Long-term Responses With Loncastuximab Tesirine: Updated Results From LOTIS-2, the Pivotal Phase 2 Study in Patients With Relapsed/Refractory Diffuse Large B-cell Lymphoma

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Conflict of Interest Disclosures

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Introduction

- Patients with R/R DLBCL after SCT or CAR-T therapy have a poor prognosis[1,2]
- Accessible therapies with manageable toxicity and long-term disease control are needed
- Loncastuximab tesirine (loncastuximab tesirine-lpyl [Lonca]) is a CD19-directed antibody–drug conjugate[3]
- Lonca demonstrated single-agent antitumor activity in heavily pretreated patients with R/R DLBCL[3,4]
  - Lonca was approved in the US in 2021 and in Europe in 2022[5,6]

CAR-T, chimeric antigen receptor T-cell; DLBCL, diffuse large B-cell lymphoma; Lonca, loncastuximab tesirine-lpyl; R/R, relapsed/refractory; SCT, stem cell transplant.

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Study Objectives

- Evaluate long-term efficacy and safety of Lonca in patients with R/R DLBCL
- Examine subgroups of patients with durable complete responses

DLBCL, diffuse large B-cell lymphoma; Lonca, loncastuximab tesirine-lpyl; R/R, relapsed/refractory.

Study Design and Patient Population

LOTIS-2 (NCT03589469): a multicenter, open-label, single-arm, phase 2 study

Patient population

R/R DLBCL[a] after ≥2 prior lines of systemic therapy, including the following:

- DLBCL NOS
- Primary mediastinal large B-cell lymphoma
- HGBCL with *MYC* and *BCL2* and/or *BCL-6* rearrangements

Primary end point

ORR by IRC of PET-CT (Lugano 2014 criteria)

Lonca (IV) was administered as a single, 30-minute outpatient infusion Q3W

Key inclusion/exclusion criteria

- Male or female patients ≥18 years of age
- Pathologic diagnosis of R/R DLBCL following ≥2 multiagent systemic treatment regimens
- ECOG performance status of 0-2
- No bulky disease (≥10 cm in longest dimension, per protocol amendment 2)

[a]Defined by the 2016 WHO classification.

CT, computed tomography; DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; HGBCL, high-grade B-cell lymphoma; IRC, independent review committee; IV, intravenous; Lonca, loncastuximab tesirine-Ipyl; NOS, not otherwise specified; ORR, overall response rate; PET, positron emission tomography; Q3W, every 3 weeks; R/R, relapsed/refractory.

Study Analysis Populations

- All-treated population
- Patients with a CR
- Patients with a CR who were event-free for ≥1 year[a]
- Patients with a CR who were event-free for ≥2 years[a]

[a]Event-free is defined as no progressive disease or death starting from day 1, cycle 1 of Lonca treatment.
CR, complete response; Lonca, loncastuximab tesirine-lpyl.

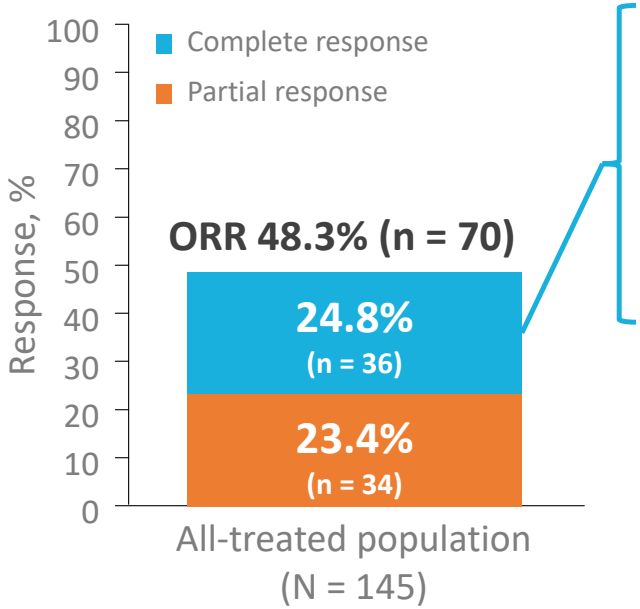
Baseline Patient Demographics and Disease Characteristics

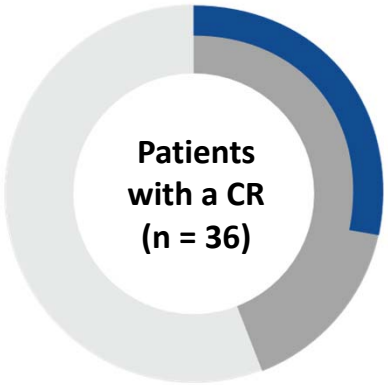
	All-treated, N = 145	Best response of CR, n = 36
Female sex, n (%)	60 (41.4)	22 (61.1)
Median age, years (range)	66.0 (23-94)	67.5 (45-94)
ECOG score, n (%)		
0	58 (40.0)	19 (52.8)
1	78 (53.8)	14 (38.9)
2	9 (6.2)	3 (8.3)
Histology, n (%)		
DLBCL, NOS	128 (88.3)	31 (86.1)
HGBCL	10 (6.9)	5 (13.9)
Transformed DLBCL, n (%)	30 (20.7)	7 (19.4)
Double/triple hit, n (%)		
Double hit	12 (8.3)	5 (13.9)
Triple hit	3 (2.1)	0
Stage, n (%)		
I-II	33 (22.8)	9 (25.0)
III-IV	112 (77.2)	27 (75.0)
Median prior systemic therapies (range)	3.0 (2-7)	3.0 (2-7)
Primary refractory, n (%)	29 (20.0)	5 (13.9)
Prior stem cell transplant, n (%)	24 (16.6)	8 (22.2)
Prior CAR-T therapy, n (%)	14 (9.7)	3 (8.3)

Data cutoff: September 15, 2022.

CAR-T, chimeric antigen receptor T-cell; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; HGBCL, high-grade B-cell lymphoma; Lonca, loncastuximab tesirine-lpyl; NOS, not otherwise specified.

Overall Response Rate and Long-term Responses Observed in the All-Treated Population





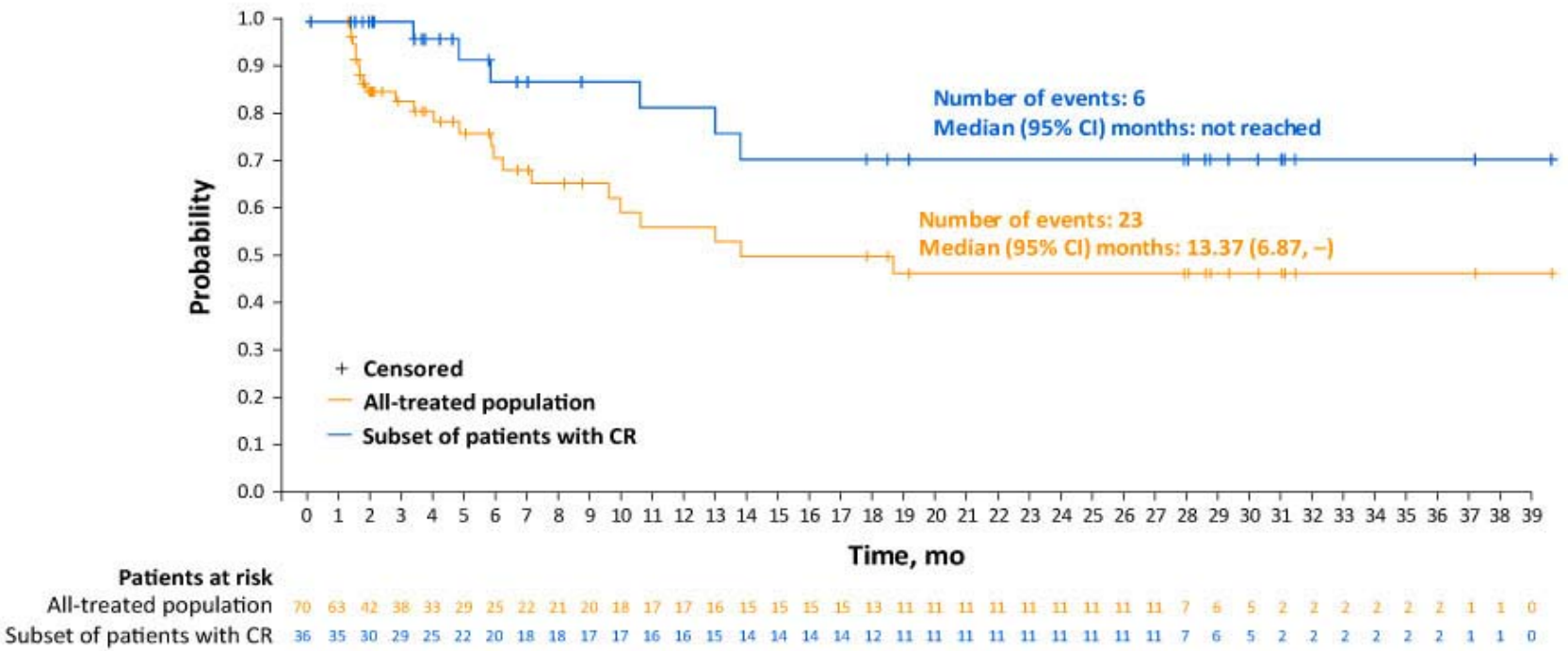
Of the patients with a CR, **44% (16 of 36)** were event-free for ≥1 year.

Of the patients with a CR, **31% (11 of 36)** were event-free for ≥2 years.

Median (range) number of treatment cycles	
All-treated population	3.0 (1-26)
Pts with a CR	8.0 (1-26)
Pts with a CR, event-free ≥1 year[a]	12.5 (1-26)
Pts with a CR, event-free ≥2 years[a]	13.0 (1-22)

Data cutoff: September 15, 2022.
The median duration of follow-up was 7.8 months (range, 0.3-42.6 months) in the all-treated population and 35.0 months (range, 4.4-42.6 months) in patients with a CR.
[a]Event-free is defined as no progressive disease or death starting from day 1, cycle 1 of Lonca treatment.
CR, complete response; Lonca, loncastuximab tesirine-lpyl; ORR, overall response rate; pts, patients.

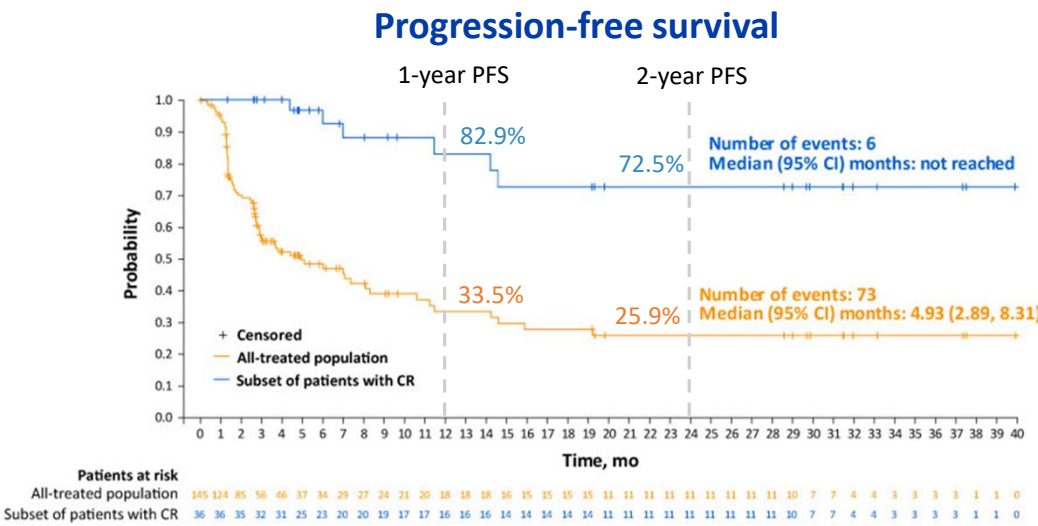
DOR: All-Treated Population and Patients With a CR

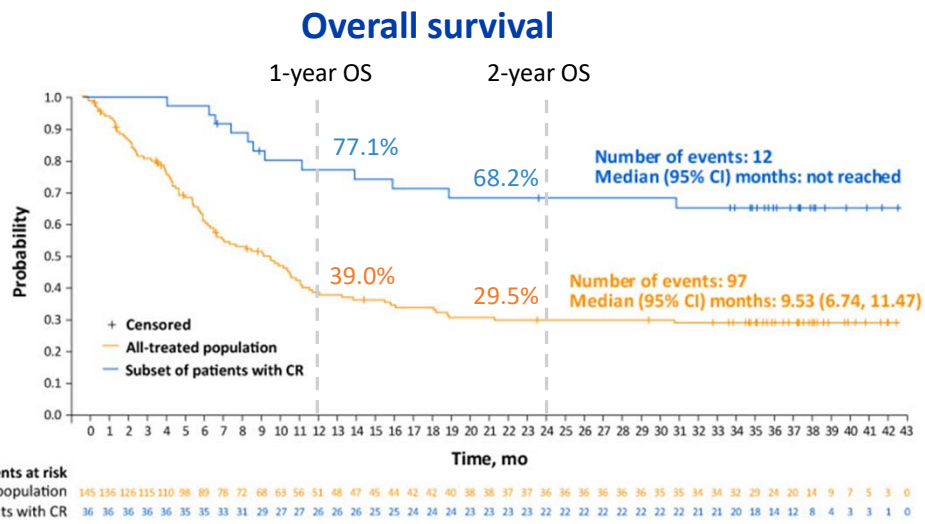


The median (range) time to response was 41 (35-247) days in the all-treated population and 42 (36-247) days for patients with a CR.

Data cutoff: September 15, 2022.
CR, complete response; DOR, duration of response.

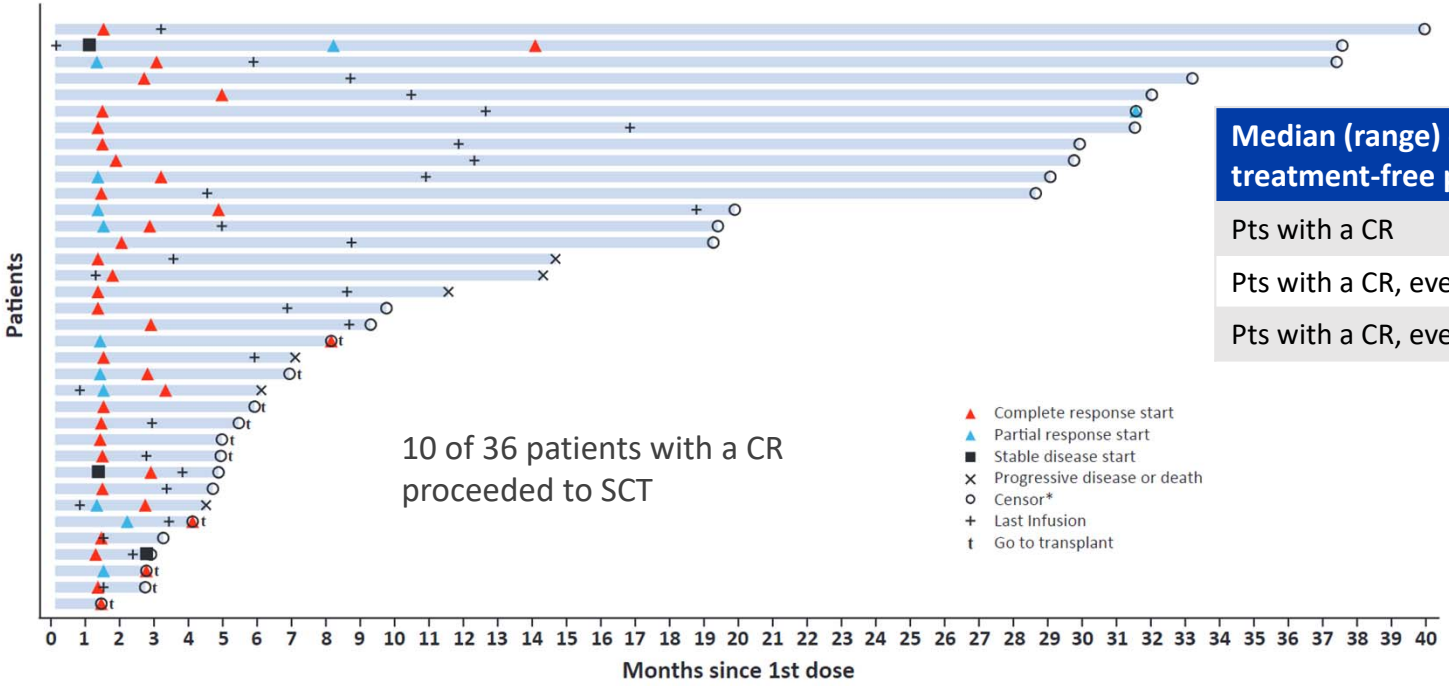
PFS and OS: All-Treated Population and Patients With a CR





Data cutoff: September 15, 2022.
CR, complete response; OS, overall survival; PFS, progression-free survival.

Swimmer Plot for Patients With a CR



Median (range) duration of time patients remained treatment-free post-Lonca discontinuation, months	
Pts with a CR	6.1 (1.0-37.5)
Pts with a CR, event-free ≥1 year[b]	24.8 (3.4-37.5)
Pts with a CR, event-free ≥2 years[b]	27.7 (20.7-37.5)

Each bar represents 1 patient in the study. Response was determined by an independent reviewer.
*Reasons for censoring included study discontinuation, new anticancer treatment started (excluding SCT), no valid post-baseline assessment, or transplant.[a]

Data cutoff: September 15, 2022.

[a]**Reasons for censoring patients with a CR included study discontinuation in 15 (41.7%) patients, SCT in 10 (27.8%) patients, and start of new anticancer therapy in 5 (13.9%) patients; 3 (8.3%) patients each experienced progressive disease and death.**

[b]Event-free is defined as no progressive disease or death starting from day 1, cycle 1 of Lonca treatment.

CR, complete response; Lonca, loncastuximab tesirine-lpyl; pts, patients; SCT, stem cell transplant.

All-Grade and Grade ≥3 Adverse Events

TEAEs, any grade in ≥30% of patients	All-treated population, N = 145	Patients with a CR, n = 36
Patients with any TEAE	98.6%	100%
Increased GGT	42%	50%
Neutropenia	40%	42%
Thrombocytopenia	33%	36%
Anemia	26%	36%
Peripheral edema	20%	33%
Nausea	23%	31%

TEAEs, grade ≥3 in ≥10% of patients	All-treated population, N = 145	Patients with a CR, n = 36
Patients with any TEAE	73.8%	75%
Neutropenia	26%	28%
Thrombocytopenia	18%	19%
Increased GGT	17%	19%
Anemia	10%	8.3%
Leukopenia	9%	14%
Hypophosphatemia	6%	11%

No new safety signals were identified during the long-term follow-up.

Data cutoff: September 15, 2022.
CR, complete response; GGT, gamma-glutamyltransferase; TEAE, treatment emergent adverse events.

Conclusions

- Among heavily pretreated patients in the LOTIS-2 study, Lonca continued to demonstrate durable, long-term responses with a manageable safety profile
  - The 2-year PFS and OS rates were 72.5% and 68.2%, respectively, in patients with a CR
  - Eleven of the 36 patients with a CR were event-free for ≥2 years with no evidence of disease and no new anticancer therapy post-Lonca
  - Patients with a CR who were event-free for ≥2 years maintained a median treatment-free period of 27.7 months from the last Lonca dose
- Further study is needed to identify factors predictive of long-term response to Lonca

CR, complete response; Lonca, loncastuximab tesirine-lpyl; OS, overall survival; PFS, progression-free survival.