Meet The Professor Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

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Chair, Professor
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The University of Texas
MD Anderson Cancer Center
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Commercial Support

This activity is supported by educational grants from ADC Therapeutics, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Genentech, a member of the Roche Group, Novartis and Seagen Inc.



Dr Love — Disclosures

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



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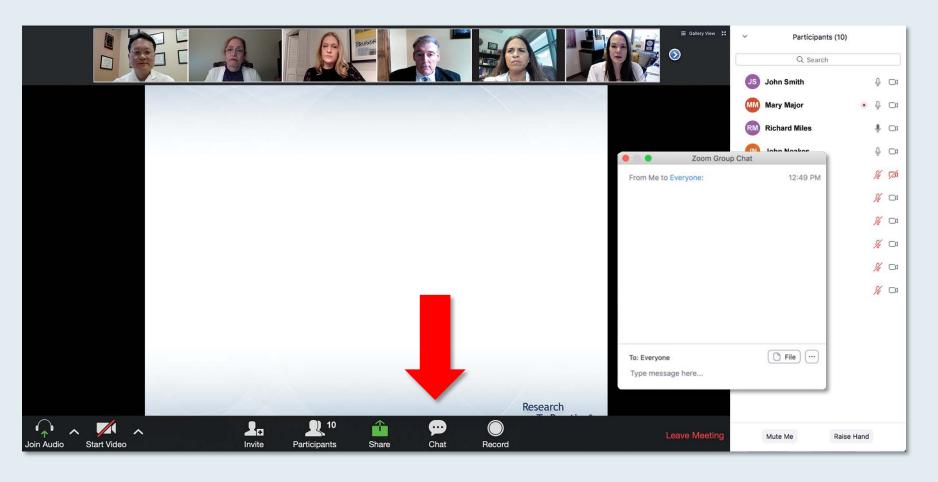


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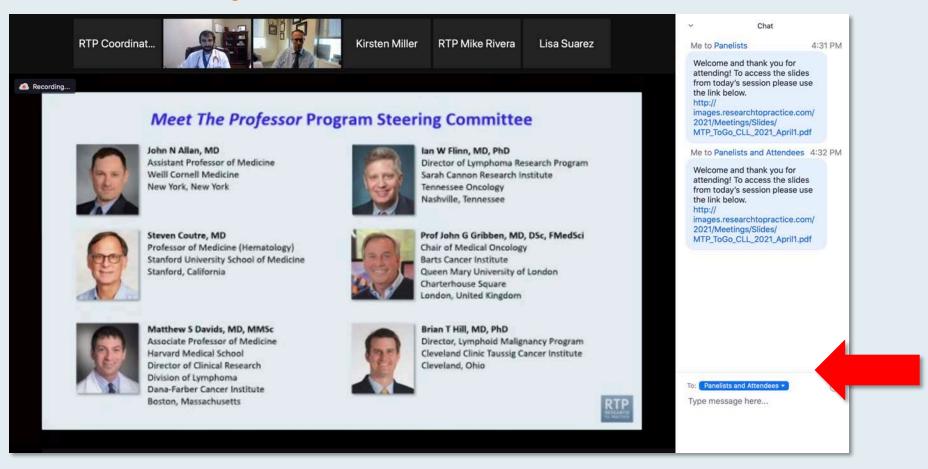


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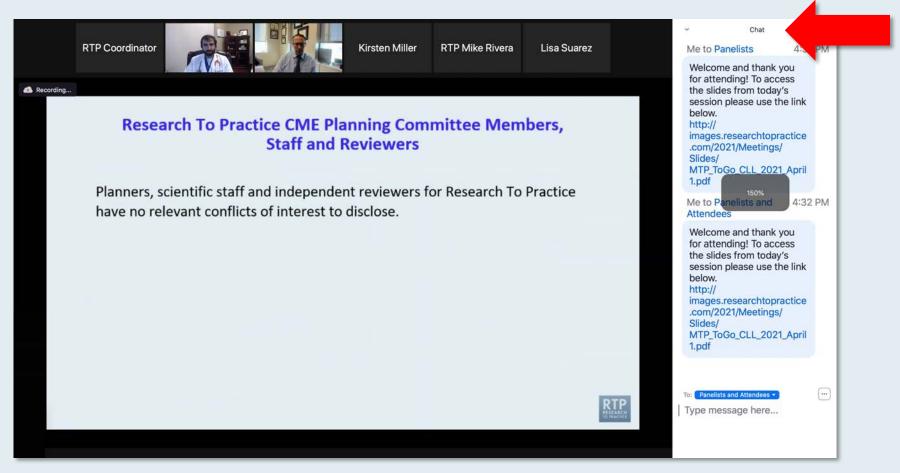


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WITH DR NEIL LOVE

CAR T-Cell Therapy in Non-Hodgkin Lymphoma



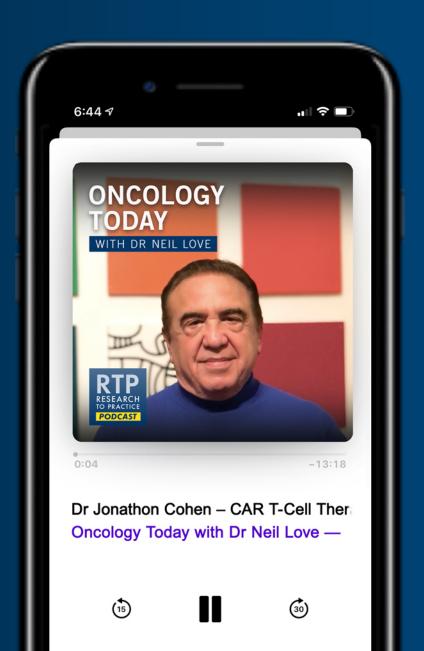
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Optimizing the Selection and Sequencing of Therapy for Patients with ER-Positive Breast Cancer

Wednesday, November 17, 2021 5:00 PM - 6:00 PM ET

Faculty
Kevin Kalinsky, MD, MS



Current and Future Role of Immunotherapy in the Management of Lung Cancer

Thursday, November 18, 2021 5:00 PM - 6:00 PM ET

Faculty
Stephen V Liu, MD



Meet The ProfessorManagement of BRAF-Mutant Melanoma

Monday, November 29, 2021 5:00 PM - 6:00 PM ET

Faculty
Jason J Luke, MD



Optimizing the Management of Metastatic Castration-Resistant Prostate Cancer

Tuesday, November 30, 2021 5:00 PM - 6:00 PM ET

Faculty
A Oliver Sartor, MD



Meet The ProfessorOptimizing the Management of Acute Myeloid Leukemia

Wednesday, December 1, 2021 5:00 PM – 6:00 PM ET

Faculty
Andrew H Wei, MBBS, PhD



Optimizing the Selection and Sequencing of Therapy for Patients with HER2-Positive Breast Cancer

Thursday, December 2, 2021 5:00 PM - 6:00 PM ET

Faculty
Hope S Rugo, MD



Thank you for joining us!

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



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Meet The Professor Program Participating Faculty



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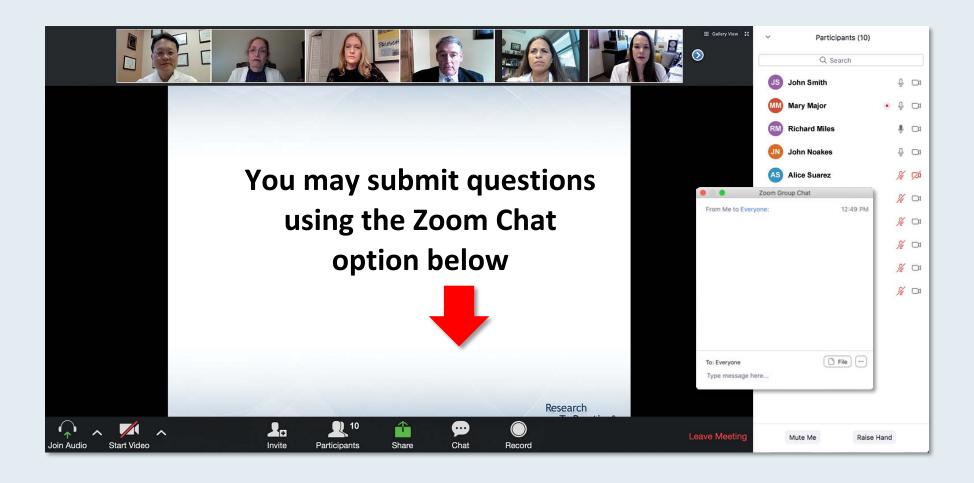
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Moderator
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Mamta Choksi, MD Florida Cancer Specialists and Research Institute New Port Richey, Florida



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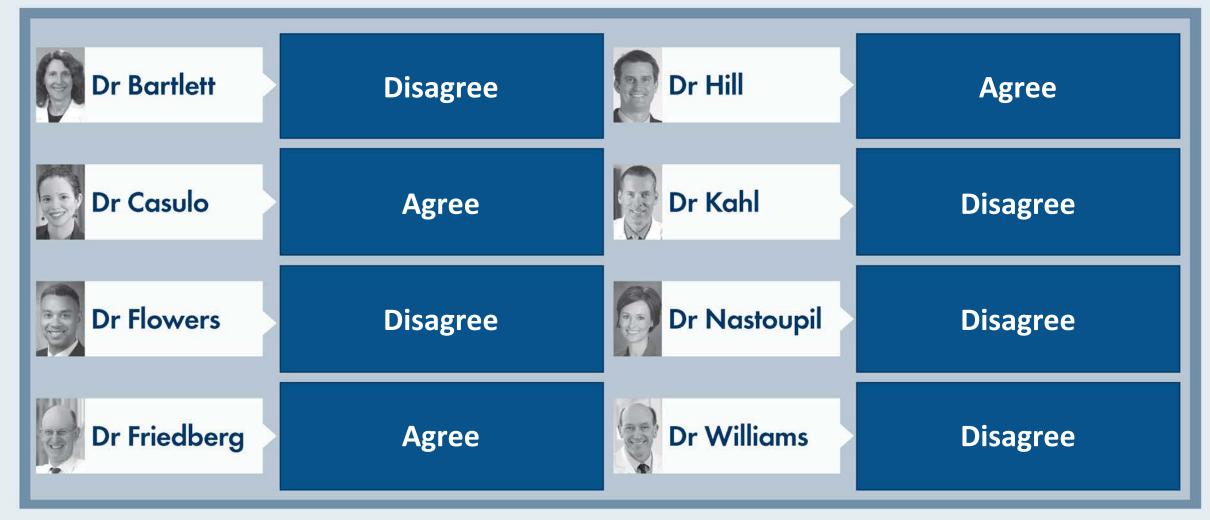
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Syed F Zafar, MD
Florida Cancer Specialists and
Research Institute
Lee Health
Fort Myers, Florida



A patient should be in adequate physical condition to undergo autologous stem cell transplant in order to be a suitable candidate for CAR T-cell therapy.





Meet The Professor with Dr Flowers

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MODULE 2: Case Presentations

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- Dr Smith: An 81-year-old man with chronic lymphocytic leukemia (CLL) and Hodgkin lymphoma
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- Dr Choksi: A 75-year-old woman with relapsed DLBCL
- Dr Zafar: An 80-year-old woman with relapsed/refractory follicular lymphoma and an EZH2 mutation
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ASH 2021 Lymphomas Preview

- POLARIX: A phase 3 study of polatuzumab vedotin plus R-CHP versus R-CHOP in patients with untreated DLBCL. ASH 2021;Late-breaking abstract.
- Locke FL et al. Primary analysis of ZUMA-7: A Phase 3 randomized trial of axicabtagene ciloleucel
 (Axi-Cel) versus standard-of-care therapy in patients with relapsed/refractory large B-cell
 lymphoma. ASH 2021; Abstract 2.
- Kamdar M et al. Lisocabtagene maraleucel (liso-cel), a CD19-directed chimeric antigen receptor (CAR) T cell therapy, versus standard of care (SOC) with salvage chemotherapy (CT) followed by autologous stem cell transplantation (ASCT) as second-line (2L) treatment in patients (pts) with relapsed or refractory (R/R) large b-cell lymphoma (LBCL): Results from the randomized phase 3 TRANSFORM study. ASH 2021; Abstract 91.



Trial-in-Progress: Randomized Phase II Trial in Early Relapsing or Refractory Follicular Lymphoma (NCT#03269669): SWOG S1608

Barr PM et al.

ASH 2021; Abstract 2425.



Ibrutinib with Rituximab and Venetoclax (IRV)
Followed By Risk-Stratified Observation or Short
Course R-Hypercvad/MTX for Young Patients with
Previously Untreated Mantle Cell Lymphoma –
Phase-II Window-2 Clinical Trial

Wang M et al.

ASH 2021; Abstract 3525.





Blood 2021 Jun 10;137(23):3272-6

Brief Report

LYMPHOID NEOPLASIA

Prognostic impact of corticosteroids on efficacy of chimeric antigen receptor T-cell therapy in large B-cell lymphoma

Paolo Strati,^{1,*} Sairah Ahmed,^{1,*} Fateeha Furqan,¹ Luis E. Fayad,¹ Hun J. Lee,¹ Swaminathan P. Iyer,¹ Ranjit Nair,¹ Loretta J. Nastoupil,¹ Simrit Parmar,¹ Maria A. Rodriguez,¹ Felipe Samaniego,¹ Raphael E. Steiner,¹ Michael Wang,¹ Chelsea C. Pinnix,² Sandra B. Horowitz,³ Lei Feng,⁴ Ryan Sun,⁴ Catherine M. Claussen,¹ Misha C. Hawkins,¹ Nicole A. Johnson,¹ Prachee Singh,¹ Haleigh Mistry,¹ Swapna Johncy,¹ Sherry Adkins,¹ Partow Kebriaei,⁵ Elizabeth J. Shpall,⁵ Michael R. Green,^{1,6} Christopher R. Flowers,¹ Jason Westin,^{1,†} and Sattva S. Neelapu^{1,†}



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Case Presentation – Dr Gupta: A 79-year-old man with relapsed mantle cell lymphoma



Dr Ranju Gupta

- 2019: Presented with lymphocytosis and mild symptoms; diagnosed with MCL
- Bendamustine/rituximab x 4, with excellent response, but relapse 3 months later
- Radiation therapy to purplish subcutaneous nodules on both legs, with rapid PD
- Ibrutinib, with no response and rapid PD
- Brexucabtagene autoleucel CAR T-cell therapy, with VGPR, but new subcutaneous nodules on left arm
- Radiation therapy
- Obinutuzumab/venetoclax

Question

• What would you do next?



Case Presentation – Dr Smith: An 81-year-old man with CLL and Hodgkin lymphoma



Dr Mitchell Smith

- CLL, IgVH mutated, del13q, under observation for several years
- Developed progressive symptomatic anemia (Hgb: 9), with minimal adenopathy, no WBC changes
- Bone marrow aspirate/biopsy: CLL, but with infiltrate c/w Hodgkin lymphoma
 - EBER-positive Reed-Sternberg cells, circulating EBV DNA in the blood

Questions

- Could this be a Hodgkin-like Richter's syndrome?
- Could this be an EBV-positive lymphoproliferative disorder, and if so, how would you treat EBV-positive proliferations in immunosuppressed patients with CLL?
- What is your approach to treatment for elderly patients with Hodgkin lymphoma, whether it's in the setting of Richter's syndrome or not?



Case Presentation – Dr Shameem: A 71-year-old woman with DLBCL

- PMH: HTN, GERD
- Presents to PCP with right neck swelling
- PET/CT: Right neck adenopathy, lymph nodes above/below diaphragm
- Biopsy: DLBCL, germinal center subtype; FISH: MYC-, BCL2- and BCL6-negative
- Echocardiogram: Normal ejection fraction

Questions

- In elderly patients with DLBCL, do you administer R-mini-CHOP more frequently than R-CHOP?
- What are your thoughts about tafasitamab/lenalidomide if her disease progresses on front-line treatment?
- For elderly patients with "double-hit" DLBCL, how would you approach treatment?



Dr Raji Shameem



Case Presentation – Dr Choksi: A 75-year-old woman with relapsed DLBCL



Dr Mamta Choksi

- 4/2019: Presents with B-symptoms
- 5/2019 CT/PET: Right hilar LAD, bilateral pulmonary nodules, large splenic nodules, peripancreatic nodes
- Biopsy: DLBCL, non-germinal center, Ki67: 80%
- 6/2019: Dose-adjusted R-EPOCH x 1 but poorly tolerated, admitted to hospital and treated for mucositis, anemia and diarrhea
- Switched to R-CHOP x 5
- 11/2019 Re-staging: Decrease in size at sites of disease
- 2/2020 Re-staging: Increase in size at sites of disease, PS ~1.5
- Lenalidomide/rituximab → maintenance lenalidomide, with stable disease 7/2021

Question

• Among the newer treatment options, such as polatuzumab vedotin, loncastuximab and CAR T-cell therapy, which do you prefer and how do you sequence them?



Case Presentation – Dr Zafar: An 80-year-old woman with relapsed/refractory follicular lymphoma and an EZH2 mutation



Dr Syed Zafar

- PMH: Parkinson's disease
- 2015: Grade 3 follicular lymphoma \rightarrow rituximab \rightarrow maintenance rituximab
- 3/2019: Recurrence, with LAD above/below the diaphragm, B symptoms, non-bulky
- Ibritumomab, with radiographic CR
- 2/2020: Recurrence, with inguinal, cervical and pelvic lymph nodes; positive bone sites; symptoms
- NGS: EZH2 mutation
- Tazemetostat
- 10/2021: New cytopenias and B symptoms

Questions

- What would you do next if she has progressive disease PI3K inhibitor, lenalidomide or other options, even CAR T-cell therapy?
- Would you have used something different from tazemetostat?



Case Presentation – Dr Gandhi: A 54-year-old man with Grade 2 follicular lymphoma

- Presents to ER with severe abdominal pain, marked LAD
 - Biopsy: Grade 2, FLIPI 2, follicular lymphoma
 - Liver metastases confirmed on biopsy
- 8/2019: R-CHOP x 6, with CR → weekly maintenance rituximab x 4 every 6 months

Question

What would you recommend next for this patient?



Dr Sunil Gandhi



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ASH 2021 Lymphomas Preview

- Bachy E et al. A propensity score-matched comparison of axi-cel and tisa-cel for relapsed/refractory diffuse large B-cell lymphoma in real-life: A lysa study from the descar-T registry. ASH 2021; Abstract 92.
- Carter J et al. A large multicenter real-world evidence (RWE) analysis of autoimmune (AI)
 diseases and lymphoma: Histologic associations, disease characteristics, survival, and
 prognostication. ASH 2021; Abstract 50.
- Di Ciaccio PR et al. Lymphoma during pregnancy: A multicentre study by the australasian lymphoma alliance. ASH 2021;Abstract 882.
- Budde LE et al. Mosunetuzumab monotherapy is an effective and well-tolerated treatment
 option for patients with relapsed/refractory (R/R) follicular lymphoma (FL) who have received ≥2
 prior lines of therapy: Pivotal results from a Phase I/II study. ASH 2021; Abstract 127.
- Herrera AF et al. Brentuximab vedotin plus cyclophosphamide, doxorubicin, etoposide, and prednisone (CHEP-BV) followed by BV consolidation in patients with CD30-expressing peripheral T-cell lymphomas. ASH 2021;Abstract 133.

ASH 2021 Lymphomas Preview (continued)

- Tomas AA et al. Novel agents may be preferable to chemotherapy for large B-cell lymphoma progressing after CD19-CAR-T: A multicenter observational study. ASH 2021; Abstract 883.
- Horwitz SM et al. The Echelon-2 trial: 5-year exploratory subgroup analyses of a randomized, double-blind, phase 3 study of brentuximab vedotin and CHP (A+CHP) vs CHOP in frontline treatment of pts with CD30-positive peripheral t-cell lymphoma. ASH 2021; Abstract 135.
- Kahl BS et al. Long term follow up of the resort study (E4402): A randomized phase III study comparing two different rituximab dosing strategies for low tumor burden follicular lymphoma. ASH 2021;Abstract 815.
- Ribrag V et al. Rituximab-lenalidomide (R²) maintenance is superior to rituximab maintenance after first line immunochemotherapy in mantle cell lymphoma: Results of the mcl R² elderly clinical trial. ASH 2021;Abstract 379.
- Wang M et al. Pirtobrutinib, a next generation, highly selective, non-covalent BTK inhibitor in previously treated mantle cell lymphoma: Updated results from the Phase 1/2 BRUIN study. ASH 2021; Abstract 381.



ASH 2021 Lymphomas Preview (continued)

- Bryan LJ et al. Pembrolizumab (PEM) added to ICE chemotherapy results in high complete metabolic response rates in relapsed/refractory classic hodgkin lymphoma (cHL): A multi-institutional Phase II trial. ASH 2021; Abstract 229.
- Lazarovici J et al. Nivolumab first-line therapy for elderly, frail hodgkin lymphoma patients: niviniho, a lysa Phase II study. ASH 2021; Abstract 232.



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Journal Club with Dr Flowers – Part 2

- Dance KV et al. Perceptions of clinical care and research among African-American patients with lymphoma. Leuk Lymphoma 2021;62(8):1860-8.
- Flowers C. Highlighting the disparities in hematologic malignancies: An epidemiologic perspective. Education Session. ASCO 2021.
- Smith-Graziani D, Flowers CR. Understanding and addressing disparities in patients with hematologic malignancies: Approaches for clinicians. Am Soc Clin Oncol Educ Book 2021;41:1-7.
- Goldman ML et al. Surveillance imaging during first remission in follicular lymphoma does not impact overall survival. Cancer 2021;127(18):3390-402.
- Payne JB et al. Supporting decision-making on fertility preservation among adolescent and young adult women with cancer. Oncology (Williston Park) 2020;34(11):494-9.



Journal Club with Dr Flowers (continued)

- Steiner RE et al. Pacific: A phase II study of brentuximab vedotin and nivolumab alone and then combined with rituximab, cyclophosphamide, doxorubicin and prednisone for patients with untreated primary mediastinal large b-cell lymphoma.
 ASH 2021; Abstract 1408.
- Zhang S et al. Longitudinal single-cell profiling reveals molecular heterogeneity and tumor-immune evolution in refractory mantle cell lymphoma. Nat Commun 2021;12(1):1-17.



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Diffuse Large B-Cell Lymphoma



Which third- and fourth-line therapy would you generally recommend first for a 65-year-old patient with DLBCL who responds to R-CHOP and then R-DHAP followed by transplant on relapse but subsequently develops disease progression?



Dr Bartlett





Dr Hill

CAR T-cell therapy → tafasitamab/ lenalidomide



Dr Casulo





Dr Kahl

CAR T-cell therapy → tafasitamab/ lenalidomide



Dr Flowers





Dr Nastoupil

CAR T-cell therapy → polatuzumab vedotin/BR



Dr Friedberg

CAR T-cell therapy →
polatuzumab
vedotin/BR



Dr Williams

CAR T-cell therapy → tafasitamab/ lenalidomide



Which third- and fourth-line therapy would you generally recommend first for an 80-year-old patient with DLBCL who experiences disease progression on front-line R-CHOP and is not eligible for high-dose therapy?



Dr Bartlett

Loncastuximab tesirine

→ tafasitamab/
lenalidomide



Dr Hill

Tafasitamab/
lenalidomide →
loncastuximab tesirine



Dr Casulo

Polatuzumab vedotin/BR → tafasitamab/lenalidomide

CAR T-cell therapy →

tafasitamab/

lenalidomide



Dr Kahl

Tafasitamab/
lenalidomide →
loncastuximab tesirine



Dr Flowers

Dr Nastoupil

CAR T-cell therapy →
polatuzumab
vedotin/BR



Dr Friedberg

Tafasitamab/
lenalidomide →
loncastuximab tesirine



Dr Williams

Tafasitamab/
lenalidomide →
loncastuximab tesirine

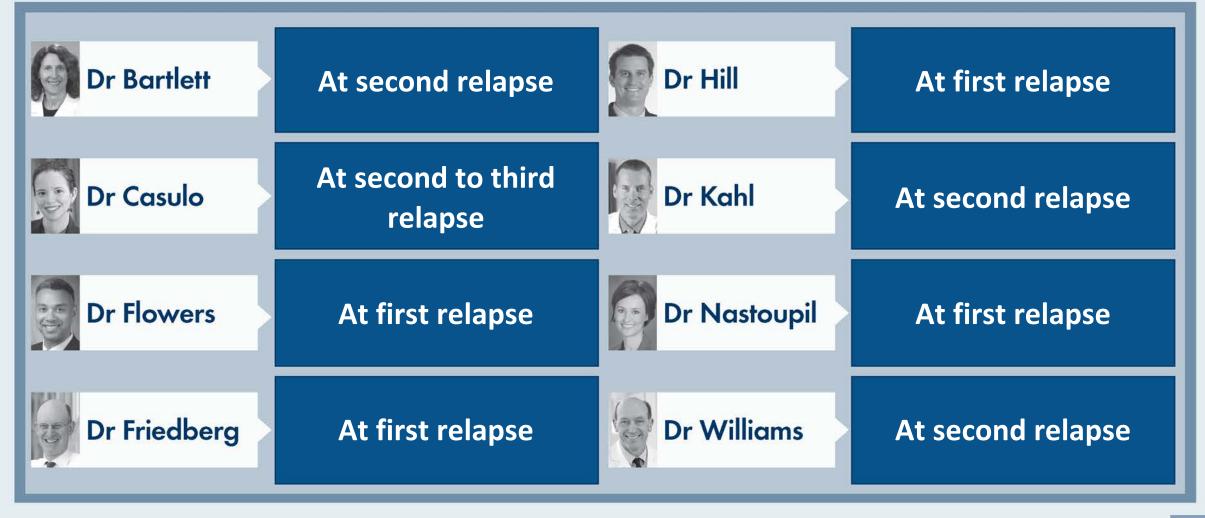


Do you generally use either tafasitamab/lenalidomide or loncastuximab tesirine in a patient who has experienced disease progression on or after CD19-directed CAR T-cell therapy?



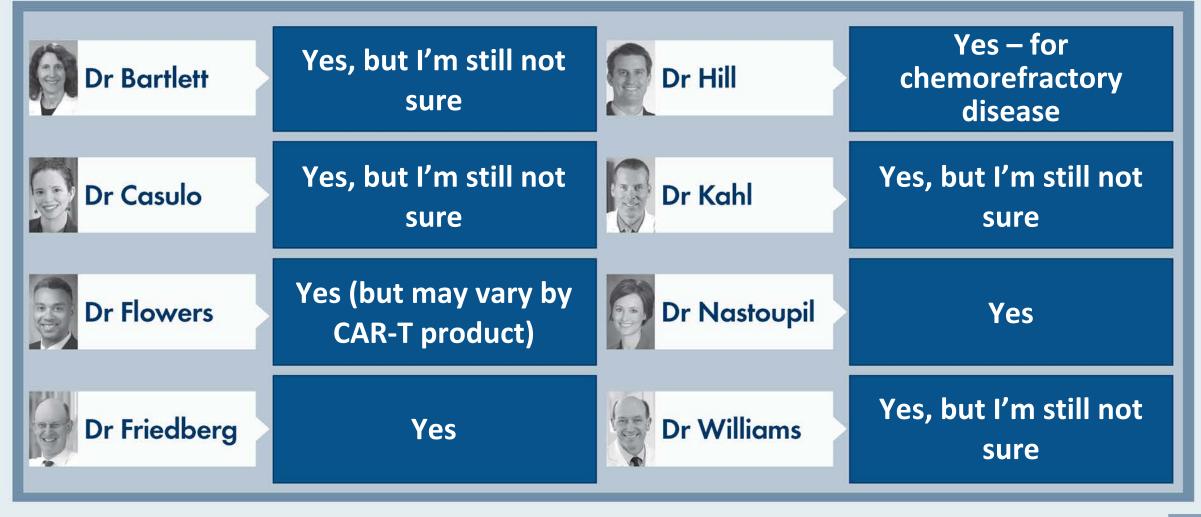


At what point in the treatment course are you referring patients with DLBCL for consultation regarding CAR T-cell therapy?



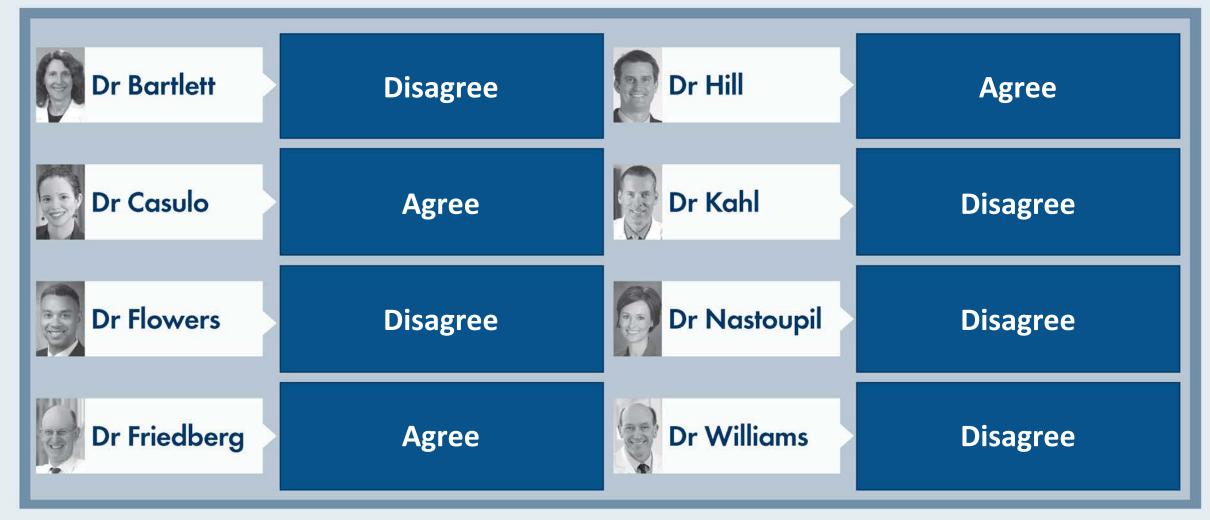


Do you believe that CAR T-cell therapy is more <u>efficacious</u> than autologous stem cell transplantation for DLBCL as second-line treatment after R-CHOP?





A patient should be in adequate physical condition to undergo autologous stem cell transplant in order to be a suitable candidate for CAR T-cell therapy.





Do you believe that CAR T-cell therapy is more <u>tolerable</u> for most patients than autologous stem cell transplantation?

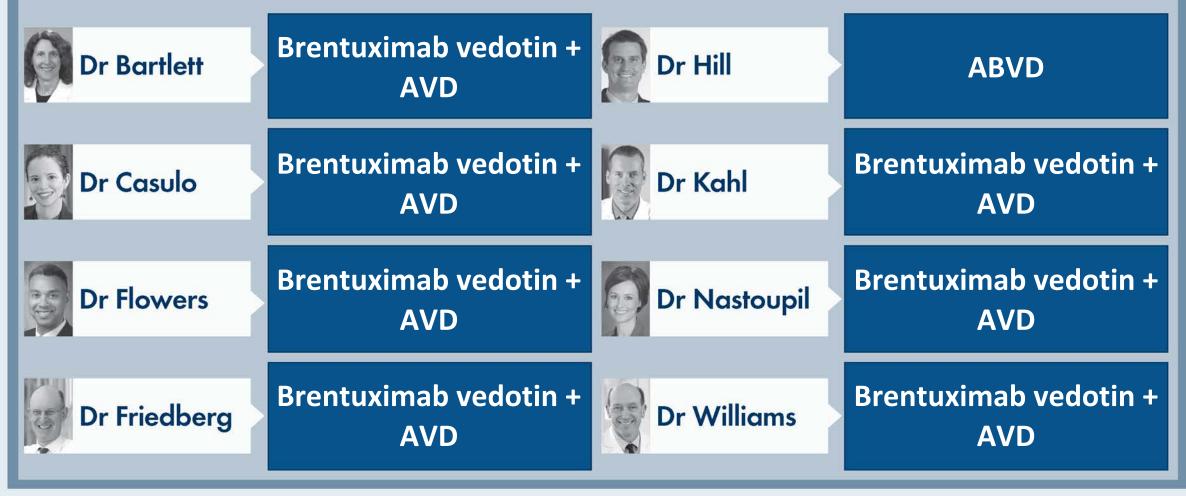




Hodgkin Lymphoma

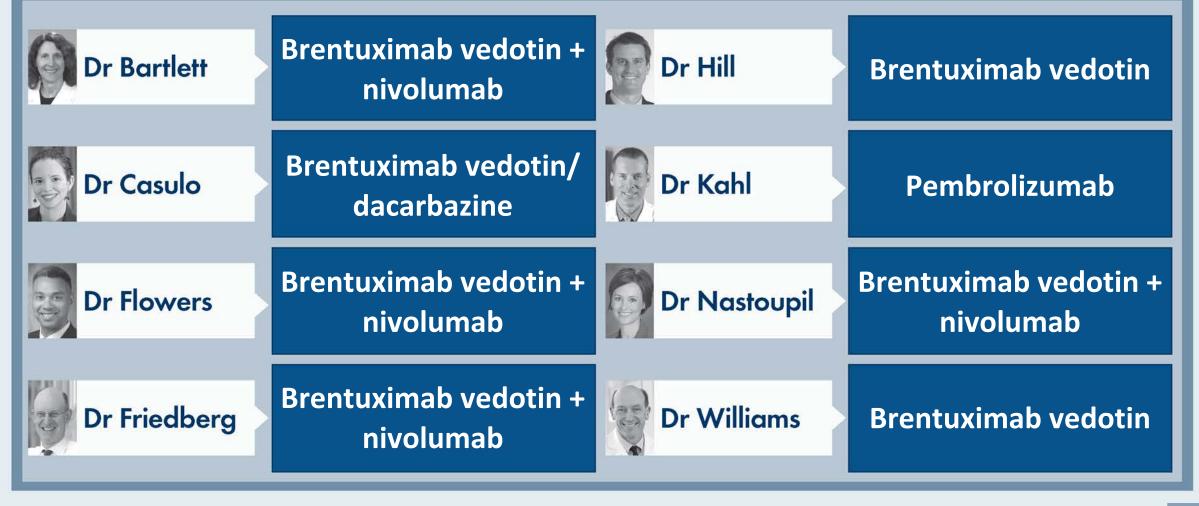


What initial treatment would you recommend for a 26-year-old patient with classical Hodgkin lymphoma (HL) with anemia, diffuse adenopathy, hepatosplenomegaly and diffuse bone marrow involvement?



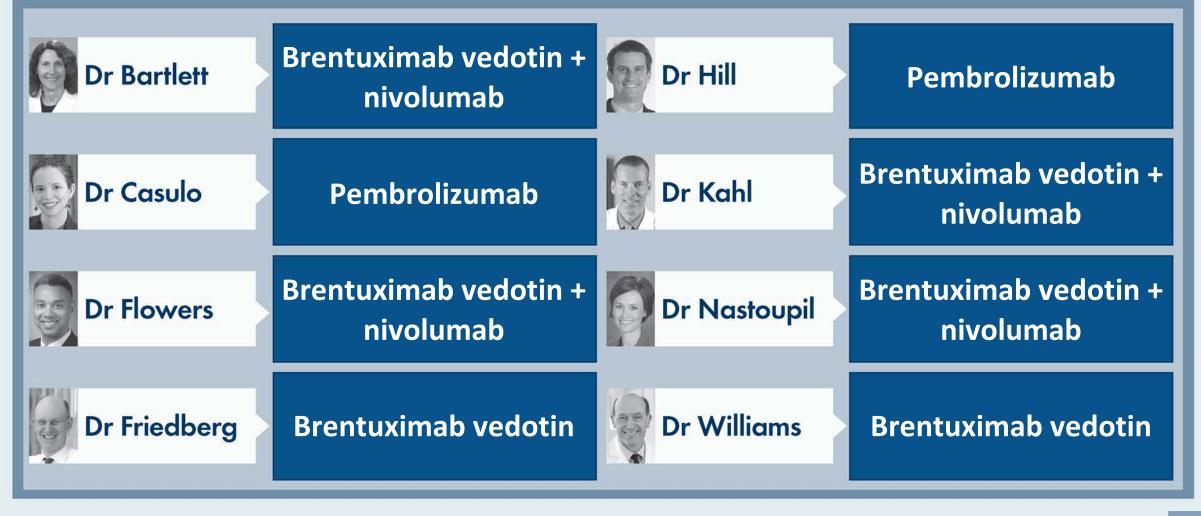


An 85-year-old frail patient with advanced-stage symptomatic HL is not a candidate for aggressive chemotherapy but is seeking active treatment. Regulatory and reimbursement issues aside, what would you recommend?



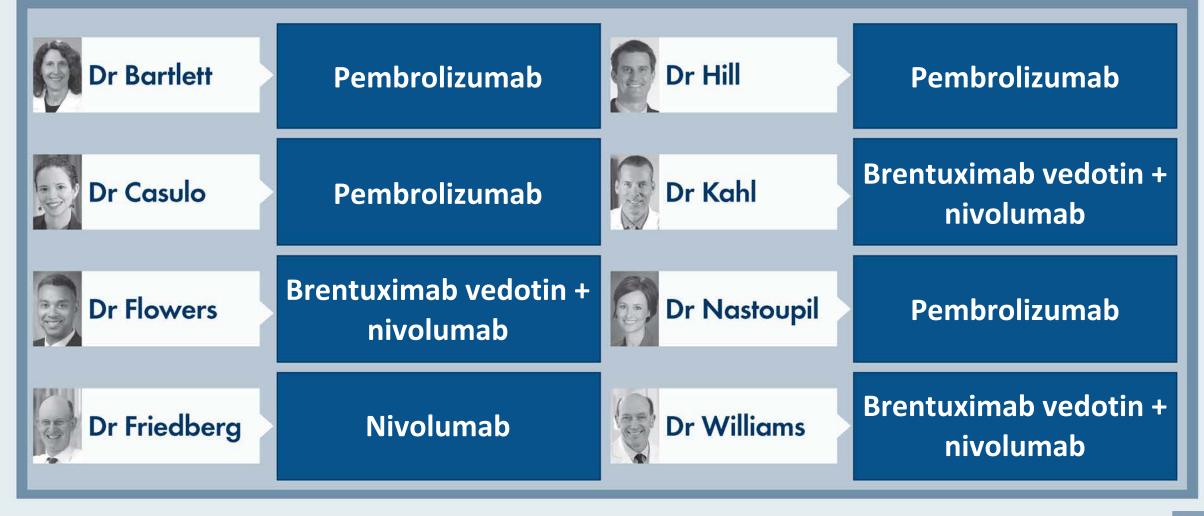


Regulatory and reimbursement issues aside, in general, what is your preferred second-line therapy for a patient with HL who is experiencing disease relapse after up-front ABVD and is not considered a candidate for transplant?





Regulatory and reimbursement issues aside, what is your preferred next line of therapy for a patient with HL who is experiencing disease relapse after ABVD and autologous stem cell transplant?





Have you administered or would you administer brentuximab vedotin in combination with an immune checkpoint inhibitor to a patient with HL outside of a clinical trial setting?





Follicular Lymphoma

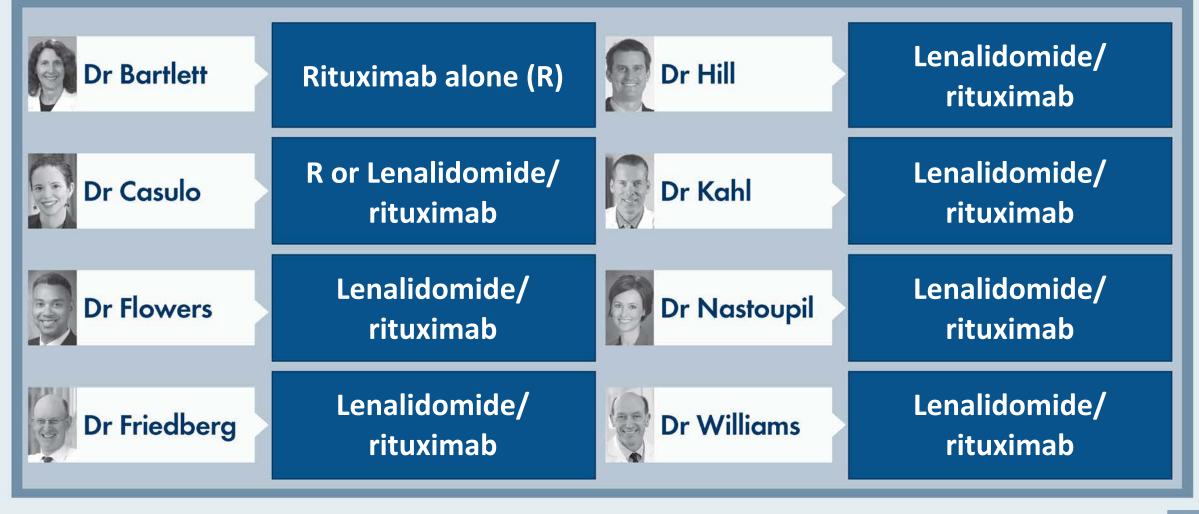


What treatment do you generally recommend for an <u>otherwise</u> <u>healthy 65-year-old</u> patient with symptomatic FL requiring treatment?

Dr Bartlett	Bendamustine/ rituximab (BR)	Dr Hill	BR
Dr Casulo	BR	Dr Kahl	BR
Dr Flowers	BR	Dr Nastoupil	BR
Dr Friedberg	BR	Dr Williams	BR

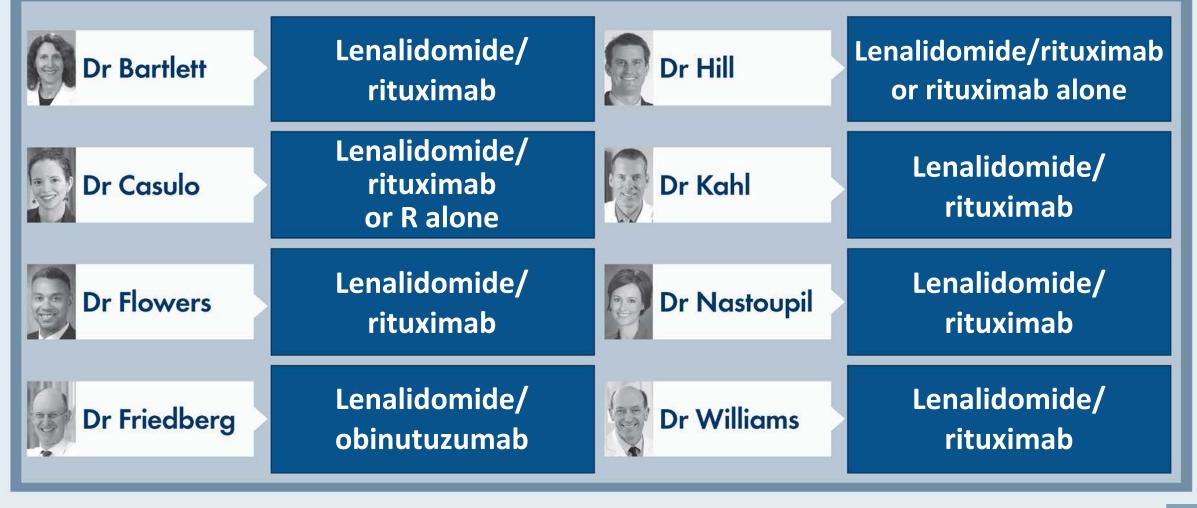


What treatment do you generally recommend for a patient with symptomatic FL requiring treatment who refuses to receive cytotoxic chemotherapy?



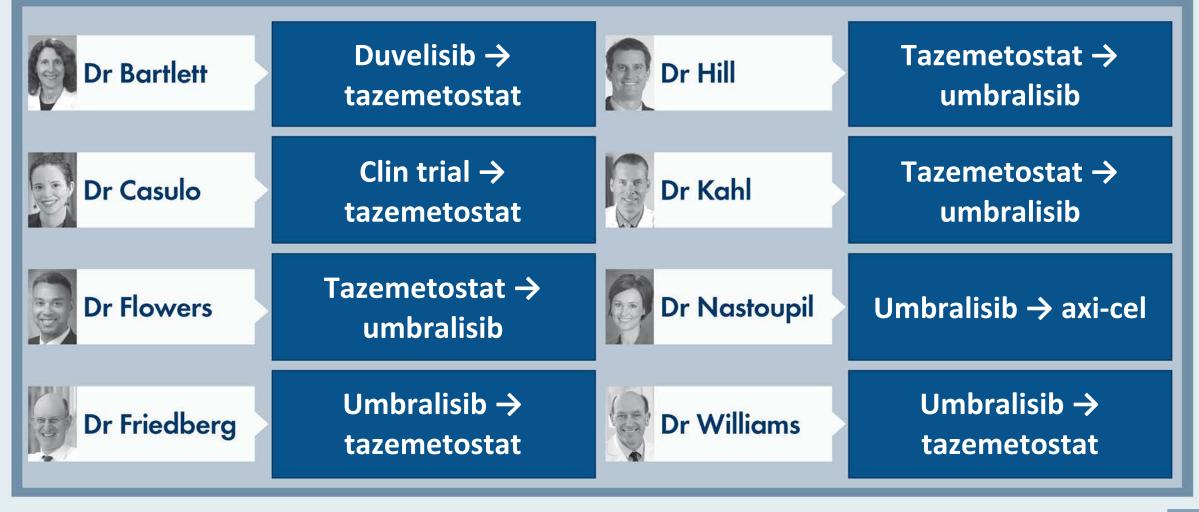


Regulatory and reimbursement issues aside, what is your usual second-line therapy for a 65-year-old patient with FL who achieves a complete response to 6 cycles of bendamustine/rituximab (BR) but then experiences disease <u>relapse 4 years later?</u>



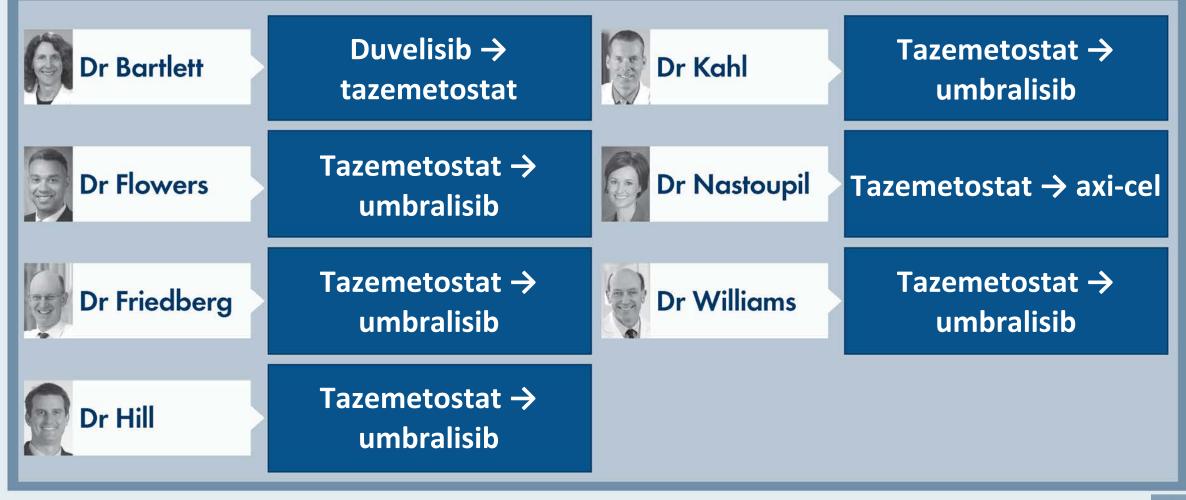


What is your usual third- and fourth-line treatment for a patient with FL (EZH2 wild type) who receives first-line BR, second-line lenalidomide/rituximab and then develops disease progression?



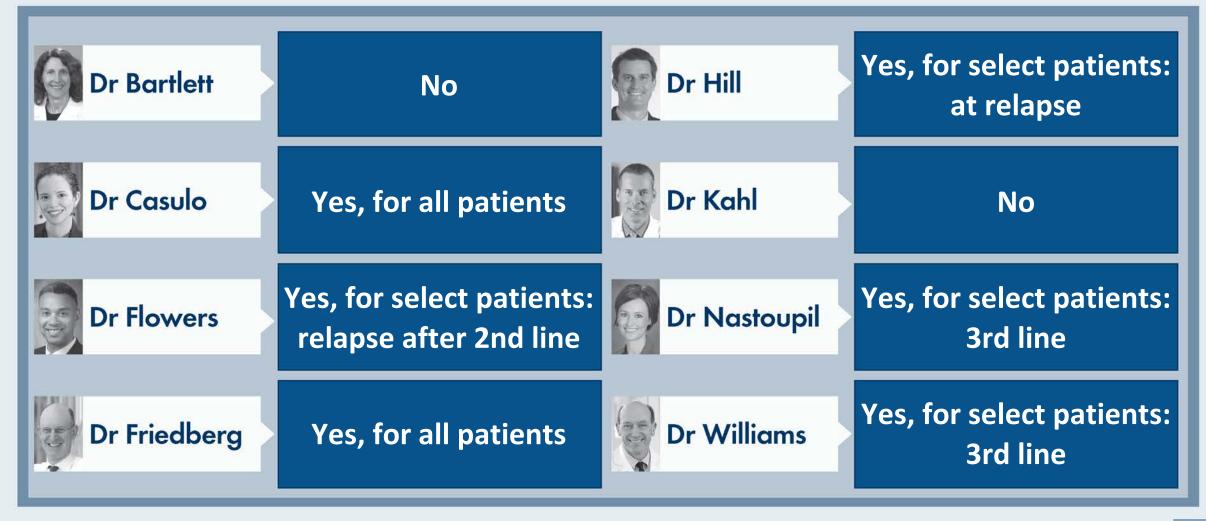


What is your usual third- and fourth-line treatment for a patient with FL with an EZH2 mutation who receives first-line BR, second-line lenalidomide/rituximab and then develops disease progression?



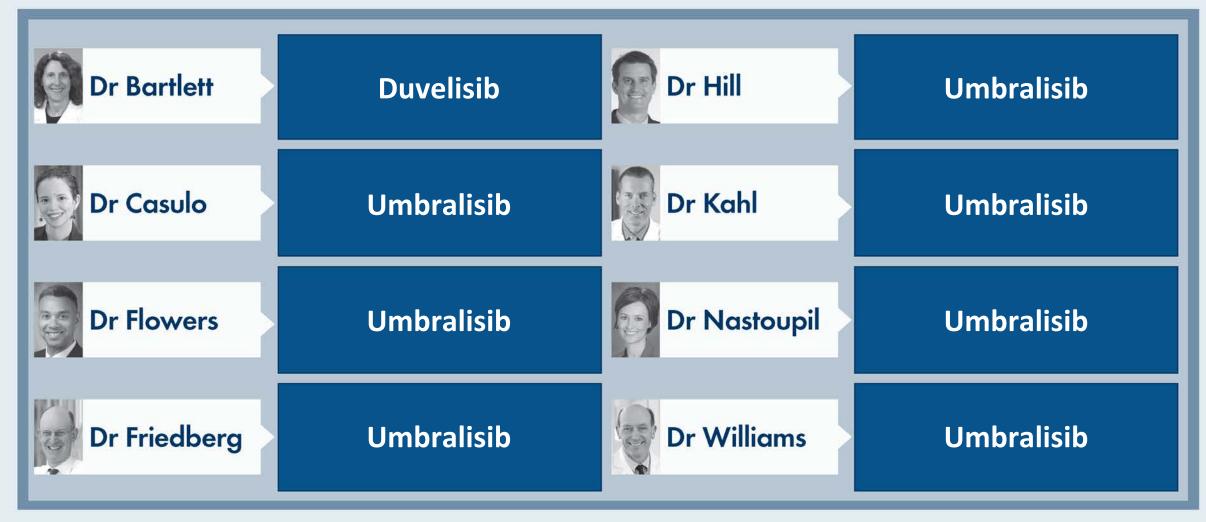


Are you typically assessing EZH2 mutation status for your patients with FL?





Which PI3K inhibitor do you use most commonly?



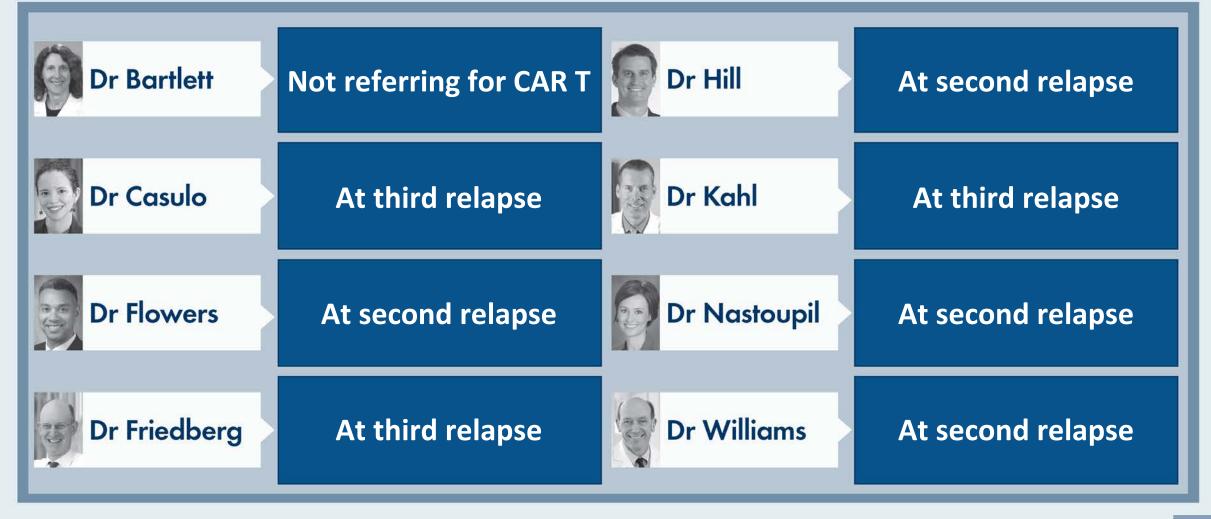


How would you generally sequence PI3K inhibitors and tazemetostat for a patient with relapsed FL who is eligible to receive both?





At what point in the treatment course are you referring patients with FL for consultation regarding CAR T-cell therapy?

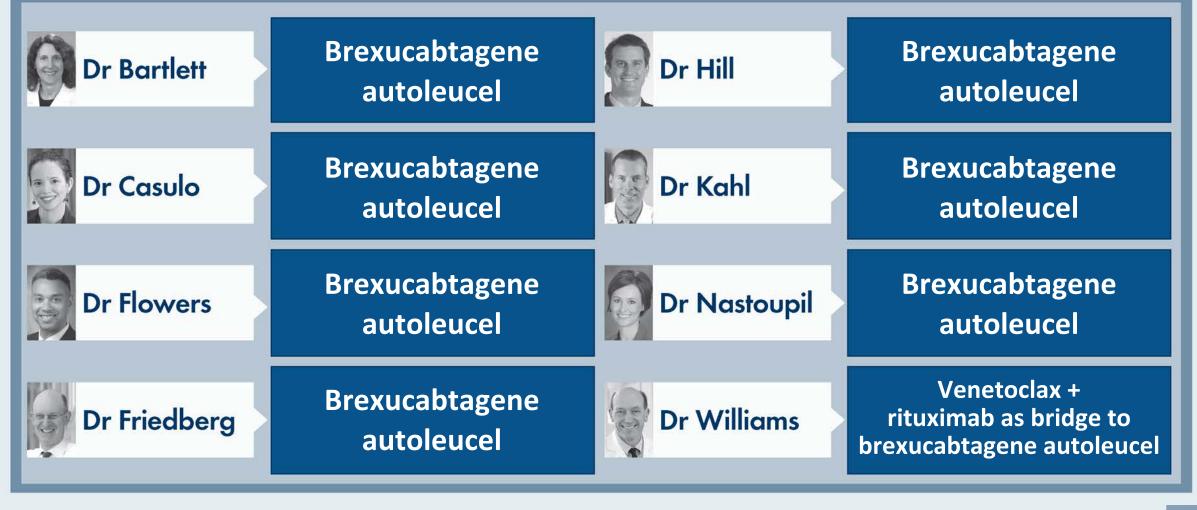




Mantle Cell Lymphoma

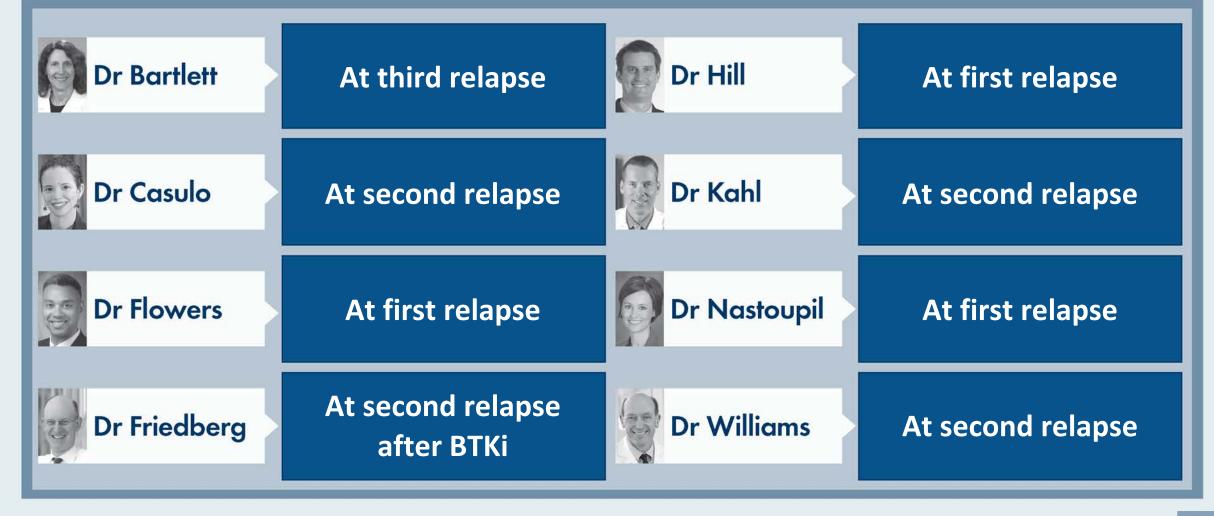


In general, what would be your most likely treatment recommendation for a 70-year-old patient with mantle cell lymphoma who responds to BR and then ibrutinib on relapse but subsequently develops rapid tumor progression?





At what point in the treatment course are you referring patients with mantle cell lymphoma for consultation regarding CAR T-cell therapy?





Meet The Professor with Dr Flowers

MODULE 1: Journal Club with Dr Flowers – Part 1

MODULE 2: Case Presentations

- Dr Gupta: A 79-year-old man with relapsed mantle cell lymphoma
- Dr Smith: An 81-year-old man with chronic lymphocytic leukemia (CLL) and Hodgkin lymphoma
- Dr Shameem: A 71-year-old woman with diffuse large B-cell lymphoma (DLBCL)
- Dr Choksi: A 75-year-old woman with relapsed DLBCL
- Dr Zafar: An 80-year-old woman with relapsed/refractory follicular lymphoma and an EZH2 mutation
- Dr Gandhi: A 54-year-old man with Grade 2 follicular lymphoma

MODULE 3: ASH 2021 Preview

MODULE 4: Journal Club with Dr Flowers – Part 2

MODULE 5: Beyond the Guidelines

MODULE 6: Key Data Sets



Diffuse Large B-Cell Lymphoma



Phase III Study Shows Polatuzumab Vedotin with R-CHP Is the First Regimen in 20 Years to Significantly Improve Outcomes in Previously Untreated Aggressive Form of Lymphoma Press Release – August 9, 2021

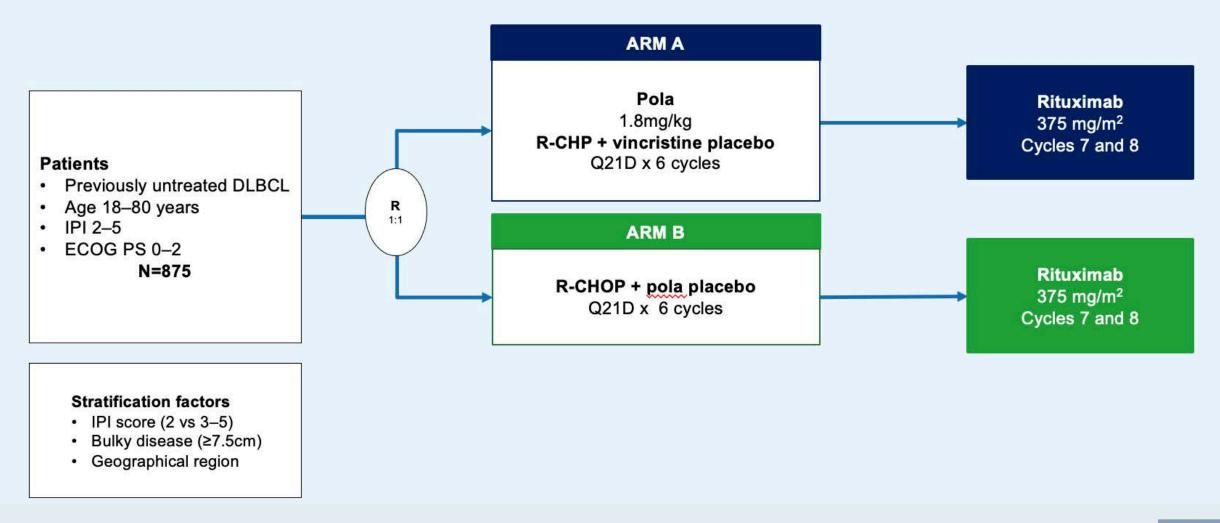
"Pivotal Phase III POLARIX trial comparing polatuzumab vedotin in combination with chemotherapy regimen R-CHP versus the standard of care R-CHOP in treatment of firstline diffuse large B-cell lymphoma (DLBCL) met its primary endpoint of investigator assessed progression-free survival.

Prolonging survival without disease advancement could be transformative for newly diagnosed DLBCL patients, as currently 40% of patients relapse after disease progression.

Data will be submitted to health authorities globally as soon as possible and presented at an upcoming medical meeting."



POLARIX Phase III Trial Design





Polatuzumab Vedotin in Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Laurie H. Sehn, MD, MPH¹; Alex F. Herrera, MD²; Christopher R. Flowers, MD, MSc³; Manali K. Kamdar, MD, MBBS⁴; Andrew McMillan, PhD⁵; Mark Hertzberg, MBBS, PhD⁶; Sarit Assouline, MDCM, MSc⁷; Tae Min Kim, MD⁸; Won Seog Kim, MD, PhD⁹; Muhit Ozcan, MD¹⁰; Jamie Hirata, PharmD¹¹; Elicia Penuel, PhD¹¹; Joseph N. Paulson, PhD¹¹; Ji Cheng, PhD¹²; Grace Ku, MD¹¹; and Matthew J. Matasar, MD¹³

J Clin Oncol 2020;38(2):155-65.

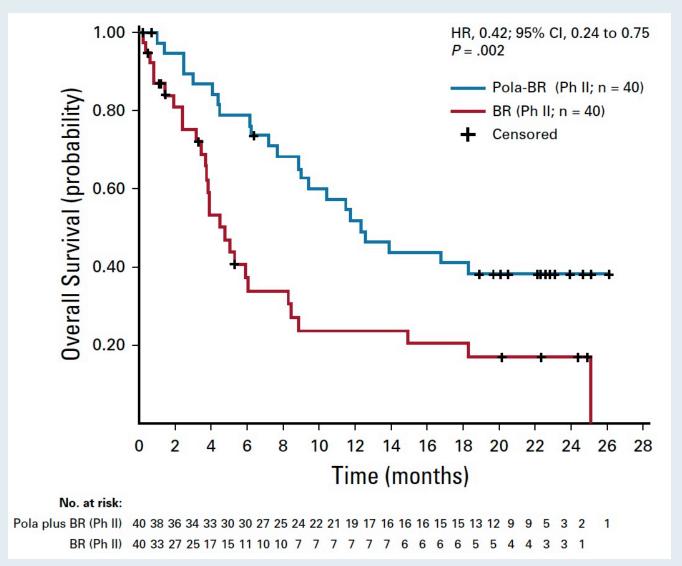


Polatuzumab Vedotin with Bendamustine/Rituximab for Transplant-Ineligible R/R DLBCL: End-of-Treatment CR Rate

	Phase II Ra	Phase II Randomized		
Outcome	Pola-BR $(n = 40)$	BR (n = 40)		
End of treatment				
IRC, objective response	18 (45.0)	7 (17.5)		
Complete response	16 (40.0)	7 (17.5)		
Partial response	2 (5.0)	0		
Stable disease	6 (15.0)	1 (2.5)		
Progressive disease	8 (20.0)	10 (25.0)		
Missing or unevaluable†	8 (20.0)	22 (55.0)		



Polatuzumab Vedotin with Bendamustine/Rituximab for Transplant-Ineligible R/R DLBCL: Overall Survival





FDA Approves Selinexor for R/R DLBCL

Press Release – June 22, 2020

"The Food and Drug Administration granted accelerated approval to selinexor for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy.

Approval was based on SADAL (KCP-330-009; NCT02227251), a multicenter, single-arm, open-label trial in patients with DLBCL after 2 to 5 systemic regimens. Patients received selinexor 60 mg orally on days 1 and 3 of each week."



Lancet Haematol 2020;7:e511-22.

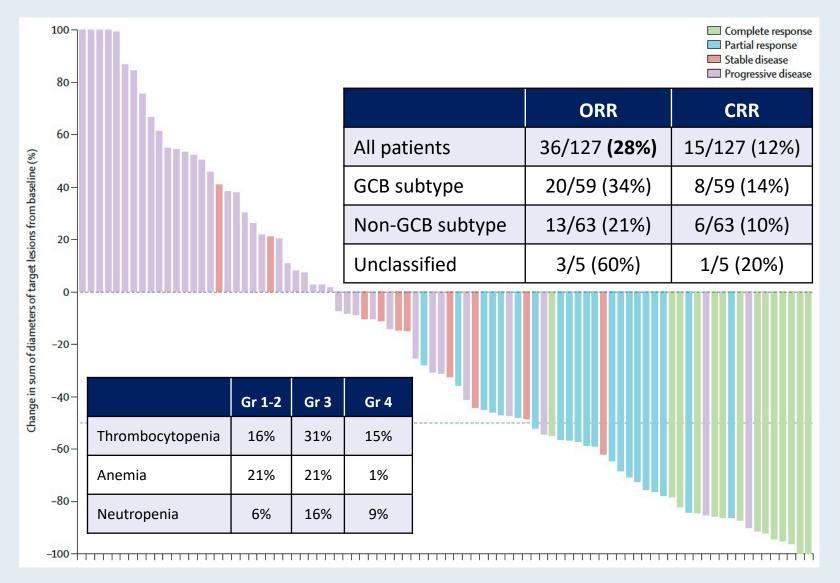
Selinexor in patients with relapsed or refractory diffuse large B-cell lymphoma (SADAL): a single-arm, multinational, multicentre, open-label, phase 2 trial



Nagesh Kalakonda*, Marie Maerevoet*, Federica Cavallo, George Follows, Andre Goy, Joost S P Vermaat, Olivier Casasnovas, Nada Hamad, Josée M Zijlstra, Sameer Bakhshi, Reda Bouabdallah, Sylvain Choquet, Ronit Gurion, Brian Hill, Ulrich Jaeger, Juan Manuel Sancho, Michael Schuster, Catherine Thieblemont, Fátima De la Cruz, Miklos Egyed, Sourav Mishra, Fritz Offner, Theodoros P Vassilakopoulos, Krzysztof Warzocha, Daniel McCarthy, Xiwen Ma, Kelly Corona, Jean-Richard Saint-Martin, Hua Chang, Yosef Landesman, Anita Joshi, Hongwei Wang, Jatin Shah, Sharon Shacham, Michael Kauffman, Eric Van Den Neste, Miguel A Canales



SADAL: Efficacy and Safety of Selinexor for R/R DLBCL After at Least 2 Previous Lines of Chemoimmunotherapy





FDA Grants Accelerated Approval to Tafasitamab-cxix for DLBCL Press Release – July 31, 2020

"The Food and Drug Administration granted accelerated approval to tafasitamab-cxix, a CD19-directed cytolytic antibody, indicated in combination with lenalidomide for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from low grade lymphoma, and who are not eligible for autologous stem cell transplant.

The efficacy of tafasitamab-cxix with lenalidomide was evaluated in L-MIND (NCT02399085), an open label, multicenter single-arm trial in 81 patients. Patients received tafasitamab-cxix 12 mg/kg intravenously with lenalidomide (25 mg orally on days 1 to 21 of each 28-day cycle) for maximum of 12 cycles, followed by tafasitamab-cxix as monotherapy."



Lancet Oncol 2020;21:978-88



Tafasitamab plus lenalidomide in relapsed or refractory diffuse large B-cell lymphoma (L-MIND): a multicentre, prospective, single-arm, phase 2 study

Gilles Salles*, Johannes Duell*, Eva González Barca, Olivier Tournilhac, Wojciech Jurczak, Anna Marina Liberati, Zsolt Nagy, Aleš Obr, Gianluca Gaidano, Marc André, Nagesh Kalakonda, Martin Dreyling, Johannes Weirather, Maren Dirnberger-Hertweck, Sumeet Ambarkhane, Günter Fingerle-Rowson, Kami Maddocks



L-MIND: Best Objective Response According to Independent Radiology Committee or Clinical Review Committee

	Patients treated with tafasitamab plus lenalidomide (n=80)*
Best objective response	
Complete response	34 (43%; 32–54)
Partial response	14 (18%; 10–28)
Stable disease	11 (14%; 7–23)
Progressive disease	13 (16%; 9–26)
Not evaluable†	8 (10%; 4–19)
PET-confirmed complete response	30/34 (88%; 73–97)
Objective response‡	48 (60%; 48–71)
Disease control§	59 (74%; 63–83)

Data are n (%; 95% CI) or n/N (%). *One patient received tafasitamab only. †Patients had no valid postbaseline response assessments. ‡Complete response plus partial response plus partial response plus stable disease.



FDA Grants Accelerated Approval to Loncastuximab Tesirine-Ipyl for Large B-Cell Lymphoma

Press Release – April 23, 2021

"The Food and Drug Administration granted accelerated approval to loncastuximab tesirine-lpyl, a CD19-directed antibody and alkylating agent conjugate, for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low grade lymphoma, and high-grade B-cell lymphoma.

Approval was based on LOTIS-2 (NCT03589469), an open-label, single-arm trial in 145 adult patients with relapsed or refractory DLBCL or high-grade B-cell lymphoma after at least two prior systemic regimens. Patients received loncastuximab tesirine-lpyl 0.15 mg/kg every 3 weeks for 2 cycles, then 0.075 mg/kg every 3 weeks for subsequent cycles. Patients received treatment until progressive disease or unacceptable toxicity."



Lancet Oncol 2021;22:790-800

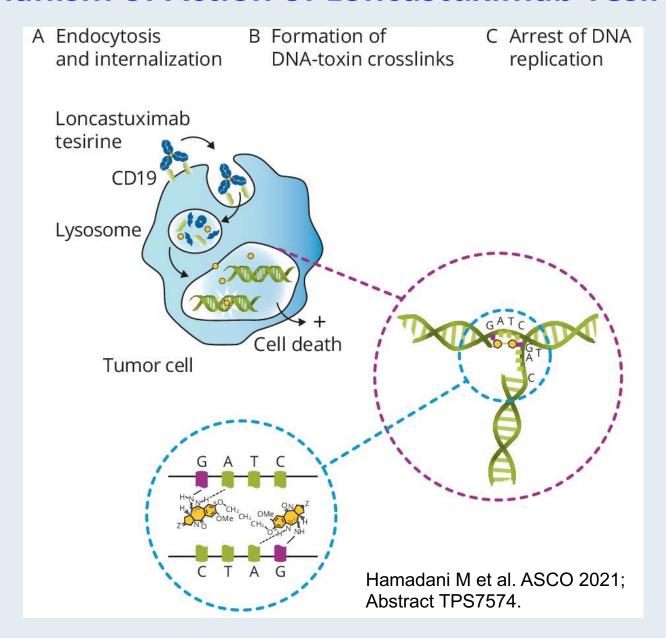


Loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma (LOTIS-2): a multicentre, open-label, single-arm, phase 2 trial

Paolo F Caimi, Weiyun Ai, Juan Pablo Alderuccio, Kirit M Ardeshna, Mehdi Hamadani, Brian Hess, Brad S Kahl, John Radford, Melhem Solh, Anastasios Stathis, Pier Luigi Zinzani, Karin Havenith, Jay Feingold, Shui He, Yajuan Qin, David Ungar, Xiaoyan Zhang, Carmelo Carlo-Stella



Mechanism of Action of Loncastuximab Tesirine





LOTIS-2: Response and Survival with Loncastuximab Tesirine for R/R DLBCL

Response	As-treated population (N = 145)		
Overall response rate	70/145 (48.3%)		
Complete response rate	35/145 (24.1%)		
Complete response	35 (24%)		
Partial response	35 (24%)		
Stable disease	22 (15%)		
Progressive disease	30 (21%)		
Not evaluable	23 (16%)		
Survival	As-treated population (N = 145)		
Median progression-free survival	4.9 months		
Median overall survival	9.9 months		



LOTIS-2: Common Treatment-Emergent Adverse Events

Treatment-Emergent AEs	Grade 1-2	Grade 3-4
Anemia	16%	10%
Thrombocytopenia	15%	18%
Neutropenia	14%	26%
Leukopenia	6%	9%



JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

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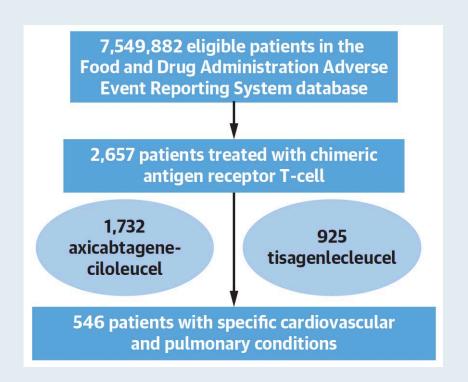
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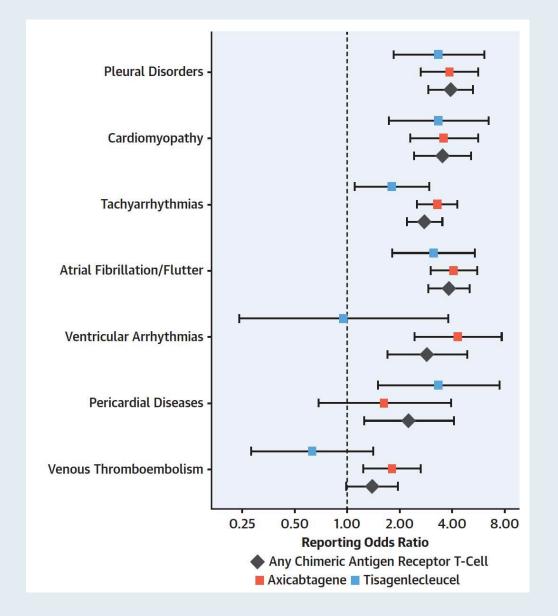
Adverse Cardiovascular and Pulmonary Events Associated With Chimeric Antigen Receptor T-Cell Therapy

Adam Goldman, MD, MPH,^{a,b} Elad Maor, MD, PhD,^{a,b} David Bomze, MD, MPH, MSc,^b Jennifer E. Liu, MD,^{c,d} Joerg Herrmann, MD,^e Joshua Fein, MD,^f Richard M. Steingart, MD,^{c,d} Syed S. Mahmood, MD, MPH,^g Wendy L. Schaffer, MD, PhD,^{c,d} Miguel-Angel Perales, MD,^{d,h} Roni Shouval, MD, PhD^{d,h}



Cardiovascular and Pulmonary Toxicities of CAR T-Cell Therapy







Phase III ZUMA-7 Trial of Axi-cel Meets Primary Endpoint Press Release – June 30, 2021

"The ZUMA-7 trial (NCT03391466) demonstrated superiority of axicabtagene ciloleucel (axi-cel) compared with standard of care (SOC) autologous stem cell transplant (ASCT) after meeting the primary end point of event-free survival (EFS) improvement for patients with relapsed or refractory large B-cell lymphoma (LBCL), according to a press release from the company responsible for manufacturing the chimeric antigen receptor (CAR) T-cell therapy. A statistically significant EFS benefit (HR, 0.398; P < 0.0001) was observed as well as improvement in the secondary end point of objective response rate (ORR).

The top-line results of the randomized ZUMA-7 trial paint the picture of a potential paradigm shift in the treatment of large B-cell lymphoma, Frederick L Locke, MD, ZUMA-7 lead principal investigator and co-leader of the Immuno-Oncology Program at Moffitt Cancer Center in Tampa, Florida, said in the press release. Investigators mentioned that these data are still immature and further analyses are planned for the future. The trial was conducted under a Special Protocol Agreement from the FDA where the trial design, end points, and statistical analysis were agreed in advance."



Phase III TRANSFORM Trial of Liso-cel Meets Primary Endpoint

Press Release – June 10, 2021

"Data from the Phase 3 TRANSFORM trial (NCT03575351) of the chimeric antigen receptor (CAR) T-cell therapy lisocabtagene maraleucel (liso-cel) as second-line therapy for patients with relapsed/refractory large B-cell lymphoma (LBCL) resulted in a statistically significant improvement in the primary end point of event-free survival versus therapy with the standard-of-care comparator arm, according to the company responsible for developing the agent.

Additionally, the toxicity profile observed with liso-cel was consistent with the safety data reported in the TRANSCEND NHL 001 trial (NCT02631044) which led to the FDA approving the CD19-directed therapy for patients with certain types of non-Hodgkin lymphoma, including diffuse large B-cell lymphoma (DLBCL), following 2 or more prior therapies. These data represent the first time a treatment for relapsed/refractory LBCL has demonstrated benefit over high-dose chemotherapy and hematopoietic stem cell transplant (HSCT).

Results regarding the primary end point will be evaluated and shared at an upcoming medical conference as well as with regulatory authorities."



BELINDA Study Investigating Tisagenlecleucel as Second-Line Treatment in Aggressive B-Cell Non-Hodgkin Lymphoma Fails to Meet Primary Endpoint

Press Release – August 24, 2021

"The Phase III BELINDA study investigating tisagenlecleucel in aggressive B-cell non-Hodgkin lymphoma (NHL) after relapse or lack of response to first-line treatment did not meet its primary endpoint of event-free survival compared to treatment with the standard-of-care (SOC). SOC was salvage chemotherapy followed in responding patients by high-dose chemotherapy and stem cell transplant. The safety profile was consistent with the established safety profile of tisagenlecleucel."



Summary of CAR T-Cell Pivotal Studies in DLBCL

	Axi-cel ZUMA-1 (N = 108 infused)	Tisagenlecleucel JULIET (N = 108 infused)	Liso-cel TRANSCEND (N = 294 infused)
CAR	α CD19	α CD19	α CD19
Transmembrane domain	CD28	CD28	CD28
Co-stimulatory doman	CD28	4-1BB	4-1BB
T-cell activation domain	CD3ζ	CD3ζ	CD3ζ
Leukapheresis	Fresh product	Cryopreserved product	Fresh product
Outpatient administration	Not allowed	Allowed	Allowed
Bridging therapy, %	Not allowed	92%	59%
Lymphodepletion chemotherapy	Cy/Flu <mark>500/30</mark> mg/m ² × 3d	Cy/Flu <mark>250/25</mark> mg/m ² x 3d Bendamustine 90 mg/m ² x 2d	Cy/Flu <mark>300/30</mark> mg/m² x 3d

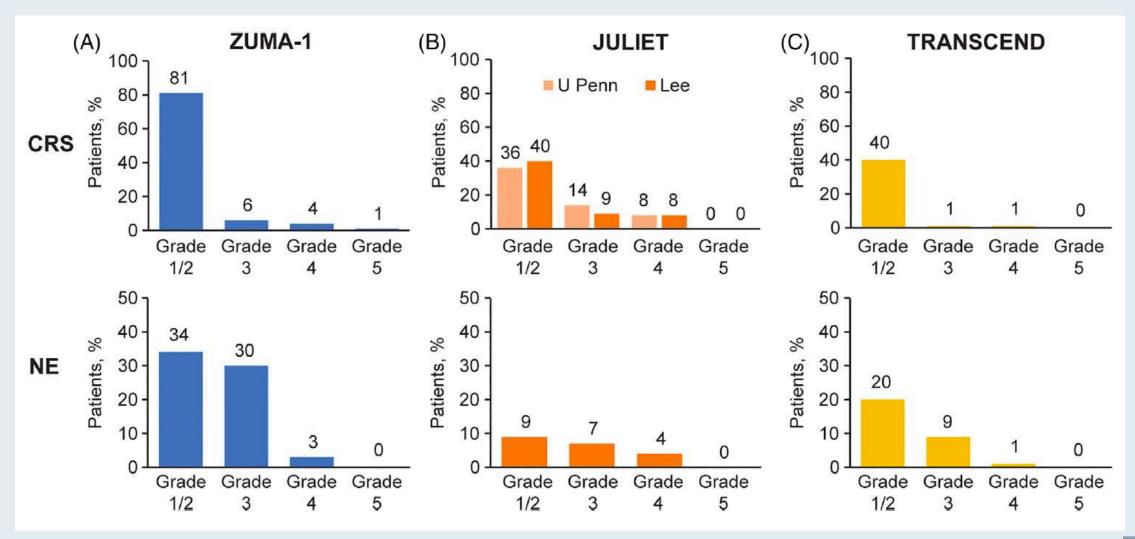


Summary of Efficacy Outcomes in Pivotal Studies of CAR T-Cell Therapy for DLBCL

	Axi-cel ZUMA-1 (N = 108 infused)	Tisagenlecleucel JULIET (N = 115 infused)	Liso-cel TRANSCEND (N = 294 infused)
Overall response rate	74%	52%	73%
Complete response rate	54%	40%	53%
24-month OS rate	50.5%	40.0%	44.9%
Indication	DLBCL, High grade, PMBCL, tFL	DLBCL, High grade, tFL	DLBCL, HGBCL, PMBCL, tFL, tIND



Cytokine Release Syndrome and Neurologic Events in Pivotal Studies of CAR T-Cell Therapy for DLBCL





CAR-T-Associated Cytokine Release Syndrome (CRS) and Neurologic Toxicity

CRS — May be mild or life-threatening

- Occurs with CART19 activation and expansion
- Dramatic cytokine elevations (IL-6, IL10, IFNy, CRP, ferritin)
- Fevers initially (can be quite high: 105°F)
- Myalgias, fatigue, nausea/anorexia
- Capillary leak, headache, hypoxia and hypotension
- CRS-related mortality 3% to 10%

Neurologic toxicity — May be mild or life-threatening

- Mechanism unclear, referred to as immune effector cell-associated neurotoxicity syndrome (ICANS)
- Encephalopathy
- Seizures
- Delirium, confusion, aphasia, agitation, sedation, coma



Hodgkin Lymphoma



Articles

Lancet Haematol 2021;8(6):e410-21

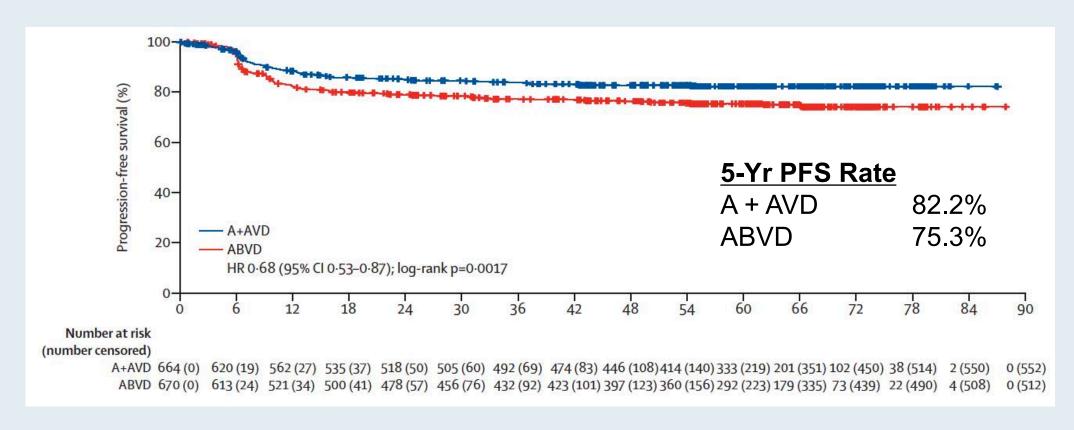


Brentuximab vedotin with chemotherapy for stage III or IV classical Hodgkin lymphoma (ECHELON-1): 5-year update of an international, open-label, randomised, phase 3 trial

David J Straus, Monika Długosz-Danecka, Joseph M Connors, Sergey Alekseev, Árpád Illés, Marco Picardi, Ewa Lech-Maranda, Tatyana Feldman, Piotr Smolewski, Kerry J Savage, Nancy L Bartlett, Jan Walewski, Radhakrishnan Ramchandren, Pier Luigi Zinzani, Martin Hutchings, Javier Munoz, Hun Ju Lee, Won Seog Kim, Ranjana Advani, Stephen M Ansell, Anas Younes, Andrea Gallamini, Rachael Liu, Meredith Little, Keenan Fenton, Michelle Fanale, John Radford



ECHELON-1: Five-Year Update



- Five-year PFS was higher with A + AVD than with ABVD for both PET-2-negative and positive patients
- Peripheral neuropathy continued to improve or resolve over time with both A + AVD and ABVD; more patients had ongoing peripheral neuropathy in the A + AVD group than in the ABVD group (19% vs 9%).



original reports

Brentuximab Vedotin Combined With Chemotherapy in Patients With Newly Diagnosed Early-Stage, Unfavorable-Risk Hodgkin Lymphoma

Anita Kumar, MD¹; Carla Casulo, MD²; Ranjana H. Advani, MD³; Elizabeth Budde, MD⁴; Paul M. Barr, MD²; Connie L. Batlevi, MD, PhD¹; Philip Caron, MD¹; Louis S. Constine, MD²; Savita V. Dandapani, MD⁴; Esther Drill, MD¹; Pamela Drullinsky, MD¹; Jonathan W. Friedberg, MD²; Clare Grieve, BA¹; Audrey Hamilton, MD¹; Paul A. Hamlin, MD¹; Richard T. Hoppe, MD³; Steven M. Horwitz, MD¹; Ashlee Joseph, BA¹; Niloufer Khan, MD¹; Leana Laraque, BA¹; Matthew J. Matasar, MD¹; Alison J. Moskowitz, MD¹; Ariela Noy, MD¹; Maria Lia Palomba, MD¹; Heiko Schöder, MD¹; David J. Straus, MD¹; Shreya Vemuri, BA¹; Joanna Yang, MD⁵; Anas Younes, MD⁶; Andrew D. Zelenetz, MD, PhD¹; Joachim Yahalom, MD¹; and Craig H. Moskowitz, MD⁵

J Clin Oncol 2021;[Online ahead of print].



Multicenter Pilot Study of BV + AVD with or without Consolidative Radiation Therapy for Early-Stage, Unfavorable-Risk Hodgkin Lymphoma

 Patients who achieved a negative end-of-therapy (EOT) PET-4 scan after 4 cycles of BV + AVD were studied with de-escalating radiation dose and field

Clinical endpoint	Cohort 1 30-Gy ISRT (n = 29)	Cohort 2 20-Gy ISRT (n = 29)	Cohort 3 30-Gy CVRT (n = 29)	Cohort 4 No radiation (n = 29)	All patients (n = 114)
EOT CR rate	27 (93%)	29 (100%)	27 (93%)	28 (97%)	111 (96%)
2-year PFS rate	93.1%	96.6%	89.7%	96.6%	94%

"BV + AVD x four cycles is a highly active and well-tolerated treatment program for ES, unfavorable-risk Hodgkin lymphoma, including bulky disease. The efficacy of BV + AVD supports the safe reduction or elimination of consolidative radiation among PET-4—negative patients."



Frontline Brentuximab Vedotin as Monotherapy or in Combination for Older Hodgkin Lymphoma Patients

Yasenchak CA et al.

ASH 2020; Abstract 471.



Best Responses per Investigator – Efficacy Evaluable Set

Efficacy Evaluable Set	Part A BV mono N=25	Part B BV+DTIC N=19	Part C BV+benda N=17	Part D BV+nivo N=19
ORR, n (%)	23 (92)	19 (100)	17 (100)	18 (95)
Best overall response				
Complete response	18 (72)	13 (68)	15 (88)	15 (79)
Partial response	5 (20)	6 (32)	2 (12)	3 (16)
Stable disease	2 (8)	0	0	1 (5)
Progressive disease	0	0	0	0
Duration of response, n	23	19	17	18
Median (min, max)	9.1 (2.8, 81.4+)	45.4 (0.0+, 67.3)	39.0 (0.0+, 56.8+)	NR (1.4+, 27.5+)

Patients who were not efficacy-evaluable included:

- Patients with no post-baseline response assessment due to deaths (n=3) and patient withdrawal (non-AE related, n=2)
 on or before the first scheduled post-baseline scan at Cycle 2
- One patient lost to follow-up
- One patient who was not an eligible cHL subtype (nodular lymphocyte-predominant HL) but still achieved partial response after receiving BV



Lancet Oncol 2021;22(4):512-24.

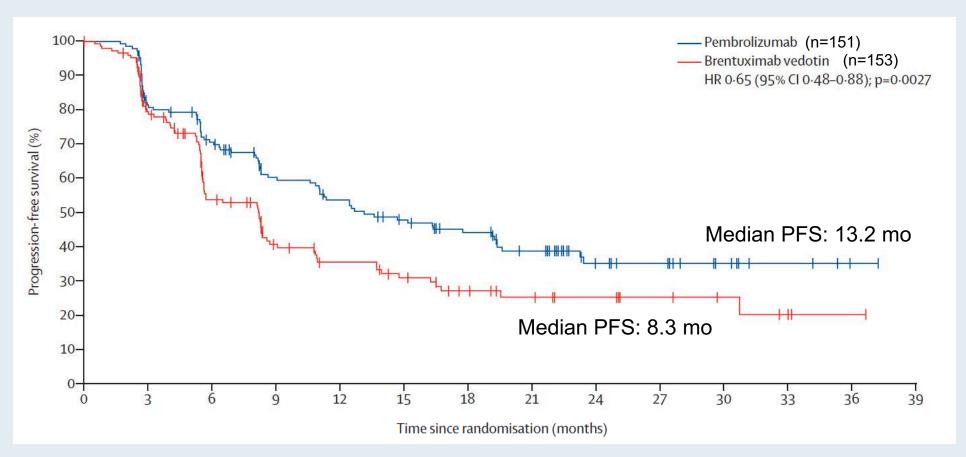


Pembrolizumab versus brentuximab vedotin in relapsed or refractory classical Hodgkin lymphoma (KEYNOTE-204): an interim analysis of a multicentre, randomised, open-label, phase 3 study

John Kuruvilla, Radhakrishnan Ramchandren, Armando Santoro, Ewa Paszkiewicz-Kozik, Robin Gasiorowski, Nathalie A Johnson, Laura Maria Fogliatto, Iara Goncalves, Jose S R de Oliveira, Valeria Buccheri, Guilherme F Perini, Neta Goldschmidt, Iryna Kriachok, Michael Dickinson, Mieczysław Komarnicki, Andrew McDonald, Muhit Ozcan, Naohiro Sekiguchi, Ying Zhu, Akash Nahar, Patricia Marinello, Pier Luigi Zinzani, on behalf of the KEYNOTE-204 investigators*



KEYNOTE-204: Interim Analysis



- The most common Grade 3-5 TRAEs in the pembrolizumab and brentuximab vedotin study arms included pneumonitis (4% vs 1%), neutropenia (2% vs 7%), and peripheral neuropathy (1% vs 3%).
- Serious TRAEs occurred in 16% of patients receiving pembrolizumab and 11% of patients receiving brentuximab vedotin.



J Clin Oncol 2020;38(32):3794-804.

Anti-CD30 CAR-T Cell Therapy in Relapsed and Refractory Hodgkin Lymphoma

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Anti-CD30 CAR T-Cell Therapy After Lymphodepletion Regimens for R/R Hodgkin Lymphoma (HL)

- Two parallel Phase I/II studies (NCT02690545 and NCT02917083) at 2 independent centers involving patients with relapsed or refractory HL
- Anti-CD30 CAR T cells were administered after lymphodepletion with either bendamustine alone,
 bendamustine and fludarabine or cyclophosphamide and fludarabine

All Patients (N = 37)	Benda (n = 5)	Benda-Flu (n = 15)	Cy-Flu (n = 17)
23 (62)	0 (0)	12 (80)	11 (65)
19 (51)	0 (0)	11 (73)	8 (47)
4 (11)	0 (0)	1 (7)	3 (18)
	(N = 37) 23 (62) 19 (51)	(N = 37) (n = 5) 23 (62) 0 (0) 19 (51) 0 (0)	(N = 37) (n = 5) (n = 15) 23 (62) 0 (0) 12 (80) 19 (51) 0 (0) 11 (73)

 Cytokine release syndrome was observed in 10 patients, all of which were Grade 1. No neurologic toxicity was observed



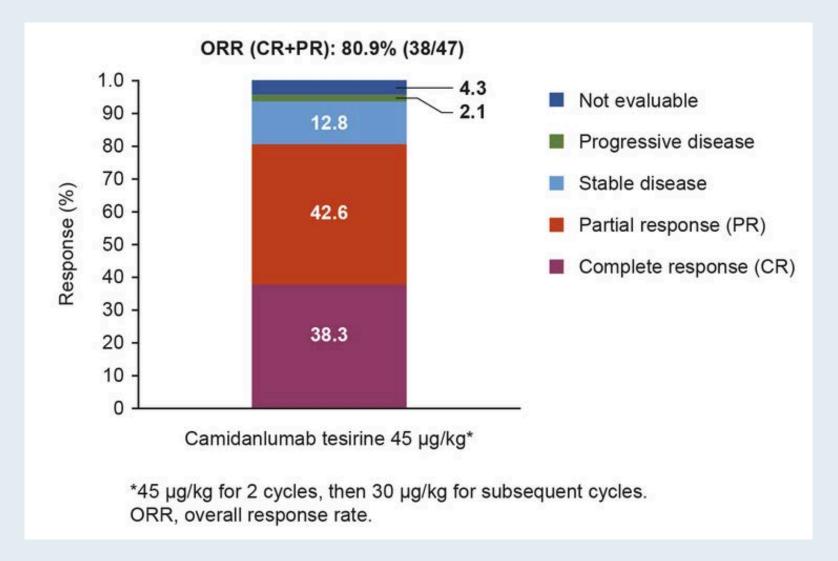
Preliminary Results of a Phase 2 Study of Camidanlumab Tesirine (Cami), a Novel Pyrrolobenzodiazepine-Based Antibody-Drug Conjugate, in Patients with Relapsed or Refractory Hodgkin Lymphoma

Herrera AF et al.

ASH 2020; Abstract 2020.



Response to Camidanlumab Tesirine in Patients with R/R Classical Hodgkin Lymphoma





Follicular Lymphoma



Approved PI3K Inhibitors for FL: Indication and Dosing

	Idelalisib ¹	Copanlisib ²	Duvelisib ³	Umbralisib ⁴
Mechanism of action	Selective PI3Kδ inhibitor	Dual inhibitor of PI3Kδ,α	Dual inhibitor of PI3Kδ,γ	Dual inhibitor of PI3Kδ and casein kinase CK1ε
Indication	Relapsed FL after at least 2 prior systemic therapies	Relapsed FL after at least 2 prior systemic therapies	R/R FL after at least 2 prior systemic therapies	R/R FL after at least 3 prior systemic therapies
Dosing	150 mg orally, twice daily	60 mg as a 1-hour IV infusion weekly (3 weeks on, 1 week off)	25 mg orally, twice daily	800 mg orally, once daily



¹Gopal AK et al. N Engl J Med 2014;370(11):1008-18; Idelalisib package insert, January 2018.

² Dreyling M et al. *J Clin Oncol* 2017;35(35):3898-905; Copanlisib package insert, September 2017.

³ Flinn IW et al. *J Clin Oncol* 2019;[Epub ahead of print]; Zinzani PL et al. EHA 2017;Abstract S777; Duvelisib package insert, September 2018. ⁴ Umbralisib package insert, February 2021.

Lancet Oncol 2021;22:678-89

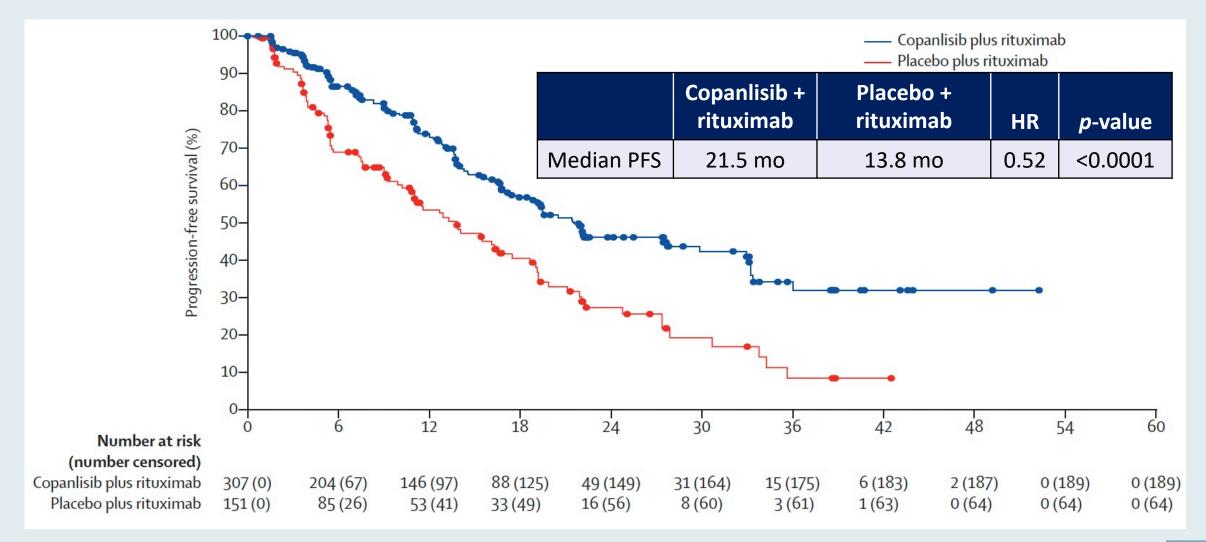


Copanlisib plus rituximab versus placebo plus rituximab in patients with relapsed indolent non-Hodgkin lymphoma (CHRONOS-3): a double-blind, randomised, placebo-controlled, phase 3 trial

Matthew J Matasar, Marcelo Capra, Muhit Özcan, Fangfang Lv, Wei Li, Eduardo Yañez, Katya Sapunarova, Tongyu Lin, Jie Jin, Wojciech Jurczak, Aryan Hamed, Ming-Chung Wang, Ross Baker, Igor Bondarenko, Qingyuan Zhang, Jifeng Feng, Klaus Geissler, Mihaela Lazaroiu, Guray Saydam, Árpád Szomor, Krimo Bouabdallah, Rinat Galiulin, Toshiki Uchida, Lidia Mongay Soler, Anjun Cao, Florian Hiemeyer, Aruna Mehra, Barrett H Childs, Yuankai Shi, Pier Luigi Zinzani



CHRONOS-3: Progression-Free Survival in R/R Indolent NHL





FDA Grants Accelerated Approval to Umbralisib for Marginal Zone Lymphoma and Follicular Lymphoma

Press Release – February 5, 2021

"The Food and Drug Administration granted accelerated approval to umbralisib, a kinase inhibitor including PI3K-delta and casein kinase CK1-epsilon, for the following indications:

- Adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based regimen;
- Adult patients with relapsed or refractory follicular lymphoma (FL) who have received at least three prior lines of systemic therapy.

Approval was based on two single-arm cohorts of an open-label, multi-center, multi-cohort trial, UTX-TGR-205 (NCT02793583), in 69 patients with MZL who received at least one prior therapy, including an anti-CD20 containing regimen, and in 117 patients with FL after at least 2 prior systemic therapies. Patients received umbralisib 800 mg orally once daily until disease progression or unacceptable toxicity."



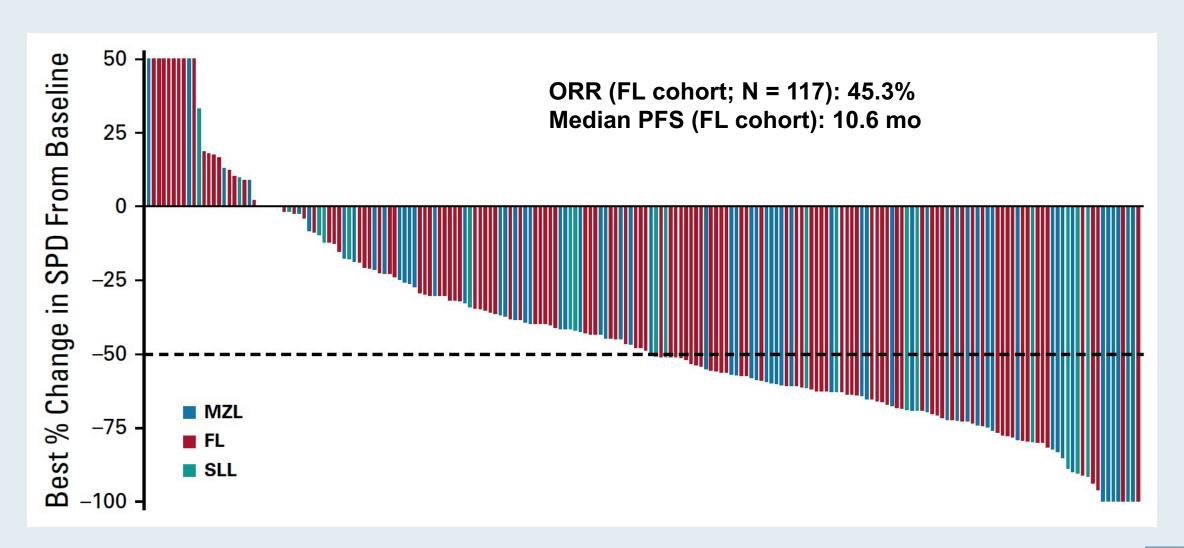
[®] Umbralisib, a Dual PI3Kδ/CK1ε Inhibitor in

Nathan H. Fowler, MD¹; Felipe Samaniego, MD¹; Wojciech Jurczak, MD, PhD²; Nilanjan Ghosh, MD, PhD³; Enrico Derenzini, MD^{4,5}; James A. Reeves, MD⁶; Wanda Knopińska-Posłuszny, MD⁷; Chan Y. Cheah, DMSc⁸; Tycel Phillips, MD⁹; Ewa Lech-Maranda, MD, PhD¹⁰; Bruce D. Cheson, MD¹¹; Paolo F. Caimi, MD¹²; Sebastian Grosicki, MD, PhD¹³; Lori A. Leslie, MD¹⁴; Julio C. Chavez, MD¹⁵; Gustavo Fonseca, MD¹⁶; Sunil Babu, MD¹⁷; Daniel J. Hodson, MD¹⁸; Spencer H. Shao, MD¹⁹; John M. Burke, MD²⁰; Jeff P. Sharman, MD²¹; Jennie Y. Law, MD²²; John M. Pagel, MD, PhD²³; Hari P. Miskin, MSc²⁴; Peter Sportelli, BS²⁴; Owen A. O'Connor, MD, PhD^{24,25}; Michael S. Weiss, JD²⁴; and Pier Luigi Zinzani, MD, PhD^{26,27}

J Clin Oncol 2021;39:1609-18



Umbralisib for Heavily Pretreated R/R Indolent NHL





FDA Grants Accelerated Approval to Tazemetostat for Follicular Lymphoma

Press Release — June 18, 2020

"The Food and Drug Administration granted accelerated approval to tazemetostat, an EZH2 inhibitor, for adult patients with relapsed or refractory (R/R) follicular lymphoma (FL) whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least 2 prior systemic therapies, and for adult patients with R/R FL who have no satisfactory alternative treatment options.

Today, the FDA also approved the cobas[®]. EZH2 Mutation Test (Roche Molecular Systems, Inc) as a companion diagnostic for tazemetostat.

Approval was based on two open-label, single-arm cohorts (Cohort 4 - EZH2 mutated FL and Cohort 5 - EZH2 wild-type FL) of a multi-center trial (Study E7438-G000-101, NCT01897571) in patients with histologically confirmed FL after at least 2 prior systemic therapies. EZH2 mutations were identified prospectively using formalin-fixed, paraffin-embedded tumor samples, which were centrally tested using the cobas EZH2 Mutation Test. Patients received tazemetostat 800 mg orally twice daily until confirmed disease progression or unacceptable toxicity."



Lancet Oncol 2020;21:1433-42

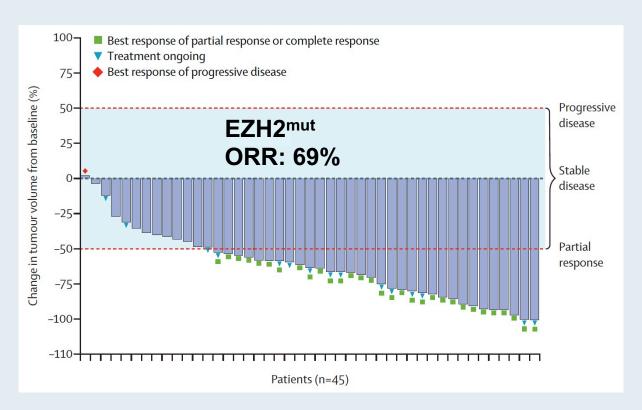
Tazemetostat for patients with relapsed or refractory follicular lymphoma: an open-label, single-arm, multicentre, phase 2 trial

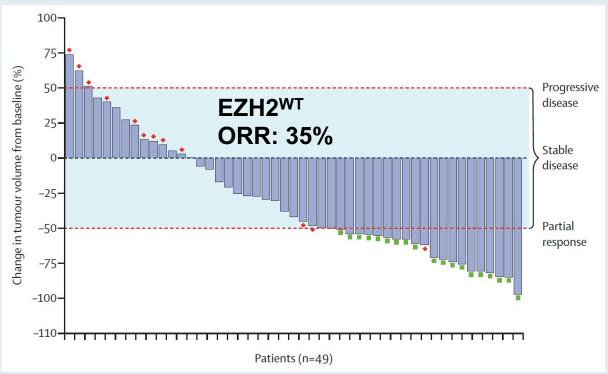


Franck Morschhauser, Hervé Tilly, Aristeidis Chaidos, Pamela McKay, Tycel Phillips, Sarit Assouline, Connie Lee Batlevi, Phillip Campbell, Vincent Ribrag, Gandhi Laurent Damaj, Michael Dickinson, Wojciech Jurczak, Maciej Kazmierczak, Stephen Opat, John Radford, Anna Schmitt, Jay Yang, Jennifer Whalen, Shefali Agarwal, Deyaa Adib, Gilles Salles



Response to Tazemetostat in Patients with R/R FL and EZH2-Mutated or EZH2 Wild-Type Tumors







Structure of Selected Bispecific Antibodies

Bi-Specific Antibody	Targets	Design	Ig Fragment Formats
blinatumomab	CD19 x CD3	CO19	two murine scFv joined by a glycine-serine linker monovalent CD19 and monovalent CD3 binding cloned from anti-CD19 (clone HD37) and anti-CD3 (clone L2K-07) murine mAbs
mosunetuzumab	CD20 x CD3		 humanized mouse heterodimeric IgG1-based antibody monovalent CD20 and monovalent CD3ε binding modified Fc devoid of FcγR and complement binding
glofitamab	(CD20) ₂ x CD3		 humanized mouse IgG1-based antibody bivalent CD20 and monovalent CD3c binding modified Fc devoid of FcyR and complement binding
odronextamab	CD20 x CD3)=(fully human IgG4-based heterodimeric antibody monovalent CD20 and monovalent CD3ε binding Fc-dependent effector function-minimized antibody with Fc of the anti-CD3ε heavy chain modified to reduce Protein A binding common κ light chain from anti-CD3ε mAb
epcoritamab	CD20 x CD3		 humanized mouse IgG1-based heterodimeric antibody monovalent CD20 and monovalent CD3 binding IgG1 Fc modified to minimize Fc-dependent effector functions and to control Fab-arm exchange of mAb half-molecules, resulting in high bispecific product yield
lg, immunoglobulin; scFv, single-chain variable fragment; mAb, monoclonal antibody; Fc, fragment crystallizable; FcγR, Fc gamma receptor			



FDA Grants Breakthrough Therapy Designation for the CD20 x CD3 Bispecific Cancer Immunotherapy Mosunetuzumab for Follicular Lymphoma

Press Release — July 14, 2020

"[The] investigational CD20xCD3 T-cell engaging bispecific mosunetuzumab has been granted Breakthrough Therapy Designation (BTD) by the US Food and Drug Administration (FDA) for the treatment of adult patients with relapsed or refractory (R/R) follicular lymphoma who have received at least two prior systemic therapies.

This designation was granted based on encouraging efficacy results observed in the phase I/Ib GO29781 study [NCT02500407] investigating mosunetuzumab in R/R non-Hodgkin lymphoma (NHL). The safety profile of this T-cell engaging bispecific was consistent with its mechanism of action."



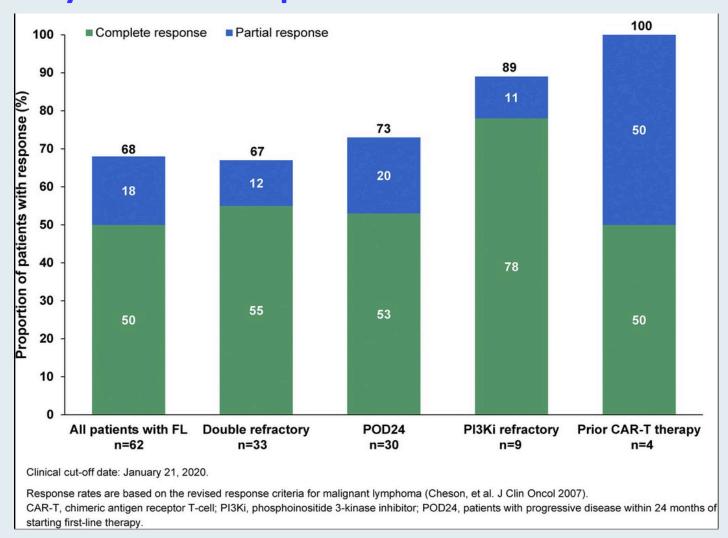
Mosunetuzumab Shows Promising Efficacy in Patients with Multiply Relapsed Follicular Lymphoma: Updated Clinical Experience from a Phase I Dose-Escalation Trial

Assouline SE et al.

ASH 2020; Abstract 702.



Investigator-Assessed Best Response to Mosunetuzumab in Patients with Follicular Lymphoma Who Have Received at Least 2 Prior Systemic Therapies



Cytokine release syndrome (CRS) rate: 35% (N = 22)

- Classified as serious adverse event in N = 4
- No patient required tocilizumab, intensive care unit admission or use of vasopressors for CRS management

Neurologic adverse event rate: 45% (N = 28)

• All Grade 1/2



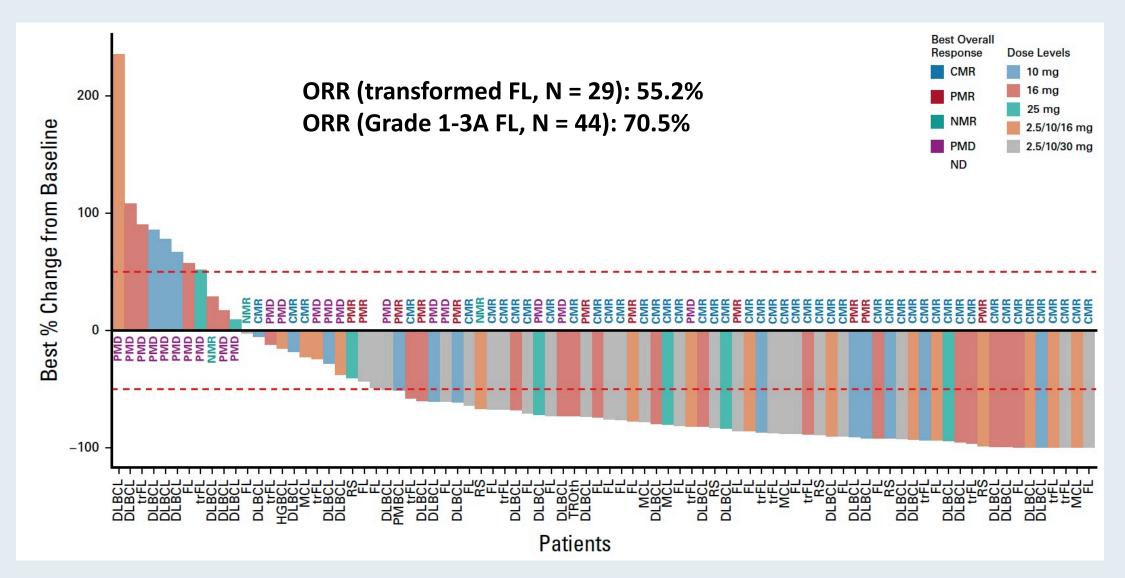
Glofitamab, a Novel, Bivalent CD20-Targeting T-Cell-Engaging Bispecific Antibody, Induces Durable Complete Remissions in Relapsed or Refractory B-Cell Lymphoma: A Phase I Trial

Martin Hutchings, PhD¹; Franck Morschhauser, MD, PhD²; Gloria Iacoboni, MD³,⁴; Carmelo Carlo-Stella, MD⁵; Fritz C. Offner, MD, PhD⁶; Anna Sureda, MD, PhDˀ; Gilles Salles, MD˚; Joaquín Martínez-Lopez, MD, PhD, MBAց; Michael Crump, MD¹o; Denise N. Thomas, MSc¹¹; Peter N. Morcos, PharmD¹¹; Cristiano Ferlini, MD¹¹; Ann-Marie E. Bröske, PhD¹²; Anton Belousov, PhD¹³; Marina Bacac, PhD¹³; Natalie Dimier, PhD¹⁴; David J. Carlile, PhD¹⁴; Linda Lundberg, PhD¹⁵; David Perez-Callejo, MD, PhD¹⁵; Pablo Umaña, PhD¹³; Tom Moore, MD¹²; Martin Weisser, MD¹²; and Michael J. Dickinson, MBBS, DMedSci¹⁶

J Clin Oncol 2021;39:1959-70.



Response to Glofitamab in Patients with R/R B-Cell Lymphomas





FDA Grants Accelerated Approval to Axicabtagene Ciloleucel for Relapsed or Refractory Follicular Lymphoma

Press Release - March 5, 2021

"The Food and Drug Administration granted accelerated approval to axicabtagene ciloleucel for adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

Approval in FL was based on a single-arm, open-label, multicenter trial (ZUMA-5; NCT03105336) that evaluated axicabtagene ciloleucel, a CD19-directed chimeric antigen receptor (CAR) T cell therapy, in adult patients with relapsed or refractory FL after two or more lines of systemic therapy, including the combination of an anti-CD20 monoclonal antibody and an alkylating agent. Following lymphodepleting chemotherapy, axicabtagene ciloleucel was administered as a single intravenous infusion."



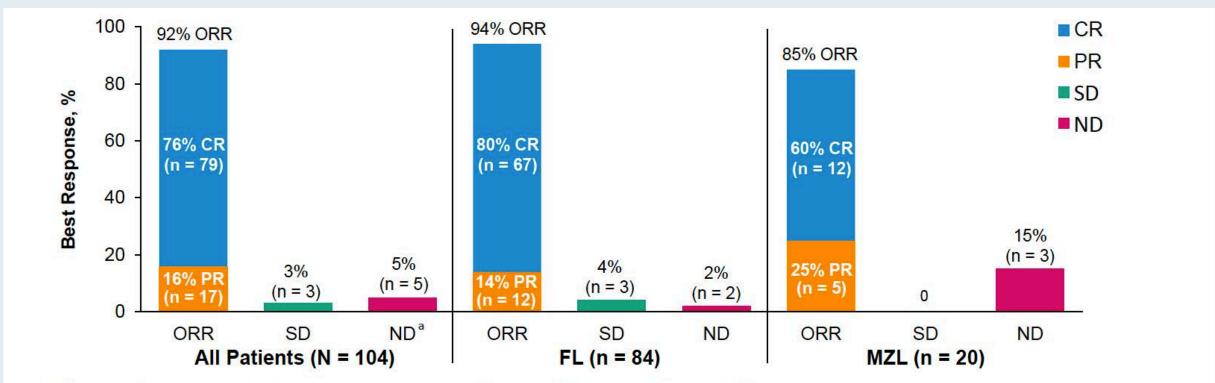
Primary Analysis of ZUMA-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

Caron Jacobson, MD¹; Julio C. Chavez, MD²; Alison Sehgal, MD³; Basem William, MD⁴; Javier Munoz, MD, MS, FACP⁵; Gilles Salles, MD, PhD⁶; Pashna Munshi, MD⁷; Carla Casulo, MD®; David Maloney, MD, PhD⁰; Sven de Vos, MD, PhD¹0; Ran Reshef, MD¹¹; Lori Leslie, MD¹²; Ibrahim Yakoub-Agha, MD, PhD¹³; Olalekan Oluwole, MD, MPH, MBBS¹⁴; Henry Chi Hang Fung, MD¹⁵; Joseph Rosenblatt, MD¹⁶; John Rossi, MS¹⁷; Lovely Goyal, PhD¹⁷; Vicki Plaks, LLB, PhD¹⁷; Yin Yang, MS¹⁷; Jennifer Lee, BS¹⁷; Wayne Godfrey, MS, MD¹⁷; Remus Vezan, MD, PhD¹⁷; Mauro Avanzi, MD, PhD¹⁷; and Sattva S. Neelapu, MD¹®

¹Dana-Farber Cancer Institute, Boston, MA, USA; ²University of South Florida H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; ³UPMC Hillman Cancer Center, Pittsburgh, PA, USA; ⁴The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; ⁵Banner MD Anderson Cancer Center, Gilbert, AZ, USA; ⁶Centre Hospitalier Lyon Sud, Pierre-Bénite, France; ⁷Georgetown Lombardi Comprehensive Cancer Center, Washington, DC, USA; ⁸University of Rochester Medical Center - James P. Wilmot Cancer Center, Rochester, NY, USA; ⁹Fred Hutchinson Cancer Research Center, Seattle, WA, USA; ¹⁰Ronald Reagan University of California Los Angeles Medical Center, Santa Monica, CA, USA; ¹¹Columbia University Herbert Irving Comprehensive Cancer Center, New York, NY, USA; ¹²John Theurer Cancer Center, Hackensack, NJ, USA; ¹³CHU de Lille, Univ Lille, INSERM U1286, Infinite, 59000 Lille, France; ¹⁴Vanderbilt University Medical Center, Nashville, TN, USA; ¹⁵Fox Chase Cancer Center, Philadelphia, PA, USA; ¹⁶University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA; ¹⁷Kite, a Gilead Company, Santa Monica, CA, USA; and ¹⁸The University of Texas MD Anderson Cancer Center, Houston, TX, USA



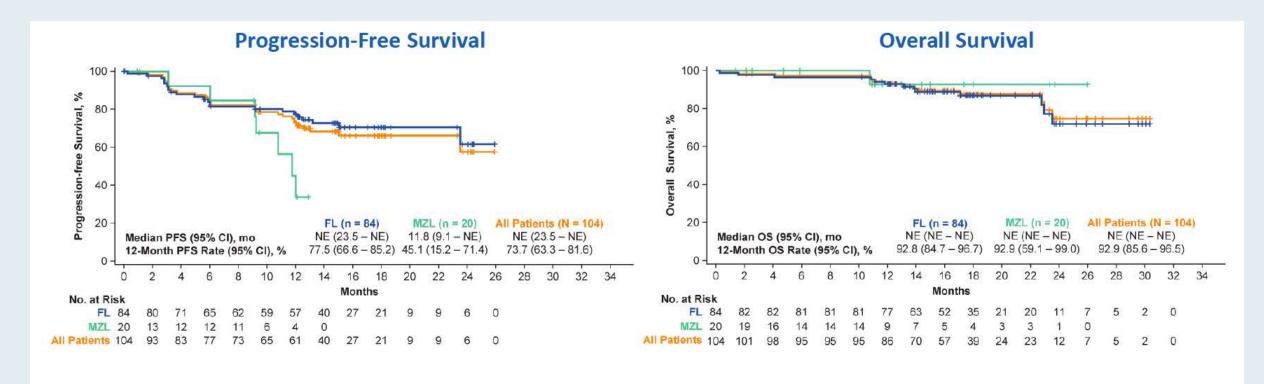
ZUMA-5: ORR by IRRC Assessment for Patients with Follicular Lymphoma Receiving Axicabtagene Ciloleucel



- The median time to first response was 1 month (range, 0.8 3.1)
- Among the 25 patients with FL who initially had a PR, 13 (52%) subsequently converted to a CR after a median of 2.2 months (range, 1.9 11.2)



ZUMA-5: Progression-Free and Overall Survival



- With a median follow-up of 17.5 months, median PFS and median OS were not reached
 - The 12-month PFS rate was 73.7% (95% CI, 63.3 81.6) for all patients
 - The 12-month OS rate was 92.9% (95% CI, 85.6 96.5) for all patients



ZUMA-5: Cytokine Release Syndrome and Neurologic Events

Cytokine release syndrome (CRS)	FL (n = 124)	MZL (n = 22)
Any grade	78%	100%
Grade ≥3	6%	9%
Median time to onset (range)	4 (1-15) days	4 (1-9) days
Median duration of events (range)	6 (1-27) days	6 (2-14) days
Patients with resolved events	99%	100%
Neurologic events		
Any grade	56%	77%
Grade ≥3	15%	41%
Median time to onset (range)	7 (1-177) days	7 (3-19) days
Median duration of events (range)	14 (1-452) days	10 (2-81) days
Patients with resolved events	96%	82%





Oral Presentation 7508

Efficacy and Safety of Tisagenlecleucel in Adult Patients With Relapsed/Refractory Follicular Lymphoma: Primary Analysis of the Phase 2 ELARA Trial

Stephen J. Schuster,¹ Michael Dickinson,² Martin Dreyling,³ Joaquin Martinez-Lopez,⁴ Arne Kolstad,⁵ Jason Butler,⁶ Monalisa Ghosh,⁷ Leslie Popplewell,⁸ Julio C. Chavez,⁹ Emmanuel Bachy,¹⁰ Koji Kato,¹¹ Hideo Harigae,¹² Marie José Kersten,¹³ Charalambos Andreadis,¹⁴ Peter A. Riedell,¹⁵ Ahmed Abdelhady,^{16a} Aiesha Zia,¹⁷ Mony Chenda Morisse,¹⁶ Nathan Hale Fowler,^{18,19,*} Catherine Thieblemont^{20,*}

¹University of Pennsylvania, Philadelphia, PA; ²Peter MacCallum Cancer Centre and Royal Melbourne Hospital, Melbourne, Australia; ³Medizinische Klinik III, LMU Klinikum, Munich, Germany; ⁴Hospital 12 De Octubre, Complutense University, CNIO, Madrid, Spain; ⁵Oslo University Hospital, Oslo, Norway; ⁶Royal Brisbane Hospital, Herston, Australia; ¬Michigan Medicine University of Michigan, Ann Arbor, MI; ³City of Hope National Medical Center, Duarte, CA; ⁶Moffitt Cancer Center, Tampa, FL; ¹⁰Hospices Civils de Lyon and Université Claude Bernard Lyon, France; ¹¹Kyushu University Hospital, Fukuoka, Japan; ¹²Tohoku University Hospital, Sendai, Japan; ¹³Amsterdam UMC, University of Amsterdam, Cancer Center Amsterdam, Netherlands, on behalf of HOVON/LLPC; ¹⁴Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, CA; ¹⁵University of Chicago, Chicago, IL; ¹⁶Novartis Pharmaceuticals Corporation, East Hanover, NJ; ¹¬Novartis Pharma AG, Basel, Switzerland; ¹⁶The University of Texas MD Anderson Cancer Center, Houston, TX; ¹⁶BostonGene, Waltham, MA; ²⁰APHP, Hôpital Saint-Louis-Université de Paris, Paris, France

*Dr Fowler and Dr Thieblemont are co-senior authors. *Analysis completed while employed by Novartis Pharmaceuticals Corporation.



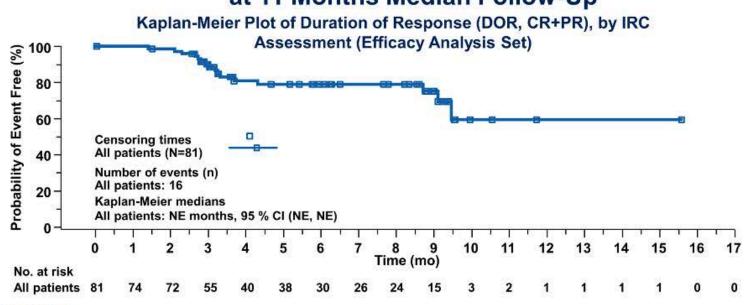
ELARA Primary Endpoint: Complete Response Rate by IRC

Best Overall Response Rate

Response Rate, %	Patients Evaluable for Efficacy ^b (n=94)
CR	66.0 ^b
PR	20.2
ORR (CR+PR)	86.2

- Investigator-assessed CRR was 69.1%^c (ORR 90.4%)
- CRRs/ORRs were comparable among key high-risk subgroups

Median DOR Was Not Reached at 11 Months Median Follow-Up



- Median follow-up for efficacy (n=94): 10.9 (4.3-19.7) months
- Probability for a responding patient to remain in response ≥6 months was 79% (95% CI, 66-87)
- 12 of 31 PRs (38.7%) converted to CRs; all but 1 occurred between Month 3 and Month 6
- Median time to next antilymphoma treatment was not reached



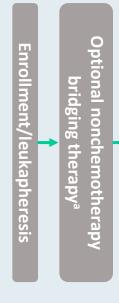
Mantle Cell Lymphoma



Multicenter Phase II ZUMA-12 Schema: First-Line Therapy

Eligibility criteria

- Age ≥ 18 years
- High-risk LBCL
 - HGBCL, with MYC and BLCL2 and/or BCL6 translocations, or
 - LBCL with IPI score ≥ 3 any time before enrollment
- 2 cycles of anti-CD20 plus anthracycline-containing regimen
- Positive interim PET (DS 4 or 5)
- ECOG PS score 0 or 1



Conditioning chemotherapy + axi-cel infusion

- Conditioning
 - Flu 30 mg/m² i.v. and Cy 500 mg/m² i.v. on Days -5, -4, and -3
- Axi-cel
 - Single i.v. infusion of 2×10^6 CAR T cells/kg on Day 0

Primary endpoint

• CRb

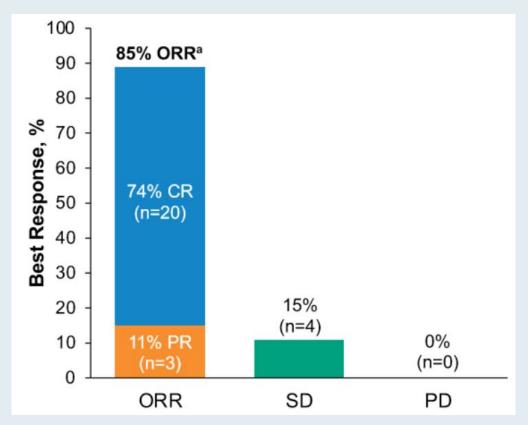
Key secondary endpoints

- ORR
- DOR
- EFS
- PFS
- OS
- Safety
- CAR T cells in blood and cytokine levels in serum



ZUMA-12: Interim Safety and Efficacy Results with Axi-cel as First-Line Treatment

ORR and CR in response-evaluable cohort (N = 27)



Safety	CRS (N = 32)	Neurologic events (N = 32)	
Any grade, n (%)	32 (100%)	22 (69%)	
Grade ≥3, n (%)	3 (9%)	8 (25%)	
Grade 4, n (%)	0	2 (6%)	
Grade 5, n (%)	0	0	
Most common any- grade symptoms, n (%)	Pyrexia: 32 (100%) Chills: 8 (25%) Hypotension: 8 (25%)	Encephalopathy: 10 (31%) Confusional state: 9 (28%)	



FDA Approves Brexucabtagene Autoleucel for Relapsed or Refractory Mantle Cell Lymphoma

Press Release – July 24, 2020

"The Food and Drug Administration granted accelerated approval to brexucabtagene autoleucel, a CD19-directed genetically modified autologous T cell immunotherapy, for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).

Approval was based on ZUMA-2 (NCT02601313), an open-label, multicenter, single-arm trial of 74 patients with relapsed or refractory MCL who had previously received anthracycline- or bendamustine-containing chemotherapy, an anti-CD20 antibody, and a Bruton tyrosine kinase inhibitor. Patients received a single infusion of brexucabtagene autoleucel following completion of lymphodepleting chemotherapy. The primary efficacy outcome measure was objective response rate (ORR) per Lugano [2014] criteria as assessed by an independent review committee."



N Engl J Med 2020;382(14):1331-42

The NEW ENGLAND JOURNAL of MEDICINE

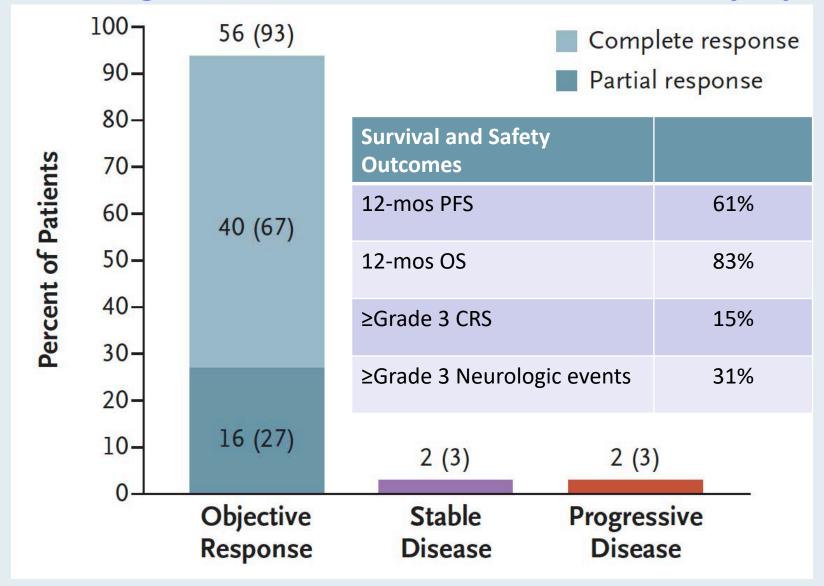
ORIGINAL ARTICLE

KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma

M. Wang, J. Munoz, A. Goy, F.L. Locke, C.A. Jacobson, B.T. Hill, J.M. Timmerman, H. Holmes, S. Jaglowski, I.W. Flinn, P.A. McSweeney, D.B. Miklos, J.M. Pagel, M.-J. Kersten, N. Milpied, H. Fung, M.S. Topp, R. Houot, A. Beitinjaneh, W. Peng, L. Zheng, J.M. Rossi, R.K. Jain, A.V. Rao, and P.M. Reagan



ZUMA-2: Response Rates, Survival and Select Safety Outcomes with Brexucabtagene Autoleucel for Mantle Cell Lymphoma





Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with ER-Positive Breast Cancer

Wednesday, November 17, 2021 5:00 PM - 6:00 PM ET

Faculty
Kevin Kalinsky, MD, MS

Moderator Neil Love, MD



Thank you for joining us!

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

