Loncastuximab Tesirine-lpyl: Administration and Patient Management Inservice

Please see Important Safety Information throughout. Full Prescribing Information is available in this presentation or at ZYNLONTAhcp.com.

THERAPEUTICS

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MA-SLD-US-LTX-00036

LONCA

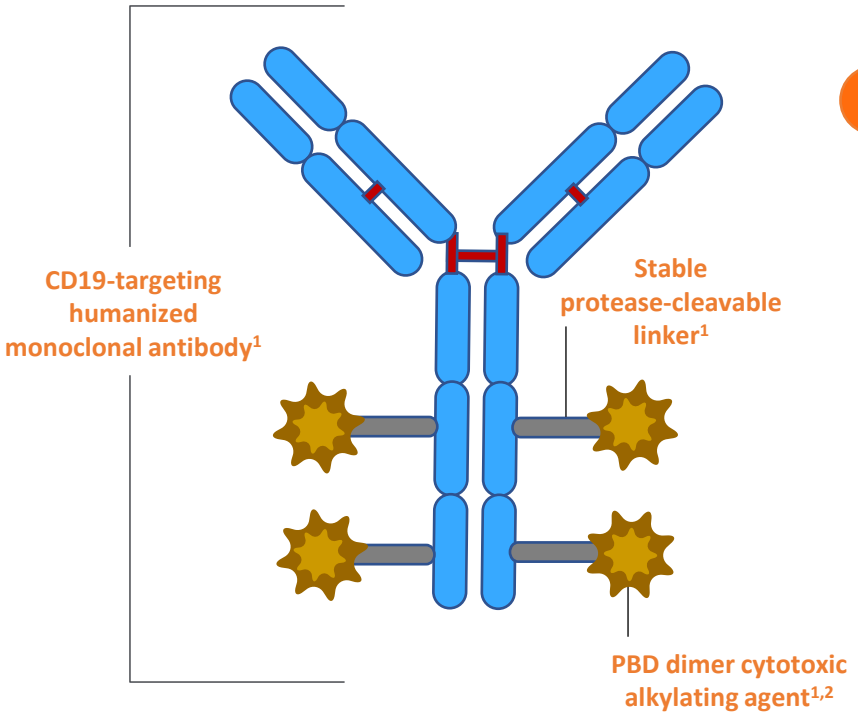
Loncastuximab tesirine-lpyl (Lonca) for the Treatment of Relapsed or Refractory DLBCL

Learning Objectives
Describe the Lonca MOA
Discuss Lonca indication and patient population studied
Describe Lonca dosing and administration
Identify Lonca side effect profile, how to identify AEs, and patient management

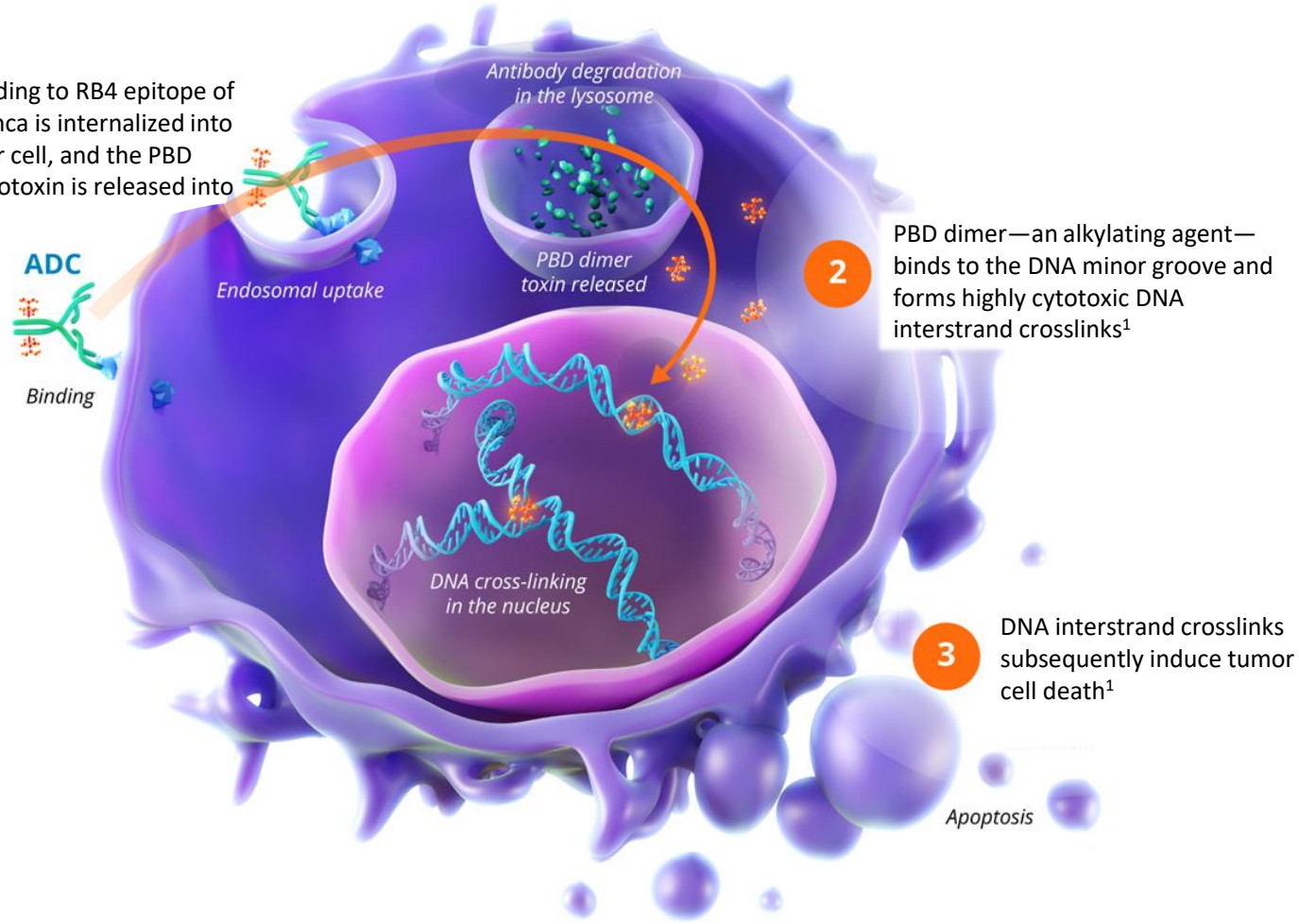
AE, adverse event; DLBCL, diffuse large B-cell lymphoma; MOA, mechanism of action.

LONCA

CD19-Directed ADC Delivers a Potent Payload



1 Upon binding to RB4 epitope of CD19, Lonca is internalized into the tumor cell, and the PBD dimer cytotoxin is released into the cell[1]



2 PBD dimer—an alkylating agent—binds to the DNA minor groove and forms highly cytotoxic DNA interstrand crosslinks[1]

3 DNA interstrand crosslinks subsequently induce tumor cell death[1]

ADC, antibody-drug conjugate; DNA, deoxyribonucleic acid; PBD, pyrrolobenzodiazepine.

1. Zynlonta (loncastuximab tesirine-lpyl) Prescribing Information. Murray Hill, NJ; ADC Therapeutics; October 2022.
2. Hartley JA. *Expert Opin Biol Ther*. 2021;21(7):931-943.

LONCA

Indication and Usage[1]

ZYNLONTA® (loncastuximab tesirine-lpyl) is indicated for the treatment of 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 (HGBCL).

This indication is approved under accelerated approval based on the overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

FDA Accelerated Approval date: April 23, 2021[2]

FDA, Food and Drug Administration.
1. Zynlonta (loncastuximab tesirine-lpyl) Prescribing Information. Murray Hill, NJ; ADC Therapeutics; October 2022. 2. U.S. Food & Drug Administration. *FDA grants accelerated approval to loncastuximab tesirine-lpyl for large B-cell lymphoma.* 2021. Accessed June 16, 2025. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-loncastuximab-tesirine-lpyl-large-b-cell-lymphoma

LONCA

Warnings and Precautions[1,a]

Effusion and Edema	Serious effusion and edema occurred in patients treated with Lonca. Withhold Lonca for grade 2 or greater effusion or edema until the toxicity resolves. Consider diagnostic imaging when symptoms develop or worsen.
Myelosuppression	Treatment with Lonca can cause serious or severe myelosuppression, including neutropenia, thrombocytopenia, and anemia. Monitor complete blood counts. Withhold, reduce, or discontinue Lonca based on the severity of cytopenia.
Infections	Fatal and serious infections, including opportunistic infections, occurred in patients treated with Lonca. Monitor for any new or worsening signs of symptoms consistent with infection. For grades 3 or 4 infection, withhold Lonca until the infection has resolved.
Cutaneous Reactions	Serious cutaneous reactions occurred in patients treated with Lonca. Monitor patients for new or worsening cutaneous reactions, including photosensitivity reactions. Advise patients to minimize or avoid exposure to direct natural or artificial sunlight and to wear sun-protective clothing and/or sunscreen products. Dermatologic consultation should be considered if skin reaction or rash develops.
Embryo-fetal Toxicity	Lonca can cause embryo-fetal harm. Advise females of reproductive potential and male patients with female partners of reproductive potential of the potential risk to a fetus and use of effective contraception.

[a]The pooled safety population described in the WARNINGS AND PRECAUTIONS reflects exposure to Lonca as a single agent at an initial dose of 0.15 mg/kg in 215 patients with DLBCL in studies ADCT-402-201 (LOTIS-2) and ADCT-402-101. In this pooled safety population of 215 patients, the most common (>20%) adverse reactions, including laboratory abnormalities, were thrombocytopenia, increased gamma-glutamyl transferase, neutropenia, anemia, hyperglycemia, transaminase elevation, fatigue, hypoalbuminemia, rash, edema, nausea, and musculoskeletal pain.

1. Zynlonta (loncastuximab tesirine-lpyl) Prescribing Information. Murray Hill, NJ; ADC Therapeutics; October 2022.

Lonca Was Investigated in LOTIS-2, the Pivotal Phase 2, Open-Label Study[1,2]

Patient Population	Primary Endpoint	Key Secondary Endpoints
R/R DLBCL after ≥2 prior lines of systemic therapy, including DLBCL-NOS, DLBCL arising from low-grade lymphoma, and high-grade B-cell lymphoma	ORR by IRC of PET-CT using Lugano 2014 criteria	DOR, CR rate

Lonca was administered as a single, 30-minute infusion Q3W[a]

Key inclusion criteria: transplant-eligible and -ineligible patients; DLBCL NOS; DLBCL arising from low-grade lymphoma; HGBCL with *MYC* and *BCL2* and/or *BCL6* rearrangements; ECOG PS 0-2; patients with prior CD19-directed therapy if CD19-positive.

Key exclusion criteria: patients with bulky disease (tumors ≥10 cm) and active CNS lymphoma.

Among the 145 patients, the median number of cycles received was 3, with 34% receiving 5 or more cycles.

[a]The average weight was 77.1 kg, requiring 2 vials for the first 2 cycles and then 1 vial for subsequent cycles.[3]

CR, complete response; CNS, central nervous system; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HGBCL, high-grade B-cell lymphoma; IRC, independent review committee; NOS, not otherwise specified; ORR, overall response rate; PET-CT, positron emission tomography-computed tomography; PS, performance status; Q3W, every 3 weeks; R/R, relapsed/refractory; SCT, stem cell transplant.

1. Zynlonta (loncastuximab tesirine-lpyl) Prescribing Information. Murray Hill, NJ; ADC Therapeutics; October 2022. 2. Caimi PF, et al. Lancet Oncol. 2021;22(6):790-800. 3. Data on file. ADC Therapeutics SA.

Lonca Dosage and Administration[1]

Administer Lonca by intravenous infusion over 30 minutes on day 1 of each 3-week cycle (with required dexamethasone premedication)

Indicated Dose[a]

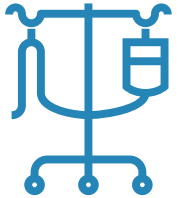
0.15 mg/kg first 2 cycles

0.075 mg/kg subsequent cycles

In LOTIS-2, Lonca was administered until progressive disease or unacceptable toxicity

For patients with a body mass index ≥35 kg/m^2, calculate the dose based on an adjusted body weight (ABW)[b]:

ABW in kg = 35 kg/m^2 × (height in meters)^2



Administration

Use a dedicated infusion line equipped with a sterile, nonpyrogenic, low-protein binding, in-line or add-on filter (0.2 or 0.22 µm pore size) and catheter[c]

Monitor the infusion site for possible subcutaneous infiltration during drug administration

[a]The Lonca prescribing information does not recommend dose adjustments for mild hepatic or mild/moderate renal impairments.
[b]Only nine patients had a body mass index of ≥35 kg/m², and therefore it was not possible to compare safety with patients with body mass index <35 kg/m².
[c]Lonca is an irritant with vesicant-like properties that may be administered into a short flexible temporary catheter in the arm or through a central venous catheter.
Lonca, loncastuximab tesirine.

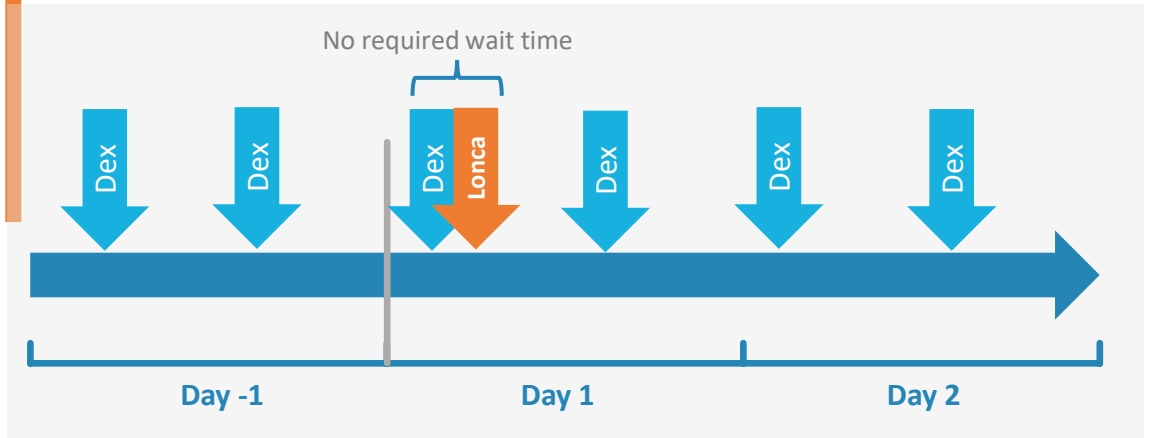
1. Zynlonta (loncastuximab tesirine-lpyl) Prescribing Information. Murray Hill, NJ; ADC Therapeutics; October 2022.

Dexamethasone Premedication[1]

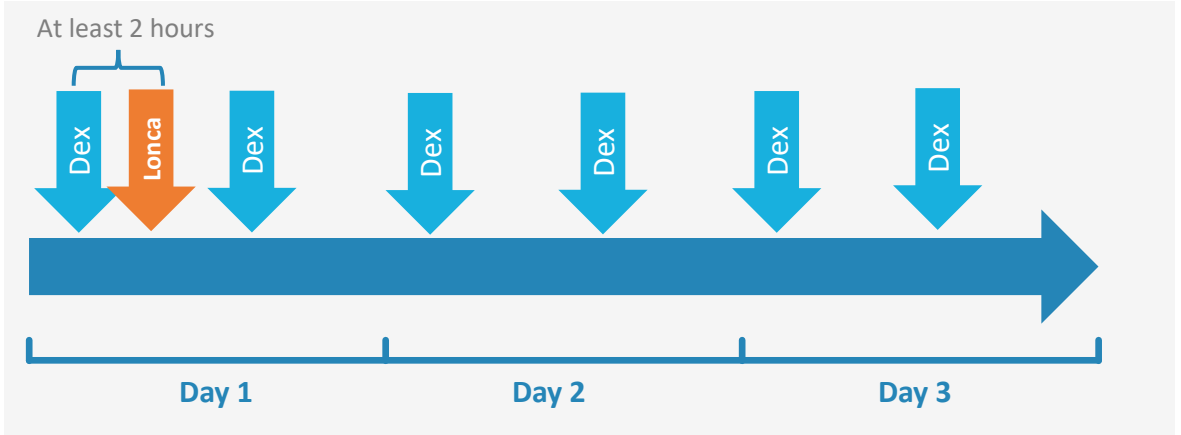
- Unless contraindicated, administer dexamethasone 4 mg orally or intravenously twice daily for 3 days beginning the day before administering Lonca.
    - If dexamethasone administration does not begin the day before Lonca, dexamethasone should begin at least 2 hours prior to administration of Lonca.

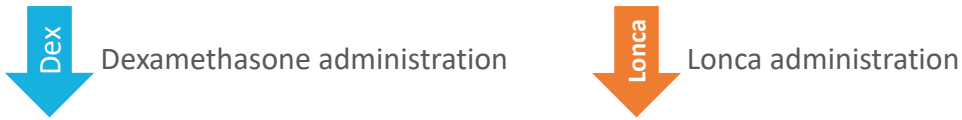
Dexamethasone Premedication Administration

If dexamethasone administration begins the day before Lonca:



If dexamethasone administration does not begin the day before Lonca:





Dex, dexamethasone; Lonca, loncastuximab tesirine; PBD, pyrrolobenzodiazepine.

1. Zynlonta (loncastuximab tesirine-lpyl) prescribing information. Murray Hill, NJ; ADC Therapeutics; October 2022.

LONCA

Reconstitution and Dilution of Lonca

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Reconstitution

- Reconstitute Lonca using 2.2 mL of sterile water for injection, USP, with the stream directed toward the inside wall of the vial to a final concentration of 5 mg/mL.
- Swirl the vial gently until the powder is completely dissolved.
  - Do not shake.
  - Do not expose to direct sunlight.
- Inspect the reconstituted solution for particulate matter and discoloration. The solution should appear clear to slightly opalescent and colorless to slightly yellow. Do not use if the reconstituted solution is discolored, is cloudy, or contains visible particulates.

Dilution

- Withdraw the required volume of reconstituted solution from the Lonca vial using a sterile syringe.
  - Discard any unused portion left in the vial.
- Add the calculated dose volume of the Lonca solution into a 50 mL infusion bag of 5% dextrose injection, USP. Gently mix the intravenous bag by slowly inverting the bag.
  - Do not shake.

- Lonca is a hazardous drug. Follow applicable special handling and disposal procedures.[a]

[a]For hazardous drugs, follow procedures for proper handling (ie, use of gloves or protective clothing).

Lonca, loncastuximab tesirine; USP, United States Pharmacopeia.

Zynlonta (loncastuximab tesirine-lpyl) prescribing information. Murray Hill, NJ; ADC Therapeutics; October 2022.

LONCA

Storage of Lonca

Storage of reconstituted vial

- After reconstitution, store the reconstituted solution in the vial for up to 4 hours:
  - Refrigerated (2°C to 8°C; 36°F to 46°F)
  - Room temperature (20°C to 25°C; 68°F to 77°F)
  - Do not freeze
- The product does not contain a preservative. Discard unused vial after reconstitution if the recommended storage time is exceeded.

Storage of diluted infusion solution

- After dilution, store the diluted Lonca infusion solution:
  - Refrigerated (2°C to 8°C; 36°F to 46°F) for up to 24 hours
  - Room temperature (20°C to 25°C; 68°F to 77°F) for up to 8 hours
  - Do not freeze
- Discard diluted infusion bag if storage time exceeds these limits.

Lonca, loncastuximab tesirine.
Zynlonta (loncastuximab tesirine-lpyl) prescribing information. Murray Hill, NJ; ADC Therapeutics; October 2022.

LONCA

Effusion and Edema: Monitoring, Patient Counseling, and Management

Incidence in LOTIS-2 (N=145)[1]

	Any Grade	Grade ≥3
Effusion	**11%** (n=16)	**2.8%** (n=4)
Edema	**27.6%** (n=40)	**3.4%** (n=5)

Monitoring

Monitor patients for new or worsening edema or effusions.[2]

Consider diagnostic imaging in patients who develop symptoms of pleural effusion or pericardial effusion, such as new or worsened dyspnea, chest pain, and/or ascites, such as swelling in the abdomen and bloating.[2]

Patient Counseling

Advise patients to contact their healthcare provider if they experience swelling, weight gain, shortness of breath, or difficult, labored breathing.[2]

Dose Modification in LOTIS-2 (N=145)[1,a]

	Dose Delay	Dose Reduction	Dose Withdrawal
Effusion	**1.4%** (n=2)	**0%** (n=0)	**2.8%** (n=4)
Edema	**5.5%** (n=8)	**0.7%** (n=1)	**2.8%** (n=4)

Dose Modifications

For grade ≥2 edema or effusion, withhold Lonca until toxicity resolves to grade ≤1.[2,b]

Management

Institute appropriate medical management for edema or effusions.[2,a]

[a]Post-hoc analysis. [b]If dosing is delayed by >3 weeks due to toxicity related to Lonca, reduce subsequent doses by 50%. If toxicity reoccurs following dose reduction, consider discontinuation. If toxicity requires dose reduction following the second dose of 0.15 mg/kg (Cycle 2), the patient should receive the dose of 0.075 mg/kg for cycle 3.[1] [c]In the LOTIS-2 trial, spironolactone diuretic therapy at standard doses was initiated in patients with weight gain >1 kg from baseline and/or new or worsening edema. Additional diuretic support was added for further increases in weight or pleural effusion.[3]
Data cutoff: April 6, 2020.
Lonca, loncastuximab tesirine; PI, prescribing information.
1. Data on file. ADC Therapeutics SA. **2.** Zynlonta (loncastuximab tesirine-lpyl) prescribing information. Murray Hill, NJ; ADC Therapeutics; October 2022. **3.** ADCT-402-201 Clinical Study Protocol. ADC Therapeutics SA.

LONCA

Myelosuppression: Monitoring, Patient Counseling, and Management

Incidence in LOTIS-2 (N=145)[1,a]

	Any Grade	Grade ≥3
Neutropenia	**53.8%** (n=78)	**29.7%** (n=43)
Thrombocytopenia	**66.2%** (n=96)	**17.9%** (n=26)
Anemia	**93.8%** (n=136)	**11.0%** (n=16)

Dose Modification in LOTIS-2 (N=145)[1,a]

	Dose Delay	Dose Reduction	Dose Withdrawal
Neutropenia	**12.4%** (n=18)	**0%** (n=0)	**0.7%** (n=1)
Thrombocytopenia	**9.0%** (n=13)	**0.7%** (n=1)	**1.4%** (n=2)
Anemia	**2.8%** (n=4)	**0%** (n=0)	**0%** (n=0)

Monitoring

Monitor complete blood counts throughout treatment.[2]

Dose Modifications

For an absolute neutrophil count $<1\times10^9$/L, withhold Lonca until neutrophil count returns to $\geq1\times10^9$/L.[2,c]

For a platelet count <50,000/µL, withhold Lonca until the platelet count returns to ≥50,000/µL.[2,c]

Patient Counseling

Advise patients to immediately contact their healthcare provider for a fever of 100.4°F (38°C) or greater or signs or symptoms of bruising or bleeding.[2]

Advise patients of the need for periodic monitoring of blood counts.[2]

Management

Consider prophylactic granulocyte colony-stimulating factor administration as applicable.[2]

[a]Incidence of hematologic abnormalities were based on laboratory reporting, while dose modifications were based on adverse event reporting. [b]Post-hoc analysis. [c]If dosing is delayed by >3 weeks due to toxicity related to Lonca, reduce subsequent doses by 50%. If toxicity reoccurs following dose reduction, consider discontinuation. If toxicity requires dose reduction following the second dose of 0.15 mg/kg (Cycle 2), the patient should receive the dose of 0.075 mg/kg for cycle 3.[1]

Lonca, loncastuximab tesirine.

1. Data on file. ADC Therapeutics SA. Data cutoff: April 6, 2020. **2.** Zynlonta (loncastuximab tesirine-lpyl) prescribing information. Murray Hill, NJ; ADC Therapeutics; October 2022.

LONCA

Infection: Monitoring, Patient Counseling, and Management

Incidence in LOTIS-2 (N=145)[1,a]

	Any Grade	Grade ≥3
Infection	**33.1%** (n=48)	**9.0%** (n=13)

Monitoring

Monitor for any new or worsening signs or symptoms consistent with infection.[2]

Patient Counseling

Advise patients to contact their healthcare provider for signs or symptoms of infection, including fever, chills, weakness and/or difficulty breathing.[2]

Dose Modification in LOTIS-2 (N=145)[1,a]

	Dose Delay	Dose Reduction	Dose Withdrawal
Infection	**7.6%** (n=11)	**0.7%** (n=1)	**1.4%** (n=2)

Dose Modifications

For grade ≥3 nonhematologic toxicity, withhold Lonca until the toxicity resolves to grade ≤1.[2,b]

[a]Post-hoc analysis. [b]If dosing is delayed by >3 weeks due to toxicity related to Lonca, reduce subsequent doses by 50%. If toxicity reoccurs following dose reduction, consider discontinuation. If toxicity requires dose reduction following the second dose of 0.15 mg/kg (Cycle 2), the patient should receive the dose of 0.075 mg/kg for Cycle 3.[2]

Lonca, loncastuximab tesirine.

1. Data on file. ADC Therapeutics SA. Data cutoff: April 6, 2020. **2.** Zynlonta (loncastuximab tesirine-lpyl) prescribing information. Murray Hill, NJ; ADC Therapeutics; October 2022.

LONCA

Cutaneous Reactions: Monitoring, Patient Counseling, and Management

Incidence in LOTIS-2 (N=145)[1,a]

	Any Grade	Grade ≥3
Photosensitivity	**10.3%** (n=15)	**2.1%** (n=3)
Nonphotosensitivity	**30.3%** (n=44)	**2.1%** (n=3)

Dose Modification in LOTIS-2 (N=145)[1,a]

	Dose Delay	Dose Reduction	Dose Withdrawal
Photosensitivity	**2.8%** (n=4)	**0%** (n=0)	**0.7%** (n=1)
Nonphotosensitivity	**4.8%** (n=7)	**0%** (n=0)	**0%** (n=0)

Monitoring

Monitor patients for new or worsening cutaneous reactions, including photosensitivity reactions.[2]

- If a skin reaction or rash develops, dermatologic consultation should be considered.[2]

Dose Modifications

For grade ≥3 nonhematologic toxicity, withhold Lonca until the toxicity resolves to grade ≤1.[2,b]

Patient Counseling

Advise patients that a skin reaction or rash can occur.[2]

Patients should be directed to minimize or avoid exposure to direct natural or artificial sunlight, including sunlight exposure through glass windows.[2]

Patients should be instructed to protect skin from exposure to sunlight by wearing sun-protective clothing and/or using sunscreen products.[2]

[a]Post-hoc analysis. [b]If dosing is delayed by >3 weeks due to toxicity related to Lonca, reduce subsequent doses by 50%. If toxicity reoccurs following dose reduction, consider discontinuation. If toxicity requires dose reduction following the second dose of 0.15 mg/kg (Cycle 2), the patient should receive the dose of 0.075 mg/kg for Cycle 3.[2]
Lonca, loncastuximab tesirine.

1. Data on file. ADC Therapeutics SA. Data cutoff: April 6, 2020. **2.** Zynlonta (loncastuximab tesirine-lpyl) prescribing information. Murray Hill, NJ; ADC Therapeutics; October 2022.

LONCA

Gamma-Glutamyl Transferase and Other Liver Enzyme Elevations: Monitoring and Management

Incidence in LOTIS-2 (N=145)[1,a]

	Any Grade	Grade ≥3
GGT elevation	**72.4%** (n=105)	**22.1%** (n=32)
AST elevation	**51.7%** (n=75)	**0.7%** (n=1)
ALT elevation	**38.6%** (n=56)	**3.4%** (n=5)
ALP elevation	**53.8%** (n=78)	**2.1%** (n=3)

Monitoring

The Lonca Prescribing Information does not make any statements or recommendations regarding the monitoring of GGT levels.[2]

Dose Modification in LOTIS-2 (N=145)[1,a]

	Dose Delay	Dose Reduction	Dose Withdrawal
GGT elevation	**20.7%** (n=30)	**4.1%** (n=6)	**10.3%** (n=15)
AST elevation	**2.1%** (n=3)	**0%** (n=0)	**0%** (n=0)
ALT elevation	**3.4%** (n=5)	**0%** (n=0)	**0%** (n=0)
ALP elevation	**4.1%** (n=6)	**0%** (n=0)	**0.7%** (n=1)

Dose Modifications

For grade ≥3 nonhematologic toxicity, withhold Lonca until the toxicity resolves to grade ≤1.[2,d]

[a]Incidence of hematologic abnormalities were based on laboratory reporting, while dose modifications were based on adverse event reporting. [b]Post hoc analysis. [c]In LOTIS-2, Lonca was withheld for grade ≥2 increased GGT until it resolved to grade ≤1.[1] [d]If dosing is delayed by >3 weeks due to toxicity related to ZYNLONTA, reduce subsequent doses by 50%. If toxicity reoccurs following dose reduction, consider discontinuation. If toxicity requires dose reduction following the second dose of 0.15 mg/kg (Cycle 2), the patient should receive the dose of 0.075 mg/kg for Cycle 3.[2]

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; Lonca, loncastuximab tesirine.

1. Data on file. ADC Therapeutics SA. Data cutoff: April 6, 2020. **2.** Zynlonta (loncastuximab tesirine-lpyl) Prescribing Information. Murray Hill, NJ; ADC Therapeutics; October 2022.

LONCA

Embryo-Fetal Toxicity and Lactation: Patient Counseling

Embryo-Fetal Toxicity Patient Counseling

Advise pregnant women of the potential risk to a fetus. Advise female patients of reproductive potential to contact their healthcare provider if they become pregnant, or if pregnancy is suspected, during treatment with Lonca.

Advise women of reproductive potential to use effective contraception during treatment with Lonca and for 10 months after the last dose.

Advise male patients with female partners of reproductive potential to use effective contraception during treatment with Lonca and for 7 months after the last dose.

Lactation Patient Counseling

Advise women not to breastfeed during treatment with Lonca and for 3 months after the last dose.

Lonca, loncastuximab tesirine.

Zynlonta (loncastuximab tesirine-lpyl) prescribing information. Murray Hill, NJ; ADC Therapeutics; October 2022.

Case Study: Photosensitivity Associated with Lonca[1]

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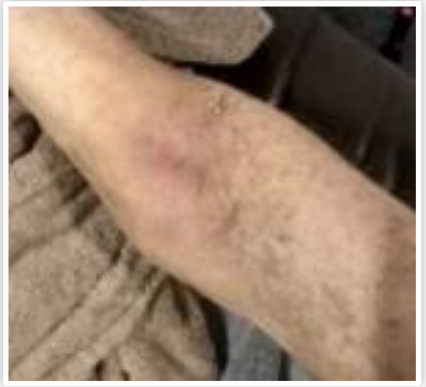
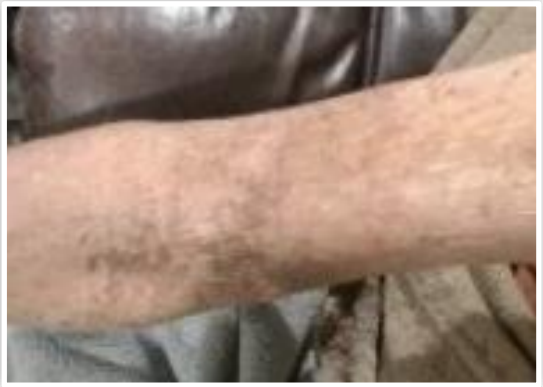
Case #1

Patient #1: 72-y/o Caucasian man with non-GCB DLBCL leg type diagnosed from thigh cutaneous biopsy treated with Lonca 3L



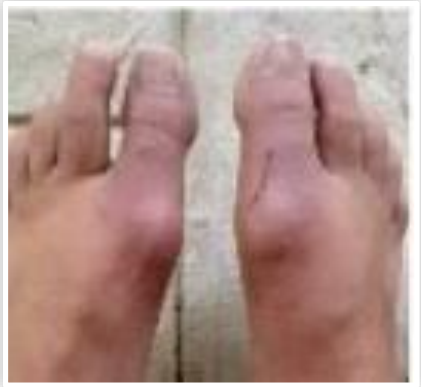


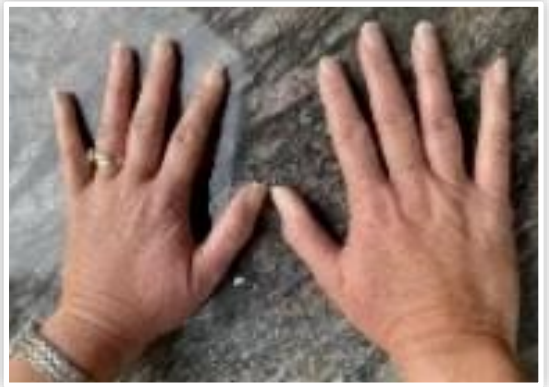
Within the first 2 cycles of Lonca, developed rash to sun-exposed areas that did not respond to OTC diphenhydramine cream, hydrocortisone, or treatment delay of 1 week

Patient responded to clobetasol cream, cetirizine, famotidine, and L-lysine with improvement within a few days, allowing patient to continue treatment with Lonca

Case #2

Patient #2: 55-y/o woman with biopsy-proven stage IV DLBCL, non-GCB subtype, with high Ki-67, originally transformed from FL treated with Lonca 3L





Within the first 2 cycles of Lonca, patient developed photosensitivity rash

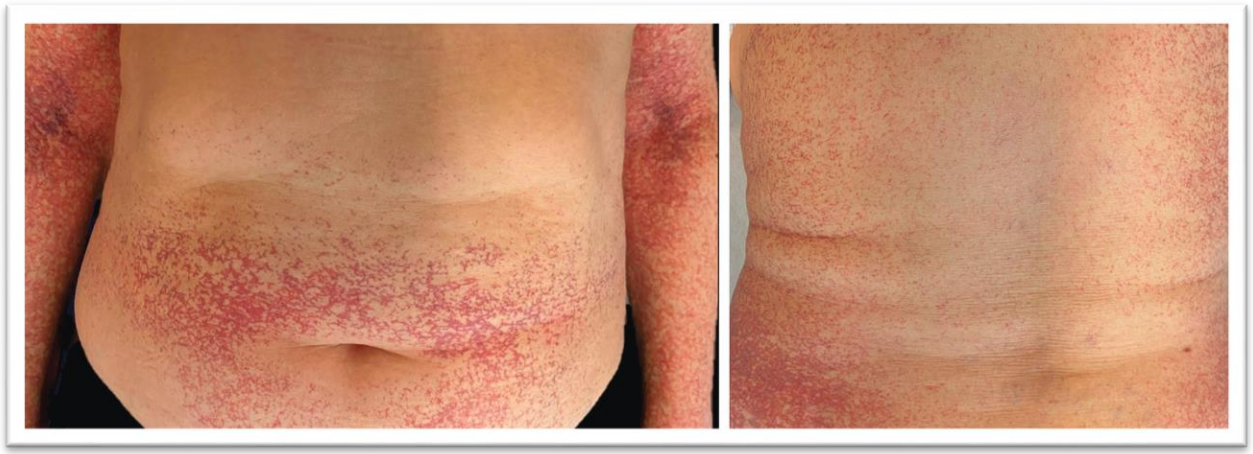
Patient responded to clobetasol cream, cetirizine, famotidine, and L-lysine with improvement within two days and was able to continue Lonca treatment without delay

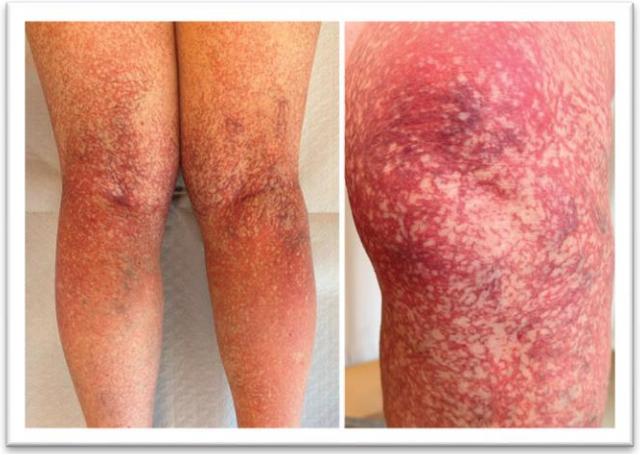
3L; third-line treatment; DLBCL, diffuse large B cell lymphoma; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; GCB, germinal center B-cell like; Lonca, loncastuximab tesirine; OTC, over the counter; y/o, year old.

1. Mistry HE, et al. Case Study: Photosensitivity Rash Associated with Loncastuximab Tesirine. Poster presented at: Pan Pacific Lymphoma Conference; July 18th, 2022; Kauai, Hawaii.

Case Study: CCV Associated with Lonca[1]

Patient: Woman in her 60s with a history of untreated hypertension who was diagnosed with DLBCL and treated with Lonca 3L





Dermatologic examination 2 years after treatment with Lonca showed diffuse, nonblanching, reticulated telangiectasias covering the trunk, flexor, and extensor surfaces of the upper and lower extremities

Although the pathogenesis remains unclear, skin biopsies were also diagnostic of CCV, a rare primary cutaneous microangiopathy typically starting as dilated small blood vessels on the lower limbs that may gradually spread

3L, third-line treatment; CCV, cutaneous collagenous vasculopathy; DLBCL, diffuse large B cell lymphoma; Lonca, loncastuximab tesirine. For Field Medical Use in Scientific Exchange

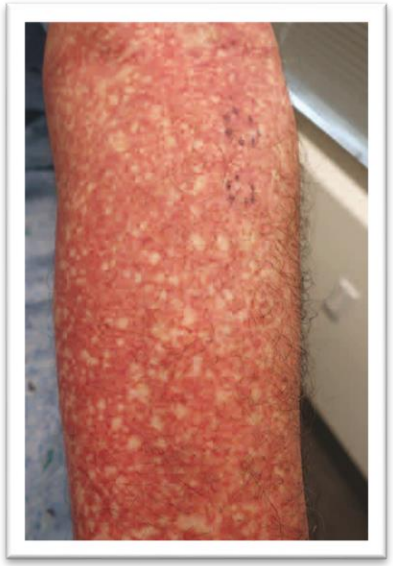
1. Michelerio A, et al. *JAMA Dermatol.* 2024;160(10):1130-1132.

Case Study: Diffuse Telangiectasia Associated with Lonca[1]

Five patients of ages ranging from early 50s to late 80s presented with asymptomatic, progressive rash during and up to 16 months post Lonca

Case #1

Patient #1: Male in his 70s with mantle cell lymphoma who was treated with Lonca

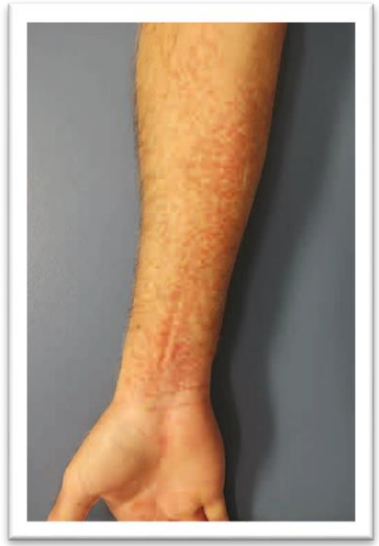


Four months after therapy with Lonca, developed rash in the upper and lower extremities, abdomen, and flanks

Patient was treated with methylprednisolone and hydrocortisone 1% ointment

Case #2

Patient #2: Male in his mid 50s with DLBCL who was treated with Lonca



During therapy with Lonca, developed rash on the upper and lower extremities, chest, abdomen, and back

The patient did not seek therapy for the rash, which persisted for 2 years

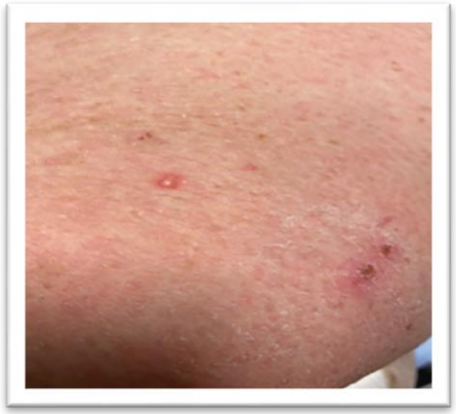
DLBCL, diffuse large B-cell lymphoma; Lonca, loncastuximab tesirine;.

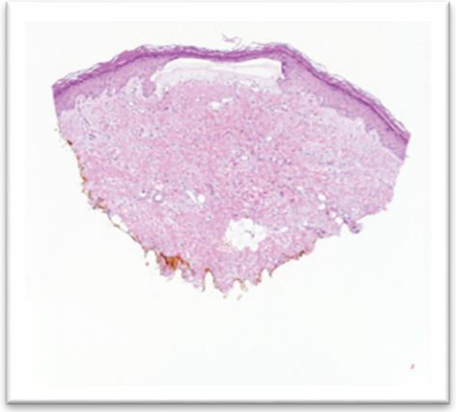
1. Sorensen EP, et al. *JAMA Dermatol.* 2020;156(5):601-603.

Case Study: Blistering Lesions Associated with Lonca[1]

Case #1

Patient #1: 89-y/o female with DLBCL, originally transformed from MZL treated with Lonca after treatment with RCHOP, BR, and ibrutinib



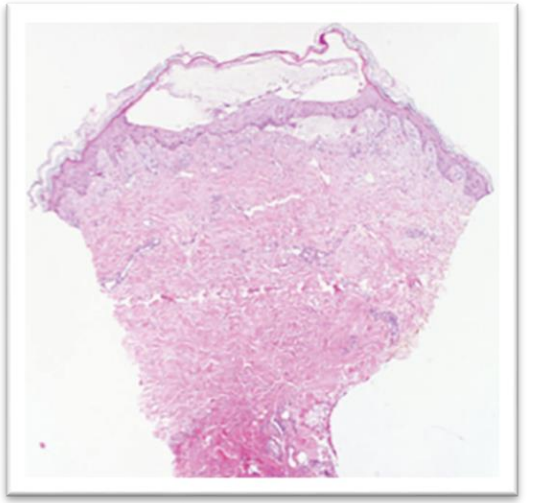


Within the first 3 cycles of Lonca, developed open blistering lesions involving other sites that preceded blisters secondary to lower extremity edema. HE staining demonstrated subepidermal vesiculation with minimal dermal inflammation.

Rash was resolved after discontinuation of Lonca for other reasons, with no recurrence to date

Case #2

Patient #2: 68-y/o male with DLBCL, originally transformed from FL treated with Lonca after treatment with RCHOP, R-GemOx, and radiotherapy



Within the first 4 cycles of Lonca, developed open blistering lesions involving other sites that preceded blisters secondary to edema. HE staining demonstrated sparse lymphohistiocytic infiltrate with rare neutrophils and mast cells.

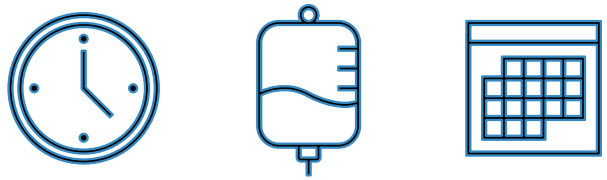
Treatment with Lonca was discontinued because of a grade 3 soft tissue infection; the course of lesions was not assessable because the patient died

BR, bendamustine, rituximab; DLBCL, diffuse large B cell lymphoma; FL, follicular lymphoma; HE, hematoxylin-eosin; Lonca, loncastuximab tesirine; RCHOP, rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone; MZL, marginal zone lymphoma; R-GemOx, gemcitabine-oxaliplatin plus rituximab; y/o, year old.

1. Gociman S, et al. *JAMA Dermatol.* 2022;158(7):831-832.

Summary of Administration: Lonca Is Administered as a Single 30-Minute Infusion Every 3 Weeks

Administer Lonca by intravenous infusion over 30 minutes on day 1 of each 3-week cycle (with required dexamethasone premedication)



Recommended Dose	Premedication
0.15 mg/kg first 2 cycles **0.075 mg/kg subsequent cycles**	**Dexamethasone 4 mg (oral or IV) twice daily for 3 days, beginning the day before Lonca infusion (unless contraindicated)**
In LOTIS-2, Lonca was administered until progressive disease or unacceptable toxicity	If dexamethasone administration does not begin the day before Lonca, it should begin at least 2 hours prior to Lonca infusion

Dosage modifications and delays

Recommended Dosage Modifications for Adverse Reactions

Adverse reactions	Lonca should be held until:
Hematologic Adverse Reactions	
Absolute neutrophil count $<1 \times 10^9$/L	Neutrophil count returns to $\geq 1 \times 10^9$/L
Platelet count <50,000/mcL	Platelet count returns to ≥50,000/mcL
Nonhematologic Adverse Reactions	
Grade ≥2 edema or effusion	Toxicity resolves to grade 1 or less
Any grade ≥3 nonhematologic toxicity	Toxicity resolves to grade 1 or less

Recommendations for Dosage Delays

If dosing is delayed by >3 weeks due to toxicity related to ZYNLONTA, reduce subsequent doses by 50%. If toxicity reoccurs following dose reduction, consider discontinuation.

Note: If toxicity requires dose reduction following the second dose of 0.15 mg/kg (Cycle 2), the patient should receive the dose of 0.075 mg/kg for Cycle 3.

IV, intravenous; Lonca, loncastuximab tesirine.

Zynlonta (loncastuximab tesirine-lpyl) Prescribing Information. Murray Hill, NJ; ADC Therapeutics; October 2022.

Lonca for Adults With R/R DLBCL After ≥2 Prior Therapies

THERAPEUTICS

Overall Response

48.3% ORR

(95% CI: 39.9, 56.7)[1,a,d]

2-year follow-up

24.8% CR; 23.4% PR[2,b]

Simple Dosing

Single-Agent IV[c]

30-minute IV infusion

Once every 3 weeks

Management

In LOTIS-2, dexamethasone premedication, the Lonca dosing schedule, and dosing modifications were used to aid in the management of adverse reactions[3]

The patient population in the LOTIS-2 clinical trial included heavily pretreated patients with difficult-to-treat disease.

Lonca can cause serious adverse reactions, including effusion and edema, serious infection, photosensitivity, and embryo-fetal toxicity. Patients should be counseled on these potential adverse reactions.

[a]**Median follow-up time:** 7.3 months (range 0.3-20.2). Of 70 patients with objective response, 25 (36%) were censored prior to 3 months; 26% of the responders had a DOR of **≥6 months.**[1]
[b]**Median follow-up time:** 7.8 months (range: 0.3 – 42.6).[2]
[c]**Premedication:** dexamethasone 4 mg (oral or IV) twice daily for 3 days, beginning the day before infusion (unless contraindicated).[1]
[d]ORR defined as the proportion of patients with a best OR of CR or PR; assessed by an independent review committee using Lugano 2014 criteria.
DLBCL, diffuse large B-cell lymphoma; CR, complete response; GGT, gamma-glutamyltransferase; IV, intravenous; DOR; duration of response; ORR, overall response rate; R/R, relapsed/refractory.
1. Zynlonta (loncastuximab tesirine-lpyl) prescribing information. Murray Hill, NJ; ADC Therapeutics; October 2022. **2.** Caimi PF, et al. Haematologica. 2024;109(4):1184-1193. **3.** Caimi PF, et al. *Lancet Oncol.* 2021;22(6):790-800.

Summary of Adverse Events in LOTIS-2

	Effusion and Edema	Myelosuppression	Infection	Cutaneous Reactions	Liver Enzyme Elevations
Grade ≥3	Effusion: 2.8% Edema: 3.4%	Neutropenia: 29.7% Thrombocytopenia: 17.9% Anemia: 11.0%	9.0%	Photosensitivity: 2.1% Nonphotosensitivity: 2.1%	GGT: 22.1% AST: 0.7% ALT: 3.4% ALP: 2.1%
Dose Delay	Effusion: 1.4% Edema: 5.5%	Neutropenia: 12.4% Thrombocytopenia: 9.4% Anemia: 2.8%	1.4%	Photosensitivity: 2.8% Nonphotosensitivity: 4.8%	GGT: 20.7%

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase.
Data on file. ADC Therapeutics SA. Data cutoff: April 6, 2020.