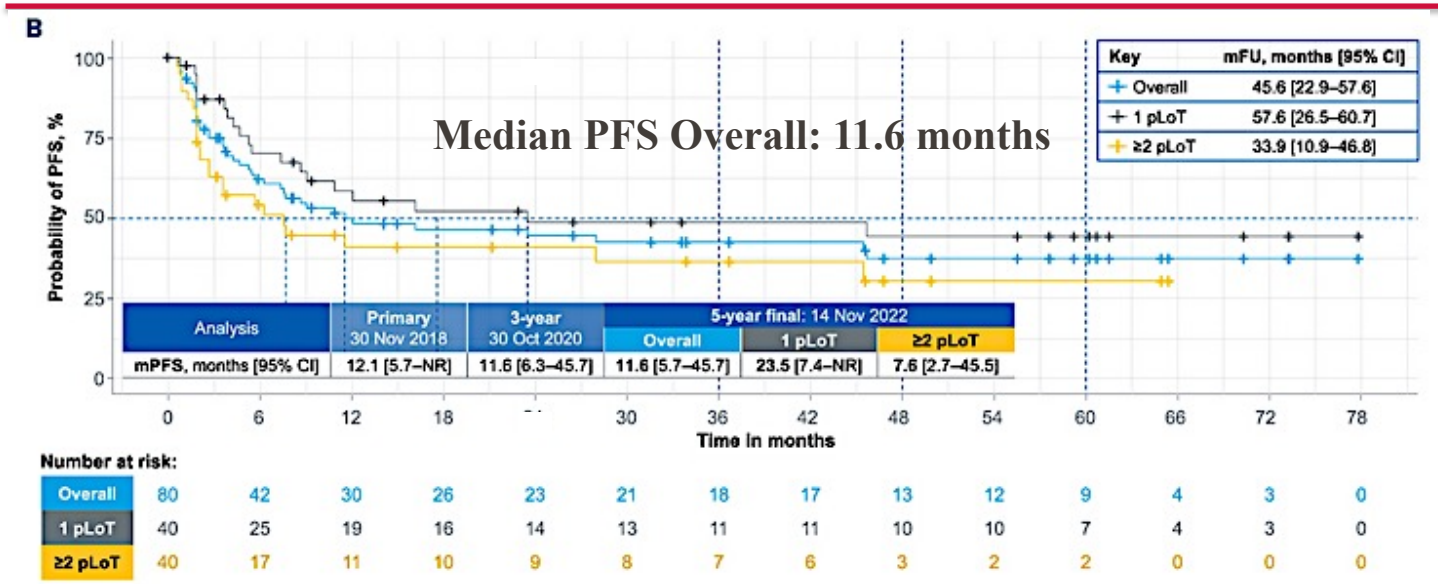


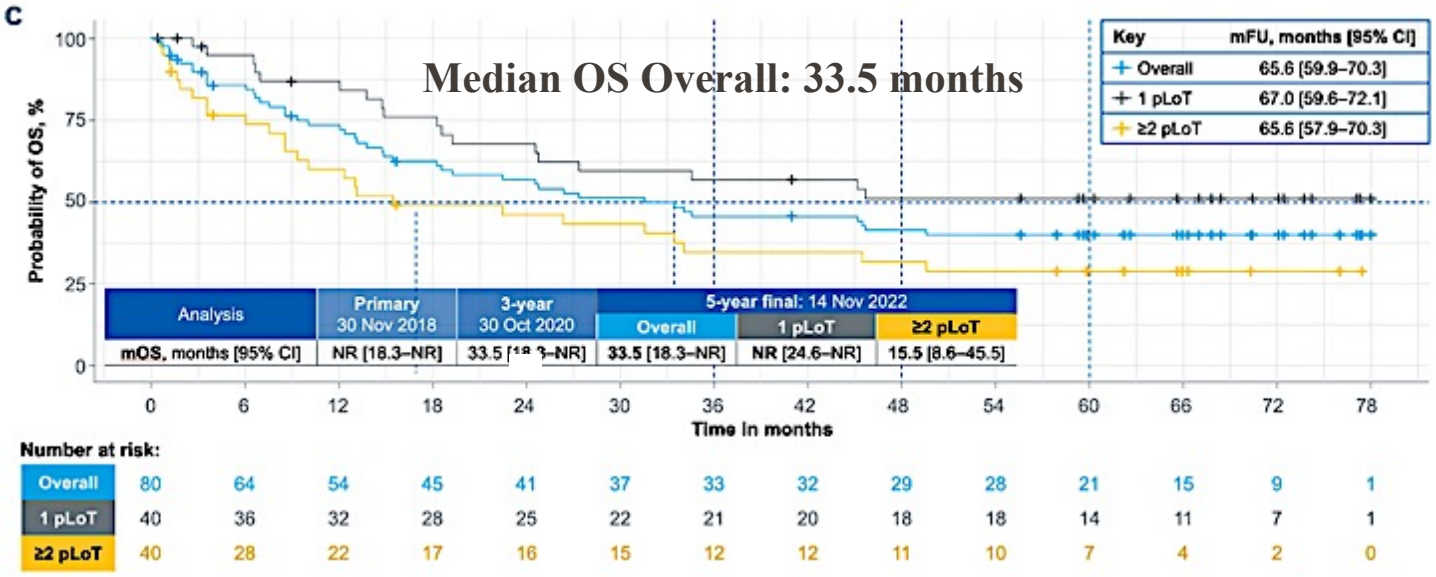
Lenalidomide enhances NK cell function with enhanced ADCC *in vitro*

Salles G et al. *Lancet Oncol* 2020;21(7):978-88.

RTP RESEARCH TO PRACTICE

Tafasitamab + Lenalidomide: Outcomes

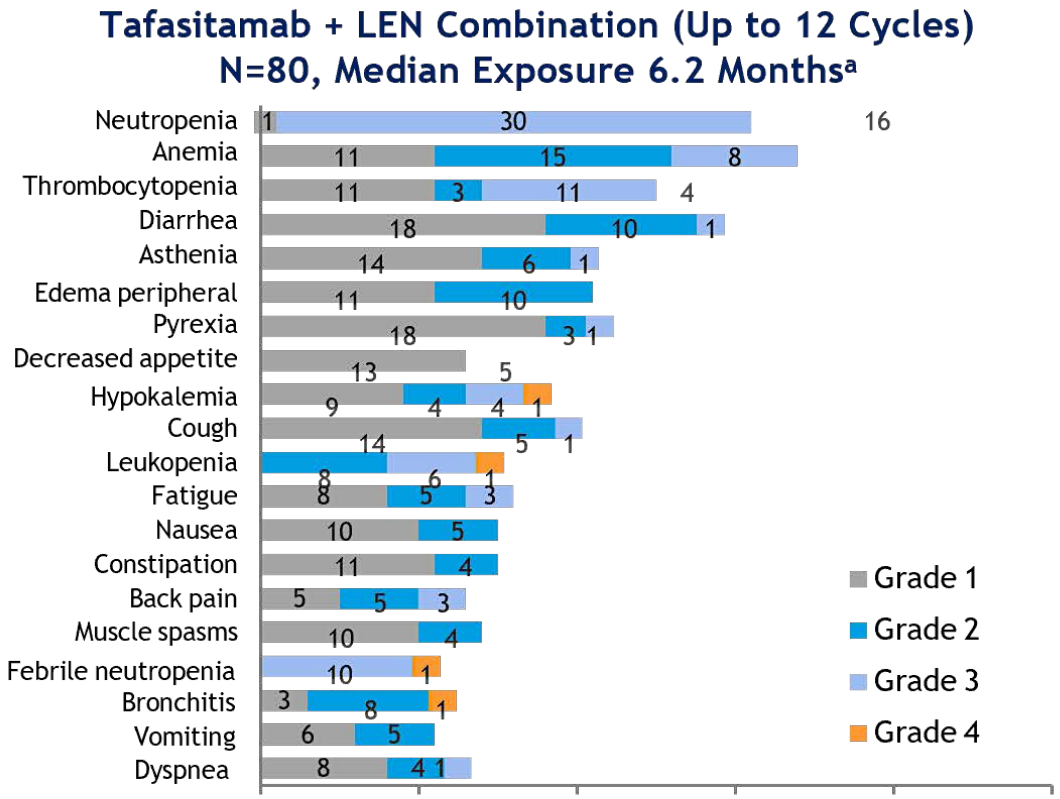


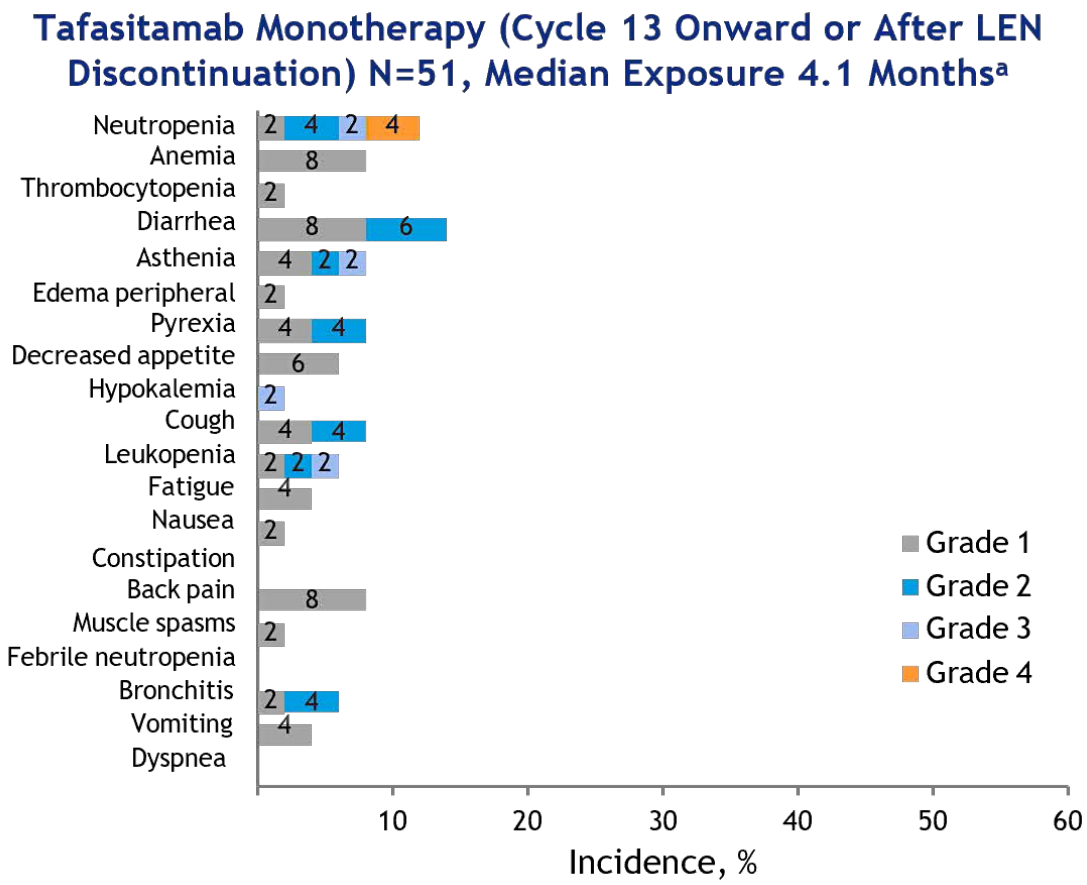


Characteristics	Primary analysis	3-year follow-up	Final 5-year data
Data cut-off date	Nov 30, 2018	Oct 30, 2020	Nov 14, 2022
Best ORR, N (%) [95% CI]	48 (60.0) [48.4-70.9]	46 (57.5) [45.9-68.5]	46 (57.5) [45.9-68.5]
CR rate, N (%) [95% CI]	34 (42.5) [32.0-54.0]	32 (40.0) [29.2-51.6]	33 (41.3) [30.4-52.8]
PR rate, N (%) [95% CI]	14 (17.5) [10.0-28.0]	14 (17.5) [9.9-27.6]	13 (16.3) [8.9-26.2]

Duell J et al. *Haematologica* 2024;109:553-66.

Tafasitamab + Lenalidomide: Safety





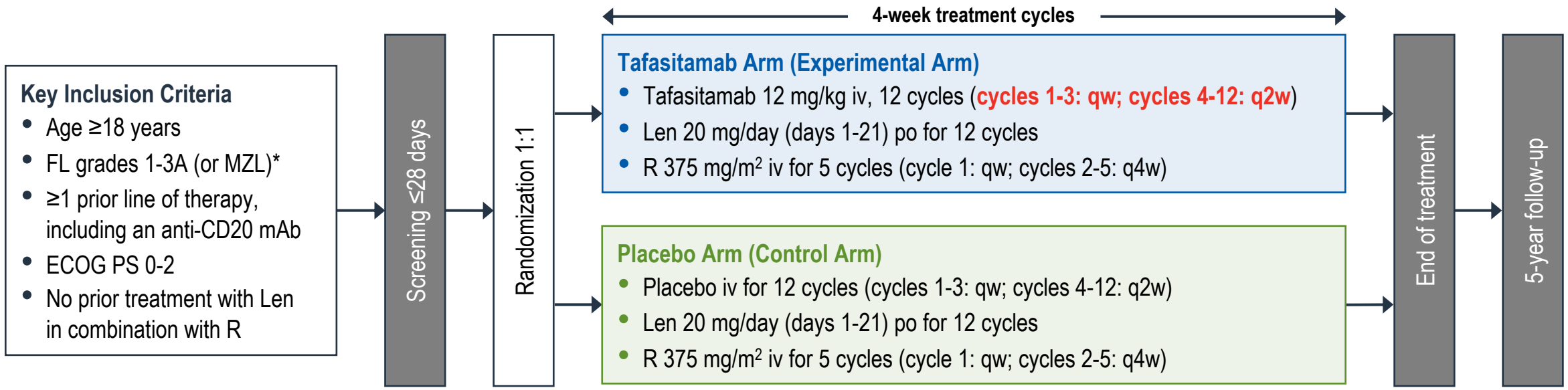
- 37 patients (43%) required lenalidomide dose reduction
- 62/80 patients (78%) were able to stay at dose ≥ 20mg/d

- Incidence and severity of TEAEs are lower during the tafasitamab monotherapy phase
- Ten patients (12%) discontinued tafasitamab + LEN because of AEs

[a]AE collection period included 30 days after end of treatment
AEs, adverse events; LEN, lenalidomide; TEAEs, treatment-emergent AEs .

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

inMIND study: phase 3, tafa-R2 vs R2



Stratification Factors (Patients With FL)

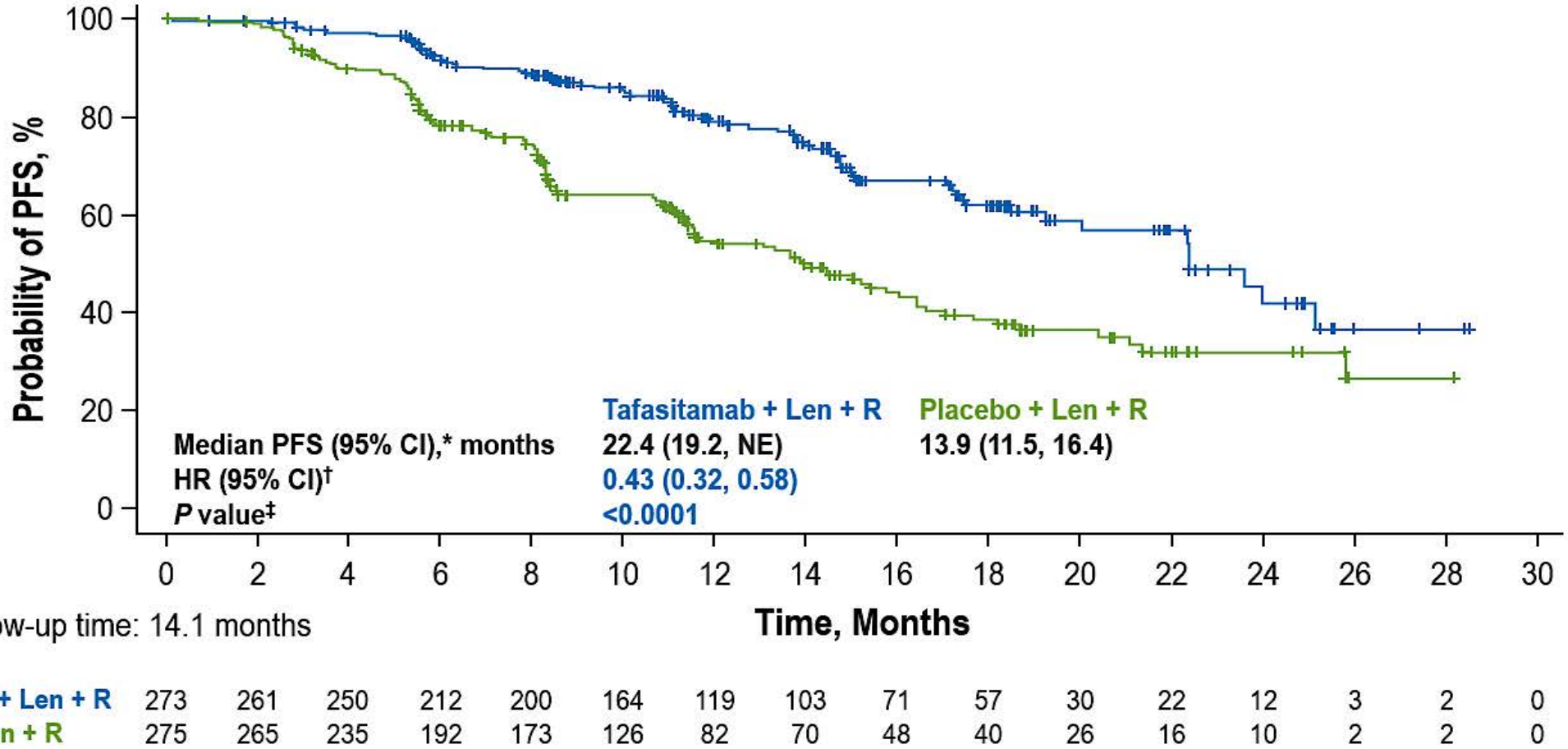
- POD24
- **Refractoriness to prior anti-CD20 mAb therapy**
- Number of prior lines of therapy (1 or ≥2)

Study Endpoints in FL Population (Investigator Assessed Unless Specified)

- **Primary study endpoint:** **PFS**
- **Key secondary:** PET-CR rate in the FDG-avid population, OS
- **Select other secondary:** PFS by IRC, ORR, DOR, safety, QoL, MRD
- **Exploratory:** TTNT, B-cell recovery, Ig levels, CD19 expression

inMIND study: phase 3, tafa-R2 vs R2

Primary endpoint: PFS



Median follow-up time: 14.1 months

No. at Risk

Tafasitamab + Len + R	273	261	250	212	200	164	119	103	71	57	30	22	12	3	2	0
Placebo + Len + R	275	265	235	192	173	126	82	70	48	40	26	16	10	2	2	0

Significant improvement in PFS was observed with tafasitamab

Sehn et al. ASH 2024

Roundtable Discussion

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Nursing Considerations for Patients Receiving Tafasitamab

Caitlin Murphy DNP, FNP-BC, AOCNP

Tafasitamab plus lenalidomide

- Adult patients with relapsed or refractory diffuse large B-cell lymphoma
- DLBCL arising from low grade lymphoma, and who are ***not*** eligible for autologous stem cell transplant

Tafasitamab package insert.

Schedule of Administration

- Dosage of is 12 mg/kg as an intravenous infusion
- Cycle 1: Days 1, 4, 8, 15 and 22 of the 28-day cycle
- Cycles 2 and 3: Days 1, 8, 15 and 22 of each 28-day cycle
- Cycle 4 and beyond: Days 1 and 15 of each 28-day cycle
- Administer tafa in combination with lenalidomide for a maximum of 12 cycles
- Lenalidomide 25 mg/day days 1-21 of 28 day cycle
- May continue tafa monotherapy until disease progression or unacceptable toxicity

Tafasitamab package insert.

Adverse Effects/Common Toxicities

- Monitor for to minimize infusion-related reactions
  - Administer premedication 30 minutes to 2 hours prior to starting infusion
  - Acetaminophen
  - histamine H_1 receptor antagonists
  - histamine H_2 receptor antagonists
  - and/or glucocorticosteroids
- Hematological AEs
  - Most notable: neutropenia, anemia, thrombocytopenia and then febrile neutropenia
- Infection—
  - Respiratory tract infections
  - UTIs
  - Bronchitis
- GI—diarrhea (36%)
- Peripheral Neuropathy
- Fatigue
  - Exercise!

Tafasitamab package insert.

Supportive Care

- 80% of infusion-related reactions occurred during cycle 1 or 2
- Monitor CBC prior to administration of each treatment cycle and throughout treatment.
- Monitor patients with neutropenia for signs of infection
- Consider granulocyte colony-stimulating factor (G-CSF) support

Lenalidomide Supportive Care

- REMS program
- May cause birth defects or embryo-fetal death
  - Counseling around safe sex practices for male and female sex patients
- Significantly increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE)
  - Anti-thrombotic prophylaxis is recommended
- Cytopenias—Neutropenia and Thrombocytopenia
  - HSV prophylaxis

Patient Case

- 72 y/o woman with notable history of IBS, HTN, HLD, and arthritis who presented with weight loss and bloating
- Underwent CT which demonstrated retroperitoneal mass about 5 x 5 cm with highest SUV 12 and pulmonary nodules
- IR guided biopsy and pathology consistent with DLBCL
- Received 6 cycles of R-CHOP
- EOT PET with persistent lung nodules

Patient Case

- Ongoing surveillance with intermittent imaging when patient noted waxing/waning cervical nodes, stable pulmonary nodes
- In 2024, cervical nodes increasing on exam; small axillary and RP nodes; biopsy consistent with DLBCL
- Treatment considerations:
  - Location of care
  - Caregiver support
  - Goals of care and intensity of treatment

Patient Case

- Community based clinic setting close to home
- No change in location of care—team consistent across all lines of therapy
- Limited caregiver support and able to have multiple caregivers for various appointments and family, friends could support patient in ways suited to their abilities

Patient Case

- HSR with cycle 1 day 1 as fever, chills, flushing
  - Managed with rescue medications; able to tolerate subsequent infusions
- Lenalidomide
  - Dose reductions over first 3 cycles and maintained 10 mg dosing
- Interim restaging PET with PR
- Continued with 12 cycles and is in ongoing surveillance with stable pulmonary nodes

Roundtable Discussion

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Understanding the Current Paradigm and New Approaches in the Care of Patients with Cancer

A Complimentary NCPD Hybrid Symposium Series Held During the 50th Annual ONS Congress

Non-Hodgkin Lymphoma

Saturday, April 12, 2025

6:00 PM – 7:30 PM

Faculty

Christopher Flowers, MD, MS
Manali Kamdar, MD, MBBS
Robin Klebig, MSN, APRN, CNP, AOCNP
Caitlin Murphy, DNP, FNP-BC, AOCNP

Moderator

Neil Love, MD

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