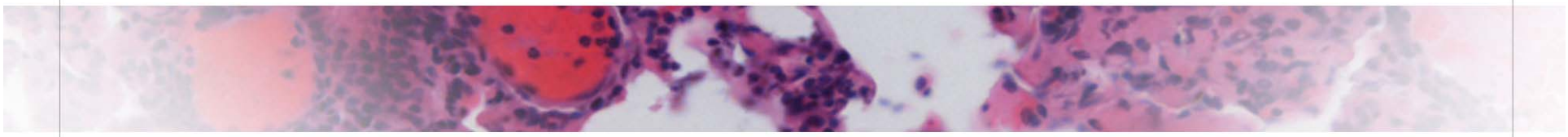


Clinical Characteristics and Responses of Patients with Relapsed or Refractory High-Grade B-Cell Lymphoma Treated with Loncastuximab Tesirine in the LOTIS-2 Clinical Trial

Poster slides, 63rd ASH Annual Meeting and Exposition Meeting, December 11-14, 2021

Juan Pablo Alderuccio, MD[1], Weiyun Z. Ai, MD, PhD[2], John Radford, MD, FRCP, FMedSci[3], Melhem Solh, MD[4], Kirit M. Ardeshna, MD, FRCP[5], Matthew Lunning, DO, FACP[6], Brian T. Hess, MD[7], Pier Luigi Zinzani, MD[8], Anastasios Stathis, MD[9], Carmelo Carlo-Stella, MD[10], Mehdi Hamadani, MD[11], Brad S. Kahl, MD[12], David Ungar, MD[13], Turk Kilavuz, MD[13], Eric Yu, PhD[13], Yajuan Qin, MD, PhD[13], Paolo Caimi, MD[14]

[1]Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, USA; [2]University of California, San Francisco, CA, USA; [3]NIHR Manchester Clinical Research Facility, University of Manchester and The Christie NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK; [4]Blood and Marrow Transplant Program at Northside Hospital, Atlanta, GA, USA; [5]University College London Hospitals NHS Foundation Trust, London, UK; [6]University of Nebraska Medical Center, Omaha, NE, USA; [7]Medical University of South Carolina, Charleston, SC, USA; [8]Institute of Hematology "Seràgnoli" University of Bologna, Bologna, Italy; [9]Oncology Institute of Southern Switzerland, Bellinzona, Switzerland; [10] Department of Biomedical Sciences, Humanitas University, and Department of Oncology and Hematology, Humanitas Research Hospital - IRCCS, Milano, Italy; [11]BMT & Cellular Therapy Program, Department of Medicine, Medical College of Wisconsin, Milwaukee, WI, USA; [12]Washington University, St. Louis, MO, USA; [13]ADC Therapeutics America, Inc., Murray Hill, NJ, USA; [14]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, USA

Introduction

DLBCL is a heterogeneous disease, with variable outcomes that are differentially characterized by clinical factors, response to therapy, and the unique biology of underlying disease subtypes[1]

High-grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* rearrangement is associated with poor patient prognosis[2,3]

Loncastuximab tesirine (loncastuximab tesirine-lpyl; Lonca) is an FDA-approved CD19-directed antibody-drug conjugate indicated in adults with R/R large B-cell lymphoma after ≥2 lines of systemic therapy, including patients with HGBCL[4]

DLBCL, diffuse large B-cell lymphoma; HGBCL, high-grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* rearrangements; R/R, relapsed or refractory.

1. Liu Y and Barta SK. *Am J Hematol*. 2019;94(5):604-616. 2. Swerdlow SH, et al. *Blood*. 2016;127(20):2375-2390. 3. Rosenwald A, et al. *J Clin Oncol*. 2019;37(35):3359-3368.
4. ZYNLOTA [package insert]. Murray Hill, New Jersey: ADC Therapeutics, SA; 2021.

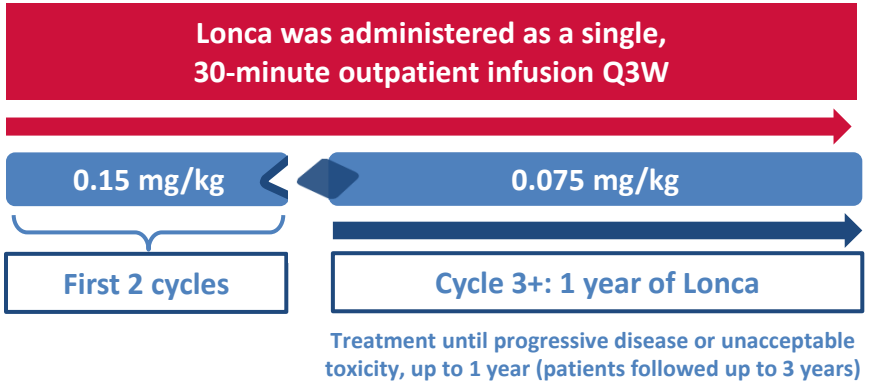
LOTIS-2: Open-Label, Single-Arm, Phase 2 Study

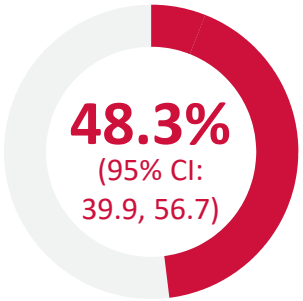
Patient Population

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

Primary Endpoint

ORR by IRC of PET-CT using Lugano 2014 criteria





ORR in the full LOTIS-2 population (N = 145)

DLBCL, diffuse large B-cell lymphoma; 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; Q3W, every 3 weeks; R/R, relapsed/refractory.

Caimi, PF, et al. *Lancet Oncol.* 2021;22(6):790-800.

Objective

To characterize the clinical characteristics and efficacy of Lonca in patients with high-grade B-cell lymphoma enrolled in the LOTIS-2 trial

- Data cutoff: March 1, 2021

LOTIS-2: Characteristics of Patients With HGBCL

Baseline Characteristics	Patients with HGBCL (n=11)	Patients with DLBCL-NOS (n=127)
Age, median (min, max), years	74.0 (53, 85)	65.0 (23, 94)
Age group, n (%) • <65 years • ≥65 to <75 years • ≥75 years	 2 (18.2) 4 (36.4) 5 (45.5)	 57 (44.9) 55 (43.3) 15 (11.8)
Diagnosis to first dose, median (min, max), months	22.2 (5.4, 86.6)	16.9 (1.4, 292.6)
Prior systemic therapies[a], n (%) • 2 prior lines • 3 prior lines • >3 prior lines	 3 (27.3) 5 (45.5) 3 (27.3)	 58 (45.7) 27 (21.3) 42 (33.1)
Prior stem-cell transplant, n (%)	1 (9.1)	21 (16.5)
Refractory to prior therapy, n (%) • Primary refractory • Refractory to most recent therapy • Refractory to all prior therapy	 3 (27.3) 5 (45.5) 3 (27.3)	 26 (20.5) 78 (61.4) 24 (18.6)

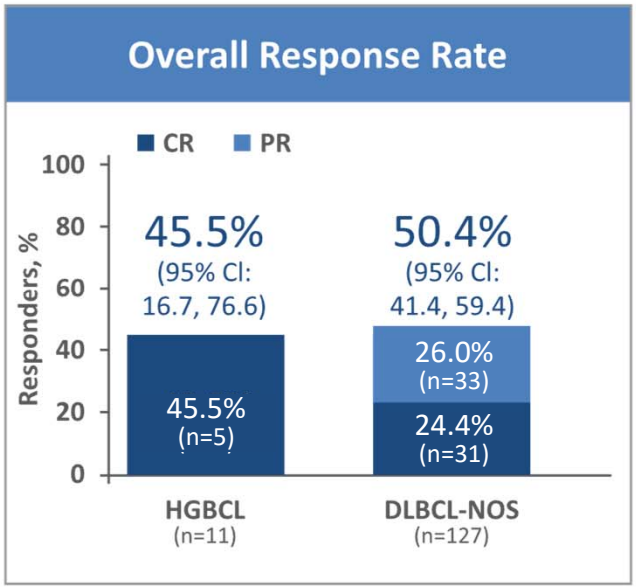
Among patients with HGBCL, 3/11 patients had prior CAR T-cell therapy, and 2/11 patients had triple-hit lymphoma.

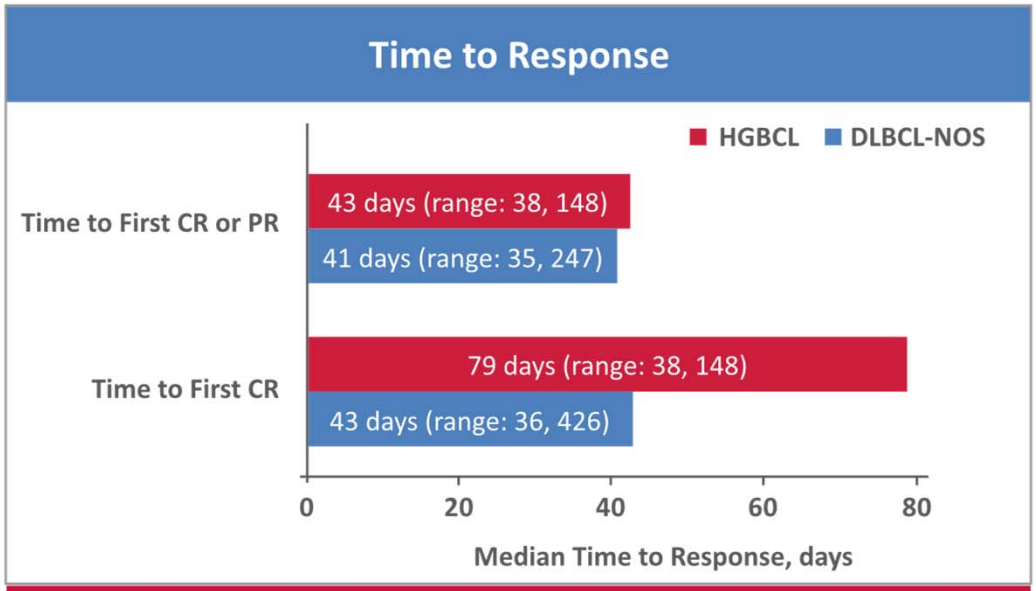
Data cutoff: March 1, 2021. Median (range) follow-up for the entire LOTIS-2 population: 7.8 (0.3-31.0) months.

[a]Prior stem cell transplant is included. For patients who received an autologous transplant, the mobilization regimen was considered a line of therapy if it was chemotherapy-based and distinct from the other previous lines of treatment.

CAR, chimeric antigen receptor; DLBCL, diffuse large B-cell lymphoma; HGBCL, high-grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* rearrangements; NOS, not otherwise specified.

LOTIS-2: Efficacy in Patients With HGBCL



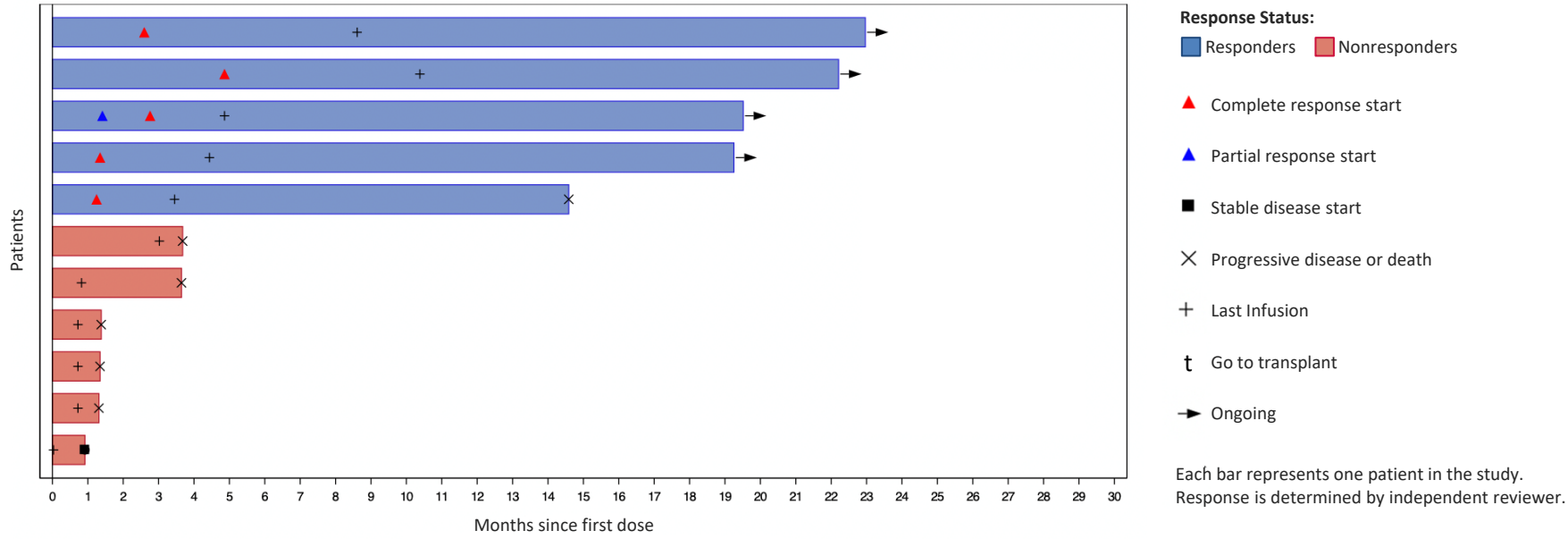


Overall responses were achieved within approximately 6 weeks of initiating Lonca.

Data cutoff: March 1, 2021.

CR, complete response; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; HGBCL, high-grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* rearrangements; NOS, not otherwise specified; PR, partial response.

LOTIS-2: Duration of Response in Patients with HGBCL



All 5 responding patients with HGBCL had a duration of response >1 year; median duration of response has not been reached at the time of data cutoff.

Data cutoff: March 1, 2021.

CR, complete response; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; HGBCL, high-grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* rearrangements; NOS, not otherwise specified; PR, partial response.

Conclusions

- In LOTIS-2, response rates in this small subgroup of patients with HGBCL (45.5%) are consistent with the DLBCL-NOS patient population (50.4%)
- All responding patients with HGBCL achieved a CR
- Overall responses were achieved within approximately the first six weeks of initiating Lonca, and long-term disease control was seen in responding patients
- These results suggest that Lonca is active in the treatment of this high-risk lymphoma subgroup

Data cutoff: March 1, 2021.
CR, complete response; DLBCL, diffuse large B-cell lymphoma; HGBCL, high-grade B-cell lymphoma; Lonca, loncastuximab tesirine; NOS, not otherwise specified.

Disclosures and Acknowledgments

J. P. Alderuccio: immediate family member has served on advisory boards for Puma Biotechnology, Inovio Pharmaceuticals, Agios Pharmaceuticals, Forma Therapeutics, and Foundation Medicine; honoraria from OncLive and Oncinfo; consult for and research funding from ADC Therapeutics.

W. Ai: consultant for ADC Therapeutics, Nurix, Kite Pharma, and Kymera Therapeutics.

J. Radford: consultant for ADC Therapeutics, Bristol-Myers Squibb, Kite Pharma, and Takeda; ownership interests with AstraZeneca (spouse) and GlaxoSmithKline (self); research funding from Takeda; honoraria from Takeda, Bristol-Myers Squibb, and ADC Therapeutics; speakers' bureau member for Takeda and ADC Therapeutics.

M. Sohl: consultant for Amgen, Bristol-Myers Squibb; research funding from ADC Therapeutics and Partner Therapeutics; speakers' bureau member for Bristol-Myers Squibb, GSK, AbbVie, and Celgene.

K. M. Ardeshna: research funding from Novartis, Bristol-Myers Squibb, Autolus Therapeutics, ADC Therapeutics, Pharmacyclics, and Janssen; honoraria from BeiGene, Celgene, Novartis, and Roche; member on Board of Directors or advisory board for Gilead, BeiGene, Celgene, Novartis, and Roche.

M. Lunning: financial relationships with BeiGene, Karyopharm, Gilead/Kite Pharma, Daiichi Sankyo, Novartis, Kyowa Kirin, AbbVie, Celgene, Verastem, Janssen, Myeloid Therapeutics, AstraZeneca, Acrotech, ADC Therapeutics, Legend, Spectrum, MorphoSys, and TG Therapeutics.

B. Hess: speakers' bureau member for Bristol-Myers Squibb; advisory board member for ADC Therapeutics; speakers' bureau member for AstraZeneca.

A. Stathis: consultant to Bayer, Eli Lilly; institutional research funding from Pfizer, ADC Therapeutics, Bayer, Roche, Merck, Novartis, MEI Therapeutics, and AbbVie; other financial relationships with AbbVie and PharmaMar.

P. L. Zinzani: consultancy services to Verastem, MSD, EUSA Pharma, and Sanofi; member on entity's board of directors, speakers' bureau or advisory committee for ADC Therapeutics (advisory board agreement), Verastem, Celltrion, Gilead, Janssen-Cilag, Bristol-Myers Squibb, Servier, Sandoz, MSD, Immune Design, Celgene, Portola, Roche, EUSA Pharma, and Kyowa Kirin.

C. Carlo-Stella: consult to Sanofi; research funding from ADC Therapeutics, Roche, and Sanofi; honoraria from AstraZeneca, Bristol-Myers Squibb, Incyte, Janssen Oncology, Takeda, and ADC Therapeutics; member on an entity's Board of Directors, speakers' bureau or advisory committee for Sanofi, ADC Therapeutics, Bristol-Myers Squibb, Celgene, Karyopharm Therapeutics, Roche.

M. Hamadani: research support/funding from Takeda Pharmaceutical Company, Spectrum Pharmaceuticals, and Astellas Pharma; consultant to Janssen, Incyte Corporation, ADC Therapeutics, Celgene Corporation, Omeros, Verastem, MorphoSys; speaker's bureau member for Sanofi Genzyme, AstraZeneca, BeiGene.

B. S. Kahl: consultant to AbbVie, ADC Therapeutics, AstraZeneca, BeiGene, Celgene, Teva, Janssen, MTEM, Bayer, Incyte, Adaptive, Genentech, Roche, MEI, KITE, TG Therapeutics, Epizyme, and Takeda.

D. Ungar, T. Kilavuz, Y. Qin: employees of ADC Therapeutics with ownership interests.

E. Yu: employee of ADC Therapeutics; ownership interests in Zentalis Pharma and Merck.

P. F. Caimi: research funding from ADC Therapeutics; grants from Genentech; consultant to ADC Therapeutics, Kite Pharmaceuticals, Verastem, Seattle Genetics, Amgen, and TG Therapeutics; speaker's bureau member for Celgene.

This study was funded by ADC Therapeutics SA (NCT03589469)

Acknowledgments

- The authors would like to thank all participating patients and their families, study co-investigators, and research coordinators.
- Medical writing support was provided by CiTRUS Health Group, funded by ADC Therapeutics.

Clinical Characteristics and Responses of Patients With Relapsed or Refractory High-Grade B-Cell Lymphoma Treated With Loncastuximab Tesirine in the LOTIS-2 Clinical Trial

Juan Pablo Alderuccio, MD[1*], Weiyun Z. Ai, MD, PhD[2], John Radford, MD, FRCP, FMedSci[3], Melhem Solh, MD[4], Kirit M. Ardeshna, MD, FRCP[5], Matthew Lunning, DO, FACP[6], Brian T. Hess, MD[7], Pier Luigi Zinzani, MD[8], Anastasios Stathis, MD[9], Carmelo Carlo-Stella, MD[10], Mehdi Hamadani, MD[11], Brad S. Kahl, MD[12], David Ungar, MD[13], Turk Kilavuz, MD[13], Eric Yu, PhD[13], Yajuan Qin, MD, PhD[13], Paolo Caimi, MD[14]

[1]Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, USA; [2]University of California, San Francisco, CA, USA; [3]NIHR Manchester Clinical Research Facility, University of Manchester and The Christie NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK; [4]Blood and Marrow Transplant Program at Northside Hospital, Atlanta, GA, USA; [5]University College London Hospitals NHS Foundation Trust, London, UK; [6]University of Nebraska Medical Center, Omaha, NE, USA; [7]Medical University of South Carolina, Charleston, SC, USA; [8]Institute of Hematology "Seràgnoli" University of Bologna, Bologna, Italy; [9]Oncology Institute of Southern Switzerland, Bellinzona, Switzerland; [10] Department of Biomedical Sciences, Humanitas University, and Department of Oncology and Hematology, Humanitas Research Hospital - IRCCS, Milano, Italy; [11]BMT & Cellular Therapy Program, Department of Medicine, Medical College of Wisconsin, Milwaukee, WI, USA; [12]Washington University, St. Louis, MO, USA; [13]ADC Therapeutics America, Inc., Murray Hill, NJ, USA; [14]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, USA

3575

INTRODUCTION

- Diffuse large B-cell lymphoma (DLBCL) is a heterogeneous disease with variable outcomes that are differentially characterized by clinical factors, response to therapy, and the unique biology of underlying disease subtypes[1]
- High-grade B-cell lymphoma with *MYC and BCL2 and/or BCL6* rearrangement (HGBCL) is associated with poor patient prognosis[2,3]
- Loncastuximab tesirine (loncastuximab tesirine-lpyl; Lonca) is an FDA-approved CD19-directed antibody-drug conjugate indicated in adults with relapsed or refractory (R/R) large B-cell lymphoma after ≥2 lines of systemic therapy, including patients with HGBCL[4]
- In the phase 2 LOTIS-2 trial (NCT03589469), Lonca was evaluated as a single agent in patients with R/R DLBCL, and the overall response rate (ORR) was 48.3%[5]

OBJECTIVE

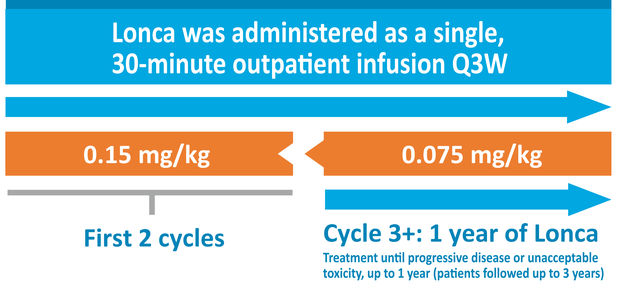
- To characterize the clinical characteristics and efficacy of Lonca in patients with HGBCL in the LOTIS-2 trial

METHODS

LOTIS-2: Open-Label, Single-Arm, Phase 2 Study

- In the phase 2 LOTIS-2 trial, Lonca was administered as a single 30-minute infusion (0.15 mg/kg for the first 2 cycles followed by 0.075 mg/kg for subsequent cycles) once every 3 weeks for up to 1 year until progressive disease or unacceptable toxicity
- **Patient Population**
  R/R DLBCL, based on pathologic diagnosis of DLBCL, as defined by the 2016 WHO classification, to include DLBCL not otherwise specified; primary mediastinal large B-cell lymphoma; and high-grade B-cell lymphoma, with *MYC* and *BCL2* and/or *BCL6* rearrangements, after ≥2 prior lines of systemic therapy

Figure 1. LOTIS-2 clinical trial design



- The primary outcome was ORR defined as the proportion of patients with best overall response of CR or PR, assessed by independent review
- Investigator assessment of histopathology according to the 2016 WHO classification was used to define HGBCL
- Data cutoff: March 1, 2021

RESULTS

LOTIS-2: Characteristics of Patients With HGBCL

The demographics and disease characteristics of the 11 patients with HGBCL are shown in Table 1

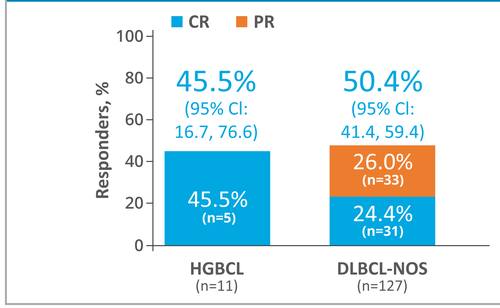
- The median age was 74 years, and 5 patients (45.5%) were age ≥75 years
- The majority of patients received ≥3 prior lines of therapy (n=8; 72.7%)
- One patient had a prior stem cell transplant (autologous; 9.1%)
- Three patients had prior CAR T-cell therapy (27.3%)
- Two patients had triple-hit lymphoma (18.2%)

Table 1. Baseline characteristics of patients with HGBCL

Baseline characteristics	Patients with HGBCL (n=11)	Patients with DLBCL-NOS (n=127)
Age, median (min, max), years	**74.0 (53, 85)**	**65.0 (23, 94)**
Age group, n (%)		
<65 years	2 (18.2)	57 (44.9)
≥65 to <75 years	4 (36.4)	55 (43.3)
≥75 years	5 (45.5)	15 (11.8)
Diagnosis to first dose, median (min, max), months	**22.2 (5.4, 86.6)**	**16.9 (1.4, 292.6)**
Prior systemic therapies, n (%)		
2 prior lines	3 (27.3)	58 (45.7)
3 prior lines	5 (45.5)	27 (21.3)
>3 prior lines	3 (27.3)	42 (33.1)
Prior stem-cell transplant, n (%)	1 (9.1)	21 (16.5)
Refractory to prior therapy, n (%)		
Primary refractory	3 (27.3)	26 (20.5)
Refractory to most recent therapy	5 (45.5)	78 (61.4)
Refractory to all prior therapy	3 (27.3)	24 (18.6)

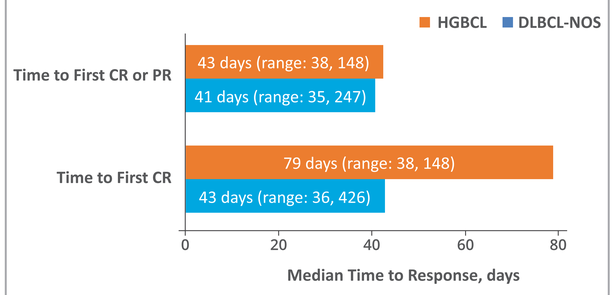
LOTIS-2: Efficacy in Patients With HGBCL

Figure 2. Overall response rate



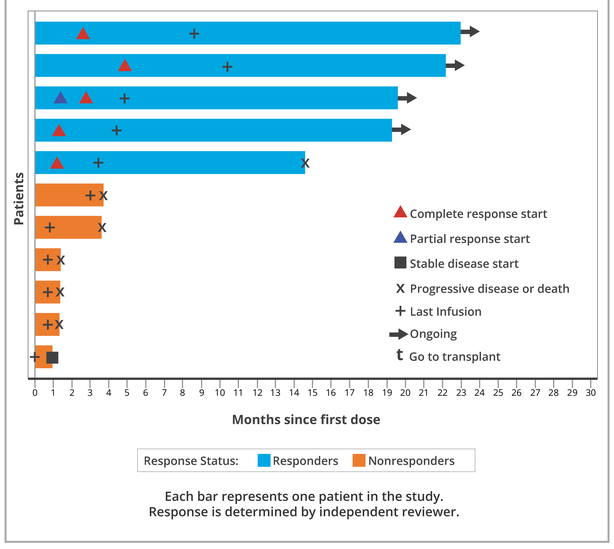
- Of the 11 patients with HGBCL, the ORR was 45.5%, with all 5 patients achieving CR
- Among patients with DLBCL-NOS (n=127), the ORR was 50.4%, with 31 patients achieving CR (Figure 2)

Figure 3. Time to first response



- Among patients with HGBCL who responded to Lonca (n=5), the median (min, max) time to first CR or PR was 43 (38, 148) days, and the median time to first CR was 79 (38, 148) days (Figure 3)
  - All five responding patients (45.5%) with HGBCL had a duration of response ≥1 year; the median duration of response has not been reached at the time of data cutoff
- Among patients with DLBCL-NOS who responded to Lonca (n=70), the median time to first CR or PR was 41 (35, 247) days, and among patients with DLBCL-NOS who achieved CR with Lonca (n=36), the median time to first CR was 43 (36, 426) days (Figure 3)

Figure 4. Duration of response in patients with HGBCL



CONCLUSIONS

- In LOTIS-2, response rates in this small subgroup of patients with HGBCL (45.5%) are consistent with the DLBCL-NOS patient population (50.4%)
- All responding patients with HGBCL achieved a CR
- Overall responses were achieved within approximately the first six weeks of initiating Lonca, and long-term disease control was seen in responding patients
- These results suggest that Lonca is active in the treatment of this high-risk lymphoma subgroup

Acknowledgments

The authors would like to thank all participating patients and their families, study co-investigators, and research coordinators. Medical writing support was provided by CiTRUS Health Group, funded by ADC Therapeutics. This study was funded by ADC Therapeutics (NCT03589469).

Disclosures

J. P. Alderuccio: immediate family member has served on advisory boards for Puma Biotechnology, Inovio Pharmaceuticals, Agios Pharmaceuticals, Forma Therapeutics, and Foundation Medicine; honoraria from OncLive and Oncinfo; consult for and research funding from ADC Therapeutics. W. Ai: consultant for ADC Therapeutics, Nurix, Kite Pharma, and Kymera Therapeutics. J. Radford: consultant for ADC Therapeutics, Bristol-Myers Squibb, Kite Pharma, and Takeda; ownership interests with AstraZeneca (spouse) and GlaxoSmithKline (self); research funding from Takeda; honoraria from Takeda, Bristol-Myers Squibb, and ADC Therapeutics; speakers' bureau member for Takeda and ADC Therapeutics. M. Sohl: consultant for Amgen, Bristol-Myers Squibb; research funding from ADC Therapeutics and Partner Therapeutics; speakers' bureau member for Bristol-Myers Squibb, GSK, AbbVie, and Celgene. K. M. Ardeshna: research funding from Novartis, Bristol-Myers Squibb, Autolus Therapeutics, ADC Therapeutics, Pharmacyclics, and Janssen; honoraria from BeiGene, Celgene, Novartis, and Roche; member on Board of Directors or advisory board for Gilead, BeiGene, Celgene, Novartis, and Roche. M. Lunning: financial relationships with BeiGene, Karyopharm, Gilead/Kite Pharma, Daiichi Sankyo, Novartis, Kyowa Kirin, AbbVie, Celgene, Verastem, Janssen, Myeloid Therapeutics, AstraZeneca, Acrotech, ADC Therapeutics, Legend, Spectrum, MorphoSys, and TG Therapeutics. B. Hess: speakers' bureau member for Bristol-Myers Squibb; advisory board member for ADC Therapeutics; speakers' bureau member for AstraZeneca. A. Stathis: consultant to Bayer, Eli Lilly; institutional research funding from Pfizer, ADC Therapeutics, Bayer, Roche, Merck, Novartis, MEI Therapeutics, and AbbVie; other financial relationships with AbbVie and PharmaMar. P. L. Zinzani: consultancy services to Verastem, MSD, EUSA Pharma, and Sanofi; member on entity's board of directors, speakers' bureau or advisory committee for ADC Therapeutics (advisory board agreement), Verastem, Celltrion, Gilead, Janssen-Cilag, Bristol-Myers Squibb, Servier, Sandoz, MSD, Immune Design, Celgene, Portola, Roche, EUSA Pharma, and Kyowa Kirin. C. Carlo-Stella: consult to Sanofi; research funding from ADC Therapeutics, Roche, and Sanofi; honoraria from AstraZeneca, Bristol-Myers Squibb, Incyte, Janssen Oncology, Takeda, and ADC Therapeutics; member on an entity's Board of Directors, speakers' bureau or advisory committee for Sanofi, ADC Therapeutics, Bristol-Myers Squibb, Celgene, Karyopharm Therapeutics, Roche. M. Hamadani: research support/funding from Takeda Pharmaceutical Company, Spectrum Pharmaceuticals, and Astellas Pharma; consultant to Janssen, Incyte Corporation, ADC Therapeutics, Celgene Corporation, Omeros, Verastem, MorphoSys; speaker's bureau member for Sanofi Genzyme, AstraZeneca, BeiGene. B. S. Kahl: consultant to AbbVie, ADC Therapeutics, AstraZeneca, BeiGene, Celgene, Teva, Janssen, MTEM, Bayer, Incyte, Adaptive, Genentech, Roche, MEI, KITE, TG Therapeutics, Epizyme, and Takeda. D. Ungar, T. Kilavuz, Y. Qin: employees of ADC Therapeutics with ownership interests. E. Yu: employee of ADC Therapeutics; ownership interests in Zentalis Pharma and Merck. P. F. Caimi: research funding from ADC Therapeutics; grants from Genentech; consultant to ADC Therapeutics, Kite Pharmaceuticals, Verastem, Seattle Genetics, Amgen, and TG Therapeutics; speaker's bureau member for Celgene.

*Contact information

Juan Pablo Alderuccio, MD: Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, USA; jalderuccio@med.miami.edu

References

1. Liu Y and Barta SK. *Am J Hematol*. 2019;94(5):604-616.
2. Swerdlow SH, et al. *Blood*. 2016;127(20):2375-2390.
3. Rosenwald A, et al. *J Clin Oncol*. 2019;37(35):3359-3368.
4. ZYNLOTA [package insert]. Murray Hill, New Jersey: ADC Therapeutics, SA; 2021.
5. Caimi PF, et al. *Lancet Oncol*. 2021;22:790-800

Poster presented at the 63rd ASH Annual Meeting and Exposition, December 11-14, 2021, Atlanta, GA, USA.