Duration of Response to Loncastuximab Tesirine in Relapsed/Refractory Diffuse Large B-cell Lymphoma by Demographic and Clinical Characteristics: Subgroup Analyses from LOTIS-2

Paolo F. Caimi[1], Weiyun Ai[2], Juan Pablo Alderuccio[3], Kirit M. Ardeshna[4], Mehdi Hamadani[5], Brian Hess[6], Brad S. Kahl[7], John Radford[8], Melhem Solh[9], Anastasios Stathis[10], Pier Luigi Zinzani[11], Jay Feingold[12], David Ungar[12], Yajuan Qin[12], Luqiang Wang[13], Carmelo Carlo-Stella[14]

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

BACKGROUND

- Outcomes for patients with relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) are poor[1,2], particularly for those with high-risk clinical characteristics
- There remains an unmet need for new treatment options for these patients[1,2]
- Loncastuximab tesirine (Lonca) is an antibody-drug conjugate comprising a humanized anti-CD19 antibody conjugated to a potent pyrrolobenzodiazepine dimer toxin[3]
- LOTIS-2 was a pivotal Phase 2 study that demonstrated substantial single-agent anti-cancer activity of Lonca in patients with R/R DLBCL (NCT03589469)[4]
- The primary efficacy and safety data were previously presented[4,5], and here we present subgroup analyses of duration of response (DoR) to Lonca by demographic and clinical characteristics

METHODS

Study Design

- Patients aged ≥18 years with R/R DLBCL who had received ≥2 prior therapies were enrolled in this Phase 2, multicenter, single-arm, open-label study of single-agent Lonca
  - Enrollment is complete
- Lonca was administered intravenously at 150 µg/kg every 3 weeks (Q3W) for 2 cycles, followed by 75 µg/kg Q3W for ≤1 year
- Patients are being followed-up Q12W for ≤3 years

Endpoints

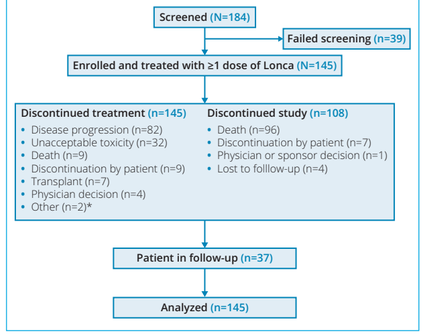
- Findings from the primary analysis of the study (where the primary endpoint was overall response rate [ORR]) have previously been reported[4,5]
- DoR was a key secondary efficacy endpoint, defined as time from the first documentation of response (central review) to disease progression or death
  - We analyzed pre-specified demographic and clinical characteristic subgroups for DoR
- Safety analysis included the frequency and severity of treatment-emergent adverse events (TEAEs)
  - Safety subgroup analyses were performed by age

RESULTS

Patient Disposition and Baseline Characteristics

- A total of 145 patients were enrolled in LOTIS-2 and treated with ≥1 dose of Lonca. As of data cut-off (March 01, 2021), 37 patients are in follow-up, and 145 patients were included in the efficacy and safety analyses (**Figure 1**)

Figure 1. Patient disposition



*Other reasons for treatment discontinuation included recurrence of metastatic colonic adenocarcinoma (n=1) and adverse event (n=1).

- Patients with high-risk characteristics were included, such as double-/triple-hit DLBCL (**Table 1**)

Table 1. Baseline characteristics

Patient characteristic	Total (N=145)
Age	
<65 years	65 (44.8)
≥65 to <75 years	59 (40.7)
≥75 years	21 (14.5)
Histology	
DLBCL	127 (87.6)
HGBCL*	11 (7.6)
PMBCL	7 (4.8)
Double-/triple-hit DLBCL	15 (10.3)
Transformed DLBCL	29 (20.0)
Disease stage	
I–II	33 (22.8)
III–IV	112 (77.2)
Response to first-line systemic therapy	
Relapse	99 (68.3)
Refractory	29 (20.0)
Other†	17 (11.7)
Response to most recent systemic therapy	
Relapse	44 (30.3)
Refractory	88 (60.7)
Other†	13 (9.0)

*HGBCL with MYC and BCL2 and/or BCL6 rearrangements. †Other defined as unknown, not evaluable or missing.

DLBCL, diffuse large B-cell lymphoma; HGBCL, high-grade B-cell lymphoma; PMBCL, primary mediastinal B-cell lymphoma.

- Median (range) patient age was 66 years (23–94)
- Patients received a median (range) of 3.0 (2–7) previous systemic therapies

Treatment

- At data cut-off, ≥12 months since all patients received their first dose of Lonca, patients received a mean (SD) of 4.6 cycles (4.3) and median (range) of 3.0 cycles (1–26) of Lonca
- Median (range) of patient follow-up was 7.8 (0.3–31.0) months

Key Message

Durable responses were observed with the recommended Phase 2 dose regimen of Lonca in heavily pre-treated patients and those with high-risk characteristics, including older patients and those with double-/triple-hit, advanced stage, or transformed DLBCL, or DLBCL refractory to first-line therapy

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Contact information

Contact Dr Paolo F. Caimi: paolo.caimi@case.edu

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Safety

- Overall, no increase in toxicity was observed in patients aged ≥65 years compared with patients aged <65 years
  - Most common all-grade TEAEs included increased gamma-glutamyltransferase (GGT) (occurring in 33 [50.8%] and 28 [35.0%] patients aged <65 years and ≥65 years, respectively), neutropenia (occurring in 34 [52.3%] and 24 [30.0%] patients aged <65 years and ≥65 years, respectively), and thrombocytopenia (occurring in 28 [43.1%] and 20 [25.0%] patients aged <65 years and ≥65 years, respectively) (**Table 2**)
  - Most common Grade ≥3 TEAEs included neutropenia (occurring in 19 [29.2%] and 19 [23.8%] patients aged <65 years and ≥65 years, respectively), thrombocytopenia (occurring in 13 [20.0%] and 13 [16.3%] patients aged <65 years and ≥65 years, respectively), and increased GGT (occurring in 17 [26.2%] and 8 [10.0%] patients aged <65 years and ≥65 years, respectively)

Table 2. TEAEs in ≥20% of the all-treated population by age group

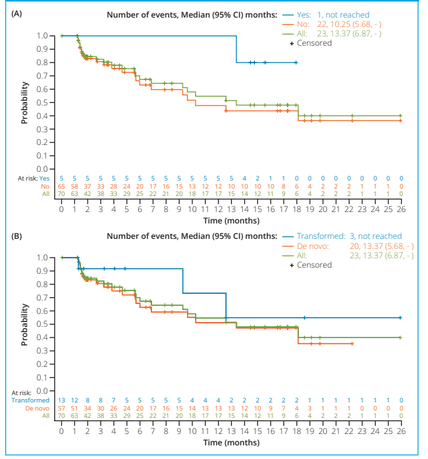
TEAE	<65 years (N=65)	≥65 to <75 years (N=59)	≥75 years (N=21)	Total (N=145)
Any TEAE	65 (100.0)	58 (98.3)	20 (95.2)	143 (98.6)
GGT increased	33 (50.8)	24 (40.7)	4 (19.0)	61 (42.1)
Neutropenia	34 (52.3)	20 (33.9)	4 (19.0)	58 (40.0)
Thrombocytopenia	28 (43.1)	17 (28.8)	3 (14.3)	48 (33.1)
Fatigue	21 (32.3)	15 (25.4)	4 (19.0)	40 (27.6)
Anemia	23 (35.4)	9 (15.3)	6 (28.6)	38 (26.2)
Nausea	17 (26.2)	13 (22.0)	4 (19.0)	34 (23.4)
Cough	19 (29.2)	9 (15.3)	4 (19.0)	32 (22.1)
Alkaline phosphatase increased	18 (27.7)	10 (16.9)	1 (4.8)	29 (20.0)
Peripheral edema	11 (16.9)	14 (23.7)	4 (19.0)	29 (20.0)

GGT, gamma-glutamyltransferase; TEAE, treatment-emergent adverse event.

DoR in Subgroups

- At data cut-off, ORR in the total population (N=145) was 48.3% (24.8% [n=36] had complete response [CR] and 23.4% [n=34] had partial response [PR])
- Median DoR for the 70 responders (CR and PR) was 13.4 months
  - Median DoR for patients with PR was 5.7 months, and not reached for patients with CR
- Patients with double-/triple-hit or transformed DLBCL each had a median DoR of not reached (**Figure 2**); patients with advanced stage disease (Stage III–IV) had a median DoR of 12.6 months
- Median DoR for older patients was longer than for younger patients (≥75 years, not reached; ≥65 to <75 years, 12.6 months; <65 years, 9.3 months) (**Figure 3A**)

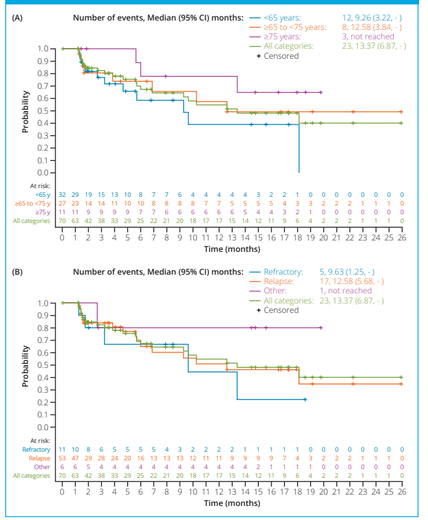
Figure 2. DoR by (A) double-/triple-hit disease (Yes/No) and (B) transformed and de novo disease



CI, confidence interval; DoR, duration of response.

- Patients with DLBCL refractory to first-line systemic therapy had a median DoR of 9.6 months compared with 12.6 months for patients who relapsed after responding to initial therapy (**Figure 3B**)

Figure 3. DoR by (A) age and (B) response to first-line systemic therapy



Other defined as unknown, not evaluable or missing. CI, confidence interval; DoR, duration of response.