Drug Updates in Hematologic Malignancies

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Disclosures

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

Objectives

1. Identify FDA drug approvals in hematologic malignancies
   - August 2020-August 2021
2. Evaluate data supporting use of these new therapies
3. Review pharmacology, pertinent drug information, and clinical management
4. Discuss supportive care management and patient counseling information

New FDA Drug Approvals in Past Year: Leukemia/Lymphoma/Multiple Myeloma

Month/Year	Drug	Disease
August 2020	**Belantamab mafodotin-blmf**	R/R MM
September 2020	**Azacitidine tablets**	AML
October 2020	**Pembrolizumab**	R/R cHL (peds & adults)
February 2021	**Umbralisib**	FL & MZL
	Melphalan Flufenamide	R/R MM
April 2021	**Loncastuximab Tesirine**	R/R LBCL
June 2021	**Asparaginase erwinia chrysanthemi (recombinant)-rywn)**	Acute lymphoblastic leukemia/lymphoma
	Avapritinib	Systemic mastocytosis & mast cell leukemia

U.S. Food and Drug Administration. Oncology (Cancer)/Hematologic Malignancies Approvals Notifications. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications

New FDA Drug Approvals in Past Year: CART Therapies

Month/Year	Drug	Disease
February 2021	**Lisocabtagene Maraleucel**	R/R LBCL
March 2021	**Idecabtagene Vicleucel**	R/R MM
	Axicabtagene Ciloleuel	R/R FL

U.S. Food and Drug Administration. Oncology (Cancer)/Hematologic Malignancies Approvals Notifications. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications

New FDA Drug Approvals in Past Year: GVHD Therapies

Month/Year	Drug	Disease
July 2021	**Belumosudil**	Chronic GVHD

U.S. Food and Drug Administration. Oncology (Cancer)/Hematologic Malignancies Approvals Notifications. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications

New Drug Approvals in Leukemia

Azacitidine Tablets (Onureg®)

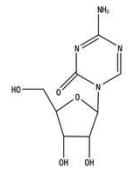
Indication

- Continuation of acute myeloid leukemia (AML) treatment in adults who achieved CR or CRi and unable to complete intensive curative therapy

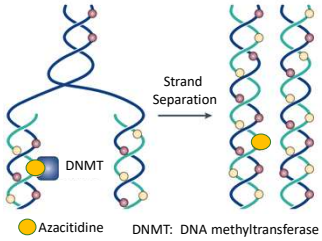
Onureg (azacitidine tablets) [package insert]. Summit, NJ: Celgene Corporation; 2020.

Azacitidine Tablets (Onureg®)

Cytidine Nucleoside Analog



Mechanism of Action



Onureg (azacitidine tablets) [package insert]. Summit, NJ: Celgene Corporation; 2020.
Adapted from Issa, JP, et al. *Nat Rev Drug Discov.* 2005;4:275–6.

Azacitidine Tablets (Onureg®): Quazar AML-001 Trial

Objective	Evaluate efficacy oral azacitidine as maintenance AML therapy	
Design	Phase 3, randomized, double blind, placebo-controlled study	
Intervention	Azacitidine 300 mg PO daily on days 1-14 of each 28-day cycle vs. Placebo	
Population	Patients treated for AML and in first remission, but ineligible for stem cell transplant Median age: 68 years	
Endpoints	**Primary**	
	• OS: 27 months vs. 14.8 months	
	Secondary	
	• RFS: 10.2 months vs. 4.8 months • QOL: FACIT Fatigue Scale and EQ-5D-3L similar between groups	Safety • Nausea and vomiting: >60% • Neutropenia: 44% • Thrombocytopenia: 33% • Time to discontinuation: 11.4 months with 60% due to relapse

Wei AH, et al. *NEJM*. 2020;383:2526-37.

Azacitidine Tablets (Onureg®)

Dosing:
• 300 mg PO daily on days 1-14 of each 28-day cycle

Administration:
•Antiemetic recommended
•Without regard to meals
•Do not crush or split

Drug-Drug Interactions:
•None

Dose Adjustments
Hematologic toxicity
Gastrointestinal toxicity

Warnings/Precautions
Not equivalent to IV or SC formulations
Increased mortality in MDS
Myelosuppression
Embryo/Fetal Toxicity

Other Adverse Effects
Nausea/Vomiting
Diarrhea
Febrile Neutropenia
Pneumonia

Monitoring/Guidance
CBC every other week x 2 cycles
Prior to start of new cycles

Onureg (azacitidine tablets) [package insert]. Summit, NJ: Celgene Corporation; 2020.

Azacitidine Tablets (Onureg®): Helpful Information

- Advise on febrile neutropenia
- Hazardous drug handling
- Dispense in manufacturer bottle with desiccants
- Available as 200 mg and 300 mg film coated tablets
- Copay assistance and free drug programs available

Onureg (azacitidine tablets) [package insert]. Summit, NJ: Celgene Corporation; 2020.

Asparaginase Erwinia Chrysanthemi (recombinant)-rywn) (Rylaze®)

Indication

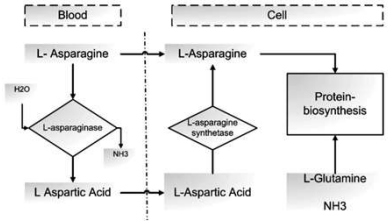
- Component of Acute lymphoblastic leukemia/lymphoma regimens for pediatric patients ≥ 1 month old and adults who developed hypersensitivity to *E.coli*-derived asparaginase products
- Was granted FDA fast track and orphan drug designation

Rylaze (asparaginase erwinia chrysanthemi (recombinant) rywn) injection) [package insert]. Palo Alto, CA: Jazz Pharmaceuticals; 2021.

Asparaginase Erwinia Chrysanthemi (recombinant)-rywn) (Rylaze®)

Mechanism of Action

Healthy Cell

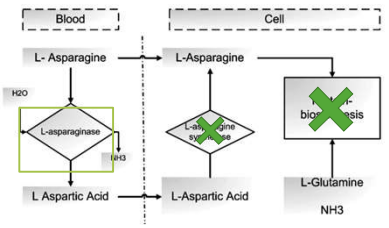


Adapted from van den Berg H. *Leuk Lymphoma*. 2011; 52 (2): 169-78.

Asparaginase Erwinia Chrysanthemi (recombinant)-rywn) (Rylaze®)

Mechanism of Action

Lymphoblast



Cell Death

Adapted from van den Berg H. *Leuk Lymphoma*. 2011; 52 (2): 169-78.

Asparaginase Erwinia Chrysanthemi (recombinant)-rywn (Rylaze®): JZP 458-201 Trial

Objective	Evaluate safety and efficacy of asparaginase Erwinia Chrysanthemi (recombinant)–rywn in acute lymphoblastic leukemia/lymphoma
Design	Multicenter, open label, Phase 2/3 single arm dose and PK study
Intervention	Asparaginase Erwinia Chrysanthemi (recombinant)–rywn x 6 doses over 2 weeks to replace a course of *E.coli*-derived product; Median age: 11; Median courses: 4
Population	Pediatrics (≥ 1 month) and adults with acute lymphoblastic leukemia/lymphoma who had grade ≥ 3 allergic reaction or silent inactivation to the *E.coli*-derived product
Endpoints	**Primary**
	• Serum asparaginase nadir concentration ≥ 0.1 units/mL: 93.6% at 48h
	Secondary
	• ORR: to be reported Safety • Elevated LFTs: 70% • Nausea: 46% • MSK pain: 39% • Infection: 30% • Febrile Neutropenia: 24% • Hyperglycemia: 21% • Discontinuation due to ADE: 9%

Rylaze (asparaginase erwinia chrysanthemi (recombinant) rywn) injection) [package insert]. Palo Alto, CA: Jazz Pharmaceuticals; 2021.

Asparaginase Erwinia Chrysanthemi (recombinant)-rywn) (Rylaze®)

Dosing:
• 25mg/m2 IM every 48 hours

Administration:
•Rotate injection sites

Drug-Drug Interactions:
•None

Dose Adjustments
Hypersensitivity
Thrombosis
Hemorrhage
Hepatotoxicity

Warnings/Precautions
Hypersensitivity
Thrombosis
Hemorrhage
Hepatotoxicity

Other Adverse Effects
Nausea/Vomiting
Diarrhea
Musculoskeletal pain
Infection

Monitoring/Guidance
Tbili, LFTs, and glucose every 2-3 weeks prior to treatment

Rylaze (asparaginase erwinia chrysanthemi (recombinant) rywn) injection) [package insert]. Palo Alto, CA: Jazz Pharmaceuticals; 2021.

Asparaginase Erwinia Chrysanthemi (recombinant)-rywn) (Rylaze®)

- Rotate injection sites
- Split volumes > 2 mL into multiple syringes
- Copay assistance and free drug programs not currently available

Rylaze (asparaginase erwinia chrysanthemi (recombinant) rywn) injection) [package insert]. Palo Alto, CA: Jazz Pharmaceuticals; 2021.

Avapritinib (Ayvakit®)

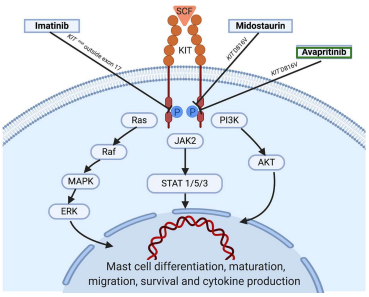
Indication

- Advanced systemic mastocytosis (ASM) in adults including:
  - Systemic mastocytosis with associated hematological neoplasm (SM-AHN)
  - Mast cell leukemia (MCL)
  - Aggressive systemic mastocytosis (ASM)

Avapritinib (Ayvakit)[package insert]. Cambridge, MA. Blueprint Medicines Corporation; 2021.

Avapritinib (Ayvakit®)

Mechanism of Action



Piris-Villaespesa M , et al. *Frontiers in Pharmacology.* 2020;11(443):1-8.

Avapritinib (Ayvakit®) PATHFINDER Trial

Objective	Evaluate efficacy in advanced systemic mastocytosis	
Design	Phase 2, single arm study	
Intervention	Avapritinib 200 mg PO daily until toxicity or progression Median Duration: 10.4 months	
Population	Advanced systemic mastocytosis: SM-AHN (81%), MCL (13%), ASM: 6% Median age: 69 years (31-88); ECOG: 0-1 (69%) Previous treatment: 68%	
Endpoints	**Primary**	
	• ORR: 75% ; median time to response: 2 months • CR or CRi: 19%	
	Secondary	
	• OS: Not reached at analysis • Predicted OS at 12 months: 87%	Safety • Edema: > 50% • Thrombocytopenia: 32% • Diarrhea: 28% • Cognitive effects: 14% • Required dose reduction: 92% • Discontinued due to ADE: 5%

DeAngelo DJ, et al. AACR. 2021:Abstr, CT023.

Avapritinib (Ayvakit®)

Dosing:
•200 mg PO daily

Administration:
• On empty stomach
•1 hour before or 2 hours after a meal
•Antiemetic premed

Drug-Drug Interactions:
•Strong and moderate CYP3A4, CYP3A5 and CYP2C9 inhibitors
• Strong and moderate CYP3A4, CYP3A5 and CYP2C9 inducers

Dose Adjustments
Thrombocytopenia

Warnings/Precautions
Intracranial Hemorrhage
Memory Impairment, Confusion
Embryo-Fetal Toxicity

Other Adverse Effects
Pancytopenia
Edema
Hyperbilirubinemia, Transaminitis
Hypophosphatemia

Monitoring/Guidance
Platelets at baseline and every 2 weeks for first 8 weeks, then every 2 weeks if platelets < 75,000 or every 4 weeks if platelets 75-100,000

Avapritinib (Ayvakit)[package insert]. Cambridge, MA: Blueprint Medicines Corporation; 2021.

Avapritinib (Ayvakit®): Helpful Information

- Not recommended platelets < 50,000
- Copay assistance and free drug program available
- Tablet sizes: 25 mg, 50 mg, 100 mg, 200 mg
- Note: target dose is different from GIST target dose
- Hazardous precautions

Avapritinib (Ayvakit) [package insert]. Cambridge, MA: Blueprint Medicines Corporation; 2021.

New Drug Approvals in Multiple Myeloma

Belantamab mafodotin-blmf (Blenrep®)

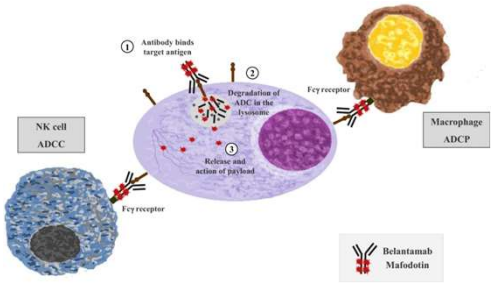
Indication

- Relapsed/refractory multiple myeloma (R/R MM) who have received at least 4 previous regimens one of which must have contained a CD38- targeted therapy, proteasome inhibitor, and an immunomodulatory agent
- Approved as a monotherapy

Belantamab mafodotin-blmf (Blenrep®) [package insert]. Research Triangle Park, NC. GlaxoSmithKline, Inc.; 2020.

Belantamab mafodotin-blmf (Blenrep®)

Mechanism of Action



Offidani M, et al. *Drug Design, Development and Therapy*. 2021:152401–2415.

Belantamab mafodotin-blmf (Blenrep®) DREAMM-2 Trial

Objective	Evaluate efficacy in relapsed/refractory MM	
Design	International, open label, Phase 2, two-arm study	
Intervention	Belantamab mafodotin-blmf 2.5 mg/kg IV every 3 weeks vs. Belantamab mafodotin-blmf 3.5 mg/kg IV every 3 weeks	
Population	R/R MM who have received a CD38 agent, a proteosome inhibitor, and immunomodulatory agent Median age: 65-67; > 50% ISS Stage II and III Median of 6-7 previous lines of therapy	
Endpoints	**Primary**	
	• ORR: 31% vs. 35%	
	Secondary	
	• DOR: NR vs 6.2 months • PFS: 2.8 months vs. 3.9 months • Probability of 1 year survival: 53%	Safety • Ocular events (>70% keratopathy) • Thrombocytopenia • Anemia • 8-10% discontinuation rate due to keratopathy

Lonial S et al. *Lancet Oncol*. 2020;21:207–221.
Lonial S et al. *J Clin Onc*. 2020;38:15. Abstr 8536.

Belantamab mafodotin-blmf (Blenrep®)

Dosing:
- 2.5 mg/kg IV every 3 weeks
- Used total body weight

Administration:
- Infuse over 30 minutes
- Use within 6 hours of preparation

Drug-Drug Considerations :
- Substrate of OATP1B1,and OATP1B3, MRP1, MRP2, MRP3, and possible Pgp

Dose Adjustments
Corneal events
Thrombocytopenia

Warnings/Precautions
Ocular Toxicity
Infusion related reactions
Embryo-Fetal Toxicity

Other Adverse Effects
Pancytopenia
Pneumonia
Renal impairment

Monitoring/Guidance
Ophthalmic exam at baseline, prior to each dose, and if symptoms develop

Belantamab mafodotin-blmf (Blenrep®) [package insert]. Research Triangle Park, NC. GlaxoSmithKline, inc.; 2020.

Belantamab mafodotin-blmf (Blenrep®): Helpful Information

REMS Program
- Restricted distribution drug
- Medication and patient guide distribution
- Ophthalmology appointments and monitoring

Ocular Toxicity Management:
- Preservative-free lubricant eyedrops
  - Corticosteroid eyedrops not as beneficial
- Avoid contact lenses
- Dose delays or omissions

Belantamab mafodotin-blmf (Blenrep®) [package insert]. Research Triangle Park, NC. GlaxoSmithKline, inc.; 2020.

Melphalan Flufenamide (Pepaxto®)

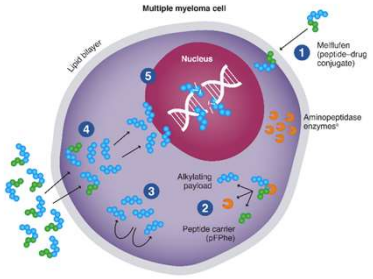
Indication

- Relapsed/refractory multiple myeloma (R/R MM) who have received at least 4 previous regimens including a CD38- targeted therapy, proteasome inhibitor, or an immunomodulatory agent
- Approved in combination with dexamethasone

Melphalan Flufenamide (Pepaxto®) [package insert]. Waltham, MA. Oncopeptides, Inc; 2021.

Melphalan Flufenamide (Pepaxto®)

Mechanism of Action



Mateos MV, et al. *J. Clin. Med.* 2020, 9, 3120.

Melphalan Flufenamide (Pepaxto®): HORIZON Trial

Objective	Evaluate efficacy with dexamethasone in relapsed/refractory MM	
Design	Multicenter, open label, Phase 2, single arm	
Intervention	• Melphalan 40 mg IV on Day 1 of every 28-day cycle • Dexamethasone 40 mg PO on Days 1,8,15,22	
Population	R/R MM who were refractory to a CD38 agent, a proteosome inhibitor, or immunomodulatory agent Median age: 65; > 50% ISS Stage I and II; Extramedullary disease: 35% 76% triple refractory; 59% alkylator refractory Median previous lines of therapy: 5	
Endpoints	**Primary**	
	• ORR: 29%	
	Secondary	
	• DOR: 5.5 months • PFS: 4.2 months • OS: 11.6 months	Safety • Neutropenia: 82%, Grade 4: 47% • Thrombocytopenia: 82%, Grade: 51% • Nausea: 32% • Diarrhea: 27% • 83% discontinuation due to progression

Richardson et al. *J Clin Oncol* 39:757-767.

Melphalan Flufenamide (Pepaxto®)

Dosing:
- 40 mg IV on Day 1
- Dexamethasone 40 mg IV/PO on Days 1,8,15,22
- 28-day cycles

Administration:
- Infuse over 30 minutes
- 5HT3 antagonist premed
- Central line administration

Preparation:
- Cold 0.9% normal saline
- Timed steps
- Use within 60 minutes; up to 6h stability refrigerated

Dose Adjustments
Hold if ANC <1000
Hold if platelets < 50,000
Neutropenia
Thrombocytopenia

Warnings/Precautions
Pancytopenia
Infections
Secondary Malignancies
Embryo-Fetal Toxicity
Potential increased mortality risk with high doses

Other Adverse Effects
Pneumonia
URI
Febrile Neutropenia

Monitoring/Guidance
CBC at baseline and prior to each cycle

Melphalan Flufenamide (Pepaxto®) [package insert]. Waltham, MA. Oncopeptides, Inc; 2021.

Melphalan Flufenamide (Pepaxto®): Helpful Information

- FDA Alert in July 2021:
  Increased risk of death in patients receiving Melphalan Flufenamide and low dose dexamethasone with R/R MM in Phase 3 OCEAN trial.
- Financial assistance is available
- Hazardous precautions

FDA Alerts: Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-patients-and-health-care-professionals-about-clinical-trial-results-showing-increased

Audience Response Question #1

True or False:

Melphalan flufenamide can be substituted for high dose melphalan in stem cell conditioning regimens.

1. True
2. False

New Drug Approvals in Lymphoma

Pembrolizumab (Keytruda®)

Indication

- Relapsed/refractory classical Hodgkin's Lymphoma (R/R cHL) in adults and pediatrics

Pembrolizumab (Keytruda) [package insert]. Whitehouse Station, NJ: Merck & Co, Inc; 2021.

Pembrolizumab (Keytruda®): Keynote 204 Trial

Objective	Assess efficacy of pembrolizumab compared to brentuximab vedotin in R/R cHL	
Design	International, Randomized Phase 3	
Intervention	Pembrolizumab 200 mg IV every 3 weeks vs. Brentuximab vedotin 1.8 mg/kg IV every 3 weeks	
Population	R/R cHL in patients who had received autoHCT or were ineligible for autoHCT Median age: 35-36 years; ECOG: 0-1 (69%); Median previous therapies: 2 vs. 3 Previous autoHCT: 37%; no previous autoHCT: 63% Previous brentuximab vedotin exposure: 3% vs. 7%	
Endpoints	**Primary**	
	• PFS: 13.2 vs. 8.3 months • OS: NR in published interim analysis; planned for third interim analysis	
	Secondary	
	• ORR: 65.6% vs. 54.2% • CR: 24.5% vs. 24.2% • DOR 20.7 months vs.13.8 months	Safety • ADEs: 74% vs. 77% • irAEs: 3% vs. 7% • Pneumonitis: 4% vs. 1% • Neutropenia: 2% vs. 7% • Peripheral neuropathy: 1% vs. 3%

Kuruvilla J, et al. *Lancet Oncol* 2021; 22: 512–24.

Umbralisib (Ukoniq®)

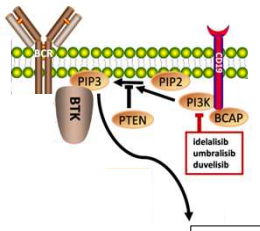
Indication

- Relapsed/refractory marginal zone lymphoma (R/R MZL) who received ≥ 1 anti-CD20 directed therapy
- Relapsed/refractory follicular lymphoma (R/R FL) who received ≥ 3 prior therapies

Umbralisib (Ukoniq) [package insert]. Edison, NJ: TG Therapeutics, Inc; 2021..

Umbralisib (Ukoniq®)

Mechanism of Action



Umbralisib
- More selective for PI3Kδ
- Inhibition of CK1ε

AKT/mTOR Pathway

Adapted from Wang L, et al. *Signal Transduction and Targeted Therapy.* 2020;5:15.
Umbralisib (Ukoniq) [package insert]. Edison, NJ: TG Therapeutics, Inc; 2021.

Umbralisib (Ukoniq®): UNITY-NHL Trial

Objective	Assess efficacy of umbralisib as monotherapy in R/R NHL	
Design	International, open label, Phase 2b, cohort trial	
Intervention	Umbralisib 800 mg PO daily	
Population	R/R MZL, FL, and SLL (also included: MCL and DLBCL) Median age: MZL: 67; FL: 65; SLL: 65 Median pervious therapies: MZL: 2; FL: 3; SLL: 2 > 50% had Stage IV disease for MZL, FL, and SLL	
Endpoints	**Primary**	
	MZL: FL: SLL: • ORR: 49.3% 53% 53%	
	Secondary	
	MZL: FL: SLL: • DOR: NR 11.1 18.3 • TTR: 2.8 4.6 2.7 • PFS: NR 10.6 20.9	Safety • Diarrhea: 53% (10.1% ≥ Grade 3) • Neutropenia: 33% • Nausea: 39.4%; Vomiting: 23.6% • ALT increased 20%

Fowler NH et al. *J Clin Onc.* 2021;39:1609-1618.

Umbralisib (Ukoniq®)

Dosing:
- 800 mg PO daily

Administration:
- With food
- Do not cut or crush

Drug-Drug Considerations:
- Substrate of CYP1A2, CYP2C9, and CYP3A4
- Inhibits CYP2C8, CYP2C9, CYP2C19, CYP3A4, and Pgp
- Induces CYP3A4

Dose Adjustments
Neutropenia
Thrombocytopenia
Hepatotoxicity
Infections
Diarrhea or colitis

Warnings/Precautions
Infections
Neutropenia
Diarrhea or colitis
Hepatoxicity
Severe cutaneous reactions
Allergic reactions (yellow dye)
Embryo-Fetal Toxicity

Other Adverse Effects
Vomiting
Increased creatinine
CMV reactivation

Monitoring/Guidance
Tbili and LFTs at baseline and through treatment

Umbralisib (Ukoniq) [package insert]. Edison, NJ: TG Therapeutics, Inc; 2021.

Umbralisib (Ukoniq®): Helpful Information

- Antiviral and *Pneumocystis jirovecii* pneumonia prophylaxis necessitated.
- Copay assistance program available
- Tablet size: 200 mg
- Patient guidance to track changes in stool to prevent colitis
- Hazardous precautions

Fowler NH et al. *J Clin Onc.* 2021;39:1609-1618.
Umbralisib (Ukoniq) [package insert]. Edison, NJ: TG Therapeutics, Inc; 2021.

Loncastuximab Tesirine (Zynlonta®)

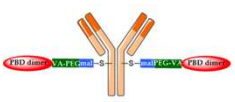
Indication

- Relapsed/refractory large B-cell lymphoma (LBCL) who have received ≥ 2 systemic treatments. Includes:
  - Diffuse large B-cell lymphoma, not otherwise specified (DLBCL)
  - Transformed indolent lymphomas
  - High-grade B-cell lymphoma (HGBCL)

Loncastuximab Tesirine (Zynlonta) [package insert]. Murray Hill, NJ: ADC Therapeutics SA; 2021.

Loncastuximab Tesirine (Zynlonta®)

Mechanism of Action



anti-CD19 Loncastuximab tesirine

Joubert N, et al. *Pharmaceuticals.* 2020;13:245).

Loncastuximab Tesirine (Zynlonta®): LOTIS-2 Trial

Objective	Assess efficacy of Loncastuximab Tesirine as monotherapy in R/R DLBCL	
Design	International, open label, Phase 2, single arm	
Intervention	Loncastuximab Tesirine 150 µg/kg IV on day 1 of 21-day cycle x 2 cycles, then 75 µg/kg IV thereafter, for up to 1 year	
Population	R/R DLBCL status post ≥ 2 multiagent lines of therapy Median age: 66 ; Previous systemic treatments: 3; Previous CART therapy: 9% DLBCL 88%, HGBCL: 8%, PMBCL: 5%l Bulky disease: 6%	
Endpoints	**Primary**	
	• ORR: 48.3% • CR: 24%	
	Secondary	
	• Time to response: 41 days • DOR: 10.3 months • PFS: 4.9 months • OS: 9.9 months	Safety • Anemia 16%, Thrombocytopenia 15% • Neutropenia 14%, Febrile neutropenia 3% • Edema 19%, pleural effusion: 8%, Pericardial effusion 1% • Increased LFTs > 13% • Rash: > 12% • 62% dose reduced or discontinued due to ADEs

Caimi PF et al. *J Lancet Oncol* 2021;22: 790-800.

Loncastuximab Tesirine (Zynlonta®)

Dosing:
- C1-2: 150 µg/kg IV on day 1
- C ≥3: 75 µg/kg IV on day 1
- 21-day cycles
- If BMI>35 kg/m2, use ADBW

Administration:
- 30-minute infusion
- Dexamethasone 4 mg PO q12h x 3 days

Preparation:
- Dilute in 50 mL D5W
- 24h under refrigeration

Drug-Drug Considerations:
- Substrate of Pgp

Warnings/Precautions
Effusions/Edema
Myelosuppression
Infections
Cutaneous reactions
Embryo-Fetal Toxicity

Warnings/Precautions
Effusions/Edema
Myelosuppression
Infections
Cutaneous reactions
Embryo-Fetal Toxicity

Other Adverse Effects
Nausea/Vomiting
Photosensitivity
URI

Monitoring/Guidance
CBC, CMP at baseline and throughout treatment

Loncastuximab Tesirine (Zynlonta) [package insert]. Murray Hill, NJ: ADC Therapeutics SA; 2021.

Loncastuximab Tesirine (Zynlonta®): Helpful Information

- Hazardous precautions
- Classified as an irritant
- Can consider addition of growth factor
- Copay and financial assistance programs available

Loncastuximab Tesirine (Zynlonta) [package insert]. Murray Hill, NJ: ADC Therapeutics SA; 2021.

Audience Response Question #2

Which of the following drug-serious toxicity pairs are incorrectly paired?

1. Umbralisib – colitis
2. Belantamab mafodotin-blmf – keratopathy
3. Avapritinib – thrombocytopenia and bleeding events
4. Loncastuximab Tesirine - Hypophosphatemia

New Drug Approvals in CART Therapies

New CART Therapies Compared

CART Product	Lisocabragene maraleucel (Breyanzi®)	Idecabtagene vicleucel (Abecma®)	Axicabtagene Ciloleuel (Yescarta®)
Approval Date	February 2021	March 2021	March 2021
Indication	R/R LBCL status post ≥2 lines of systemic therapy & FL grade 3B	R/R MM status post ≥4 lines of therapy including proteasome inhibitor, immunomodulatory agent, and anti-38 antibody	R/R FL (indication added)
Construct: Target and Co-stimulatory Domain	CD19 CD3ζ 4-1BB	BCMA CD3ζ 4-1BB	CD19 CD3ζ CD28

Lisocabragene maraleucel (Breyanzi®) [package insert]. Bothell, WA: Juno Therapeutics Inc.;2021.
Idecabtagene vicleucel (Abecma®) [package insert]. Summit, NJ: Celgene Corporation; 2021.
Axicabtagene ciloleuel (Yescarta®) [package insert]. Santa Monica, CA: Kite Pharma Inc.; 2021.

New CART Therapies Compared

CART Product	Lisocabragene maraleucel (Breyanzi®)	Idecabtagene vicleucel (Abecma®)	Axicabtagene Ciloleuel (Yescarta®)		
Pivotal Trial	Transcend NHL 001	KarMMa	ZUMA-5		
ORR **CR**	73% 53%	73% 33%	Overall: 92% 76%	FL: 94% 80%	MZL: 85% 60%
PFS **OS**	6.8 months 21.1 months	8.8 months 19.4 months	Overall: NR NR	FL: NR NR	MZL: 11.8 m NR
CRS **CRS Grade ≥ 3**	42% 2%	84% 5%	Overall: 82% 7%	FL: 78% 6%	MZL: 100% 9%
ICANS **ICANS Grade ≥ 3**	30% 10%	18% 3%	Overall: 60% 19%	FL: 56% 15%	MZL: 77% 41%

Abramson JS, et al. Lancet. 2020; 396(10254):839-852.
Munshi, NC, et al. NEJM. 2021;384(8):705-716.
Jacobson, et al. ASH 2020. Abstr 700.

New CART Therapies Compared

CART Product	Lisocabragene maraleucel (Breyanzi®)	Idecabtagene vicleucel (Abecma®)	Axicabtagene Ciloleuel (Yescarta®)
REMS	Yes		
Lymphodepletion	Fludarabine 30 mg/m^2 + Cyclophosphamide 300 mg/m^2 x 3 days		Fludarabine 30 mg/m^2 + Cyclophosphamide 500 mg/m^2 x 3 days
Premedication	Acetaminophen Diphenhydramine		
Other Considerations	CD8 and CD4 components are separate. Prepare CD8 component first	HLH/MAS additional label warning	• Can consider early levetiracetam prophylaxis • Avoid operating vehicle and machinery x8 weeks

Lisocabragene maraleucel (Breyanzi®) [package insert]. Bothell, WA: Juno Therapeutics Inc.;2021.
Idecabtagene vicleucel (Abecma®) [package insert]. Summit, NJ: Celgene Corporation; 2021.
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Jacobson, et al. ASH 2020. Abstr 700.

Audience Response Question #3

Which of the following CART co-stimulatory domains is associated with greater incidence of CRS and neurotoxicity?

1. 4-1BB
2. CD28

New Drug Approval in GVHD

Belumosudil (Rezurock®)

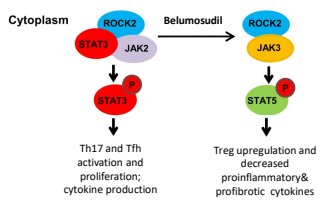
Indication

- Chronic GVHD (cGVHD) after failure of ≥ 2 systemic therapies
- Adults and pediatrics ≥ 12 years of age

Belumosudil (Rezurock®) [package insert]. Warrendale, PA: Kadmon Pharmaceuticals; 2021.

Belumosudil (Rezurock®)

Mechanism of Action



Adapted from: Chen W, et al. *Sci Rep.* 2018;8 (1): 16636.

Belumosudil (Rezurock®): ROCKstar Trial

Objective	Assess efficacy of addition of belumosudil in cGVHD
Design	Multicenter, randomized, Phase 2, 2 arm study
Intervention	Belumosudil 200 mg PO daily (or Belumosudil 200 mg PO BID)
Population	cGVHD in patients ≥ 12 years old 70% severe cGVHD; skin: 83%, joints/fascia: 77%, eyes: 73%, lungs: 36%, GI 29% Median age: 53 Previous treatments: 3; Previous ruxolitinib: 30%, Previous ibrutinib: 33%
Endpoints	**Primary** • ORR: 75% (CRs achieved in each organ subgroup) **Secondary** • TTR: 4 weeks • DOR: 54 weeks • FFS: 73% at 6 months • > 7-point Lee Symptom Scale reduction: 52% • Corticosteroid reductions: 64% • Corticosteroid discontinuation: 20% • Calcineurin inhibitor reductions: 42% • Calcineurin inhibitor discontinuations: 17% • OS: 87% at 2 years Safety • Infections 53% • Asthenia: 46% • Nausea: 42% • Hemorrhage: 23% • Hypertension: 21% • Hyperglycemia: 5% • 12% discontinued due to ADEs

Cutler CS, et al. *Blood.* 2021.
The ROCKstar Study Efficacy. Available at: https://rezurockhcp.com/rockstar-study-efficacy-data/

Belumosudil (Rezurock®)

Dosing:
• 200 mg PO daily

Administration:
• With food
• Do not cut, crush, or chew

Drug-Drug Interactions:
• String CYP3A inducers
• Proton pump inhibitors

Dose Adjustments
Hepatoxicity
Interacting Medications

Warnings/Precautions
Embryo-Fetal Toxicity

Other Adverse Effects
Infections
Nausea, Diarrhea
Cough
Bleeding
MSK Pain
Hypertension
Reduced Lymphocytes
Hypophosphatemia
Increased LFTs and Tbili

Monitoring/Guidance
Tbili/LFTs at baseline and monthly thereafter

Belumosudil (Rezurock®) [package insert]. Warrendale, PA: Kadmon Pharmaceuticals; 2021.

Belumosudil (Rezurock®): Helpful Information

- Hazardous precautions
- Copay and financial assistance programs available
- 30-day free supply to prevent delays in treatment due to insurance approvals
- Tablet size: 200 mg

Belumosudil (Rezurock®) [package insert]. Warrendale, PA: Kadmon Pharmaceuticals; 2021

Audience Response Question #4

Concomitant administration of which of the following necessitate a dose adjustment for belumosudil?

1. Strong CY3A inducers
2. Pgp inhibitors
3. Proton pump inhibitors
4. Both 1 and 3
5. Both 2 and 3

Conclusions

- Many novel therapeutics have been approved for diseases in relapsed/refractory disease states
- Focus on optimizing efficacy while minimizing toxicity
- Many agents received Accelerated Approval or Orphan Drug designations. Finalized results anticipated in future
- New regimens for AML and agents for cGVHD currently under FDA review
- Financial barriers to access

Drug Updates in Hematologic Malignancies

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