So Many Options, So Little Time

Relapsed/Refractory Diffuse Large B-Cell Lymphoma

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Disclosures

I have nothing to disclose. I *will not* be discussing off-label indications.

Objectives

Review epidemiology, risk factors, and pathophysiology of diffuse large B-cell lymphoma (DLBCL)

Describe treatment approaches of relapsed/refractory DLBCL

Discuss the role of novel agents for the treatment of relapsed/refractory DLBCL

Develop a proposed treatment algorithm based on key primary literature

DLBCL Overview

Aggressive (fast growing) non-Hodgkin lymphoma (NHL) that occurs in B-lymphocytes

Most common subtype of NHL (30%)
- Estimated 150,000 new cases annually with 5-year relative survival is 63.85

Epidemiology
- Male predominance (55%) with median age at diagnosis of 64 years old

Subtypes:
- Germinal center B-cell-like (GCB)
- Activated B-cell-like (ABC)

Pathology: pan B cell antigens
- CD19, CD20, CD22, CD30, CD45, CD79b
- FISH or Karyotype testing for *MYC, BCL2, BCL6* gene rearrangements

Risk Factors
- Immunosuppression
- Infectious
- Environmental

NATIONAL COMPREHENSIVE CANCER CENTER NETWORK (NCCN) GUIDELINE VERSION 4.2021. B-CELL LYMPHOMAS.
SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS (SEER) PROGRAM. CANCER STAT FACTS: B-CELL LYMPHOMAS. 2000-2017.

Clinical presentation & Work up

International Prognostic Index (IPI)

All Patients	International Index
Age > 60 years	Low: 0-1
Serum LDH > normal	Low – intermediate: 2
Performance status 2-4	High– intermediate: 3
Stage III or IV	High: 4-5
Extranodal involvement > 1 site	

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Audience Response

Which of the following is **not** a CD (cell surface) marker of DLBCL?

A. CD 20
B. CD 30
C. CD 45
D. CD 79b
E. CD 80

DLBCL: First Line Treatment

Systemic cytotoxic chemotherapy

+

Rituximab

- **CHOP** (cyclophosphamide, doxorubicin, vincristine, prednisone)
- **EPOCH** (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)

Duration: 3 to 6 cycles

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DLBCL: Relapsed/refractory

Approximately 30-40% of patients will experience relapsed/refractory (R/R) disease

- Relapsed: disease recurrence after achievement of complete response (CR)
  - Approximately 10%
- Refractory: failure to respond to therapy
  - Approximately 20%

Treatment goal?

- Cure

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Autologous hematopoietic stem cell transplant

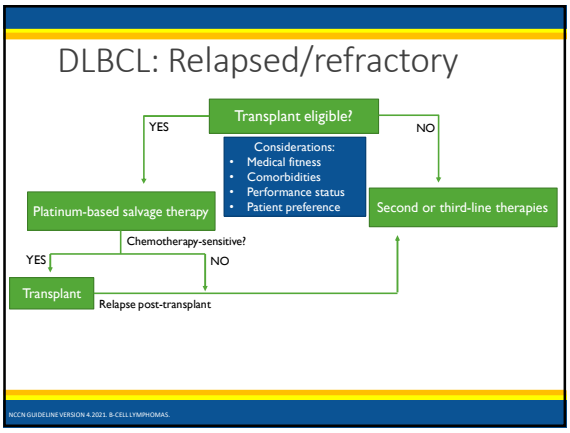
Requires chemotherapy-sensitive disease

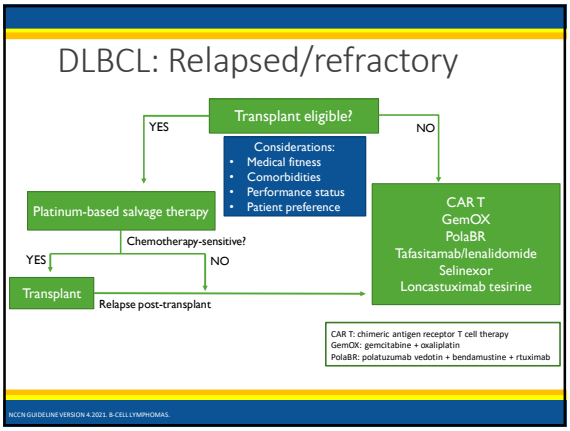
- Give up to a total of 6 cycles to reach complete response (CR)
- Once CR is achieved, proceed to autologous hematopoietic stem cell transplant (aHCT)

Selected salvage regimens

- DHAP (dexamethasone, cisplatin, cytarabine) ± rituximab
  - Myelosuppression, nausea/emesis, dermatologic changes
  - Supportive care: high emetogenecity, hydration, artificial tears and steroid eye drops
- ICE (ifosfamide, carboplatin, etoposide) ± rituximab
  - Myelosuppression, hemorrhagic cystitis, hepatotoxicity, nephrotoxicity, neurotoxicity
  - Supportive care: high emetogenecity, hydration, mesna, growth factor

NCCN GUIDELINE VERSION 4.2021. B-CELL LYMPHOMAS.
VELASQUEZ WS ET AL. *BLOOD*. 1988;71(1):117-122.; KEWALRAMANI T ET AL. *BLOOD*. 2004;103(10):3684-3688


DLBCL: Relapsed/refractory
Transplant eligible?
YES
NO
Considerations:
• Medical fitness
• Comorbidities
• Performance status
• Patient preference
Platinum-based salvage therapy
Second or third-line therapies
Chemotherapy-sensitive?
YES
NO
Transplant
Relapse post-transplant
NCCN GUIDELINE VERSION 4.2021. B-CELL LYMPHOMAS.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Considerations:
• Medical fitness
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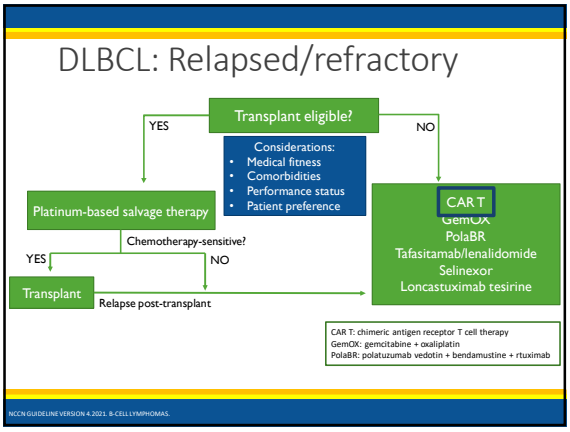
• Patient preference
Platinum-based salvage therapy
CAR T
GemOX
PolaBR
Tafasitamab/lenalidomide
Selinexor
Loncastuximab tesirine
Chemotherapy-sensitive?
YES
NO
Transplant
Relapse post-transplant
CAR T: chimeric antigen receptor T cell therapy
GemOX: gemcitabine + oxaliplatin
PolaBR: polatuzumab vedotin + bendamustine + rtuximab
NCCN GUIDELINE VERSION 4.2021. B-CELL LYMPHOMAS.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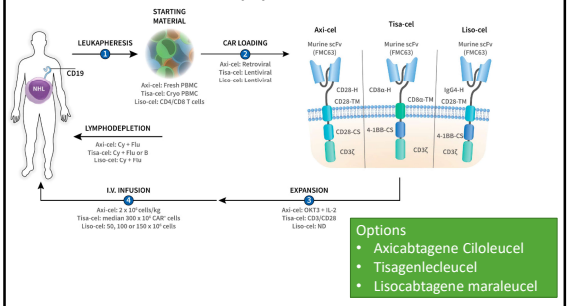
CAR-T Therapy



Options
- Axicabtagene Ciloleucel
- Tisagenlecleucel
- Lisocabtagene maraleucel

"ADOPTIVE IMMUNOTHERAPY FOR SELECT B CELL MALIGNANCIES." *CAR T SCIENCE: MECHANISM OF ACTION (MOA) | FOR HCPS*, WWW.CARTCELLSCIENCE.COM/CAR-T-CELL-SCIENCE.

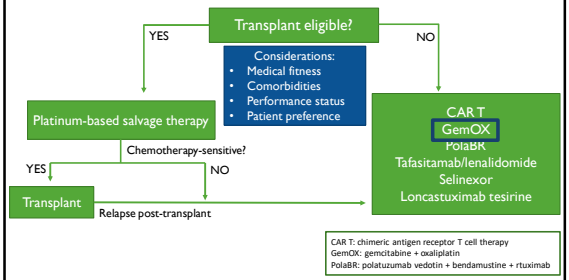
ZUMA-1

Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma	
Study Design	Multicenter, phase 2
Methods	Conditioning chemotherapy • Fludarabine 30mg/m2/day + cyclophosphamide 500 mg/m2/day on days -5, -4, -3 Axi-cel infusion at a target dose of 2x10^6 CAR T cells per kilogram of body weight on day 0
Inclusion	• Adequate organ function
Patient characteristics	• N = 101 (DLBCL, primary mediastinal DLBCL) • Median age of 58 with majority having stage III or IV disease • Majority were resistant to second-line therapies and 21% had disease relapse after transplant
Results	• Overall response rate (ORR) = 92 (82%), Complete response (CR) (54%) • Median time to response = 1 month with a median duration of response of 8.1 months • 4 year overall survival data = 44%
Selected adverse effects	• Pyrexia (14%), hypotension (14%), encephalopathy (21%), neutropenia (78%), febrile neutropenia (31%), anemia (43%), thrombocytopenia (38%), cytokine release syndrome (13%)

NEELAPU SS ET AL. *N ENGL J MED.* 2017 DEC 28;377(26):2531-2544.

Regimen	Population	Pro	Con	Toxicities	Cost
Axicabtagene ciloleucel (CD19)	GCB Non-GCB IPI score 0-4 Double or triple HIT	• Response rate (consistent amongst covariates) • Rapid response • Durable response	• Access to therapy • Non-comparator trial • Cytokine release syndrome • Neurotoxicity	+++++	$$$$$

DLBCL: Relapsed/refractory



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GemOX

Dose
- Gemcitabine 1000 mg/m2, Oxaliplatin 100 mg/m2, ± Rituximab 375 mg/m2
- Repeat cycle every 21 days for a total of 6-8 cycles
- Renal: If CrCl < 30mL/min, reduce initial dose of oxaliplatin
- Hepatic: none

Grade 3-4 adverse events:
- Anemia (10%), neutropenia (43-73%), thrombocytopenia (26-44%), neuropathy (7%)

Other adverse events: nausea/emesis (52-100%)

LOPEZ A. ET AL. *EUR J HAEMATOL* 2008 FEB;80(2):127-32 .; CORAZZELLI G. ET AL. *CANCER CHEMOTHER PHARMACOL* 2009 OCT;64(5):907-16.
MOLINER N. ET AL. *HAEMATOLOGICA*. 2013;98(11):1726-1731.

GemOX

Patient characteristics
- Median age was 67 years old with a median of 1.8 prior lines of therapy

Prophylaxis
- No use of prophylactic growth factors

Multiple studies demonstrate response
- ORR = 43-78%, CR = 34-50%, PR = 17%
- Overall survival (OS) 13.9-41% and 5-year progression-free survival (PFS) 12.8-29%

LOPEZ A. ET AL. *EUR J HAEMATOL* 2008 FEB;80(2):127-32 .; CORAZZELLI G. ET AL. *CANCER CHEMOTHER PHARMACOL* 2009 OCT;64(5):907-16.
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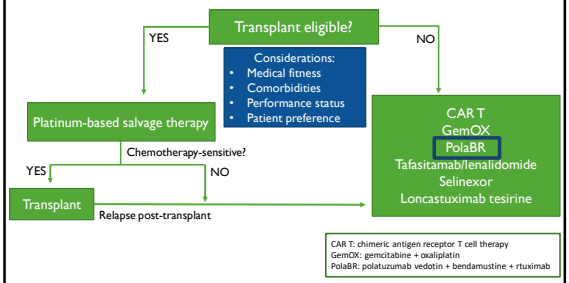
GemOx (Cytoxic)	GCB Non-GCB IPI score 0-4 Double or triple HIT	• Response rate • Durable response • Most available data	• Difficult to tolerate	++++	$

DLBCL: Relapsed/refractory



CAR T: chimeric antigen receptor T cell therapy
GemOX: gemcitabine + oxaliplatin
PolaBR: polatuzumab vedotin + bendamustine + rituximab

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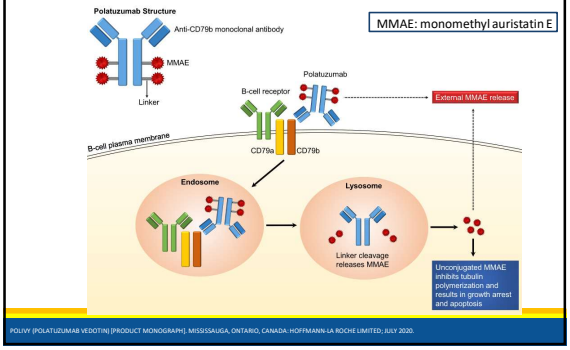
Polatuzumab vedotin



POLIVY (POLATUZUMAB VEDOTIN) [PRODUCT MONOGRAPH]. MISSISSAUGA, ONTARIO, CANADA: HOFFMANN-LA ROCHE LIMITED; JULY 2020.

Polatuzumab vedotin

Dose
- Polatuzumab vedotin 1.8 mg/kg intravenously once every 21 days in combination with bendamustine 90 mg/m2 and rituximab 375 mg/m2
- Administer for a maximum of 6 cycles
- Renal adjustments: none
- Hepatic adjustments: avoid use with AST/ALT >2.5x ULN or total bilirubin > 1.5x ULN

Grade 3-4 adverse events
- Neutropenia (66%), thrombocytopenia (56%), anemia (24%), lymphoctyopenia (22%), febrile neutropenia (15%), peripheral neuropathy (2%)

Other notable adverse events
- Diarrhea (38%), increase AST (36%), increase ALT (38%), increase serum creatinine (87%), pneumonia (22%)

Drug-Drug Interactions: minor substrate of CYP3A4

POLIVY (POLATUZUMAB VEDOTIN) [PRODUCT MONOGRAPH]. MISSISSAUGA, ONTARIO, CANADA: HOFFMANN-LA ROCHE LIMITED; JULY 2020.

Polatuzumab vedotin plus bendamustine and rituximab in relapsed/refractory DLBCL

Study Design	Multicenter, open-label, phase Ib/II trial
Methods	Bendamustine with rituximab or obintuzumab ± Polutuzumab vedotin (BR, PolaBR)
Inclusion	• ECOG 0-2 • Baseline grade ≤ 1 peripheral neuropathy • Transplant ineligible
Patient characteristics	• N = 80 • Median age of 67 and 71 (Pola-BR group, BR group) • Majority of patients with IPI score of 3-5 having received 1-3 lines of previous therapy
Results (PolaBR vs BR)	• ORR = 28 (70%) vs 13 (32.5%), CR = 23 (57.5%) vs 8 (20%), PR = 5 (12.5%) vs 5 (12.5%) • Median duration of response = 10.3 months vs 4.1 months • OS =12.4 months (PolaBR) vs 4.7 months (BR)
Selected adverse events (PolaBR vs BR)	• Grade 3/4: anemia (28% vs 18%), neutropenia (46% vs 33%), thrombocytopenia (41% vs 23%), lymphopenia (13% vs 0%), febrile neutropenia (10% vs 13%), infections (23% vs 21%) • Diarrhea (39% vs 28%), constipation (18% vs 21%), peripheral neuropathy (44% vs 8%)

SEHN LH ET AL. *J CLIN ONCOL.* 2020;38(2):155-165.

Polatuzumab vedotin plus bendamustine and rituximab in relapsed/refractory DLBCL

Limitations	• Small sample size • Confounded by addition of novel agent to historical treatment regimen • 31% of patients discontinued all treatment due to toxicities
Clinical Pearls	• Due to high risk of infection, prophylaxis for *Pneumocystis jivroveci* and *Herpes*virus must be administered • Consider use of prophylactic granulocyte colony-stimulating factors
Author conclusion	PolaBR resulted in statistically significant improvement in CR, ORR, and PFS compared with BR
Reviewer conclusions	• PolaBR has demonstrated response in R/R DLBCL, including high-risk subgroups • Higher rates of grade 3/4 myelosuppression than with BR alone • The toxicity profile of PolaBR impacts utilization

SEHN LH ET AL. *J CLIN ONCOL.* 2020;38(2):155-165.

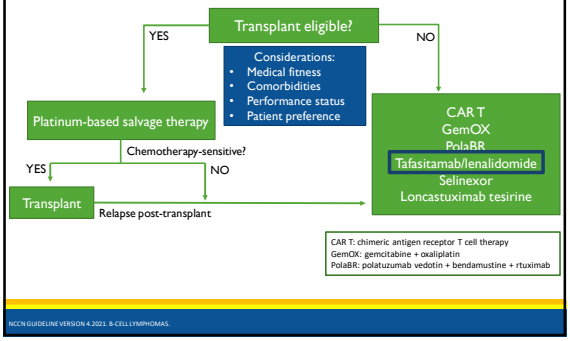
Regimen	Population	Pro	Con	Toxicities	Cost
Axicabtagene ciloleucel (CD19)	GCB Non-GCB IPI score 0-4 Double or triple HIT	• Response rate (consistent amongst covariates) • Rapid response • Durable response	• Access to therapy • Non-comparator trial • Cytokine release syndrome • Neurotoxicity	+++++	$$$$$
GemOx (Cytoxic)	GCB Non-GCB IPI score 0-4 Double or triple HIT	• Response rate • Durable response • Most available data	• Difficult to tolerate	++	$
PolaBR (CD79b)	GCB Non-GCB IPI score 0-5 Double or triple HIT	• Definitive treatment course • Inclusion of high relapse risk patient population • Response rate • Overall survival benefit	• Small sample size (n=40) • High infection risk • Lymphosuppression limits use, including ability to receive CART • Moderate duration of response • Transplant ineligible criteria	++++	$$$

Audience Response

Which prophylaxis is required when starting patients on treatment with polatuzumab vedotin?

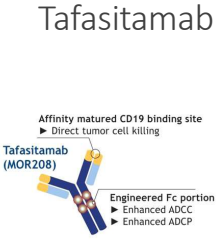
A. Sulfamethoxazole-trimethoprim
B. Acyclovir
C. Granulocyte-colony stimulating factor (G-CSF)
D. A & B
E. All of the above

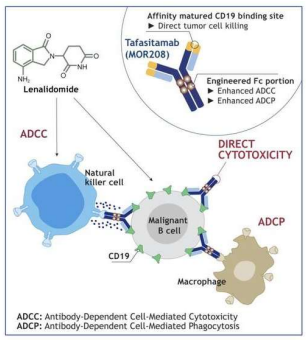
DLBCL: Relapsed/refractory



NCCN GUIDELINE VERSION 4.2021. B-CELL LYMPHOMAS.

Tafasitamab





MONJUVI (TAFASITAMAB) [PRESCRIBING INFORMATION]. BOSTON, MA: MORPHOSYS US INC; AUGUST 2020.

Tafasitamab

Dose
- Tafasitamab 12 mg/kg intravenously in combination with oral lenalidomide 25 mg on days 1-21 of each 28-day cycle
- Administer for a maximum of 12 cycles, followed by tafasitamab monotherapy indefinitely
- Renal adjustments: none
- Hepatic adjustments: none

Selected grade 3/4 adverse events
- Anemia (7%), febrile neutropenia (12%), neutropenia (50%), prolonged partial thromboplastin time (4%), thrombocytopenia (18%)

Other notable adverse events
- Peripheral edema (24%), increase glucose (49%), increase uric acid (20%), diarrhea (36%), infection (73%)

Drug-Drug Interactions: none

MONJUVI (TAFASITAMAB) [PRESCRIBING INFORMATION]. BOSTON, MA: MORPHOSYS US INC; AUGUST 2020.

L-MIND

Study Design	International multi-center, open-label, single-arm, phase 2
Methods	Tafasitamab (weekly) in combination with lenalidomide (on days 1-21) for up to 12 cycles followed by tafasitamab monotherapy
Inclusion	• Transplant ineligible
Exclusion	• Double or triple-hit lymphoma, primary refractory DLBCL • Previous treatment with CD19 therapy (including CART)
Patient characteristics	• N = 80 • Median age of 72 years old with majority being an ECOG 0-1 and 1-2 previous lines of therapy
Results	• ORR = 48 (60%), CR = 34 (43%), PR = 14 (18%) • Median duration of response = 21.7 months
Selected adverse events	• Grade 3/4: Neutropenia (48%), thrombocytopenia (17%), febrile neutropenia (12%), hypokalemia (6%), pneumonia (6%), pulmonary embolism (4%) • Diarrhea (33%), rash (36%)

SALLES G ET AL. *LANCET ONCOL*. 2020;21(7):978-988.

L-MIND

Limitations	• Excluded patients at higher risk of relapse • Transplant ineligible criteria • Primary endpoint of response rate • No comparator arm
Clinical pearls	• Regimen requires venous thromboembolism (VTE) prophylaxis with the inclusion of lenalidomide
Author conclusion	In R/R DLBCL transplant ineligible patients, the combination of tafasitamab and lenalidomide shows high clinical activity with a durable response
Reviewer conclusions	• Difficult to generalize the results to the broad R/R DLBCL patient population due to strict exclusion criteria and high dropout rate • Clinical activity is shown in lower-risk patient subgroups • Median overall survival data is still pending

SALLES G ET AL. *LANCET ONCOL.* 2020;21(7):978-988.

Regimen	Population	Pro	Con	Toxicities	Cost
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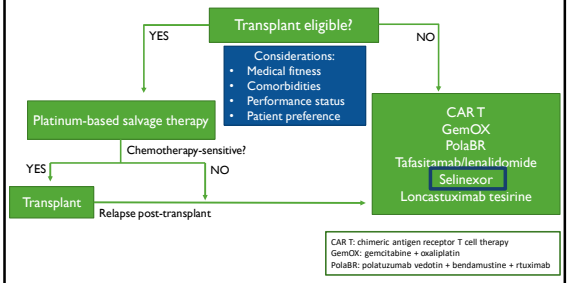
GemOx (Cytoxic)	GCB Non-GCB IPI score 0-4 Double or triple HIT	• Response rate • Durable response • Most available data	• Difficult to tolerate	++	$
PolaBR (CD79b)	GCB Non-GCB IPI score 0-5 Double or triple HIT	• Definitive treatment course • Inclusion of high relapse risk patient population • Response rate • Overall survival benefit	• Small sample size (n=40) • High infection risk • Lymphosuppression limits use, including ability to receive CART • Moderate duration of response • Transplant ineligible criteria	++++	$$$
Tafasitamab (CD19) + lenalidomide	GCB Non-GCB IPI 0-2	• Durable response	• Excluded patients at higher risk of relapse • Extensive treatment period • Concern if CAR-T is future option or used prior	+++	$$$

Audience Response

What is the dose limiting toxicity of using tafasitamab/lenalidomide?

A. Hepatotoxicity
B. Infection
C. Nausea and vomiting
D. Neutropenia
E. Renal impairment

DLBCL: Relapsed/refractory



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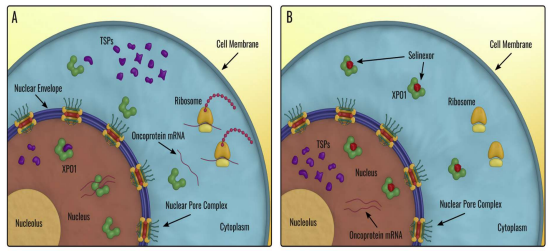
Selinexor



BENKOVA K, ET AL. *BLOOD REV.* 2021 MAR;46:100758. DOI: 10.1016/J.BLRE.2020.100758.

Selinexor

Dose:
- 60 mg/dose orally twice weekly on days 1 and 3 (total selinexor dose per week is 120 mg)
- Renal adjustments: none
- Hepatic adjustments: none

Selected grade 3/4 adverse events
- Anemia (40%), leukopenia (11%), lymphoctyopenia (15%), neutropenia (30%), thrombocytopenia (70%)

Other notable adverse events
- Weight loss (30-47%), hypotension (13%), infections (49-52%), diarrhea (37-44%), nausea (57-72%), emesis (28-41%), hyponatremia (39-62%)

Drug-Drug Interactions: none

XPOVIO (SELINEXOR) [PRESCRIBING INFORMATION]. NEWTON, MA: KARYOPHARM THERAPEUTICS INC; DECEMBER 2020.

SADAL

Study Design	Multicenter, multinational, open-label, phase 2b
Methods	Selinexor 60 mg orally administered on days 1 and 3 of each week
Inclusion	• R/R disease to two to five lines of previous therapy • Transplant ineligible
Exclusion	• Primary mediastinal B-cell lymphoma
Patient characteristics	• N = 127 • Median age of 67 years old with majority being an ECOG 0-1
Results	• ORR = 36 (28%), CR 15 (12%), PR 21 (17%) • Median progression free survival was 2.6 months and median overall survival was 9.1 months
Selected adverse events	• Grade 3/4: thrombocytopenia (46%), nausea (6%), anemia (22%), neutropenia (25%) • Diarrhea (35%), hypotension (13%)

KALAKONDA N. ET AL. *LANCET HAEMATOL.* 2020 JUL;7(7):E511-E522.

SADAL

Limitations	• No comparator arm • Adverse events significantly limited treatment as 17% of patients discontinued and 70% requiring dose modifications • Median duration of treatment was 9 weeks
Clinical Pearls	• Due to high rates of nausea/emesis, an antiemetic is required before the first dose
Author conclusion	In heavily pre-treated R/R DLBCL that are not candidates for transplant, treatment with selinexor has the potential to provide disease control and tumor reduction
Reviewer conclusions	Selinexor is an option in patients with greater than 2 lines of previous therapy where their comorbidities would preclude them from other therapies that have more substantial survival outcomes

KALAKONDA N. ET AL. *LANCET HAEMATOL.* 2020 JUL;7(7):E511-E522.

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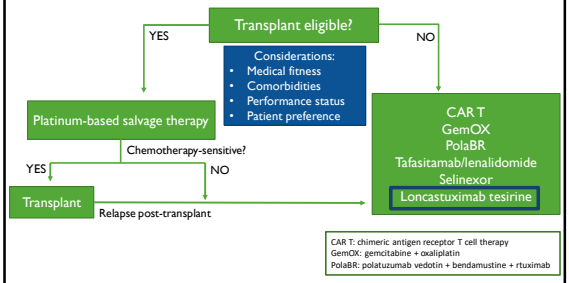
Tafasitamab (CD19) + lenalidomide	GCB Non-GCB IPI 0-2	• Durable response	• Excluded patients at higher risk of relapse • Extensive treatment period • Concern if CAR-T is future option or used prior	+++	$$$
Selinexor (XPO1 inhibitor)	GCB Non-GCB Double or triple HIT	• Oral	• Low duration of response • High rates of treatment modifications or interruptions	++++	$$

DLBCL: Relapsed/refractory



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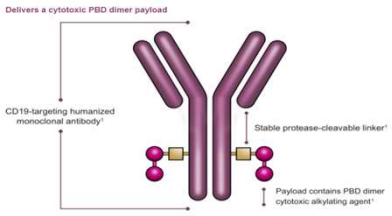
Loncastuximab tesirine



ZYNLONTA (LONCASTUXIMAB TESIRINE) [PRESCRIBING INFORMATION]. MURRAY HILL, NJ: ADC THERAPEUTICS AMERICA; APRIL 2021.

Loncastuximab tesirine

Dose:
- 0.15 mg/kg IV on day 1 every 3weeks for 2 cycles, followed by 0.075 mg/kg IV on day 1 every 3 weeks until disease progression or toxicity
- Renal adjustments: none
- Hepatic adjustments: none

Selected grade 3/4 adverse events
- Anemia (12%), neutropenia (32%), thrombocytopenia (20%), peripheral edema (3%), ascites (3%)

Other notable adverse events
- Edema (28%), skin rash (30%), increased serum glucose (48%), increased AST (41%), ALT (34%), muscloskeletal pain (23%), nausea (23%), diarrhea (17%)

Drug-Drug Interactions: CYP3A4 (minor substrate), P-glycoprotein (minor substrate)

ZYNLONTA (LONCASTUXIMAB TESIRINE) [PRESCRIBING INFORMATION]. MURRAY HILL, NJ: ADC THERAPEUTICS AMERICA; APRIL 2021.

LOTIS-2

Study Design	Multicenter, open-label, single-arm, phase 2 trial
Methods	Loncastuximab tesirine 150 ug/kg IV over 30 minutes on day 1 of each 21-day cycle for the first 2 cycles followed by 75 ug/kg for subsequent cycles
Inclusion	• R/R disease to two or more previous lines of therapy
Exclusion	• Bulky disease (tumor >10 cm) • Diagnosis of Burkitt lymphoma
Patient characteristics	• N = 145 • Median age of 66 years old with majority being an ECOG 0-1
Results	• ORR = 70 (48%), CR 35 (24%), PR 35 (24%) • Median duration of response 13.4 months (CR) and 5.7 months (PR) • Median progression free survival of 4.9 months, median overall survival of 9.9 months
Selected adverse events	• Grade 3/4: anemia (10%), thrombocytopenia (18%), neutropenia (26%), febrile neutropenia (3%) • Nausea (23%), cough (22%), peripheral edema (20%), diarrhea (17%), rash (13%), pleural effusion (10%)

CAIMI PF. ET AL. LANCET OCOL. 2021 JUN;22(6):790-800.

LOTIS-2

Limitations	• No comparator arm • Subgroup analysis limited by size of subgroup population • Patients remain in follow-up
Clinical Pearls	• Premedication with dexamethasone 4 mg twice daily is required for 3 days, starting the day before the first infusion
Author conclusion	Loncastuximab tesirine has considerable single-agent antitumor activity and is able to produce durable responses in a broad range of patients with tolerable adverse effects
Reviewer conclusions	Loncastuximab tesirine is an option for patients, especially those heavily pretreated, and produces durable responses with a manageable side effect profile

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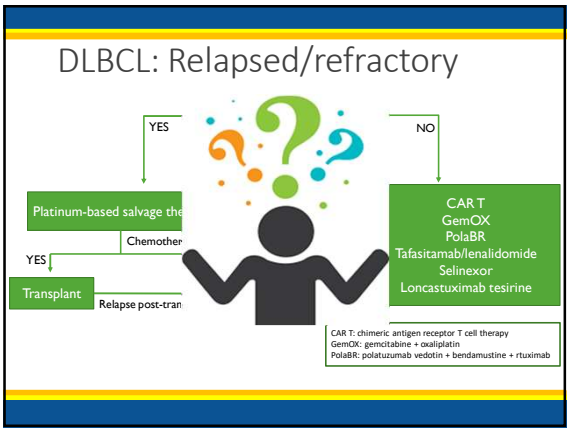
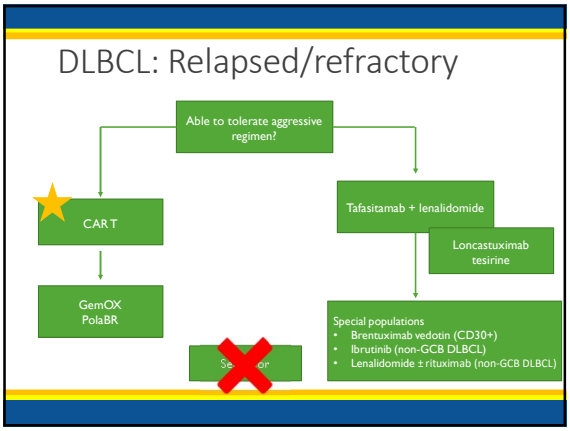
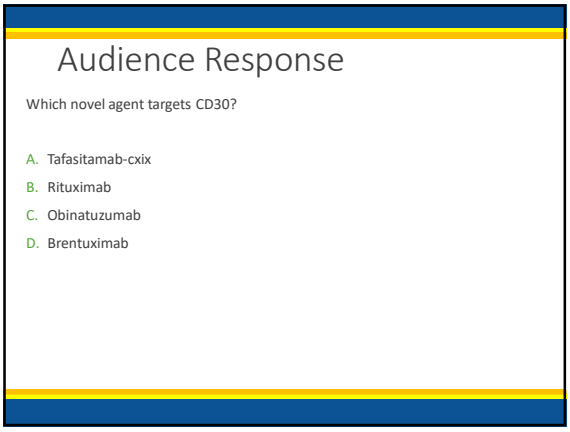
Regimen	Population	Pro	Con	Toxicities	Cost
Axicabtagene ciloleucel (CD19)	GCB Non-GCB IPI score 0-4 Double or triple HIT	• Response rate (consistent amongst covariates) • Rapid response • Durable response	• Access to therapy • Non-comparator trial • Cytokine release syndrome • Neurotoxicity	+++++	$$$$$
GemOx (Cytoxic)	GCB Non-GCB IPI score 0-4 Double or triple HIT	• Response rate • Durable response • Most available data	• Difficult to tolerate	++	$
PolaBR (CD79b)	GCB Non-GCB IPI score 0-5 Double or triple HIT	• Definitive treatment course • Inclusion of high relapse risk patient population • Response rate • Overall survival benefit	• Small sample size (n=40) • High infection risk • Lymphosuppression limits use, including ability to receive CART • Moderate duration of response • Transplant ineligible criteria	++++	$$$
Tafasitamab (CD19) + lenalidomide	GCB Non-GCB IPI 0-2	• Durable response	• Excluded patients at higher risk of relapse • Extensive treatment period • Concern if CAR-T is future option or used prior	+++	$$$
Selinexor (XPO1 inhibitor)	GCB Non-GCB Double or triple HIT	• Oral	• Low duration of response • High rates of treatment modifications or interruptions	++++	$$
Loncastuximab tesirine (CD19)	GCB Non-GCB Double or triple HIT	• Response rate • Inclusion criteria • Dosing schedule	• Small subgroup samples • Durability of response • Concern if CAR-T is future option or used prior	++	$$$


DLBCL: Relapsed/refractory
YES
NO
Platinum-based salvage the
Chemother
YES
Transplant
Relapse post-tran
CAR T
GemOX
PolaBR
Tafasitamab/lenalidomide
Selinexor
Loncastuximab tesirine
CAR T: chimeric antigen receptor T cell therapy
GemOX: gemcitabine + oxaliplatin
PolaBR: polatuzumab vedotin + bendamustine + rituximab


DLBCL: Relapsed/refractory
Able to tolerate aggressive regimen?
CAR T
GemOX
PolaBR
Tafasitamab + lenalidomide
Loncastuximab tesirine
Special populations
• Brentuximab vedotin (CD30+)
• Ibrutinib (non-GCB DLBCL)
• Lenalidomide ± rituximab (non-GCB DLBCL)


Audience Response
Which novel agent targets CD30?
A. Tafasitamab-cxix
B. Rituximab
C. Obinatuzumab
D. Brentuximab

Key Points

DLBCL is an aggressive form of NHL in which approximately 50% of patients will relapse or have refractory disease

The preferred option for patients that have access and can tolerate aggressive treatment is an aHCT

Subsequent options for R/R DLBCL are fragmented and lack a standard of care

Second and third-line therapies are selected based on limited data and patient specific factors

Future options are growing for treatment of R/R DLBCL

Future Directions

- **CAR T therapy with universal donors**
- **Antibody-drug conjugates**
- **Bispecific T-cell antibodies**
  - Blinatumomab (CD19-CD3)
  - Mosunetuzumab (CD20-CD3)
  - Glofitamab (CD20-CD3)
  - Odronextamab (CD20-CD3)
  - Epcoritamab (CD20-CD3)
- **Checkpoint inhibitor**
  - Nivolumab (PD-1)
  - Magrolimab (CD47)
- **BL2-inhibitor**
  - Venetoclax
- **Epigenetic modifier**
  - Tazemetostat (EZH2)

So Many Options, So Little Time

Relapsed/Refractory Diffuse Large B-Cell Lymphoma

GRACE ELSEY, PHARMD

ATRIUM HEALTH- LEVINE CANCER INSTITUTE

CNS Disease Risk & Prophylaxis Indications

Prognostic Model: Risk of CNS Disease	
Age > 60 years	Low risk: 0-1
Serum LDH > normal	Intermediate risk: 2-3
Performance status > 1	High risk: 4-6 or kidney or adrenal gland involement
Stage III or IV	
Extranodal involvement > 1 site	
Kidney or adrenal gland involvement	

- Additional indications for CNS prophylaxis
  - Independent of risk score
    - HIV-associated lymphoma
    - Testicular lymphoma
    - High-grade B-cell lymphomas with translocations of MYC and BLC2 and/or BCL6
    - Primary cutaneous DLBCL, leg type
    - Stage IE DLBCL of the breast