LOTIS-2 follow-up analysis: Updated results from a Phase 2 study of loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma

BS Kahl[1], M Hamadani[2], PF Caimi[3], C Carlo-Stella[4], W Ai[5], JP Alderuccio[6], KM Ardeshna[7], B Hess[8], J Radford[9], M Solh[10], A Stathis[11], J Feingold[12], D Ungar[12], Y Qin[12], L Wang[13], PL Zinzani[14]

[1]Department of Medicine, Oncology Division, Washington University, St. Louis, MO, USA; [2]Division of Hematology and Oncology, Medical College of Wisconsin, Milwaukee, WI, USA; [3]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, USA; [4]Department of Oncology and Hematology, Humanitas Clinical and Research Center – IRCCS, and Humanitas University, Rozzano, Milan, Italy; [5]Division of Hematology and Oncology, Department of Medicine, University of California, San Francisco, CA, USA; [6]Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, USA; [7]Department of Haematology, University College London Hospitals NHS Foundation Trust, London, UK; [8]Division of Hematology and Medical Oncology, Department of Medicine, Medical University of South Carolina, Charleston, SC, USA; [9]NIHR Clinical Research Facility, Christie NHS Foundation Trust and the University of Manchester, Manchester, UK; [10]Blood and Marrow Transplant Program at Northside Hospital, Atlanta, GA, USA; [11]Oncology Institute of Southern Switzerland, Bellinzona, Switzerland; [12]Clinical Development, ADC Therapeutics America, Inc., Murray Hill, NJ, USA; [13]Biometrics, ADC Therapeutics America, Inc., Murray Hill, NJ, USA; [14]IRCCS Azienda Ospedaliero-Universitaria di Bologna Istituto di Ematologia “Seràgnoli”, and Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale Università di Bologna, Bologna, Italy

Society of Hematologic Oncology (SOHO) Annual Meeting, September 8–11, 2021, Houston, Texas, USA

Disclosures

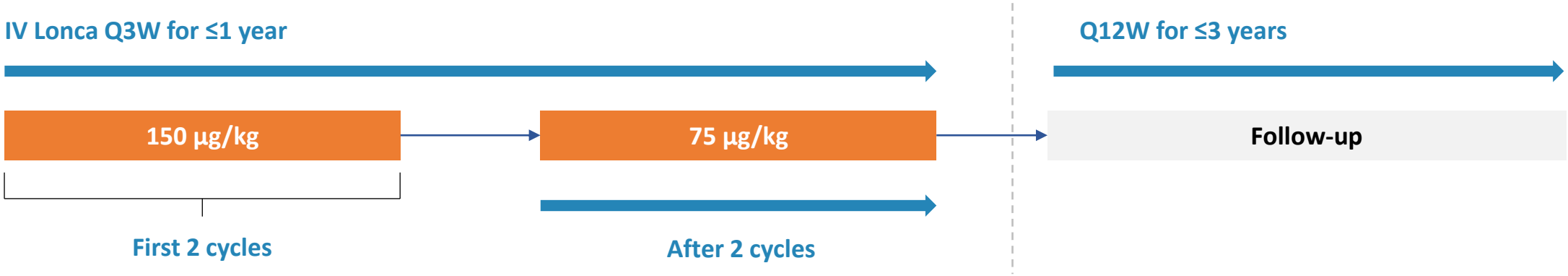
BS Kahl: Consultant/advisor for ADC Therapeutics, Genentech, and Roche; and research funding from ADC Therapeutics
M Hamadani: Consultant/advisor for AbGenomics, ADC Therapeutics, AstraZeneca, Celgene Corporation, Incyte Corporation, Janssen R&D, Omeros, Pharmacyclics, Sanofi Genzyme, TeneoBio, and Verastem; and research funding from Astellas Pharma, Spectrum Pharmaceuticals, and Takeda Pharmaceutical
PF Caimi: Consultant/advisor for ADC Therapeutics, Amgen, Bayer, Celgene, Genentech, Kite Therapeutics, TG Therapeutics, and Verastem; and research funding from ADC Therapeutics and Genentech
C Carlo-Stella: Consultant/advisor for ADC Therapeutics, Boehringer Ingelheim, Genenta Science srl, Karyopharm Therapeutics, Novartis, Roche, Sanofi, and Servier; honoraria from AstraZeneca, Bristol-Myers Squibb, Janssen Oncology, and Merck Sharpe & Dohme; and research funding from ADC Therapeutics and Rhizen Pharmaceuticals
W Ai: Consultant/advisor for ADC Therapeutics, Kymera, and Nurix; and research funding from Nurix
JP Alderuccio: Consultant/advisor for ADC Therapeutics (self), Agios Pharmaceuticals (immediate family member), FORMA Therapeutics (immediate family member), Foundation Medicine (immediate family member), Inovio Pharmaceuticals (immediate family member), Puma Biotechnology (immediate family member); and other remuneration from OncLive and Oncology Information Group (paid expert testimony)
KM Ardeshna: Consultant/advisor for ADC Therapeutics; honoraria from BeiGene, Celgene, Gilead, Roche, and Takeda; and other renumeration from University College London (UCL)/UCL Hospitals Biomedical Research Unit
B Hess: Consultant/advisor for ADC Therapeutics, AstraZeneca and Bristol-Myers Squibb

J Radford: Consultant/advisor for ADC Therapeutics, Bristol-Myers Squibb, Kite Pharmaceuticals, Novartis, Seattle Genetics, and Takeda; stock ownership for AstraZeneca and GlaxoSmithKline (spouse); research funding from Takeda; and other remuneration from ADC Therapeutics, Seattle Genetics (paid expert testimony), and Takeda
M Solh: Consultant/advisor for Amgen, Celgene; and research funding from ADC Therapeutics
A Stathis: Research funding from ADC Therapeutics, Bayer, MEI-Pharma, Merck, Novartis, Pfizer, and Roche; and other remuneration from AbbVie and PharmaMar
J Feingold, D Ungar, Y Qin, and L Wang: Employment or leadership positions for ADC Therapeutics; and stock ownership for ADC Therapeutics

PL Zinzani: Consultant/advisor for ADC Therapeutics, Bristol-Myers Squibb, Celltrion, EUSA Pharma, Gilead, Janssen-Cilag, Kyowa Kirin, Merck Sharpe & Dohme, Roche, Sandoz, Sanofi, Servier, Takeda, TG Therapeutics, and Verastem

Introduction and Methods

- Patients with R/R DLBCL for whom salvage chemotherapy/SCT is unsuccessful have a poor prognosis and limited treatment options[1,2]
- Loncastuximab tesirine (loncastuximab tesirine-lpyl; Lonca) comprises a humanized anti-CD19 antibody conjugated to a potent PBD dimer toxin[3]
- LOTIS-2 is a multicenter, open-label, single-arm, Phase 2 study in patients (≥18 years) with pathologically defined R/R DLBCL and ≥2 prior systemic treatments[4–6]



Primary efficacy and safety data have been published (**≥6 months** since first dose)[4]

- Here, we present updated results (**≥17 months** since first dose)

1. Crump M et al. *Blood* 2017;130(16):1800–1808; 2. Gisselbrecht C and Van Den Neste E. *Br J Haematol* 2018;182(5):633–643; 3. Zammarchi F et al. *Blood* 2018;131(10):1094–1105;
4. Caimi PF et al. *Lancet Oncol* 2021;22(6):790–800; 5. Caimi PF et al. *ASH 2020*; abstract 1183; 6. Caimi PF et al. *ASCO 2021*; abstract 7546.
Study findings were previously presented as a poster at the International Conference on Malignant Lymphoma (ICML) Virtual Congress, June 18-22, 2021.
DLBCL, diffuse large B-cell lymphoma; IV, intravenous; PBD, pyrrolobenzodiazepine; Q3W, every 3 weeks; Q12W, every 12 weeks; R/R, relapsed or refractory; SCT, stem cell transplant.

Treatment and Safety Results

Mean (SD) Lonca cycles: **4.6 (4.3)**

- 24 (34.3%) responders received ≥7 cycles

Overall TEAEs	Patients[a], n (%) (N=145)
Patients with any TEAE	143 (98.6)
Grade ≥3 TEAE	107 (73.8)
TEAE related to Lonca[b]	118 (81.4)
TEAE leading to Lonca dose delay or reduction	75 (51.7)
TEAE leading to Lonca discontinuation	36 (24.8)
Serious TEAE	57 (39.3)
TEAE with a fatal outcome	8 (5.5)

Grade ≥3 TEAEs

- Most common (≥10%)[c] :
  - Neutropenia: 26.2% (38/145)
  - Thrombocytopenia: 17.9% (26/145)
  - Increased GGT: 17.2% (25/145)
  - Anemia: 10.3% (15/145)

All-Grade TEAEs considered likely related to the PBD warhead

- Edema/effusion: 31.0% (45/145)
- Skin reactions and nail disorders: 43.4% (63/145)
- Liver enzyme abnormalities: 52.4% (76/145)

All-Grade Treatment-Related TEAEs

- Led to treatment discontinuation[d]: 18.6% (27/145)
- Led to dose delay[d]: 42.8% (62/145)

[a]Median (range) patient age was 66 years (23–94); [b]Related defined as possibly related, probably related, or related including missing relationship; [c]Most were reflective of laboratory abnormalities rather than clinical symptoms; [d]Increased GGT was the most common reason leading to treatment discontinuation (n=17, 11.7%) and dose delay (n=26, 17.9%).
Data cut-off: March 01, 2021.
GGT, gamma-glutamyltransferase; Lonca, loncastuximab tesirine; PBD, pyrrolobenzodiazepine; SD, standard deviation; TEAE, treatment-emergent adverse event.

Efficacy Results – ORR and DoR

ORR (Primary Endpoint)

- ORR by central review: 48.3% (70/145)

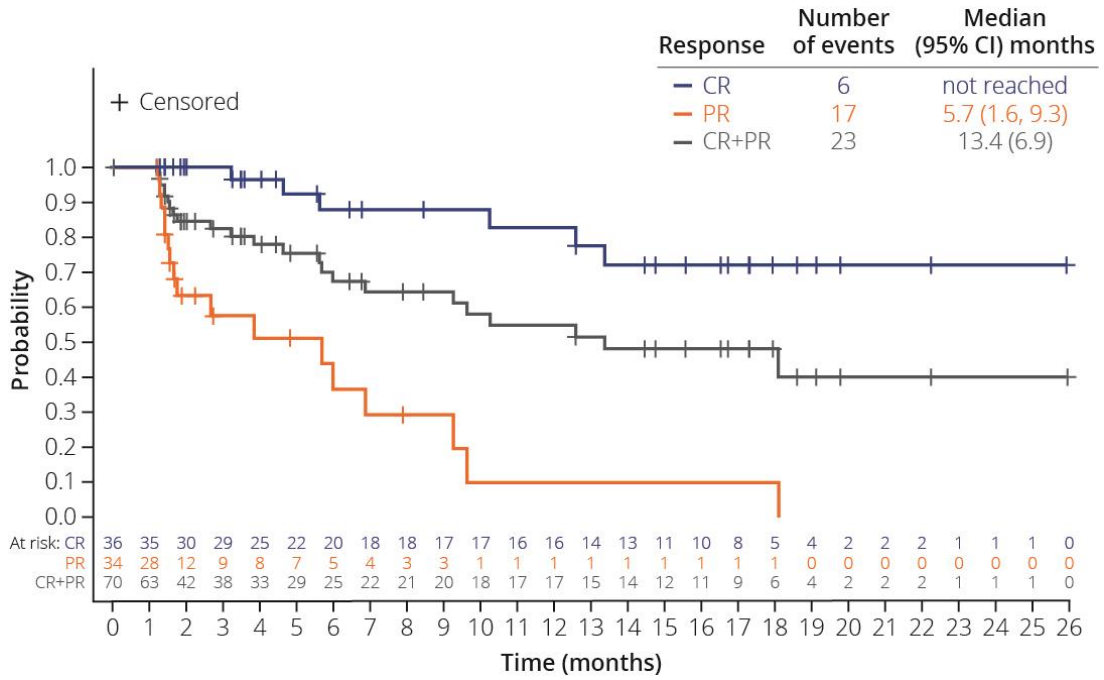
CR and PR

- CR: 24.8% (36/145)
- PR: 23.4% (34/145)

Median DoR

- 70 responders (CR + PR): 13.4 months
- Patients with a CR: not reached
- Patients with a PR: 5.7 months

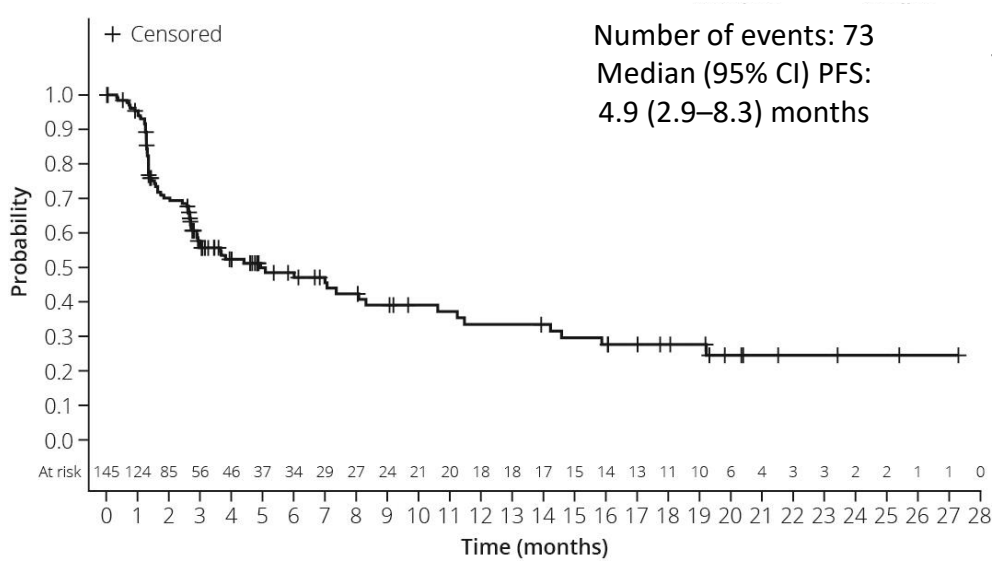
DoR by Best Overall Response



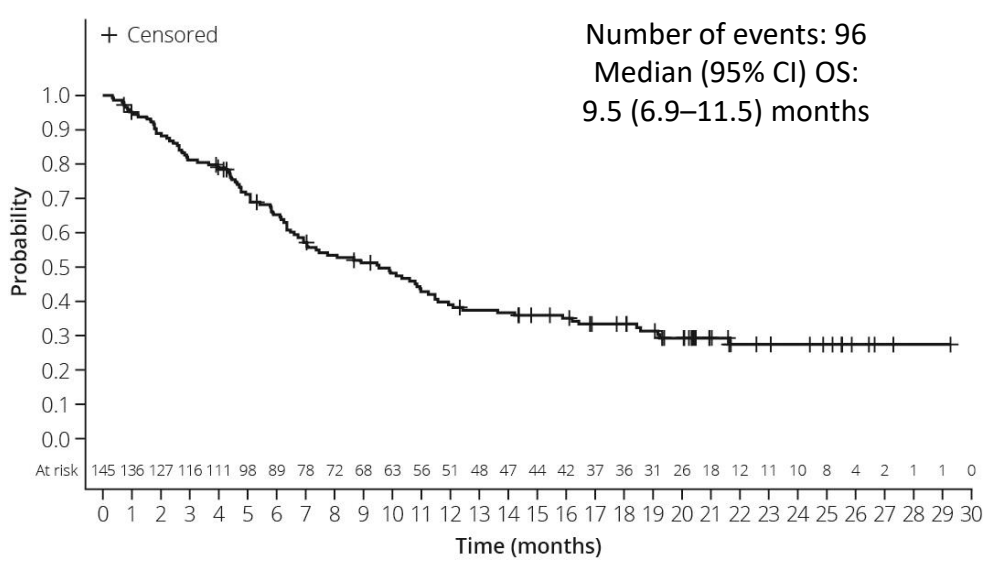
Data cut-off: March 01, 2021. All-treated population.
CI, confidence interval; CR, complete response; DoR, duration of response; ORR, overall response rate; PR, partial response.

Efficacy Results – PFS and OS

PFS



OS



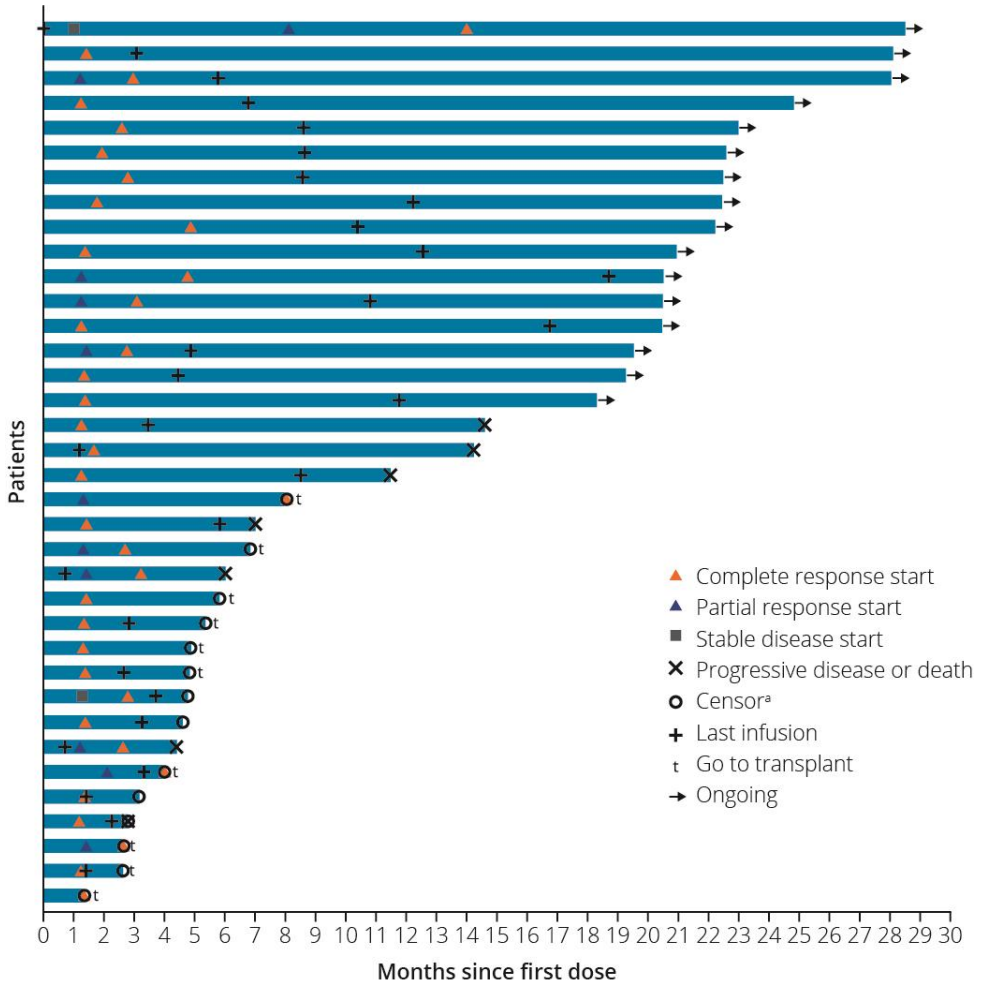
Following Lonca treatment, **16 patients received CD19-directed CAR-T therapy**, with an investigator-assessed ORR of 43.8%

- **11 patients proceeded to SCT** as consolidation after responding to Lonca

Data cut-off: March 01, 2021. All-treated population.
CAR-T, chimeric antigen receptor T-cell; CI, confidence interval; PFS, progression-free survival; ORR, overall response rate; OS, overall survival; SCT, stem cell transplant.

Efficacy Results – Complete Responders

Swimmer plot of complete responders



	Remained in CR with no further treatment % (n/N)	PD or death % (n/N)
Complete remission	44.4 (16/36)	36.1 (13/36)
Complete remission excluding 10 patients censored due to SCT	61.5 (16/26)	34.6 (9/26)

Data cut-off: March 01, 2021. All-treated population.
Each bar represents one patient. [a]Only for censored patients who discontinued the trial due to reasons other than progression or who went onto a different anticancer treatment other than SCT.
CR, complete response; PD, progressive disease; SCT, stem cell transplant.

Conclusions

- After longer follow-up in LOTIS-2, durable responses (median 13.4 months) to Lonca continue to be observed in heavily pre-treated patients with R/R DLBCL
- No new safety concerns were reported
- Efficacy and safety continue to be monitored

The authors would like to thank and acknowledge the participating patients and their families, and all study co-investigators and research coordinators

The authors also thank Shui He, formerly of ADC Therapeutics SA, for his contributions to the development of the abstract

The authors received editorial/writing support in the preparation of this poster provided by Sally Hassan of Fishawack Communications Ltd, part of Fishawack Health, funded by ADC Therapeutics SA

Study findings were previously presented at the International Conference on Malignant Lymphoma (ICML) Virtual Congress, June 18–22, 2021

This study (NCT03589469) is sponsored by ADC Therapeutics SA

Study findings were previously presented as a poster at the International Conference on Malignant Lymphoma (ICML) Virtual Congress, June 18-22, 2021.
DLBCL, diffuse large B-cell lymphoma; R/R, relapsed or refractory.