PRACTICE POINTS

Expert Tumor Board to Address Challenging Cases of RELAPSED/REFRACTORY AGGRESSIVE AND INDOLENT LYMPHOMAS

STRATEGIES TO ADDRESS CHALLENGING CASES OF R/R AGGRESSIVE LYMPHOMAS

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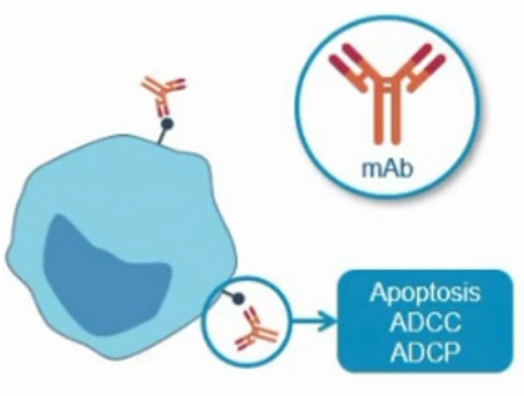
Recent Approvals for Novel Treatment Strategies for Indolent and Aggressive Lymphomas

Antibody-Based Therapies

Tafasitamab-cxix Summary

Tafasitamab-cxix: a CD19-directed cytolytic antibody, indicated in combination with lenalidomide



FDA approval: 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 (ASCT)

DOSING AND SCHEDULING

The recommended dose is 12 mg/kg as an IV infusion according to a 28-day cycle

- **Cycle 1: Days 1, 4, 8, 15 and 22**
- **Cycles 2 and 3: Days 1, 8, 15 and 22**
- **Cycle 4 and beyond: Days 1 and 15**

- Administer in combination with lenalidomide for a maximum of 12 cycles and then continue tafasitamab as monotherapy until disease progression or unacceptable toxicity

Salles G, et al. *Lancet Oncol*. 2020;21:978-988. FDA website. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed August 25, 2021. MONJUVI [package insert]. Boston, MA: Morphosys US Inc.; 2021.

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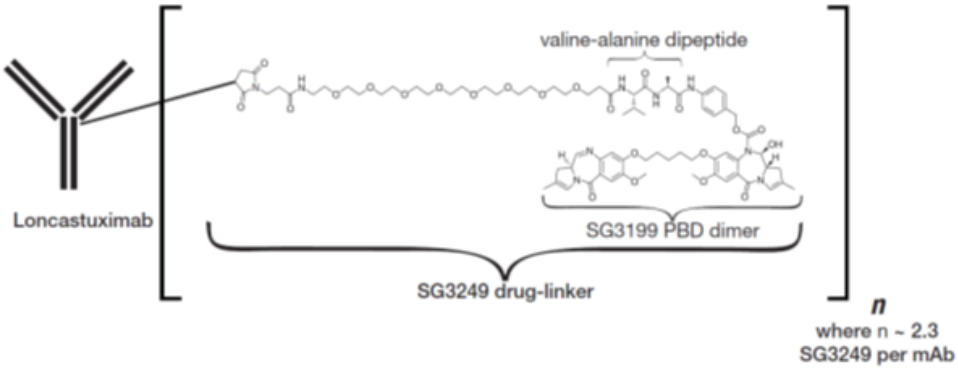
Loncastuximab Tesirine-Ipyl Summary

Loncastuximab tesirine-Ipyl: a CD19-directed antibody and alkylating agent conjugate



FDA approval: Adult patients with relapsed or refractory large B-cell lymphoma after 2 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

DOSING

IV infusion over 30 minutes on day 1 of each 3-week cycle
- **0.15 mg/kg Q3W for 2 cycles**
- **0.075 Q3W for subsequent cycles**

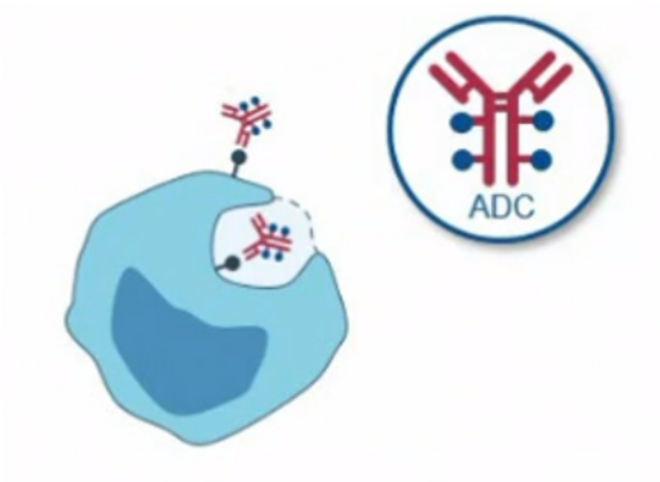
- Patients should be premedicated with dexamethasone 4 mg orally or intravenously twice daily for 3 days beginning the day before infusion

- Patients should be monitored for effusion and edema, myelosuppression, infections, and cutaneous reactions

FDA website. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed August 25, 2021.
ZYLONTA [package insert]. Murray Hill, NJ: ADC Therapeutics America; 2021.

Polatuzumab Vedotin-piiq Summary

Polatuzumab Vedotin-piiq: a CD79b-directed antibody-drug conjugate indicated in combination with bendamustine and a rituximab



FDA approval: Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, after at least 2 prior therapies.

DOSING

- **1.8 mg/kg as an intravenous infusion over 90 minutes every 21 days for 6 cycles in combination with bendamustine and rituximab**
- **Subsequent infusions may be administered over 30 minutes if the previous infusion is tolerated**

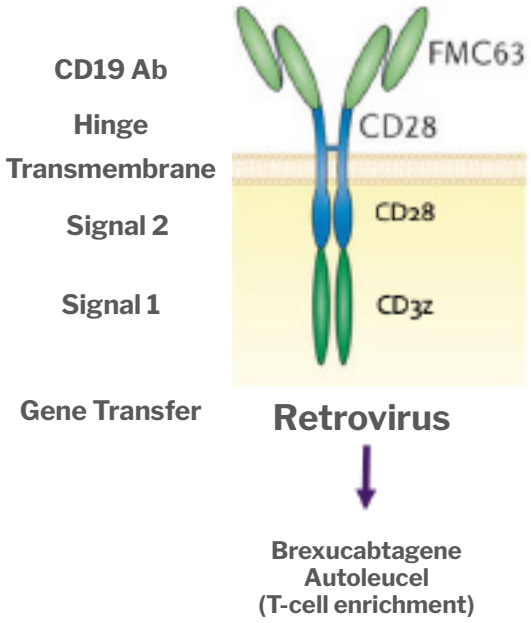
- Patients should be premedicated with an antihistamine and antipyretic

Sehn L, et al. ASH 2020 (abstr 3020). FDA website. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed August 25, 2021. POLIVY [package insert]. South San Francisco, CA: Genentech, Inc.; 2020.

CAR T Cells

Brexucabtagene Autoleucel Summary

Brexucabtagene Autoleucel: a CD19-directed genetically modified autologous T-cell immunotherapy



FDA approval: Treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL)

DOSING

Comprises a suspension of 2×10^6 CAR-positive viable T cells per kg of body weight, with a maximum of 2×10^8 CAR-positive viable T cells in approximately 68 mL

PREMEDICATION

Premedicate with acetaminophen and diphenhydramine or another H1-antihistamine approximately 30 to 60 minutes prior to infusion. Avoid prophylactic use of systemic corticosteroids as it may interfere with the activity of brexucabtagene autoleucel

Wang M, et al. *N Engl J Med.* 2020;382:1331-1342. FDA website. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed August 25, 2021. TECARTUS [package insert]. Santa Monica, CA: Kite Pharma Inc.; 2021.

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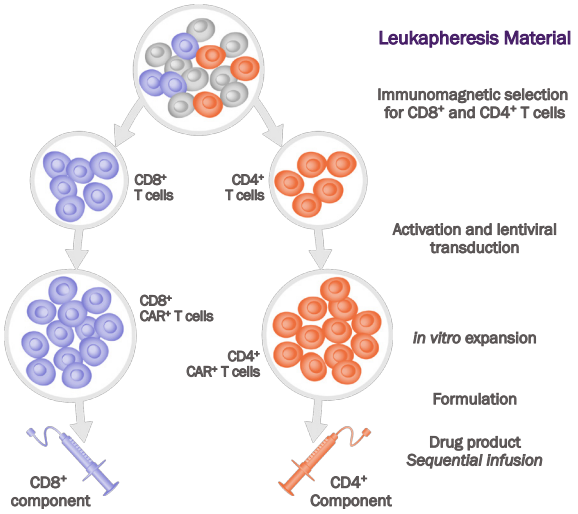
Lisocabtagene Maraleucel Summary

Lisocabtagene maraleucel: a CD19-directed chimeric antigen receptor (CAR) T-cell immunotherapy. It consists of autologous T cells that are genetically modified to produce a CAR protein, allowing the T cells to identify and eliminate CD19-expressing normal and malignant cells



FDA approval: Adult patients with relapsed or refractory (R/R) large B-cell lymphoma after 2 or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B

DOSING

A single dose contains 50 to 110 × 10^6 CAR+ T cells (consisting of 1:1 CAR+ viable CD4 and CD8 T-cell components), with each component supplied separately in one to four single-dose 5 mL vials. Each mL contains 1.5 × 10^6 to 70 × 10^6 CAR-positive viable T cells

- Administer a lymphodepleting regimen of fludarabine and cyclophosphamide before infusion
- Premedicate with acetaminophen and an H^1 antihistamine

Palomba ML, et al. ASH 2020 (abstr 118). FDA website. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed August 25, 2021. BREYANZI [package insert]. Bothell, WA: Juno Therapeutics, Inc., a Bristol-Myers Squibb Company; 2021.

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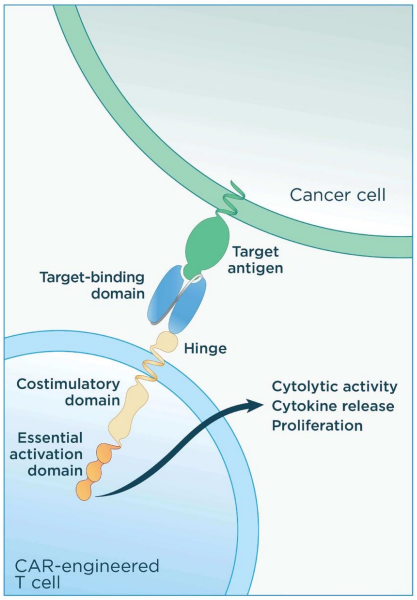
Axicabtagene Ciloleucel Summary

Axicabtagene ciloleucel: a CD19-directed genetically modified autologous T cell immunotherapy

CHIMERIC ANTIGEN RECEPTOR (CAR)



FDA approval:

- Adult patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma
- Adult patients with relapsed or refractory follicular lymphoma (FL) after 2 or more lines of systemic therapy

DOSING

A suspension of 2×10^6 CAR-positive viable T cells per kg of body weight, with a maximum of 2×10^8 CAR-positive viable T cells in approximately 68 mL

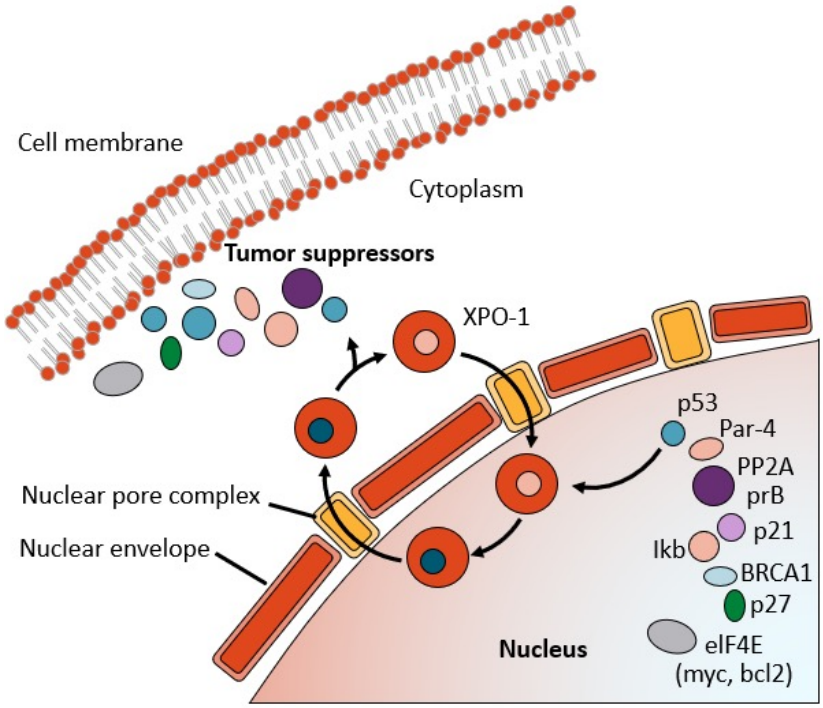
- Administer a lymphodepleting regimen of cyclophosphamide and fludarabine before infusion
- Premedicate with acetaminophen and an H^1-antihistamine

NCI website. https://www.cancer.gov/news-events/cancer-currents-blog/2017/yescarta-fda-lymphoma . Accessed August 26, 2021. FDA website. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed August 25, 2021. YESCARTA [package insert]. Santa Monica, CA: Kite Pharma, Inc.;2021.

Targeted Therapies

Selinexor Summary

Selinexor: a nuclear transport inhibitor



FDA approval: 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

DOSING

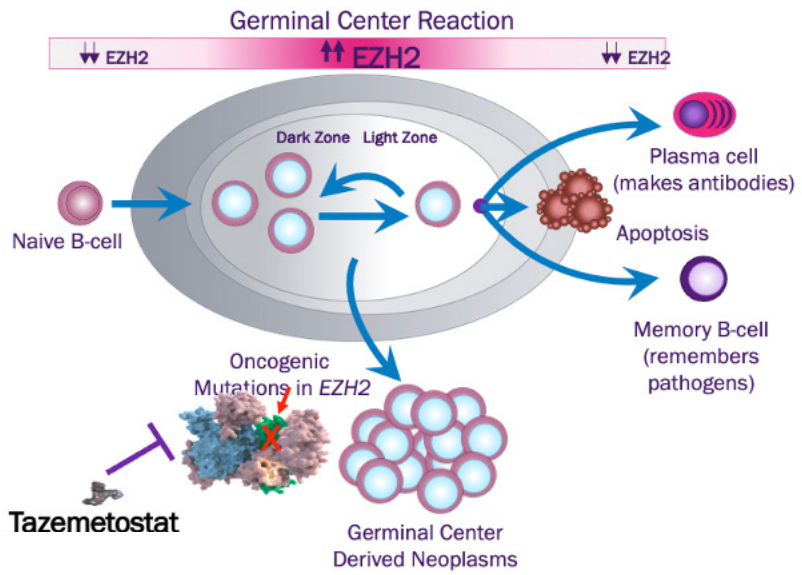
60 mg taken orally on days 1 and 3 of each week

- Provide prophylactic antiemetics
- Administer a 5-HT3 receptor antagonist and other anti nausea agents prior to and during treatment
- Advise patients to maintain adequate fluid and caloric intake throughout treatment
- Consider intravenous hydration for patients at risk of dehydration

Kalakonda N, et al. *Lancet Haematol*. 2020; 7: e511-e522. FDA website. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed August 25, 2021. XPOVIO [package insert]. Newton, MA: Karyopharm Therapeutics Inc.; 2021.

Tazemetostat Summary

Tazemetostat: an EZH2 inhibitor



FDA approval:

- Adult patients with relapsed or refractory (R/R) follicular lymphoma (FL) whose tumors are positive for an EZH2 mutation and who have received at least 2 prior systemic therapies
- Adult patients with R/R FL who have no satisfactory alternative treatment options

DOSING

800 mg taken orally twice daily with or without food (tablets are 200 mg)

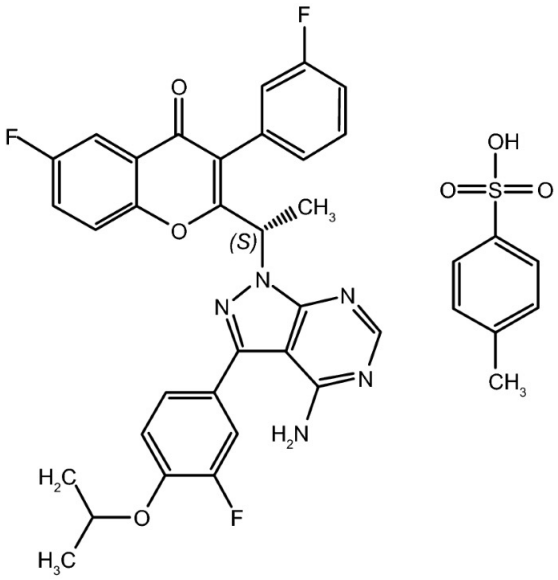
DOSE REDUCTIONS FOR ADVERSE EVENTS

- **First dose reduction: 600 mg PO BID**
- **Second dose reduction: 400 mg PO BID**
- **Discontinue in patients who are unable to tolerate 400 mg PO BID**

FDA website. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed August 25, 2021.
TAZVERIK [package insert]. Cambridge, MA: Epizyme, Inc.; 2020.

Umbralisib Summary

Umbralisib: a kinase inhibitor including PI3K-delta and casein kinase CK1-epsilon



FDA approval:

- 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 3 prior lines of systemic therapy

DOSING

800 mg orally once daily with food (tablets are 200 mg)

PROPHYLAXIS

- **Provide prophylaxis for *Pneumocystis jirovecii* pneumonia (PJP) during treatment**
- **Consider prophylactic antivirals during treatment to prevent cytomegalovirus (CMV) infection, including CMV reactivation**

Dhillon S and Keam SJ. Drugs. 2021;81:857-866. FDA website. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed August 25, 2021. UKONIQ [package insert]. Edison, NJ: TG Therapeutics, Inc.; 2021.

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Investigational Treatment Strategies for Patients With Peripheral T-Cell Lymphoma

Drug Class	Drug
EZH1/2 inhibitor	Valemetostat
PI3K inhibitors	Duvelisib Copanlisib
JAK inhibitors	Cerdulatinib Ruxolitinib
Farnesyltransferase inhibitor	Tipifarnib
Inducible costimulatory	ICOS Ab
Immunotherapy	Avelumab Pembrolizumab CD47-directed approaches

Mehata-Shah N. *Hematology AM Soc Hematol Educ Program*. 2019;1:41-46. Lee WH, et al. *Clin Cancer Res*. 2020;26:5113-5119. Poggio T, et al. *Cancer (Basel)*. 2018;10:339; Zhang W, et al. *Front Immunol*. 2020;11:1-15. ClinicalTrials.gov

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