Inside the Issue: The Current and Future Role of CD20 x CD3 Bispecific Antibodies in the Management of Non-Hodgkin Lymphoma

A CME/MOC-Accredited Live Webinar

Wednesday, August 2, 2023
5:00 PM – 6:00 PM ET

Faculty

Martin Hutchings, MD, PhD
Loretta J Nastoupil, MD

Moderator

Neil Love, MD

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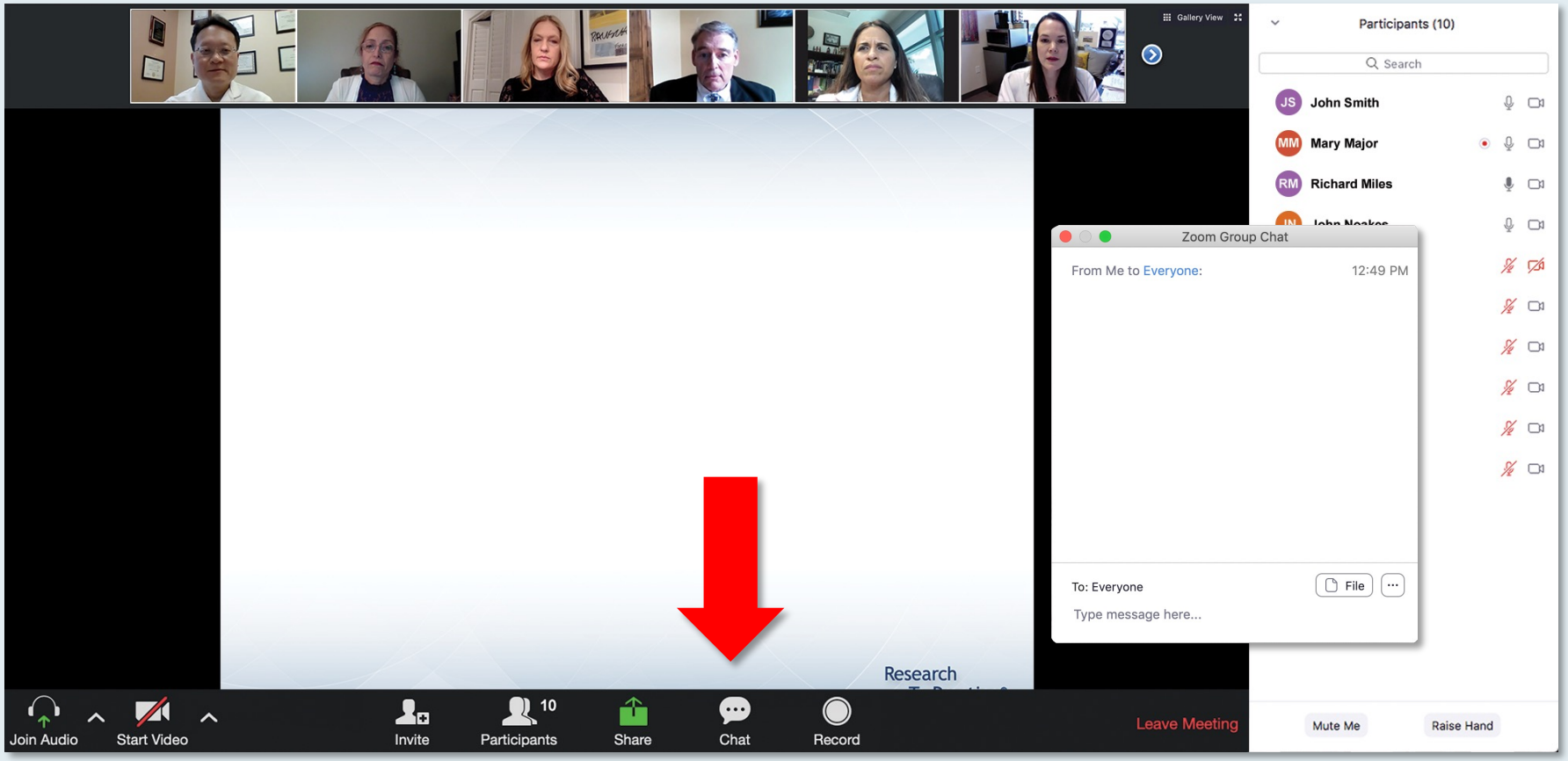

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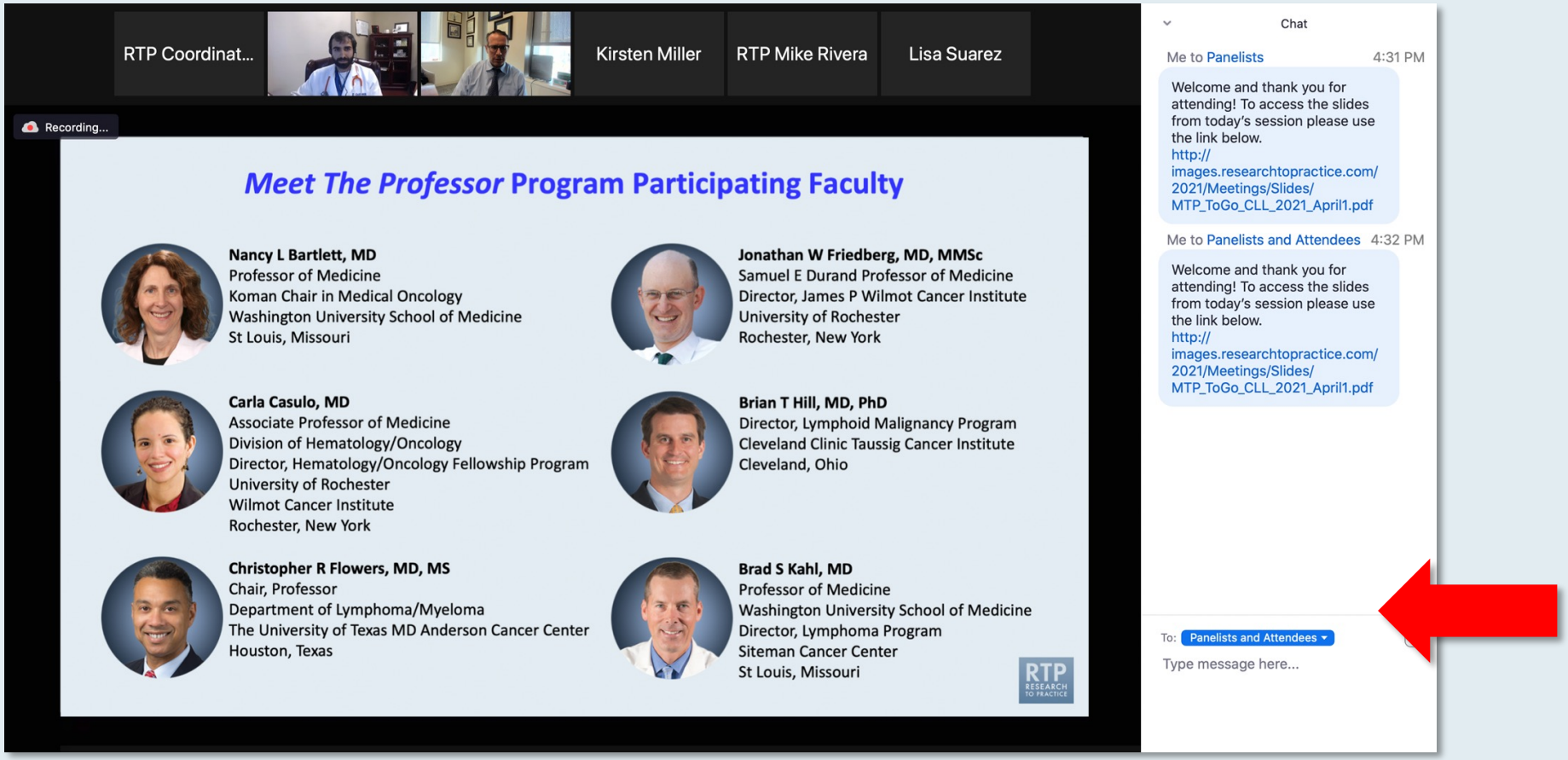

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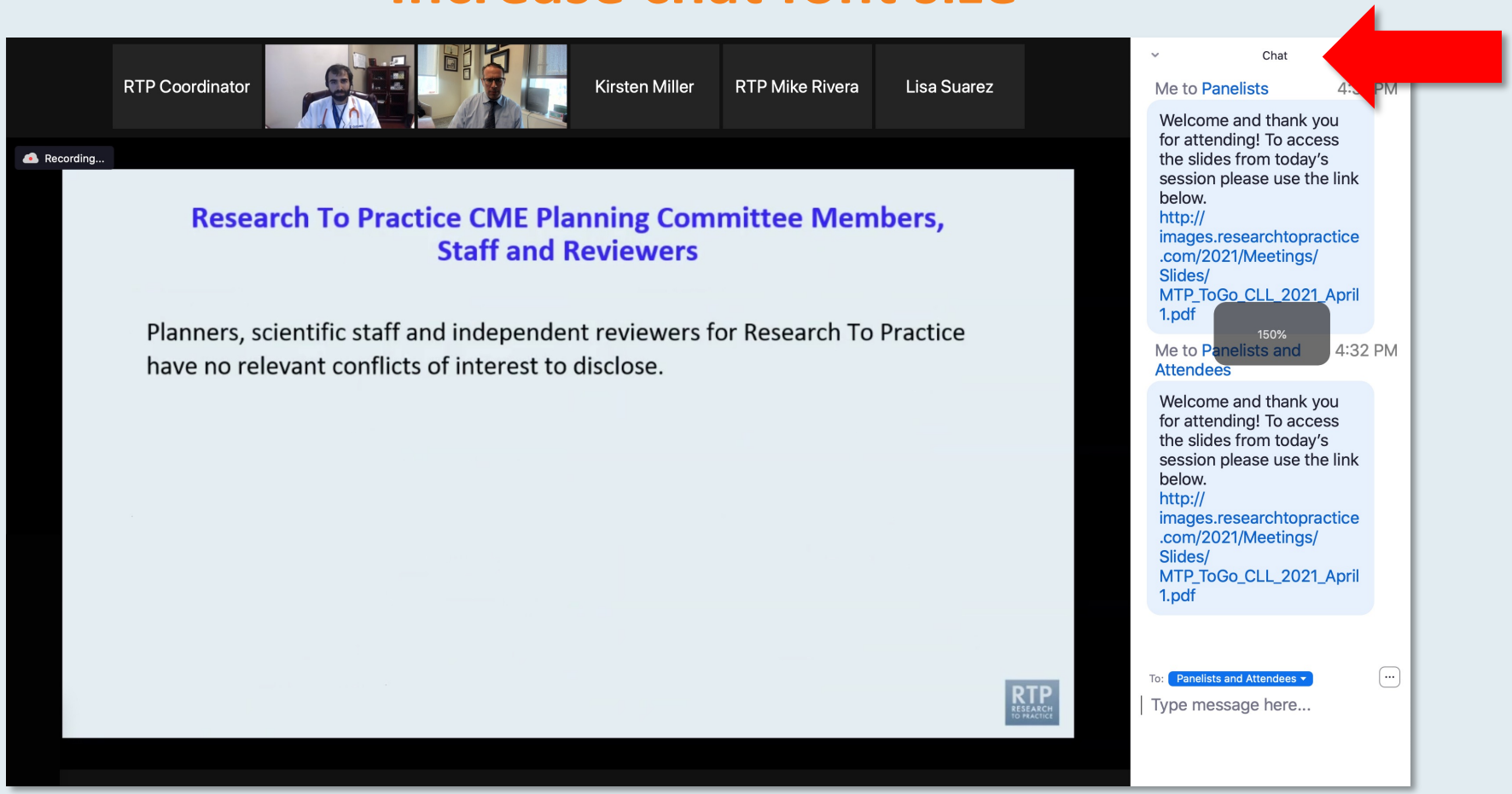

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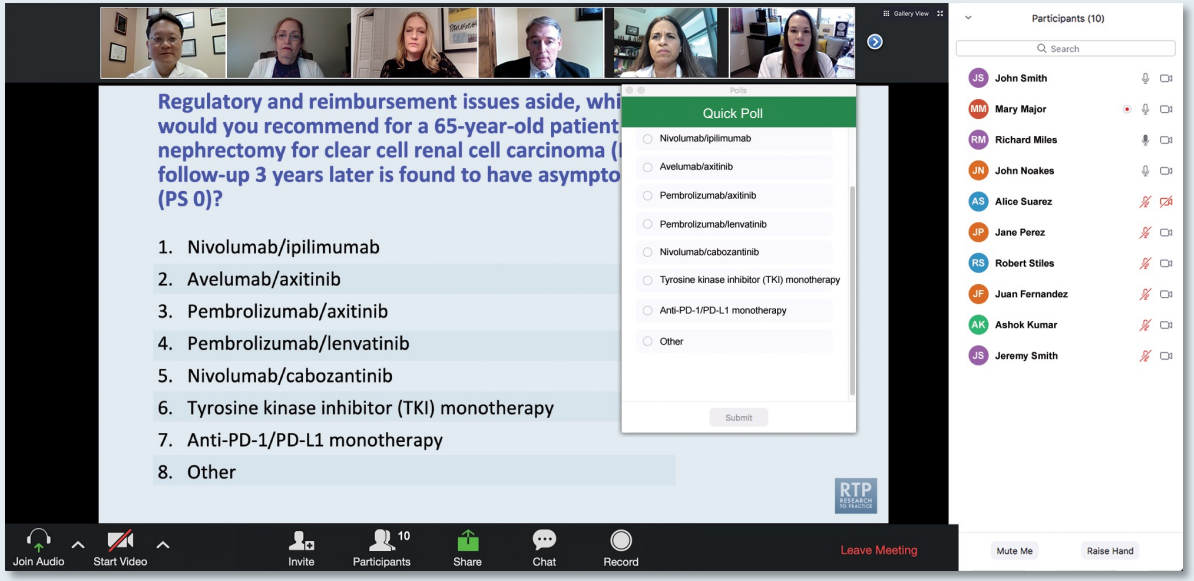

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WITH DR NEIL LOVE

Meet The Professor: The Current and Future Management of Hodgkin and Non-Hodgkin Lymphoma

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Inside the Issue: Optimizing the Management of Metastatic Pancreatic Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, August 8, 2023
5:00 PM – 6:00 PM ET

Faculty

Eileen M O'Reilly, MD
Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Melanoma

Thursday, August 10, 2023
5:00 PM – 6:00 PM ET

Faculty

Prof Georgina Long, AO, BSc, PhD, MBBS

Moderator

Neil Love, MD

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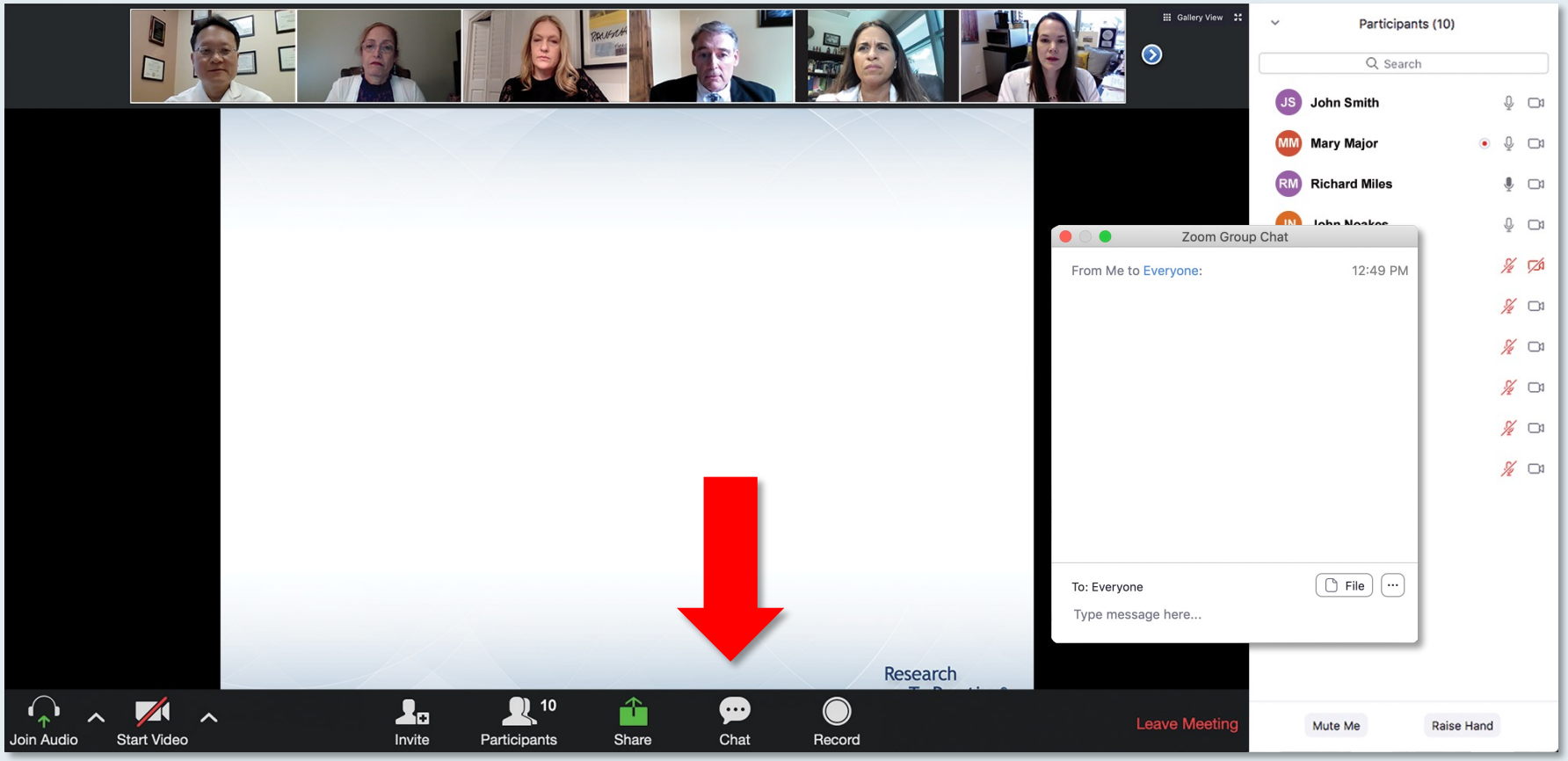

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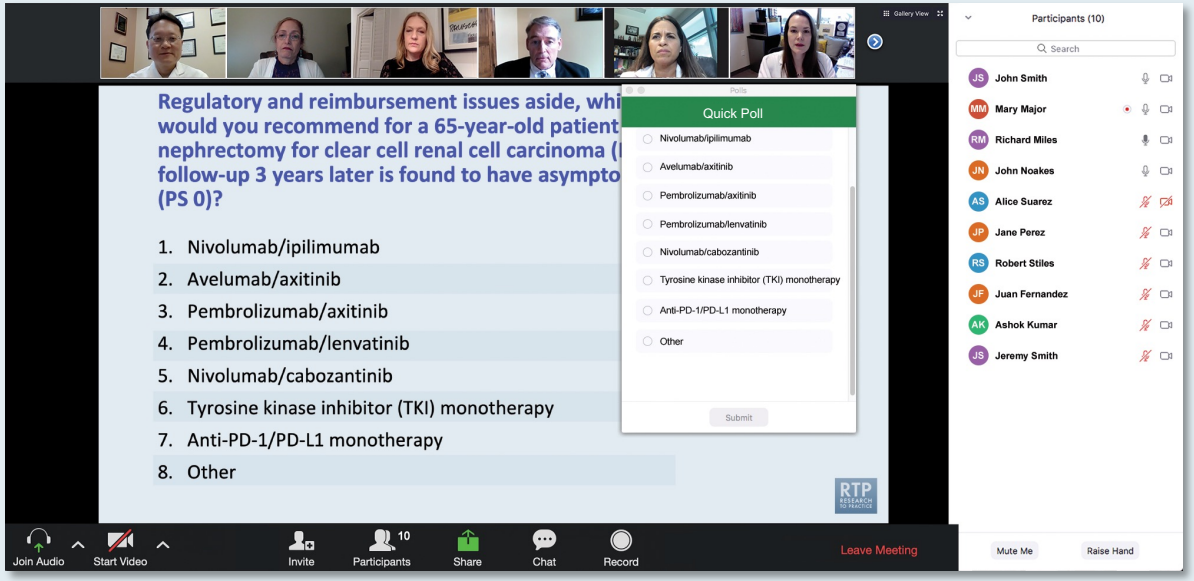

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Role of Bispecific Antibody Therapy in Follicular Lymphoma

Loretta J. Nastoupil, MD
Associate Professor
UT MD Anderson Cancer Center
Houston, TX USA

Key data on bispecific antibodies in DLBCL

Inside the Issue Live Webinar

02 August 2023

Professor Martin Hutchings
Department of Haematology and Phase 1 Unit
Rigshospitalet, Copenhagen, Denmark

Key Data Sets

Loretta J Nastoupil, MD

- Lee DW et al. ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. *Biol Blood Marrow Transplant* 2019;25(4):625-38.
- Jemaa S et al. Full automation of total metabolic tumor volume from FDG-PET/CT in DLBCL for baseline risk assessments. *Cancer Imaging* 2022;22(1):39.
- Bartlett NL et al. Mosunetuzumab monotherapy demonstrates durable efficacy with a manageable safety profile in patients with relapsed/refractory follicular lymphoma who received >2 prior therapies: Updated results from a pivotal phase II study. ASH 2022;Abstract 610.
- Kim TM et al. Odronextamab in patients with relapsed/refractory (R/R) follicular lymphoma (FL) grade 1-3a: Results from a prespecified analysis of the pivotal phase II study ELM-2. ASH 2022;Abstract 949.

Key Data Sets

Loretta J Nastoupil, MD (continued)

- Falchi L et al. Subcutaneous epcoritamab with rituximab + lenalidomide in patients with relapsed or refractory follicular lymphoma: Phase 1/2 trial update. ASH 2022;Abstract 609.
- Morschhauser F et al. Glofitamab as monotherapy and in combination with obinutuzumab induces high complete response rates in patients with multiple relapsed or refractory (R/R) follicular lymphoma (FL). ASH 2021;Abstract 128.

Key Data Sets

Martin Hutchings, MD, PhD

- Budde E et al. Single-agent mosunetuzumab shows durable complete responses in patients with relapsed or refractory B-cell lymphomas: Phase I dose-escalation study. *J Clin Oncol* 2022;40(5):481-91.
- Bannerji R et al. Odronextamab, a human CD20×CD3 bispecific antibody in patients with CD20-positive B-cell malignancies (ELM-1): Results from the relapsed or refractory non-Hodgkin lymphoma cohort in a single-arm, multicentre, phase 1 trial. *Lancet Haematol* 2022;9(5):e327-39.
- Hutchings M et al. Glofitamab, a novel, bivalent CD20-targeting T-cell-engaging bispecific antibody, induces durable complete remissions in relapsed or refractory B-cell lymphoma: A phase I trial. *J Clin Oncol* 2021;39(18):1959-70.
- Hutchings M et al. Dose escalation of subcutaneous epcoritamab in patients with relapsed or refractory B-cell non-Hodgkin lymphoma: An open-label, phase 1/2 study. *Lancet* 2021;398(10306):1157-69.

Key Data Sets

Martin Hutchings, MD, PhD (continued)

- Bartlett NL et al. Mosunetuzumab monotherapy is active and tolerable in patients with relapsed/refractory diffuse large B-cell lymphoma. *Blood Adv* 2023;[Online ahead of print].
- Walewski J et al. Odronextamab in patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL): Results from a prespecified analysis of the pivotal phase II study ELM-2. EHA 2023;Abstract P1115.
- Dickinson MJ et al. Glofitamab for relapsed or refractory diffuse large B-cell lymphoma. *N Engl J Med* 2022;387(24):2220-31.
- Thieblemont C et al. Epcoritamab, a novel, subcutaneous CD3xCD20 bispecific T-cell-engaging antibody, in relapsed or refractory large B-cell lymphoma: Dose expansion in a phase I/II trial. *J Clin Oncol* 2023;41(12):2238-47.
- Kim WS et al. Odronextamab in patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL): Results from a prespecified analysis of the pivotal phase II study ELM-2. ASH 2022;Abstract 444.

Key Data Sets

Martin Hutchings, MD, PhD (continued)

- Hutchings M et al. Glofitamab in combination with polatuzumab vedotin: Phase Ib/II preliminary data support manageable safety and encouraging efficacy in relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL). ASH 2021;Abstract 525.
- Hutchings M et al. RG6333 (CD19-CD28), a CD19-targeted affinity-optimized CD28 bispecific antibody, enhances and prolongs the anti-tumor activity of glofitamab (CD20-TCB) in preclinical models. ASH 2022;Abstract P4259.

Agenda

MODULE 1: Follicular Lymphoma

MODULE 2: Diffuse Large B-Cell Lymphoma

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Agenda

Module 1: Follicular Lymphoma

- Select Key Questions
- Case Presentations
- Faculty Survey

Module 2: Diffuse Large B-Cell Lymphoma

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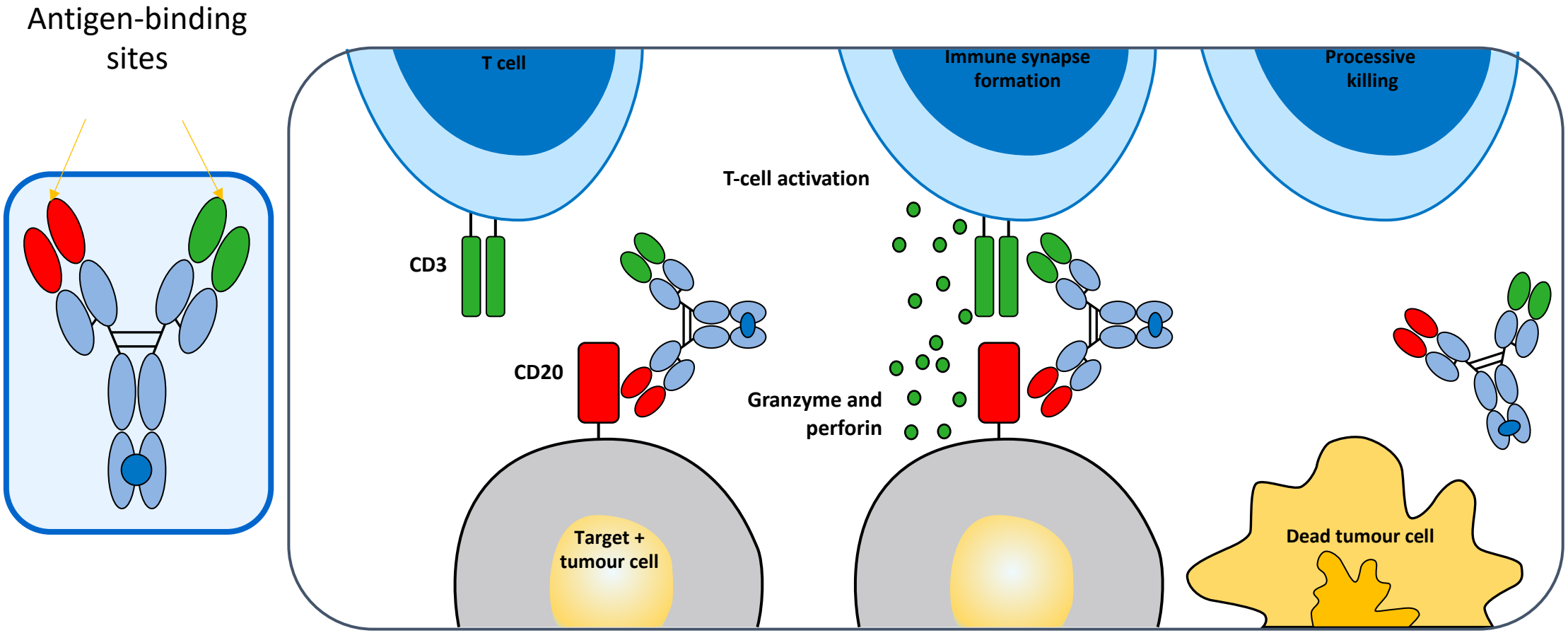
What is known about the mechanism of action of bispecific antibodies when used alone or in combination with other agents in the management of FL?

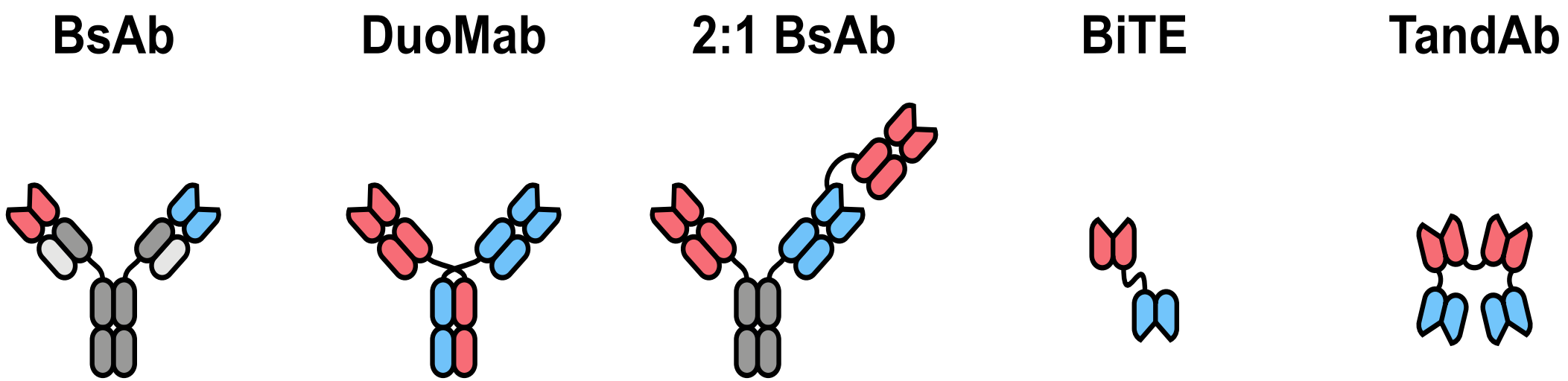
Bispecific antibodies bind two different epitopes – One on malignant cells and one on T-cells



Courtesy of Loretta J Nastoupil, MD

Csizmar CM, Ansell SM. Int J Mol Sci. 2021 Mar 24;22(7):3302.

Bispecific antibody Constructs



Courtesy of Loretta J Nastoupil, MD

Csizmar CM, Ansell SM. Int J Mol Sci. 2021 Mar 24;22(7):3302.

What is known about the global efficacy and toxicity of these agents in FL, and what difference, if any, exists among them?

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Summary- Mosunetuzumab

- In this pivotal Phase II study, fixed-duration mosunetuzumab monotherapy demonstrated a **high CR rate at EOT** in pts with R/R FL
- **Durable responses** were observed in pts with a CR at EOT; a high proportion of pts remained **event free 2 years after EOT**
- In exploratory analyses, a **similar DOR benefit** was observed regardless of whether pts achieved an **early or late CR**
- No correlation was observed between TMTV at baseline and BOR
- CRS was **predominantly low grade**; Grade ≥2 CRS events were more frequently observed in pts with bone/bone marrow metabolic disease burden versus those without

Courtesy of Loretta J Nastoupil, MD

Odronextamab Summary

- Odronextamab is an off-the-shelf, investigational CD20 × CD3 bispecific antibody
- First results from the pivotal Phase 2 trial of odronextamab demonstrate a new benchmark for efficacy in heavily pretreated, R/R FL
  - ORR 81.8%, CR 75.2%; 92% of responders were complete responders
  - Reponses were deep and durable with a mPFS of 20.2 months
- Odronextamab has a generally manageable safety profile with the optimized step-up regimen
  - CRS was mostly grade 1 and generally occurred with Cycle 1 step-up
  - No cases of ICANS or TLS
  - Treatment-related adverse events leading to treatment discontinuation occurred infrequently (7.6%)
- Phase 3 randomized controlled studies will be initiating in follicular lymphoma in earlier lines of therapy

CD, cluster of differentiation; CR, complete response; CRS, cytokine release syndrome; FL, follicular lymphoma; ICANS, immune effector cell-associated neurotoxicity syndrome; mPFS, median progression-free survival; TLS, tumor lysis syndrome; ORR, objective response rate; R/R, relapsed/refractory.

Courtesy of Loretta J Nastoupil, MD

Kim TM et al. ASH 2022;Abstract 949.

Summary: Epcoritamab + R2

- **Epcoritamab + R² showed potent antitumor activity**
  - High response rates: ORR 96.2%, CMR 83.5%; majority achieved at first assessment
  - Deep responses observed across high-risk subgroups
  - Durable responses have been observed
- **Safety remained consistent with previous reports**
  - No grade ≥3 CRS observed; CRS events mostly occurred after the first full dose
- **Ongoing phase 3 trial, EPCORE FL-1, is evaluating fully outpatient epcoritamab + R² in patients with R/R FL**
  - Trial-in-progress poster 4206 (Monday, December 12, 2022, 6:00 PM–8:00 PM)

Courtesy of Loretta J Nastoupil, MD

Glofitamab – Summary

- Glofitamab demonstrated high response rates as monotherapy or in combination with obinutuzumab in patients with heavily pre-treated R/R FL, including in high-risk subgroups (dose-escalation data)
- Glofitamab monotherapy and in combination with obinutuzumab
  - CR rates were high and comparable, conclusions on durability are limited by short follow-up
  - Increased myelosuppression in glofitamab in combination with obinutuzumab cohort, although clinical consequences were not different
- No clear benefit in CRS mitigation was observed with extended versus standard step-up dosing of glofitamab
- Phase II expansion cohort with glofitamab monotherapy (2.5mg/10mg/30mg) is being prioritised based on these data

Morschhauser F et al. ASH 2021;Abstract 128.

Courtesy of Loretta J Nastoupil, MD

Future Directions

- Mosunetuzumab
  - CELESTIMO: randomized phase 3 of mosunetuzumab +lenalidomide vs. R^2 in 2L+ FL
  - Frontline monotherapy
- Odronextamab
  - Frontline combination
- Epcoritamab
  - Still haven’t seen single arm phase 2 data?
  - In combination with R^2 in 2L+ and 1L

Courtesy of Loretta J Nastoupil, MD

Conclusions

- Efficacy observed with bispecific antibodies in R/R FL is very favorable
  - More similar than different
- CRS appears to be a frequent AE that is manageable with dose step up and corticosteroid pre-meds
  - Understanding those at risk for grade 2 or higher CRS will be critical to outpatient management
- More readily available than CAR T cell therapy, but still requires understanding of CRS management
  - Guidelines are desired to share best practices regarding CRS management
- Understanding the preferred sequencing of therapy is also desirable
  - Bispecifics will likely move into earlier lines of therapy, in combination

Courtesy of Loretta J Nastoupil, MD

What is the usual time course and presentation of cytokine release syndrome observed with bispecific antibody therapy for FL, and how can this be prevented and managed, particularly in older patients?

Based on currently available data and personal clinical experience, when in the treatment course is the optimal time to use a bispecific antibody for FL?

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Does CD20 need to be measured in patients receiving bispecific antibody therapy for FL?

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Patient Case

- 54 y/o F who received frontline R-CHOP followed by R maintenance 7 years ago when she presented with advanced stage, high tumor burden FL, grade 3a. At relapse, she was treated with BR and is now relapsing 2 years after completion of 2nd line. Imaging reveals adenopathy above and below the diaphragm, largest node is < 7 cm. She is otherwise well. Biopsy confirms FL.
  - How would you approach this young/fit patient in 3rd line?

Courtesy of Loretta J Nastoupil, MD

Patient case #2

- A 75 y/o M with HTN, DM2, mild CKD presents with symptomatic adenopathy. He was first diagnosed with FL, low grade 12 years ago. At that time, he was treated with RCVP and was in remission for approx. 4 years. At his first relapse, he received single agent rituximab x 4 cycles followed by 2 years of maintenance. He remained in remission for approx. 2 years. With his 2nd relapse, he was treated with lenalidomide and rituximab and completed 12 cycles. He was in remission for approx. 2.5 years. At relapse, he was observed but now with progressive disease is becoming symptomatic and is in need of therapy.
  - How would you approach this patient with comorbidities and advanced age?

Courtesy of Loretta J Nastoupil, MD

Patient Case #3

- A 65 y/o F who is now relapsing with FL and in need of therapy. At her initial presentation, she received BR. Within 18 months, she progressed. Biopsy revealed DLBCL and FL at the time. She received R-CHOP and remained in remission for 4 years. At relapse, biopsy revealed only recurrent FL. At that time, she was treated with lenalidomide and rituximab and was in remission for approximately 2 years. She is now relapsing and in need of therapy.
  - How would you approach this patient?

Courtesy of Loretta J Nastoupil, MD

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Based on your personal clinical experience and knowledge of available data, do you believe 1 or more CD20 x CD3 bispecific antibodies are more efficacious than others when used in the management of FL?

 Prof Hutchings	Yes, epcoritamab and glofitamab appear most potent
 Dr Nastoupil	No
 Dr Abramson	No
 Dr Kahl	No
 Dr Matasar	No
 Dr Phillips	No

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Based on your personal clinical experience and knowledge of available data, do you believe 1 or more CD20 x CD3 bispecific antibodies are more convenient than others when used in the management of FL?

 Prof Hutchings	Yes, mosunetuzumab
 Dr Nastoupil	Yes, mosunetuzumab
 Dr Abramson	Yes, mosunetuzumab and epcoritamab
 Dr Kahl	Yes, mosunetuzumab
 Dr Matasar	Yes, mosunetuzumab
 Dr Phillips	Yes, mosunetuzumab

Based on your personal clinical experience and knowledge of available data, do you believe 1 or more CD20 x CD3 bispecific antibodies are safer/less toxic than others when used in the management of FL?

 Prof Hutchings	Yes, mosunetuzumab
 Dr Nastoupil	Yes, mosunetuzumab and epcoritamab
 Dr Abramson	Yes, mosunetuzumab and epcoritamab
 Dr Kahl	Yes, mosunetuzumab
 Dr Matasar	Yes, mosunetuzumab
 Dr Phillips	Yes, mosunetuzumab

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Based on your personal clinical experience and knowledge of available data, how would you compare the global efficacy and tolerability of CD20 x CD3 bispecific antibodies to those of CAR T-cell therapy for patients with FL?

	Efficacy	Tolerability
 Prof Hutchings	About the same	Bispecific antibodies are more tolerable than CAR T-cell therapy
 Dr Nastoupil	Bispecific antibodies are less efficacious than CAR T-cell therapy	Bispecific antibodies are more tolerable than CAR T-cell therapy
 Dr Abramson	About the same	Bispecific antibodies are more tolerable than CAR T-cell therapy
 Dr Kahl	Bispecific antibodies are less efficacious than CAR T-cell therapy	Bispecific antibodies are more tolerable than CAR T-cell therapy
 Dr Matasar	Bispecific antibodies are less efficacious than CAR T-cell therapy	Bispecific antibodies are more tolerable than CAR T-cell therapy
 Dr Phillips	Bispecific antibodies are less efficacious than CAR T-cell therapy	Bispecific antibodies are more tolerable than CAR T-cell therapy

Regulatory and reimbursement issues aside, at what point would you like to use a bispecific CD20 x CD3 antibody for a patient with Stage III FL?

 Prof Hutchings	First line and beyond
 Dr Nastoupil	Third line
 Dr Abramson	Third line
 Dr Kahl	Second line
 Dr Matasar	First line
 Dr Phillips	Third line

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, would you like to use a CD20 x CD3 antibody or CAR T-cell therapy first for a patient with FL and no significant comorbidities who experienced disease progression on first-line bendamustine/rituximab (BR) → maintenance rituximab and second-line lenalidomide/rituximab (R^2)?

 Prof Hutchings	CD20 x CD3 bispecific antibody
 Dr Nastoupil	CD20 x CD3 bispecific antibody
 Dr Abramson	CD20 x CD3 bispecific antibody
 Dr Kahl	CD20 x CD3 bispecific antibody
 Dr Matasar	CD20 x CD3 bispecific antibody
 Dr Phillips	CD20 x CD3 bispecific antibody

RTP RESEARCH TO PRACTICE

In general, what is your usual preferred first-line therapy for a 60-year-old patient with FL and no significant comorbidities? Would you recommend maintenance therapy for this patient, and if so, for what duration?

	First-line therapy	Maintenance
 Prof Hutchings	Bendamustine/rituximab	Yes, rituximab for 2 years (depending on depth of response)
 Dr Nastoupil	Bendamustine/rituximab	No
 Dr Abramson	Obinutuzumab/bendamustine	Yes, obinutuzumab for 2 years
 Dr Kahl	Bendamustine/rituximab	No
 Dr Matasar	Bendamustine/rituximab	No
 Dr Phillips	Bendamustine/rituximab	No

Regulatory and reimbursement issues aside, what would you generally recommend as second-line therapy for a 60-year-old patient with Stage IV FL and no significant comorbidities who received first-line BR and then experienced disease progression 2 years after completing maintenance rituximab?

 Prof Hutchings	Epcoritamab, glofitamab or mosunetuzumab
 Dr Nastoupil	Lenalidomide/rituximab (R^2)
 Dr Abramson	Lenalidomide/rituximab (R^2)
 Dr Kahl	Lenalidomide/rituximab (R^2)
 Dr Matasar	Lenalidomide/rituximab (R^2)
 Dr Phillips	Lenalidomide/rituximab (R^2)

Regulatory and reimbursement issues aside, what would you generally recommend as second-line therapy for a 60-year-old patient with Stage IV FL and no significant comorbidities who received first-line BR and then experienced disease progression 1 year after starting maintenance rituximab?

 Prof Hutchings	Epcoritamab, glofitamab or mosunetuzumab
 Dr Nastoupil	Lenalidomide/rituximab (R^2)
 Dr Abramson	Lenalidomide/rituximab (R^2)
 Dr Kahl	Obinutuzumab/CHOP
 Dr Matasar	Odronextamab
 Dr Phillips	Lenalidomide/rituximab (R^2)

O-CHOP = obinutuzumab with CHOP

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would you recommend as third-line therapy for a 60-year-old patient with Stage IV FL and no significant comorbidities who received first-line BR and experienced disease progression on R^2?

 Prof Hutchings	Epcoritamab, glofitamab or mosunetuzumab
 Dr Nastoupil	Mosunetuzumab
 Dr Abramson	Mosunetuzumab
 Dr Kahl	Mosunetuzumab
 Dr Matasar	Mosunetuzumab
 Dr Phillips	Mosunetuzumab

RTP RESEARCH TO PRACTICE

In general, what is your preferred first-line therapy for an 80-year-old patient with FL and significant comorbidities including hypertension, chronic renal failure and Type 2 diabetes mellitus (DM)? Would you recommend maintenance therapy for this patient, and if so, for what duration?

	First-line therapy	Maintenance
 Prof Hutchings	Rituximab	Yes, rituximab for 6-12 months
 Dr Nastoupil	Rituximab	No
 Dr Abramson	Rituximab	Yes, rituximab x 4, q8wk
 Dr Kahl	Rituximab	No
 Dr Matasar	Rituximab	No
 Dr Phillips	Bendamustine/rituximab	Yes, rituximab for 2 years

In general, what would you recommend as second-line therapy for an 80-year-old patient with Stage IV FL and significant comorbidities including hypertension, chronic renal failure and Type 2 DM who received first-line rituximab?

 Prof Hutchings	Tazemetostat
 Dr Nastoupil	Lenalidomide/rituximab (R^2)
 Dr Abramson	Lenalidomide
 Dr Kahl	Tazemetostat
 Dr Matasar	Tazemetostat
 Dr Phillips	Tazemetostat

Regulatory and reimbursement issues aside, what would you recommend as third-line therapy for an 80-year-old patient with Stage IV FL and significant comorbidities including hypertension, chronic renal failure and Type 2 DM who received first-line rituximab and experienced disease progression while receiving second-line tazemetostat?

 Prof Hutchings	Epcoritamab, glofitamab or mosunetuzumab
 Dr Nastoupil	Mosunetuzumab
 Dr Abramson	Mosunetuzumab
 Dr Kahl	Mosunetuzumab
 Dr Matasar	Mosunetuzumab
 Dr Phillips	Mosunetuzumab

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Follicular Lymphoma

Module 2: Diffuse Large B-Cell Lymphoma

- **Select Key Questions**
- **Case Presentations**
- **Faculty Survey**

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1: Follicular Lymphoma

Module 2: Diffuse Large B-Cell Lymphoma

- **Select Key Questions**
- **Case Presentations**
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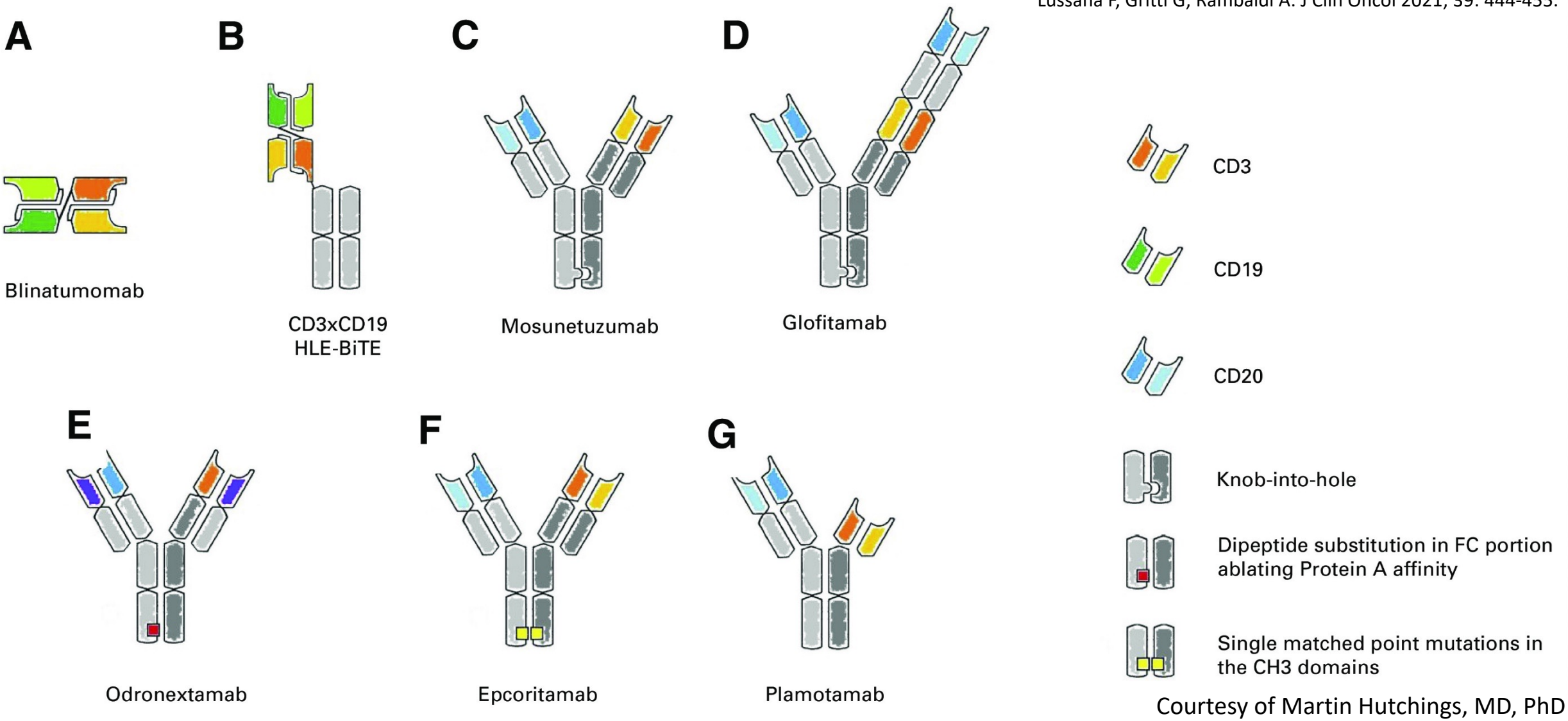
RTP
RESEARCH
TO PRACTICE

What is known about the mechanism of action of bispecific antibodies when used alone or in combination with other agents in the management of DLBCL?

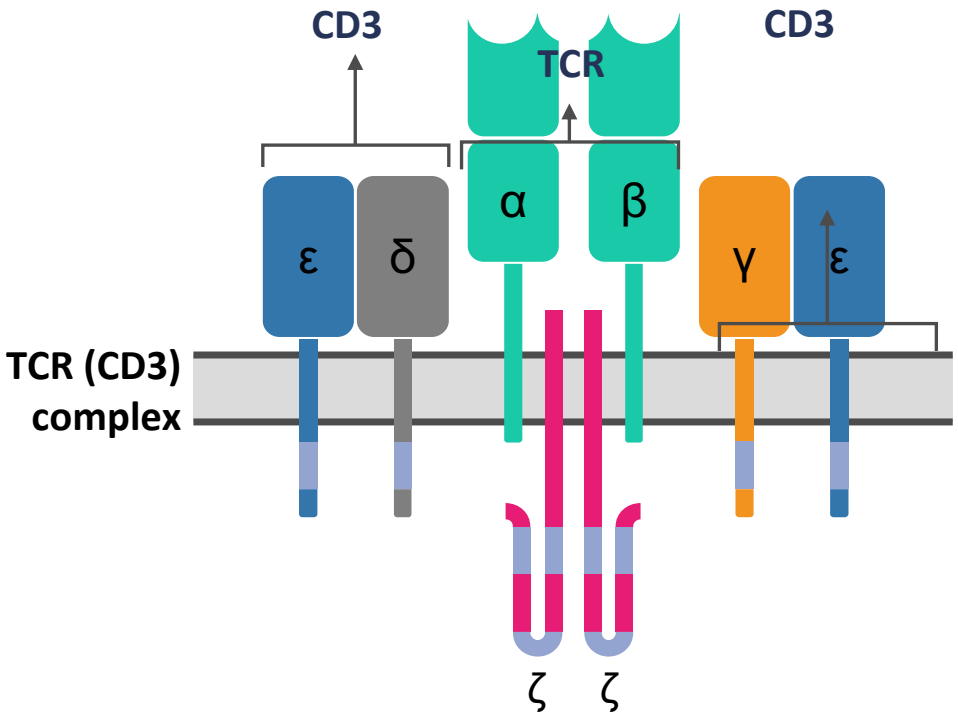
Bispecific CD3/CD20 antibodies in B-NHL

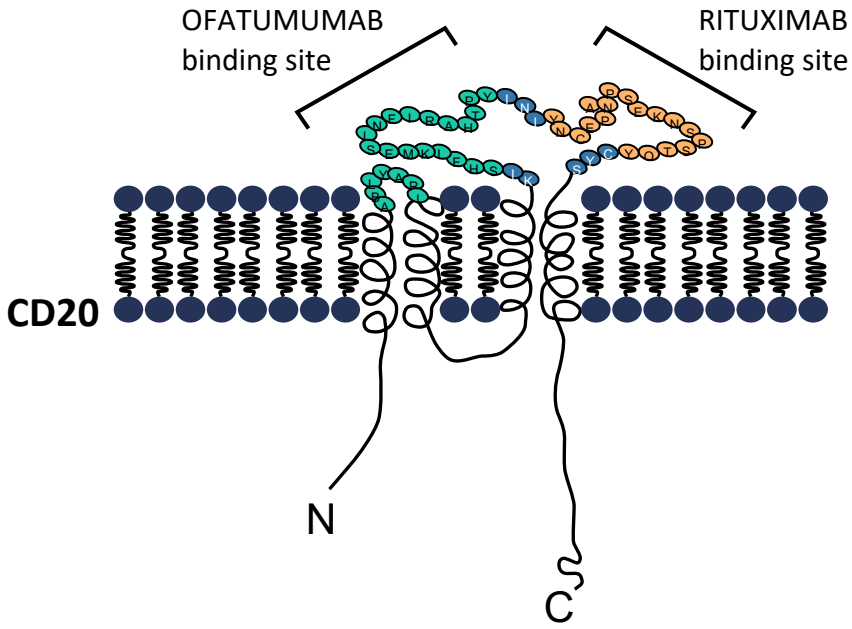


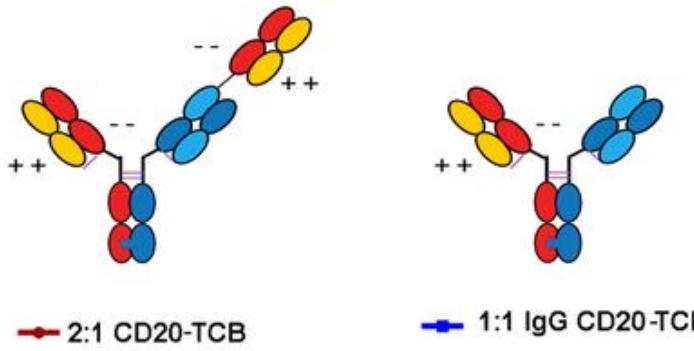
Lussana F, Gritti G; Rambaldi A. J Clin Oncol 2021; 39: 444-455.

Courtesy of Martin Hutchings, MD, PhD

Binding sites and structure of CD3xCD20 antibodies



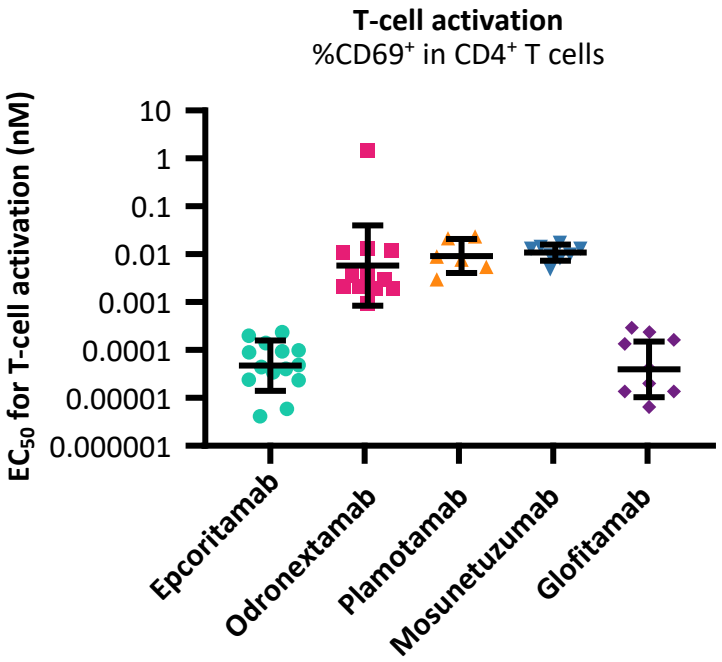


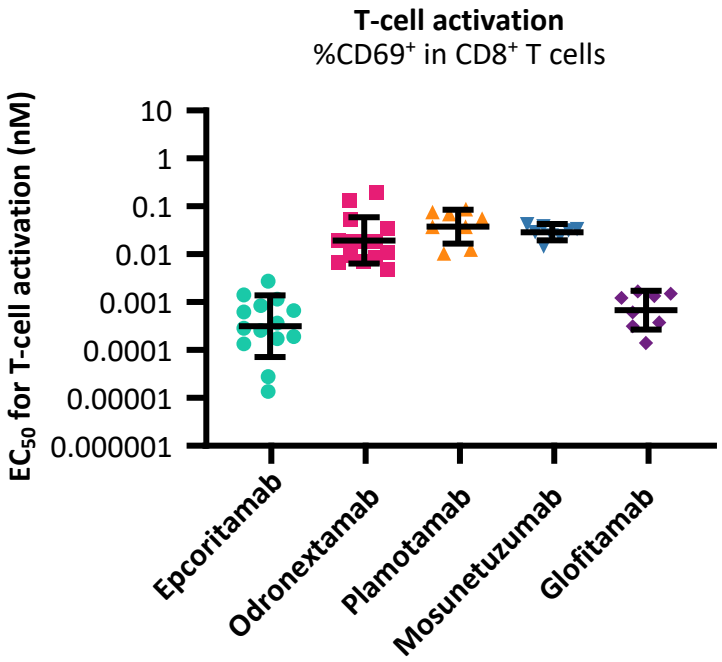


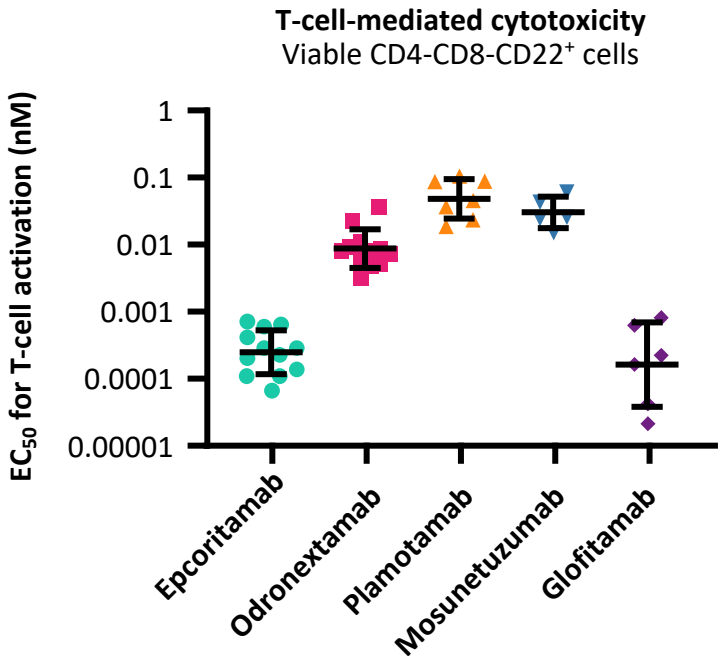
1. Franco R, *et al. Front Pharmacol* 2016; **7:** 1–10; 2. Klein C, *et al. Mabs* 2013; **5:** 22–33; 3. Bacac M, *et al. Clin Cancer Res* 2018; **24**;4785–97.

Courtesy of Martin Hutchings, MD, PhD

In vitro T-cell activation of CD3xCD20 antibodies



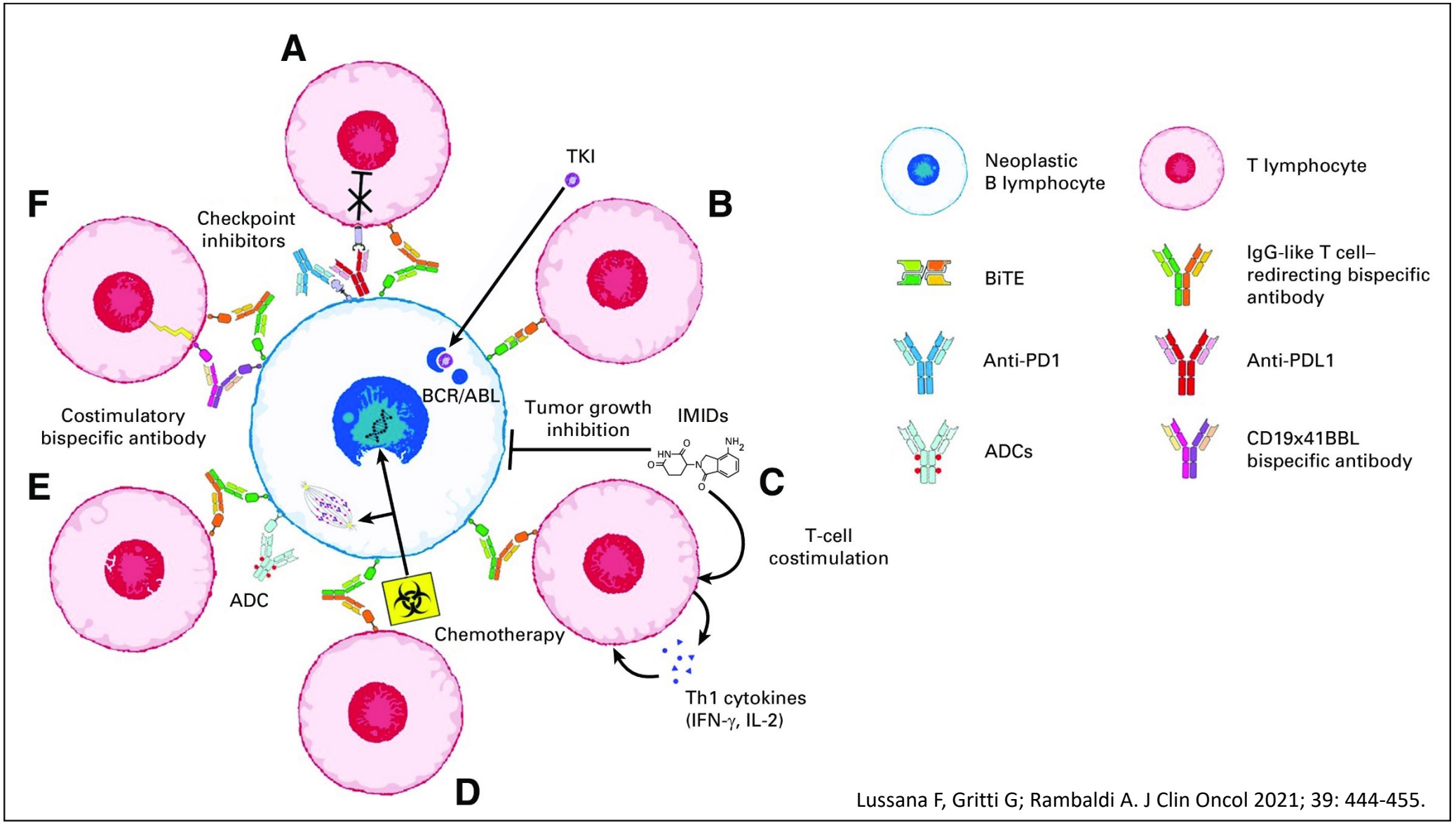




Hiemstra IH, *et al.* EHA 2019: poster presentation PS1301.

Courtesy of Martin Hutchings, MD, PhD

How to get deeper and more durable responses?

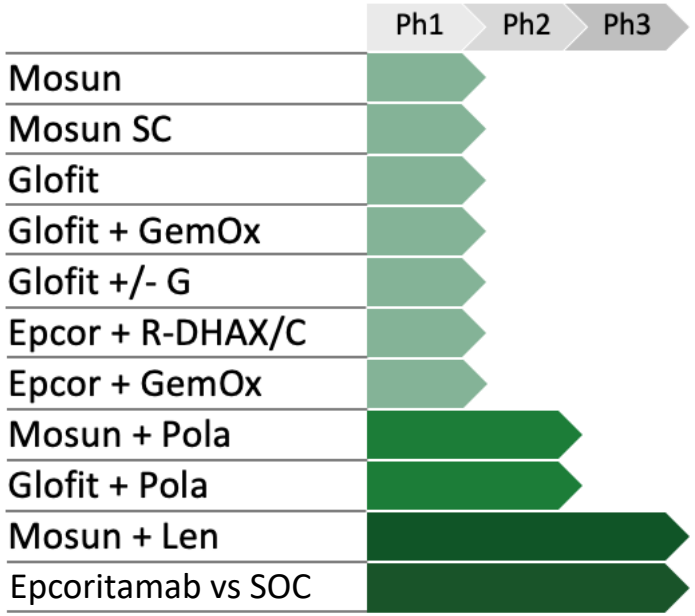


Lussana F, Gritti G; Rambaldi A. J Clin Oncol 2021; 39: 444-455.

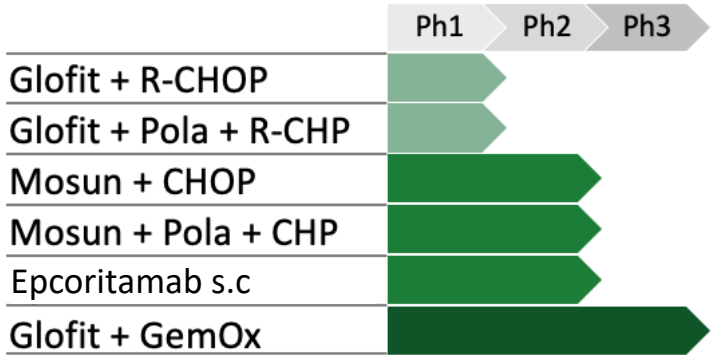
Courtesy of Martin Hutchings, MD, PhD

Ongoing combination studies with bispecific CD3/CD20 antibodies in DLBCL

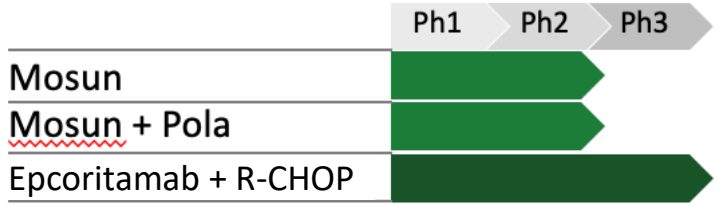
R/R DLBCL



1st Line DLBCL



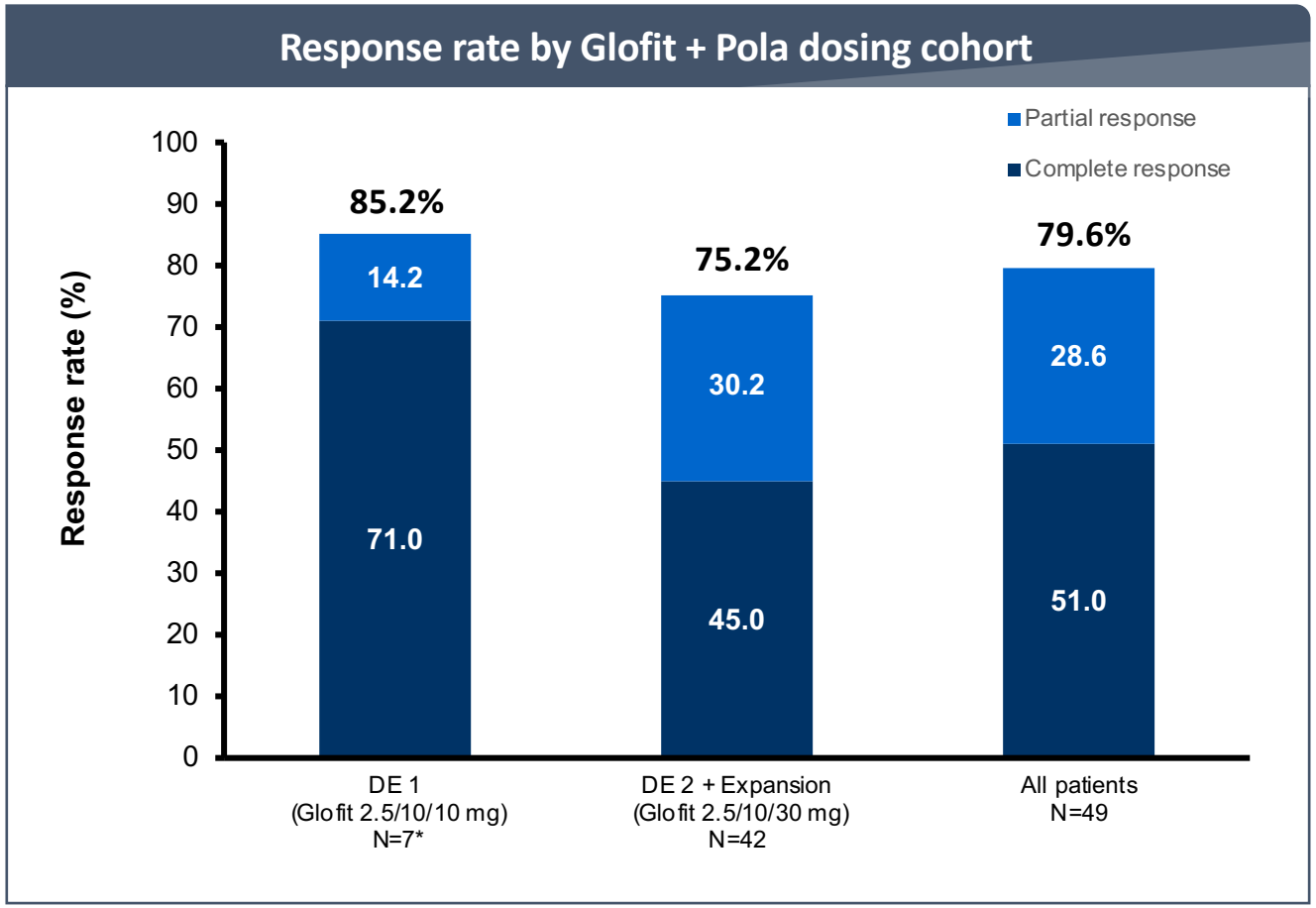
Elderly/Unfit DLBCL



Courtesy of Martin Hutchings, MD, PhD

Slide courtesy of Marion Subklewe

NP39488: Glofitamab and Polatuzumab vedotin in DLBCL



- **49/59 patients were evaluable for interim response**
- **7/49 (14.3%) patients had PD as best response and discontinued study treatment**
- **Encouraging ORR and CR rates in patients with:**
  - trFL: ORR, 8/11 and CR, 7/11
  - HGBCL: ORR, 5/8 and CR, 4/8

Update at ICML:

SESSION 15 - IMMUNOTHERAPY FOR AGGRESSIVE LYMPHOMAS. 17June 08:45.

Abstract 92: Martin Hutchings, et al.

- **Glofit + Pola combination resulted in high response rates**

Courtesy of Martin Hutchings, MD, PhD

Hutchings M, et al. ASH 2021. Abstract 525.

Summary

- The CD3/CD20 bispecific antibodies show an antitumor activity which is unprecedented in heavily pretreated r/r B-NHL
- Data from DLBCL phase 2 expansion cohorts (35-40% with prior CAR-T):
  - Odronextamab: PRR 49%, CRR 31%
  - Glofitamab: ORR 52%, CRR 39% *(FDA approved June 2023 and EMA approved July 2023 for LBCL 3+ line)*
  - Epcoritamab: ORR 63%, CRR 39% *(FDA approved May 2023 and EMA CHMP positive opinion July 2023 for LBCL 3+ line)*
- Complete responses are highly durable (for glofitamab also beyond EOT)
  - Suggests a curative potential even when given as single agents
- The toxicity profile is favourable:
  - Very little CRS > grade 2
  - Very little treatment-related CNS toxicity
- The toxicity profile and mechanism of action make the bispecifics ideal for combination strategies
  - Dose-escalation and combination studies with Obinutuzumab, R-chemo, Polatuzumab vedotin, Atezolizumab (anti-PD-L1), lenalidomide, and targeted immune agonists are ongoing

Courtesy of Martin Hutchings, MD, PhD

What is known about the global efficacy and toxicity of these agents in DLBCL, and what difference, if any, exists among them?

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TO PRACTICE

Based on currently available data and personal clinical experience, when in the treatment course is the optimal time to use a bispecific antibody for a patient with DLBCL?

Does CD20 need to be measured in patients receiving bispecific antibody therapy for DLBCL?

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RESEARCH
TO PRACTICE

Agenda

Module 1: Follicular Lymphoma

Module 2: Diffuse Large B-Cell Lymphoma

- **Select Key Questions**
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- **Faculty Survey**

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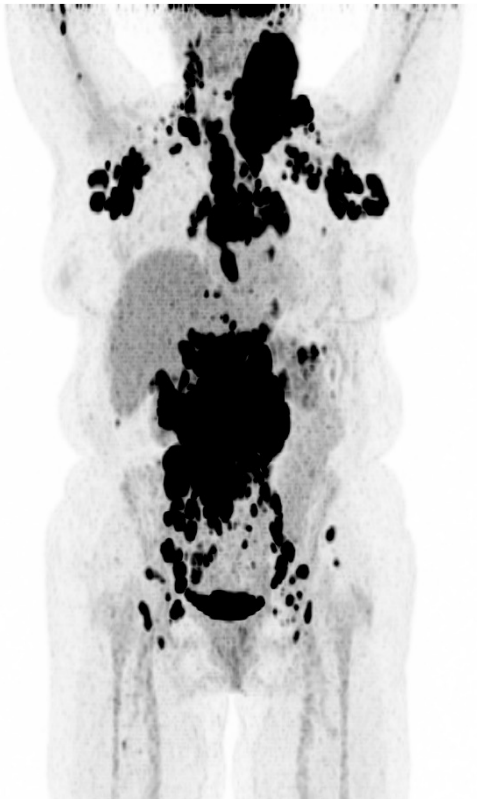
TO PRACTICE

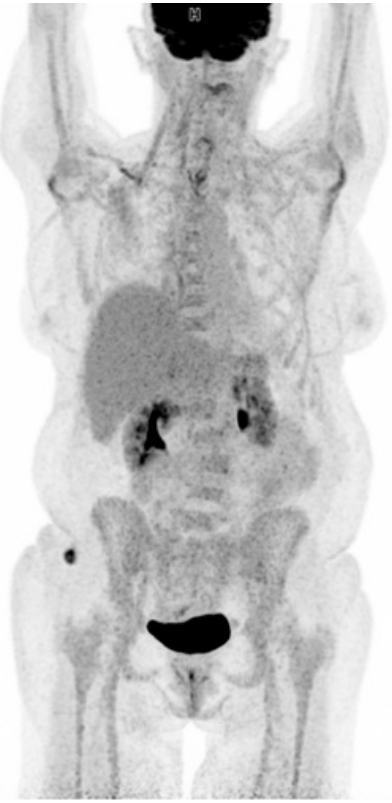
Patient case #1 – DLBCL (Richter transformation) treated with glofitamab

- 76 y.o. lady with > 20 years' history of CLL
- 5 prior treatment lines for CLL
- January 2020 Richter transformation
- 3 treatment lines for RT:
  - R-CHOP – no response
  - R-Benda – no response
  - R-GemOx – no response
- August 2020: Glofitamab
- CRS grade IV during C1 – 1 week in ICU
- CR after 2 cycles and after 5 cycles
- After 8 cycles, PET/CT showed PD
- Biopsy showed CD20-negative disease
- The patient died from progressive disease a few months later

Before treatment



After 2 cycles = CR

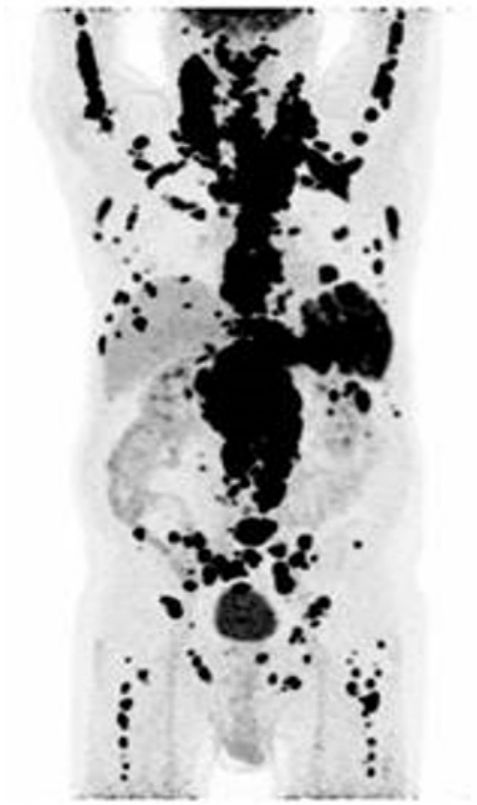


Courtesy of Martin Hutchings, MD, PhD

Patient case #2 – DLBCL (transformed FL) treated with glofitamab

- 69 y.o. man with a transformed FL
- 3 prior lines of treatment
- Refractory to the 2 most recent lines
- Begins glofitamab in late 2018
- CRS grade 1 during C1
- PR after 2 cycles and CR after 5 cycles
- Still in CR at the end of 12 cycles of glofitamab in June 2019
- Remained in CR for more than 2 years after last treatment
- Died from a chemotherapy-related MDS/AML in 2021

Before treatment

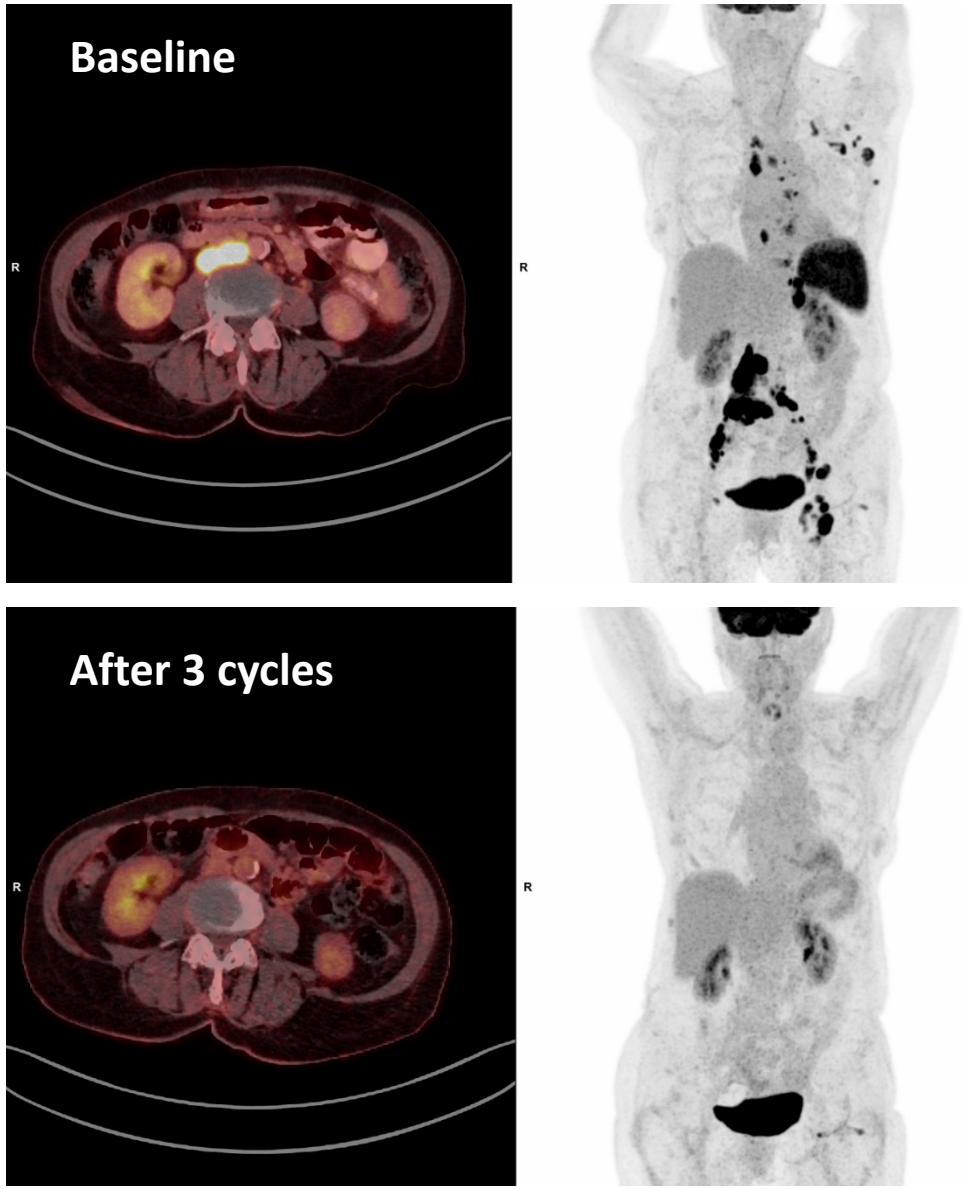


After 2 cycles = PR

Courtesy of Martin Hutchings, MD, PhD

Patient case #3 – ABC-subtype DLBCL treated with epcoritamab

- 81 y.o. lady with ABC-type DLBCL 2017
- 3 prior lines of treatment:
  - R-CHOP – CR
  - R-Gemcitabine – refractory
  - R-ICE - refractory
- Begins epcoritamab in October 2019
- ISR and CRS grade 1 after C1D15
- PR after 6 weeks
- CR after 12 weeks
- Still in CR
- A recent COVID infection is the first treatment-related AE since cycle 1



Courtesy of Martin Hutchings, MD, PhD

Agenda

Module 1: Follicular Lymphoma

Module 2: Diffuse Large B-Cell Lymphoma

- **Select Key Questions**
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Based on your personal clinical experience and knowledge of available data, do you believe 1 or more CD20 x CD3 bispecific antibodies are more efficacious than others when used in the management of DLBCL?

 Prof Hutchings	Yes, epcoritamab and glofitamab appear most potent
 Dr Nastoupil	No
 Dr Abramson	Yes, glofitamab, epcoritmab and odronextamab appear more efficacious
 Dr Kahl	Yes, epcoritamab and glofitamab appear more efficacious
 Dr Matasar	Yes, glofitamab, epcoritmab and odronextamab appear more efficacious
 Dr Phillips	Yes, epcoritamab and glofitamab appear more efficacious

RTP RESEARCH TO PRACTICE

Based on your personal clinical experience and knowledge of available data, how would you compare the global efficacy and tolerability of CD20 x CD3 bispecific antibodies to those of CAR T-cell therapy for patients with DLBCL?

	Efficacy	Tolerability
 Prof Hutchings	About the same	Bispecific antibodies are more tolerable than CAR T-cell therapy
 Dr Nastoupil	Bispecific antibodies are less efficacious than CAR T-cell therapy	Bispecific antibodies are more tolerable than CAR T-cell therapy
 Dr Abramson	Bispecific antibodies are less efficacious than CAR T-cell therapy	Bispecific antibodies are more tolerable than CAR T-cell therapy
 Dr Kahl	Bispecific antibodies are less efficacious than CAR T-cell therapy	Bispecific antibodies are more tolerable than CAR T-cell therapy
 Dr Matasar	Bispecific antibodies are less efficacious than CAR T-cell therapy	Bispecific antibodies are more tolerable than CAR T-cell therapy
 Dr Phillips	Bispecific antibodies are less efficacious than CAR T-cell therapy	Bispecific antibodies are more tolerable than CAR T-cell therapy

Regulatory and reimbursement issues aside, at what point would you like to use a bispecific CD20 x CD3 antibody for a patient with Stage IV DLBCL?

 Prof Hutchings	Second line and beyond
 Dr Nastoupil	Third line
 Dr Abramson	Third line
 Dr Kahl	Third line
 Dr Matasar	First line
 Dr Phillips	Third line

Regulatory and reimbursement issues aside, would you like to use a CD20 x CD3 bispecific antibody, CAR T-cell therapy or autologous stem cell transplant first for a patient with Stage IV DLBCL and no significant comorbidities who experienced disease progression on first-line R-CHOP?

 Prof Hutchings	CAR T-cell therapy
 Dr Nastoupil	CAR T-cell therapy
 Dr Abramson	CAR T-cell therapy
 Dr Kahl	CAR T-cell therapy
 Dr Matasar	CAR T-cell therapy
 Dr Phillips	CAR T-cell therapy

RTP RESEARCH TO PRACTICE

Which first-line therapy would you generally recommend for a 60-year-old patient with no significant comorbidities and Stage IV DLBCL that was …

	ABC type	GCB type
 Prof Hutchings	R-CHOP or R-CHOEP; R-CHP + polatuzumab vedotin if reimbursed	R-CHOP or R-CHOEP; R-CHP + polatuzumab vedotin if reimbursed
 Dr Nastoupil	R-CHP + polatuzumab vedotin	R-CHOP
 Dr Abramson	R-CHP + polatuzumab vedotin	R-CHOP
 Dr Kahl	R-CHP + polatuzumab vedotin	R-CHOP
 Dr Matasar	R-CHP + polatuzumab vedotin or R-CHOP/bortezomib	R-CHOP or R-CHP + polatuzumab vedotin depending on IPI
 Dr Phillips	R-CHP + polatuzumab vedotin	R-CHOP

ABC = activated B cell; GCB = germinal center B cell; R-CHOEP = etoposide with R-CHOP

Which second-line therapy would you generally recommend for a 60-year-old patient with Stage IV DLBCL and no significant comorbidities who experienced disease relapse 18 months after starting treatment with first-line R-CHOP?

 Prof Hutchings	Axicabtogene ciloleucel or lisocabtagene maraleucel
 Dr Nastoupil	RICE
 Dr Abramson	RICE and ASCT if chemosensitive
 Dr Kahl	Lisocabtagene maraleucel
 Dr Matasar	RICE or RDHAX towards autotransplant
 Dr Phillips	RICE

RICE = rituximab/ifosfamide/carboplatin/etoposide; ASCT = autologous stem cell transplant;
RDHAX = rituximab/dexamethasone/cytarabine/oxaliplatin

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which third-line therapy would you recommend for a 60-year-old patient with Stage IV DLBCL and no significant comorbidities who received first-line R-CHOP and subsequently experienced disease progression on second-line R-DHAP?

 Prof Hutchings	Axicabtagene ciloleucel or lisocabtagene maraleucel
 Dr Nastoupil	Axicabtagene ciloleucel
 Dr Abramson	Axicabtagene ciloleucel
 Dr Kahl	Axicabtagene ciloleucel
 Dr Matasar	Lisocabtagene maraleucel
 Dr Phillips	Lisocabtagene maraleucel

R-DHAP = rituximab with dexamethasone/ara-C/cisplatin

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Which first-line therapy would you generally recommend for an 80-year-old patient with significant comorbidities, including hypertension, chronic renal failure and Type 2 DM, and Stage IV DLBCL that was …?

	ABC type	GCB type
 Prof Hutchings	R-mini-CHOP	R-mini-CHOP
 Dr Nastoupil	R-mini-CHOP	R-mini-CHOP
 Dr Abramson	R-CHP + polatuzumab vedotin	R-CHOP
 Dr Kahl	R-mini-CHOP	R-mini-CHOP
 Dr Matasar	R-mini-CHOP	R-mini-CHOP
 Dr Phillips	R-mini-CHOP	R-mini-CHOP

ABC = activated B cell; GCB = germinal center B cell; R-mini-CHOP = rituximab with low-dose CHOP

Which second-line therapy would you generally recommend for an 80-year-old patient with Stage IV DLBCL and significant comorbidities including hypertension, chronic renal failure and Type 2 DM who experienced disease progression 18 months after receiving R-mini-CHOP?

 Prof Hutchings	Polatuzumab vedotin/BR or tafasitamab/lenalidomide
 Dr Nastoupil	Lisocabtagene maraleucel
 Dr Abramson	Tafasitamab/lenalidomide
 Dr Kahl	Tafasitamab/lenalidomide
 Dr Matasar	Tafasitamab/lenalidomide
 Dr Phillips	Tafasitamab/lenalidomide

R-mini-CHOP = rituximab with low-dose CHOP

RTP RESEARCH TO PRACTICE

Which third-line therapy would you generally recommend for an 80-year-old patient with Stage IV DLBCL and significant comorbidities including hypertension, chronic renal failure and Type 2 DM who received first-line R-mini-CHOP and second-line polatuzumab vedotin/BR?

 Prof Hutchings	Epcoritamab or glofitamab
 Dr Nastoupil	Lisocabtagene maraleucel
 Dr Abramson	Lisocabtagene maraleucel
 Dr Kahl	Glofitamab
 Dr Matasar	Glofitamab
 Dr Phillips	Lisocabtagene maraleucel

R-mini-CHOP = rituximab with low-dose CHOP

RTP RESEARCH TO PRACTICE

Inside the Issue: Optimizing the Management of Metastatic Pancreatic Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, August 8, 2023
5:00 PM – 6:00 PM ET

Faculty

Eileen M O'Reilly, MD
Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open up to 5 minutes after the meeting ends.

CME and MOC credit information will be emailed to each participant within 5 business days.

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