Loncastuximab Tesirine Clinical Overview

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Introduction to Loncastuximab Tesirine (Lonca)

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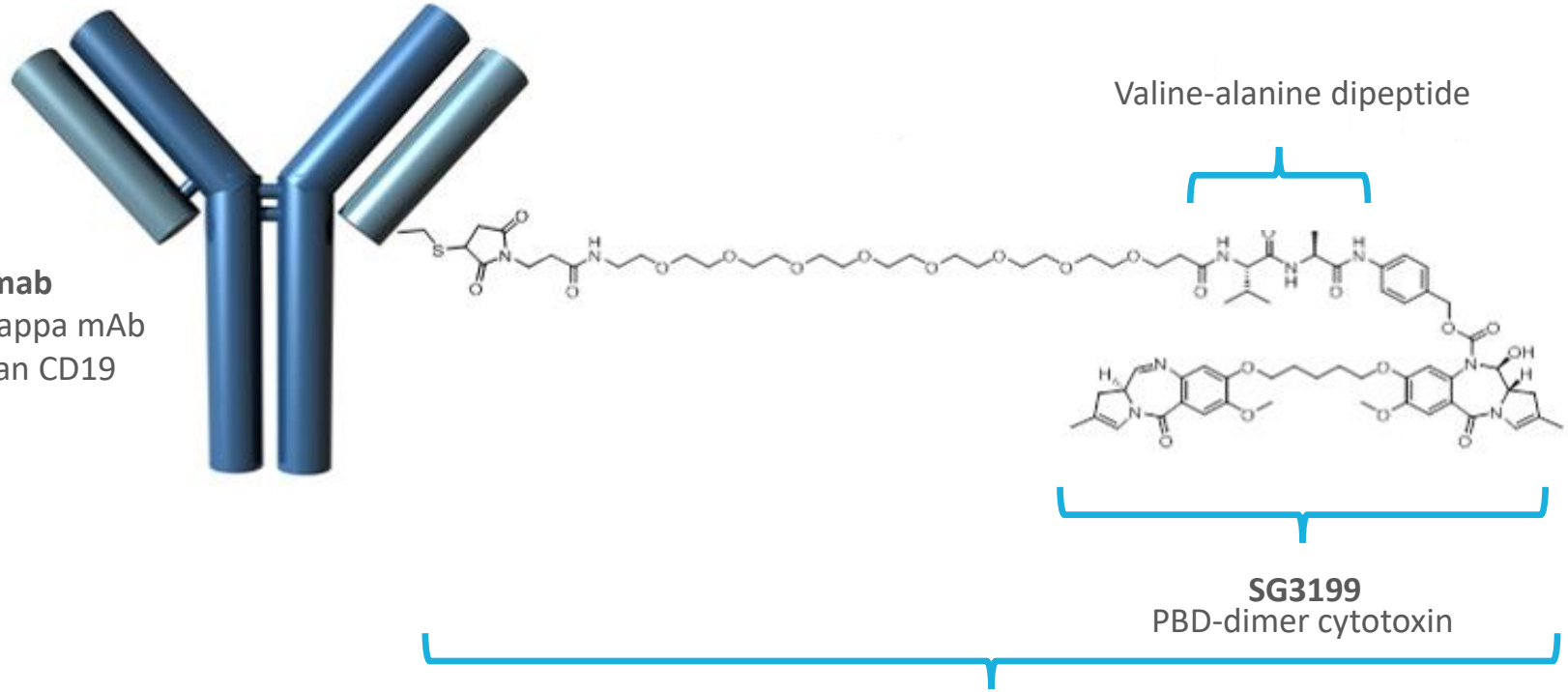
Molecular Structure of Lonca[1,2]

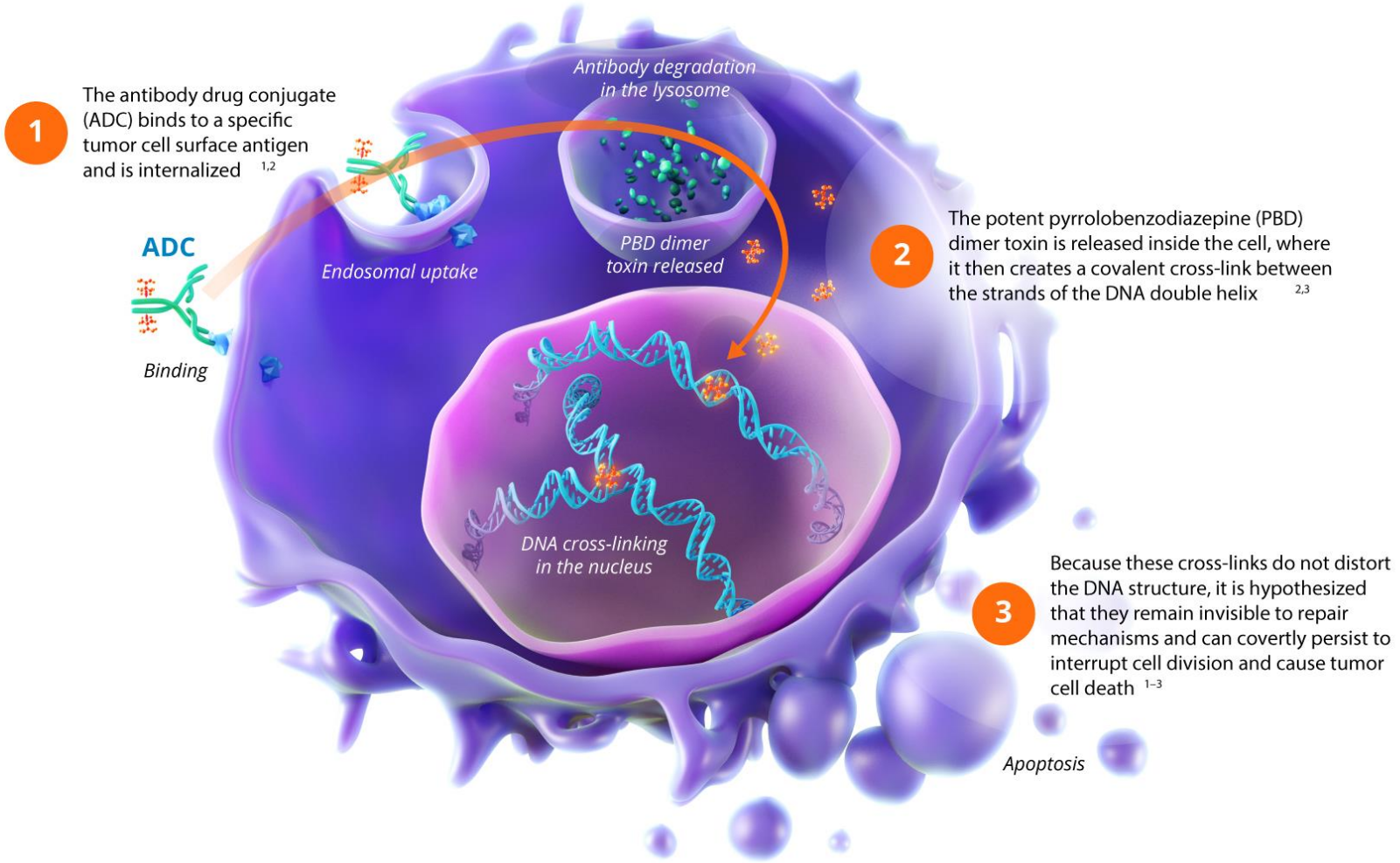


Loncastuximab
Humanized IgG1 kappa mAb specific for human CD19

SG3199
PBD-dimer cytotoxin

Tesirine/SG3249
PBD linker comprising the PBD dimer SG3199 and all linker components (stochastic conjugation)
[n, where n=~2.3 SG3249 per mAb]

Mechanism of Action[1-3]



REFERENCES

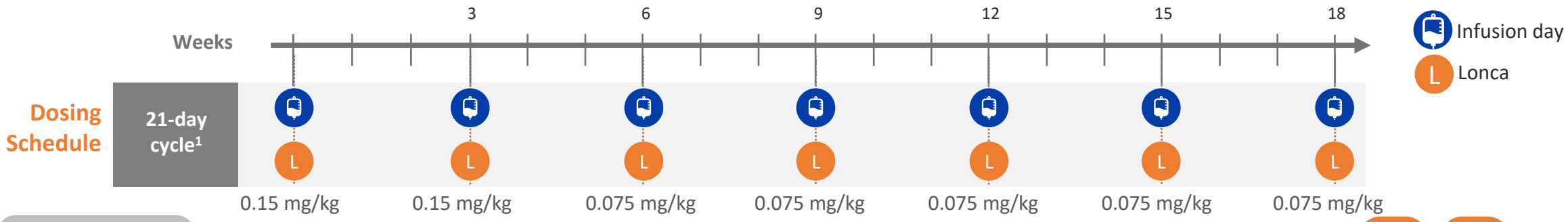
Indication and Usage

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.

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).

Lonca Dosing and Administration

Recommended Dose	Premedication	Administration
0.15 mg/kg first 2 cycles **0.075 mg/kg subsequent cycles**	**Dexamethasone 4 mg (oral or intravenous) twice daily for 3 days beginning the day before Lonca infusion (unless contraindicated)**	**Administer by intravenous infusion over 30 minutes every 3 weeks**
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	



REFERENCES

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

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LOTIS-2: Open-Label, Single-Arm, Phase 2 Study[1,2]

Patient Population[1,2]

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[1,2]

ORR by IRC of PET-CT using Lugano 2014 criteria

Lonca was administered as a single, 30-minute infusion Q3W[1,2]

Treatment until progressive disease or unacceptable toxicity, up to 1 year (patients followed up to 3 years)

Select Patient and Disease Characteristics[1]	LOTIS-2 (N=145)
Age, median years (range)	66 (23–94)
Histology,[a] n (%)	
DLBCL NOS	128 (88)
HGBCL[b]	10 (7)
Primary mediastinal DLBCL	7 (5)
Transformed DLBCL, n (%)	30 (21)

Prior Therapies[1]	LOTIS-2 (N=145)
Prior systemic therapy, median (range)	3 (2–7)
Prior stem-cell transplant, n (%)	24 (17)
Prior CAR-T, n (%)	14 (10)
Primary refractory, n (%)	29 (20)
Refractory to last LOT, n (%)	89 (61)

REFERENCES

[a]Relapsed/refractory DLBCL was classified according to the 2016 WHO classification.
[b]The primary analysis reported HGBCL in 11 patients.

LOTIS-2 Study Criteria

KEY SELECT INCLUSION CRITERIA[1,2]

- Male or female patients ≥18 years or older
- Pathologic diagnosis of R/R DLBCL following ≥2 multiagent systemic treatment regimens
- ECOG performance status 0-2
- Adequate organ function
- Biopsy-proven CD19 expression for patients who received prior CD19-targeted therapy

KEY SELECT EXCLUSION CRITERIA[1,2]

- Bulky disease (≥10 cm in longest dimension)
- Burkitt lymphoma diagnosis
- History of hypersensitivity to a CD19 antibody
- Prior treatment with Lonca
- Autologous or allogeneic SCT within 30 or 60 days, respectively, prior to initiation of study treatment
- Active central nervous system (CNS) lymphoma
- Significant comorbidities

The median (range) number of treatment cycles was 3 in the all-treated population (N=145)[3]

LOTIS-2 Patient Baseline Characteristics and Demographics

Patient characteristics

Characteristic, n (%)[a]	All-treated (N = 145)	Patients with CR (n = 36)	CR + ≥1 year EF (n = 16)[b]	CR + ≥2 years EF (n = 11)[b]
Female	60 (41.4)	22 (61.1)	13 (81.3)	9 (81.8)
Age (years)				
Median (range)	66.0 (23-94)	67.5 (45-94)	71.0 (53-84)	70.0 (53-82)
<65	65 (44.8)	13 (36.1)	3 (18.8)	3 (27.3)
≥65 to <75	59 (40.7)	15 (41.7)	7 (43.8)	5 (45.5)
≥75	21 (14.5)	8 (22.2)	6 (37.5)	3 (27.3)
Race				
White	130 (89.7)	34 (94.4)	15 (93.8)	11 (100)
Black or AA	5 (3.4)	1 (2.8)	0	0
Asian	3 (2.1)	0	0	0
Other	7 (4.8)	1 (2.8)	1 (6.3)	0
ECOG score				
0	58 (40.0)	19 (52.8)	9 (56.3)	7 (63.6)
1	78 (53.8)	14 (38.9)	6 (37.5)	3 (27.3)
2	9 (6.2)	3 (8.3)	1 (6.3)	1 (9.1)

Refractoriness

Primary refractory	29 (20.0)	5 (13.9)	2 (12.5)	0
Refractory to LT	89 (61.4)	11 (30.6)	5 (31.3)	4 (36.4)

Disease characteristics

Characteristic, n (%)[a]	All-treated (N = 145)	Patients with CR (n = 36)	CR + ≥1 year EF (n = 16)[b]	CR + ≥2 years EF (n = 11)[b]
Histology[c]				
DLBCL, NOS	128 (88.3)	31 (86.1)	11 (68.8)	8 (72.7)
HGBCL[d]	10 (6.9)	5 (13.9)	5 (31.3)	3 (27.3)
Primary mediastinal DLBCL	7 (4.8)	0	0	0
Transformed DLBCL	30 (20.7)	7 (19.4)	4 (25.0)	2 (18.2)
Double hit	12 (8.3)	5 (13.9)	5 (31.3)	3 (27.3)
Triple hit	3 (2.1)	0	0	0
Stage I-II	33 (22.8)	9 (25.0)	3 (18.8)	2 (18.2)
Stage III-IV	112 (77.2)	27 (75.0)	13 (81.3)	9 (81.8)

Prior lines of therapy

Median (range) prior lines	3.0 (2-7)	3.0 (2-7)	2.0 (2-7)	2.0 (2-7)
2 prior lines, n (%)	63 (43.4)	15 (41.7)	10 (62.5)	8 (72.7)
3 prior lines, n (%)	34 (23.4)	5 (13.9)	2 (12.5)	1 (9.1)
>3 prior lines, n (%)	48 (33.1)	16 (44.4)	4 (25.0)	2 (18.2)
Prior SCT, n (%)	24 (16.6)	8 (22.2)	1 (6.3)	1 (9.1)
Prior CAR-T, n (%)	14 (9.7)	3 (8.3)	2 (12.5)	0

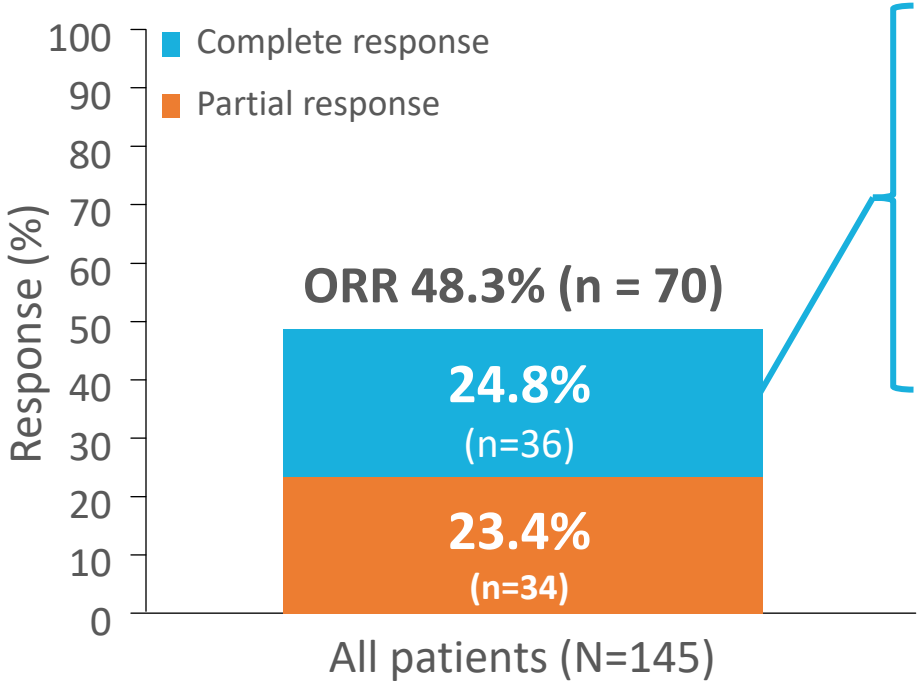
[a]Data are presented as n(%) unless otherwise specified.
[b]Event-free is defined as no progressive disease or death starting from D1C1 of Lonca treatment.
[c]R/R DLBCL was classified according to the 2016 WHO classification.
[d]The primary analysis reported HGBCL in 11 patients.

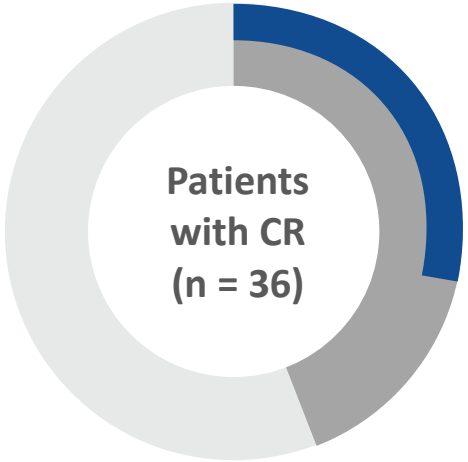
REFERENCES

LOTIS-2 Final Analysis: Lonca Administration and Extent of Exposure

	All-treated population (N = 145)	Best response of CR (n = 36)	Patients with CR who were event-free ≥1 year (n = 16)	Patients with CR who were event-free ≥2 years (n = 11)
Median duration of treatment, days (range)	45.0 (1-569)	150.0 (1-569)	262.5 (1-569)	316.0 (1-510)
Median number of treatment cycles (range)	3.0 (1-26)	8.0 (1-26)	12.5 (1-26)	13.0 (1-22)
Mean number of treatment cycles (SD)	4.6 (4.26)	8.7 (5.91)	11.6 (7.05)	11.8 (6.32)
Median average weight-adjusted dose per cycle, mg/kg (range)	0.11350 (0.0492-0.1606)	0.09136 (0.0492-0.1500)	0.08679 (0.0492-0.1498)	0.08464 (0.0492-0.1475)
Median relative dose intensity, % (range)	98.16 (41.3-107.1)	95.30 (41.3-102.8)	94.39 (41.3-100.0)	90.67 (41.3-98.3)

LOTIS-2 Final Analysis Efficacy Results: ORR[1]





44% (16/36) of patients with CR were event-free for ≥1 year

31% (11/36) of patients with CR were event-free for ≥2 years

Median (range) time to response in the all-treated population:
41 days
(35-247)

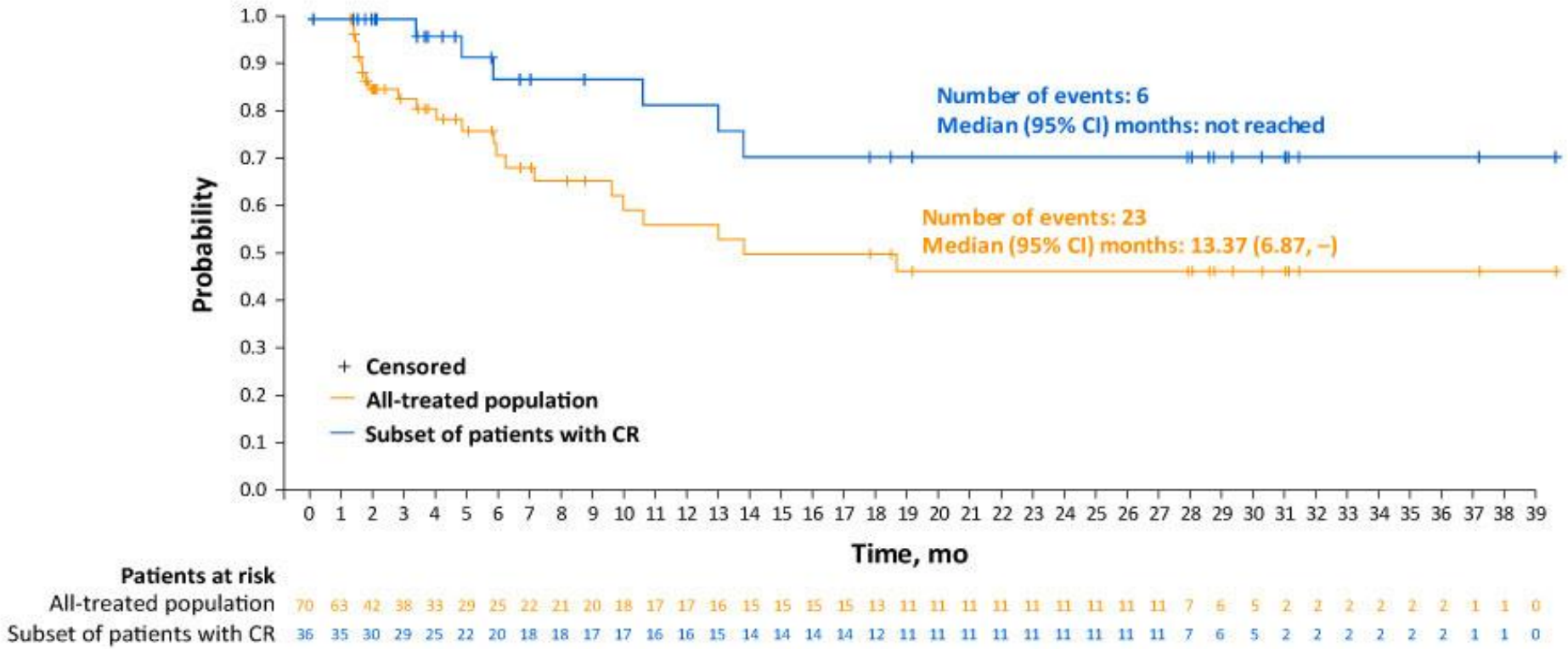
Median (range) time to response in patients with CR as BOR[2]:
42 days
(36-247)

Median (range) Lonca cycles: 3.0 (1-26)
Median (range) Lonca cycles in patients with a CR: 8.0 (1-26)

[a]Data cutoff: September 15, 2022. The median duration of follow-up was 7.8 months (range: 0.3 – 42.6) in the all-treated population and 35.0 months in patients with a CR (37.2 months for patients who were event-free ≥1 year and 37.5 months for patients who were event-free ≥2 years).
[b]ORR was assessed by independent reviewer.

REFERENCES

Median DOR of 13.4 Months Was Achieved by Patients Who Responded to Lonca[a,b]



mDOR for the 70 responders:
13.4 months
(95% CI: 6.9, NE)

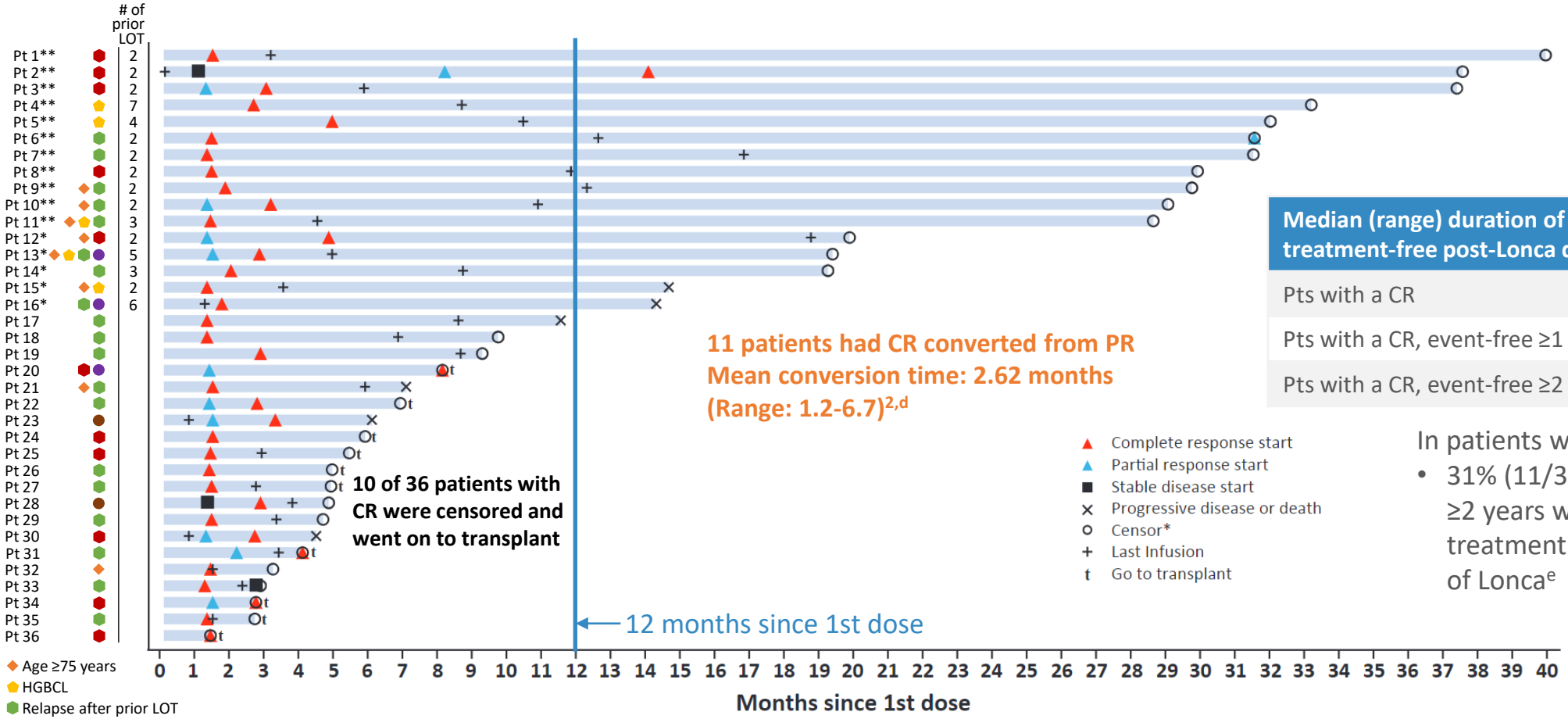
mDOR for patients with a CR:
Not reached

[a]Data cutoff: September 15, 2022. The median duration of follow-up was 7.8 months (range: 0.3 – 42.6) in the all-treated population and 35.0 months in patients with a CR (37.2 months for patients who were event-free ≥1 year and 37.5 months for patients who were event-free ≥2 years).
[b]DOR was defined as the time from earliest date of first response until the first date of either disease progression or death due to any cause.

REFERENCES

LOTIS-2: Ongoing Complete Responses ≥1 Year[1,2]

Swimmers Plot of Complete Responders (n = 36)[a-c]



11 patients had CR converted from PR
Mean conversion time: 2.62 months
(Range: 1.2-6.7)[2,d]

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[e]	24.8 (3.4-37.5)
Pts with a CR, event-free ≥2 years[e]	27.7 (20.7-37.5)

In patients with a CR:

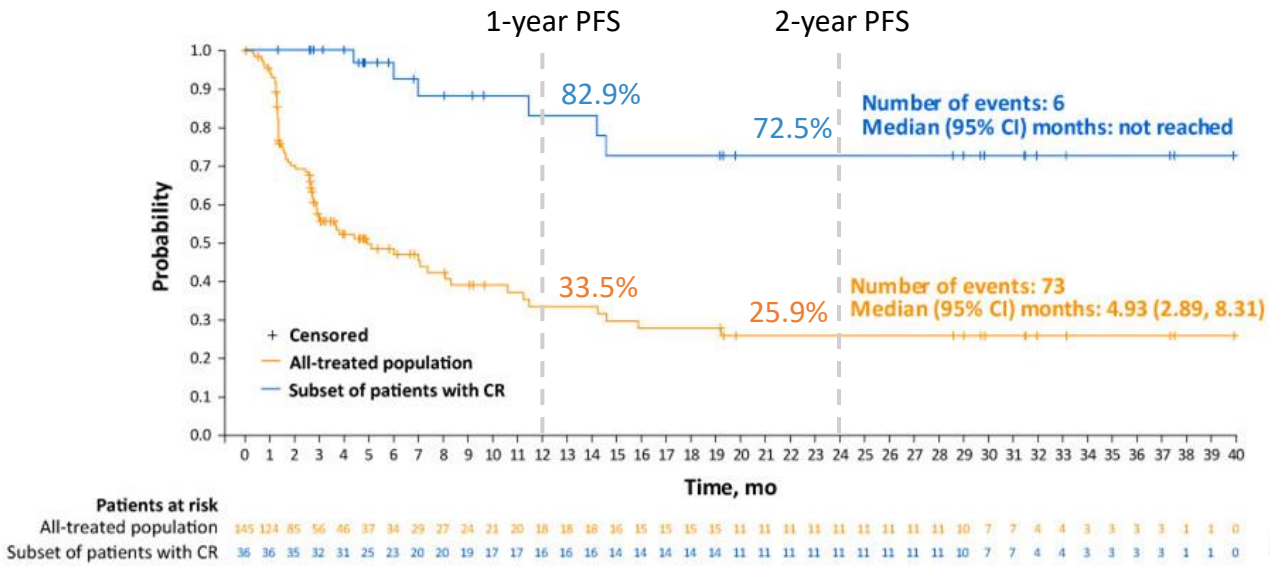
- 31% (11/36) were event-free for ≥2 years with no new anticancer treatment after discontinuation of Lonca[e]

[a]Data cutoff: September 15, 2022.
[b]Each bar represents 1 patient; patients were treated until progressive disease or unacceptable toxicity.
[c]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.
[d]Conversion time is calculated as first CR date – first PR date.
[e]Event-free is defined as no progressive disease or death starting from day 1, cycle 1 of Lonca treatment.
* Denotes CR patients who were event free for at least 12 months.
** Denotes CR patients who were event free for at least 24 months.

REFERENCES

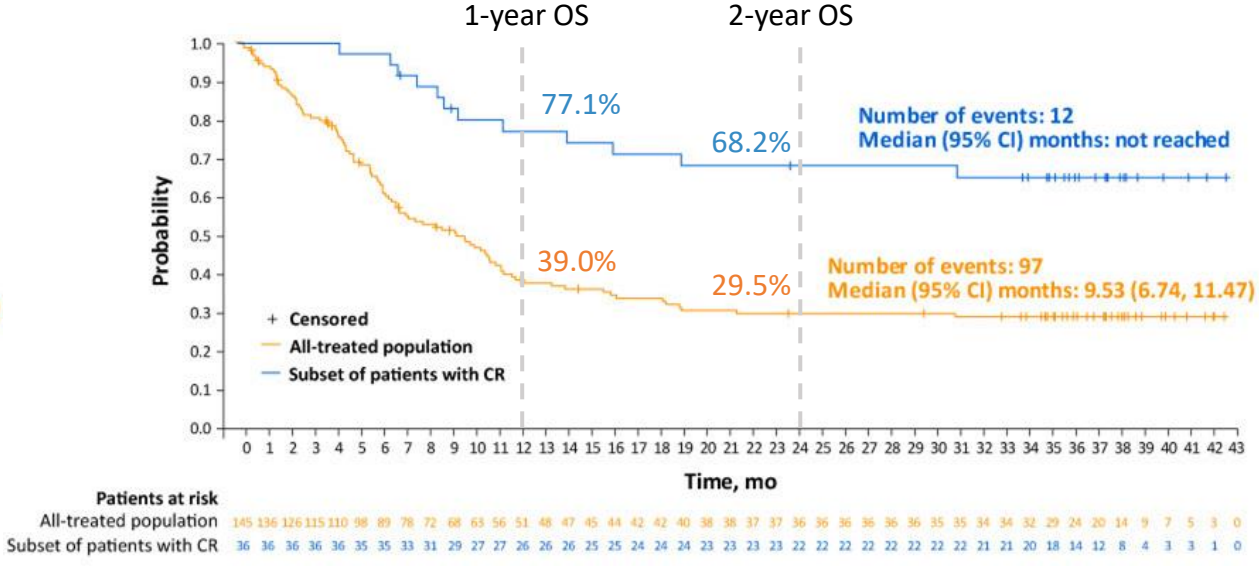
LOTIS-2 Final Analysis: Progression-Free and Overall Survival[a]

Progression-free survival



Median PFS, all-treated population
4.93 months
(95% CI: 2.98, 8.31)

Overall survival



Median OS, all-treated population
9.53 months
(95% CI: 6.74, 11.47)

REFERENCES

[a]Data cutoff: September 15, 2022. The median duration of follow-up was 7.8 months (range: 0.3 – 42.6) in the all-treated population and 35.0 months (range: 4.4 - 42.6) in patients with a CR.

Safety Profile in LOTIS-2[1]

Adverse reactions in ≥10% of patients in LOTIS-2 (N=145)	All Grades, %	Grades 3 or 4,%
General disorders and administration site conditions		
Fatigue	38	1
Edema	28	3
Skin and subcutaneous tissue disorders		
Rash	30	2
Pruritus	12	0
Photosensitivity reaction	10	2
Gastrointestinal disorders		
Nausea	23	0
Diarrhea	17	2
Abdominal pain	14	3
Vomiting	13	0
Constipation	12	0
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain	23	1
Metabolism and nutrition disorders		
Decreased appetite	15	0
Respiratory disorders		
Dyspnea	13	1
Pleural effusion	10	2
Infection		
Upper respiratory tract infection	10	<1

Serious adverse reactions occurred in 28% of patients.

The most common serious adverse reactions that occurred in ≥2% of patients were febrile neutropenia, pneumonia, edema, pleural effusion, and sepsis. Fatal adverse reactions occurred in 1% of patients due to infection.

No new safety concerns were reported in the final analysis.[2]

Pooled safety analysis (N = 215)

- The pooled safety population reflects exposure to Lonca as a single agent at an initial dose of 0.15 mg/kg in 215 patients with DLBCL in the Phase 1 and LOTIS-2 studies.
- The most common (>20%) ARs, including laboratory abnormalities: thrombocytopenia, increased GGT, neutropenia, anemia, hyperglycemia, transaminase elevation, fatigue, hypoalbuminemia, rash, edema, nausea, and musculoskeletal pain.

Safety Profile and Laboratory Abnormalities

Permanent treatment discontinuation due to an AR occurred in 19% of patients (N = 145)

ARs resulting in permanent discontinuation in ≥2% were GGT increase, edema, and effusion.

Dose reductions due to an AR of Lonca occurred in 8% of patients

ARs resulting in dose reduction in ≥4% were GGT increase.

Dosage interruptions due to an AR occurred in 49% of patients

Adverse reactions leading to dose interruption in ≥5% were GGT increase, neutropenia, thrombocytopenia, and edema.

Specific populations

In LOTIS-2, 55% of patients were ≥65 years of age, and 14% were ≥75 years of age. No overall differences in safety or effectiveness were observed between these patients and younger patients.

Select laboratory abnormalities in ≥10% of patients[a]	All grades, %	Grades 3 or 4,%
Hematologic		
Platelets decreased	58	17
Neutrophils decreased	52	30
Hemoglobin decreased	51	10[b]
Chemistry		
GGT increased	57	21
Glucose increased	48	8
AST increased	41	<1[b]
Albumin decreased	37	<1[b]
ALT increased	34	3

Routine GGT monitoring is not included in Lonca prescribing information

[a]The denominator used to calculate the rate varied from 143 to 145 based on the number of patients with a baseline value and at least one posttreatment value.

[b]No grade 4 adverse reactions occurred.

REFERENCES

LOTIS-2 Final Analysis: Safety Profile

	All-treated Population (N = 145)			All-treated Population (N = 145)	
	All grades, n (%)	Grade ≥3, n (%)		All grades, n (%)	Grade ≥3, n (%)
Any TEAE	143 (98.6)	107 (73.8)	Increased ALT	22 (15.2)	4 (2.8)
Increased GGT	61 (42.1)	25 (17.2)	Decreased appetite	22 (15.2)	-
Neutropenia	58 (40.0)	38 (26.2)	Leukopenia	21 (14.5)	13 (9.0)
Thrombocytopenia	48 (33.1)	26 (17.9)	Hypomagnesemia	20 (13.8)	1 (0.7)
Fatigue	40 (27.6)	2 (1.4)	Pruritus	19 (13.1)	-
Anemia	38 (26.2)	15 (10.3)	Rash	19 (13.1)	1 (0.7)
Nausea	34 (23.4)	-	Vomiting	19 (13.1)	-
Cough	33 (22.8)	1 (0.7)	Abdominal pain	17 (11.7)	4 (2.8)
Increased blood ALP	29 (20.0)	1 (0.7)	Constipation	17 (11.7)	-
Peripheral edema	29 (20.0)	2 (1.4)	Dyspnea	17 (11.7)	2 (1.4)
Pyrexia	28 (19.3)	2 (1.4)	Insomnia	16 (11.0)	-
Diarrhea	25 (17.2)	3 (2.1)	Pleural effusion	16 (11.0)	3 (2.1)
Increased AST	23 (15.9)	1 (0.7)	Erythema	15 (10.3)	1 (0.7)
Hypokalemia	23 (15.9)	6 (4.1)	Headache	15 (10.3)	1 (0.7)
Hypophosphatemia	23 (15.9)	8 (5.5)	Photosensitivity reaction	15 (10.3)	3 (2.1)

No new safety concerns were reported in the final analysis

REFERENCES

LOTIS-2 Safety Profile in Patients With CR Who Were Event-Free for ≥1 or ≥2 years

TEAE[a]	Patients with CR, event-free ≥1 year (n = 16)		Patients with CR, event-free ≥2 years (n = 11)		TEAE[a]	Patients with CR, event-free ≥1 year (n = 16)		Patients with CR, event-free ≥2 years (n = 11)	
	All grades, n (%)	Grade ≥3, n (%)	All grades, n (%)	Grade ≥3, n (%)		All grades, n (%)	Grade ≥3, n (%)	All grades, n (%)	Grade ≥3, n (%)
Any TEAE	16 (100)	13 (81.3)	11 (100)	9 (81.8)	Rash	5 (31.3)	—	4 (36.4)	—
Increased GGT	8 (50.0)	2 (12.5)	7 (63.6)	2 (18.2)	Vomiting	3 (18.8)	—	2 (18.2)	—
Neutropenia	6 (37.5)	6 (37.5)	4 (36.4)	4 (36.4)	Abdominal pain	1 (6.3)	—	1 (9.1)	—
Thrombocytopenia	6 (37.5)	2 (12.5)	4 (36.4)	1 (9.1)	Constipation	3 (18.8)	—	3 (27.3)	—
Fatigue	4 (25.0)	—	1 (9.1)	—	Dyspnea	4 (25.0)	—	2 (18.2)	—
Anemia	5 (31.3)	2 (12.5)	3 (27.3)	1 (9.1)	Pleural effusion	3 (18.8)	0	1 (9.1)	0
Nausea	5 (31.3)	—	4 (36.4)	—	Erythema	2 (12.5)	0	2 (18.2)	0
Cough	5 (31.3)	—	2 (18.2)	—	Headache	2 (12.5)	—	2 (18.2)	—
Increased blood ALP	2 (12.5)	—	2 (18.2)	—	Asthenia	2 (12.5)	—	2 (18.2)	—
Peripheral edema	7 (43.8)	1 (6.3)	5 (45.5)	1 (9.1)	Facial edema	3 (18.8)	1 (6.3)	1 (9.1)	1 (9.1)
Pyrexia	3 (18.8)	—	2 (18.2)	—	Arthralgia	2 (12.5)	—	1 (9.1)	—
Diarrhea	5 (31.3)	2 (12.5)	3 (27.3)	1 (9.1)	Back pain	2 (12.5)	—	1 (9.1)	—
Increased AST	3 (18.8)	—	3 (27.3)	—	Dizziness	2 (12.5)	—	2 (18.2)	—
Hypokalemia	3 (18.8)	1 (6.3)	2 (18.2)	0	Lymphopenia	2 (12.5)	1 (6.3)	2 (18.2)	1 (9.1)
Hypophosphatemia	3 (18.8)	3 (18.8)	2 (18.2)	2 (18.2)	Muscle weakness	3 (18.8)	—	1 (9.1)	—
Increased ALT	1 (6.3)	0	1 (9.1)	0	Nasal congestion	3 (18.8)	—	1 (9.1)	—
Decreased appetite	4 (25.0)	—	2 (18.2)	—	Hyperglycemia	2 (12.5)	—	2 (18.2)	—
Leukopenia	4 (25.0)	4 (25.0)	3 (27.3)	3 (27.3)	Localized edema	2 (12.5)	—	1 (9.1)	—
Hypomagnesemia	2 (12.5)	0	1 (9.1)	0	Peripheral neuropathy	2 (12.5)	—	2 (18.2)	—
Pruritus	4 (25.0)	—	3 (27.3)	—	Skin hyperpigmentation	2 (12.5)	—	2 (18.2)	—

[a]TEAEs occurring in ≥10% of patients.

LOTIS-2: Exploratory Subgroup Analyses of the Primary Endpoint (ORR)

Patient subgroups to be explored include:

- Age (<65 years, ≥65 to < 75 years, ≥75 years)
- WHO Classification (DLBCL NOS, PMBCL, HGBCL)
- Double/triple hit lymphoma
- Double/triple expressor
- Transformed disease
- Cell of origin
- Response to first-line therapy
- Prior stem-cell transplant
- Prior CAR-T therapy
- Number of prior systemic therapies

LOTIS-2 Exploratory Analyses of Primary Endpoint (ORR)[1,2]

Response in select patient subgroups

Subgroup	Patients (N)	ORR[a] (n) [95% CI]	CRR[b] (n) [95% CI]
All	145	**48.3 (70)** [39.9, 56.7]	**24.8 (36)** [18.0, 32.7]
Age			
<65 years	65	**49.2 (32)** [36.6, 61.9]	**20.0 (13)** [11.1, 31.8]
≥65 to < 75 years	59	**45.8 (27)** [32.7, 59.2]	**25.4 (15)** [15.0, 38.4]
≥75 years	21	**52.4 (11)** [29.8, 74.3]	**38.1 (8)** [18.1, 61.6]
WHO classification			
DLBCL NOS	128	**50.0 (64)** [41.4, 59.0]	**24.2 (31)** [17.1, 32.6]
PMBCL	7	**14.3 (1)** [0.4, 57.9]	0
HGBCL[c]	10	**50.0 (5)** [18.7, 81.3]	**50.0 (5)** [18.7, 81.3]
Double/triple hit[d]			
No	130	**50.0 (65)** [41.1, 58.9]	**23.8 (31)** [16.8, 32.1]
Yes	15	**33.3 (5)** [11.8, 61.6]	**33.3 (5)** [11.8, 61.6]
Double/triple expressor			
No	125	**48.0 (60)** [39.0, 57.1]	**25.6 (32)** [18.2, 34.2]
Yes	20	**50.0 (10)** [27.2, 72.8]	**20.0 (4)** [5.7, 43.7]
Transformed disease			
Transformed	30	**43.3 (13)** [25.5, 62.6]	**23.3 (7)** [9.9, 42.3]
De novo	115	**49.6 (57)** [40.1, 59.0]	**25.2 (29)** [17.6, 34.2]
Cell-of-origin[e]			
GCB	49	**53.1 (26)** [38.3, 67.5]	**26.5 (13)** [14.9, 41.1]
ABC	23	**47.8 (11)** [26.8, 69.4]	**21.7 (5)** [7.5, 43.7]

Subgroup	Patients (N)	ORR[a] (n) [95% CI]	CRR[b] (n) [95% CI]
All	145	**48.3 (70)** [39.9, 56.7]	**24.8 (36)** [18.0, 32.7]
First-line response			
Relapse	99	**53.5 (53)** [43.2, 63.6]	**27.3 (27)** [18.8, 37.1]
Refractory	29	**37.9 (11)** [20.7, 57.7]	**17.2 (5)** [5.8, 35.8]
Prior stem-cell transplant			
Yes	24	**58.3 (14)** [36.6, 77.9]	**33.3 (8)** [15.6, 55.3]
No	121	**46.3 (56)** [37.2, 55.6]	**23.1 (28)** [16.0, 31.7]
Prior CAR-T therapy			
Yes	14	**42.9 (6)** [17.1, 71.1]	**21.4 (3)** [4.7, 50.8]
No	131	**48.9 (64)** [40.0, 57.7]	**25.2 (33)** [18.0, 33.5]
Prior systemic therapies			
2 prior lines	63	**47.6 (30)** [34.9, 60.6]	**23.8 (15)** [14.0, 36.2]
3 prior lines	34	**50.0 (17)** [32.4, 67.6]	**14.7 (5)** [5.0, 31.1]
>3 prior lines	48	**47.9 (23)** [33.3, 62.8]	**33.3 (16)** [20.4, 48.4]

Data cut-off: September 15, 2022.
[a]ORR is defined as the proportion of patients with the best overall response of a complete or partial response. [b]CR is defined as the percentage of patients with a best overall response of a complete response. [c]HGBCL with *MYC* and *BCL2* and/or *BCL6* rearrangements defined by the 2016 revision of the World Health Organization (WHO) classification of lymphoid neoplasms.
[d]Some patients had a diagnosis of double-/triple-hit lymphoma based on institutional pathology prior to the WHO classification of HGBCL with *MYC* and *BCL2* and/or *BCL6* rearrangements.
[e]ABC and GCB were investigator-reported with no independent testing.

Patient Subgroup and Retrospective Analyses

Age, Response to First-Line Therapy, Double-/Triple-Hit, Transformed DLBCL, HGBCL, Prior CAR-T, and Subsequent CAR-T

LOTIS-2 Subgroup: Baseline Characteristics by Age

Characteristic, n (%)		<70 years (n = 95)	≥70 years (n = 50)	Total (N = 145)
Sex	Female	34 (35.8)	26 (52.0)	60 (41.4)
	Male	61 (64.2)	24 (48.0)	85 (58.6)
Age (years), median (range)		59 (23-69)	74 (70-94)	66 (23-94)
ECOG performance status score	0	36 (37.9)	22 (44.0)	58 (40.0)
	1	57 (60.0)	21 (42.0)	78 (53.8)
	2	2 (2.1)	7 (14.0)	9 (6.2)
Primary DLBCL category (WHO 2016)	DLBCL, NOS	87 (91.6)	41 (82.0)	128 (88.3)
	HGBCL with *MYC* and *BCL2* and/or *BCL6* rearrangements	2 (2.1)	8 (16.0)	10 (6.9)
	DLBCL, primary mediastinal	6 (6.3)	1 (2.0)	7 (4.8)
Transformed DLBCL	Transformed DLBCL	21 (22.1)	9 (18.0)	30 (20.7)
	Transformed follicular	17 (17.9)	9 (18.0)	26 (17.9)
	Richter's transformation	2 (2.1)	0	2 (1.4)
	Transformed lymphoplasmacytic	1 (1.1)	0	1 (0.7)
	Transformed MZBCL	1 (1.1)	0	1 (0.7)

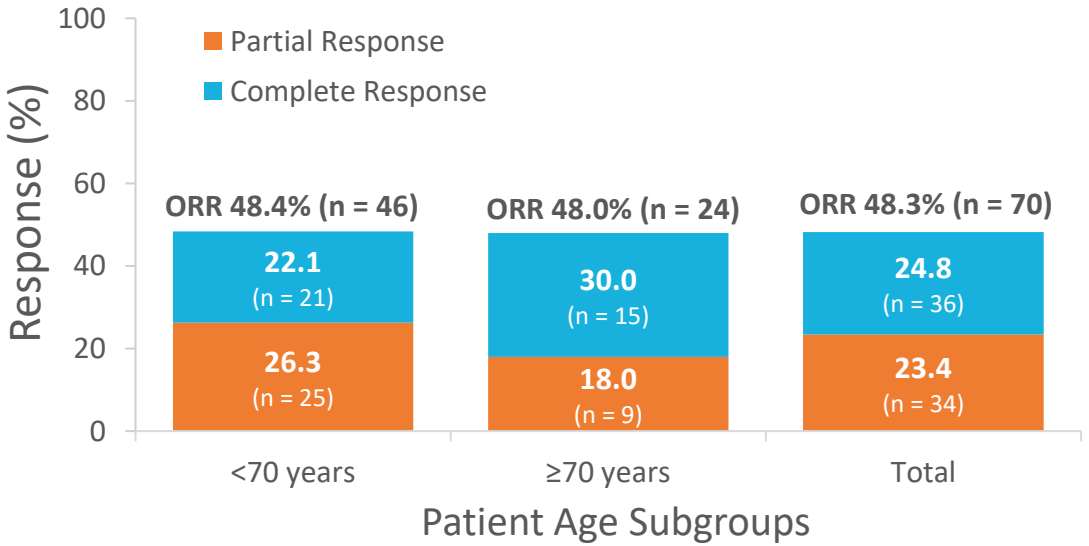
Characteristic, n (%)		<70 years (n = 95)	≥70 years (n = 50)	Total (N = 145)
DLBCL double/triple hit	Double hit	5 (5.3)	7 (14.0)	12 (8.3)
	Triple hit	1 (1.1)	2 (4.0)	3 (2.1)
Prior systemic therapies	2	37 (38.9)	26 (52.0)	63 (43.4)
	3	20 (21.1)	14 (28.0)	34 (23.4)
	>3	38 (40.0)	10 (20.0)	48 (33.1)
Prior systemic therapies, median (min, max)		3.0 (2, 7)	2.0 (2, 5)	3.0 (2, 7)
Any prior SCT	Yes	21 (22.1)	3 (6.0)	24 (16.6)
Response to 1L systemic therapy	Relapse	63 (66.3)	36 (72.0)	99 (68.3)
	Refractory	22 (23.2)	7 (14.0)	29 (20.0)
	Other	10 (10.5)	7 (14.0)	17 (11.7)
Response to prior last-line therapy	Relapse	29 (30.5)	14 (28.0)	43 (29.7)
	Refractory	58 (61.1)	31 (62.0)	89 (61.4)
	Other	8 (8.4)	5 (10.0)	13 (9.0)

Patients were heavily pretreated, with 43.4% receiving 2 prior lines and a median of 3 prior systemic therapies, and 16.6% had received prior stem cell transplant.

REFERENCES

Data cutoff: March 1, 2021.

LOTIS-2 Subgroup: Responses by Age



BOR, n (%)	<70 years (n = 95)	≥70 years (n = 50)	Total (n = 145)
CR	21 (22.1)	15 (30.0)	36 (24.8)
PR	25 (26.3)	9 (18.0)	34 (23.4)
ORR (CR + PR)	46 (48.4)	24 (48.0)	70 (48.3)
95% CI for ORR	38.0 – 58.9	33.7 – 62.6	39.9 – 56.7
95% CI for CR	14.2 – 31.8	17.9 – 44.6	18.0 – 32.7
SD	16 (16.8)	6 (12.0)	22 (15.2)
PD	18 (18.9)	12 (24.0)	30 (20.7)
Not evaluable	15 (15.8)	8 (16.0)	23 (15.9)

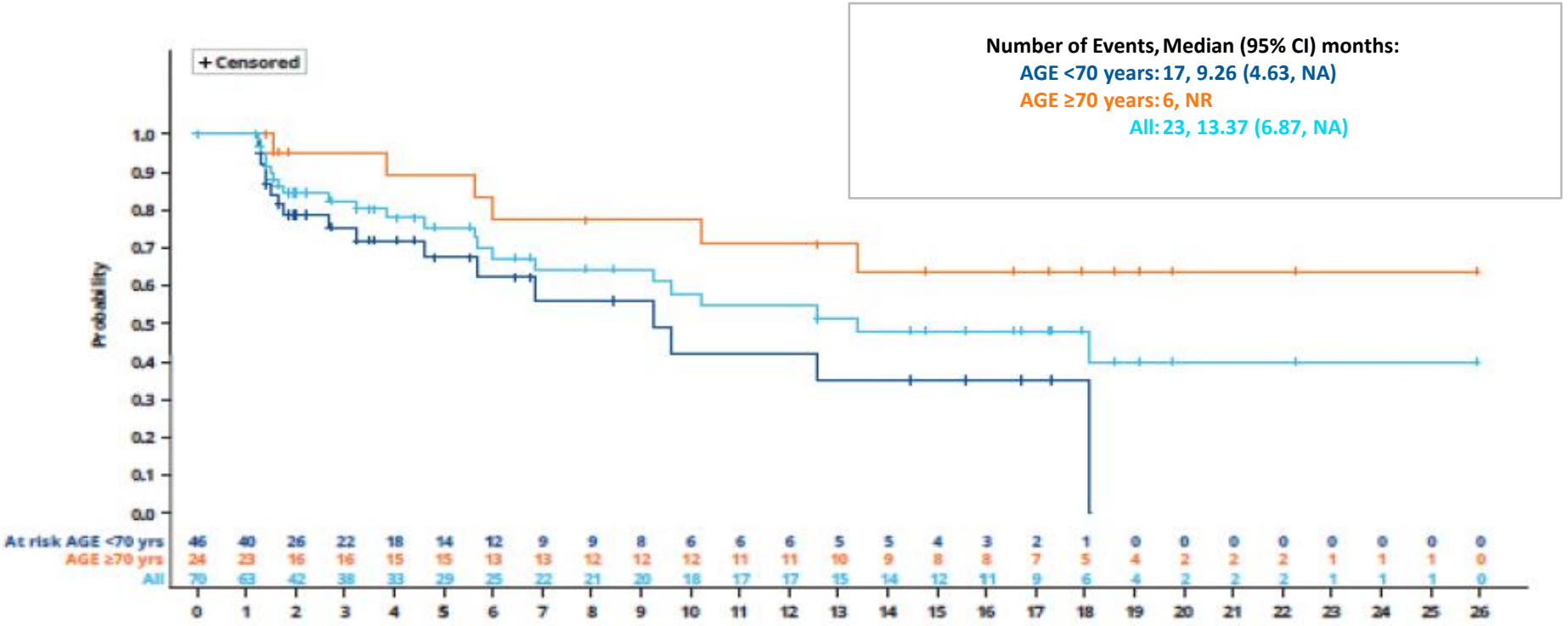
Time to Response	<70 years	≥70 years	Total
Time to CR/PR, days, median (min, max)	n = 46	n = 24	n = 70
	41.5 (35, 247)	41.0 (36, 142)	41.0 (35, 247)
Time to CR, days, median (min, max)	n = 21	n = 15	n = 36
	42.0 (37, 247)	41.0 (36, 59)	42.0 (36, 247)

Patients in the younger (aged <70 years) and older (aged ≥70 years) groups had similar responses across nearly all efficacy measures.

REFERENCES

Data cutoff: March 1, 2021.

LOTIS-2 Subgroup: Duration of Response to Lonca by Age



- Median DOR was 9.26 months (95% CI, 4.63-NA) in the younger group and not reached in the older group.[a]

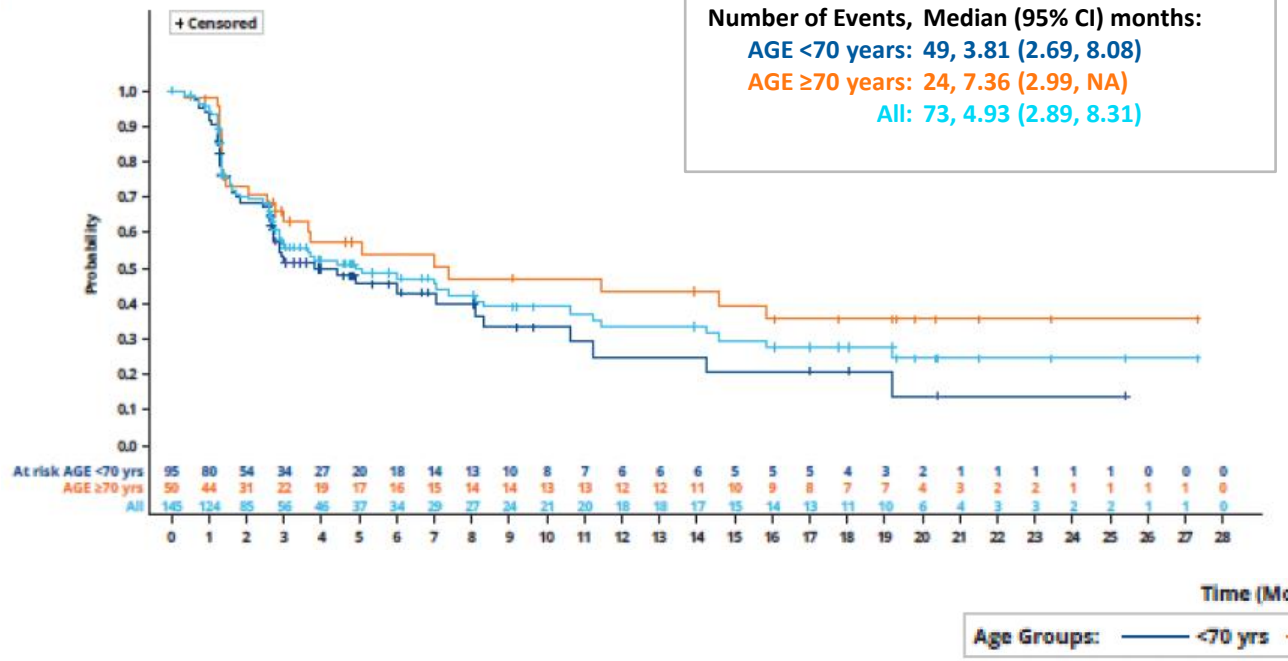
REFERENCES

Data cutoff: March 1, 2021.

[a]Comparative analyses between age groups were not performed with statistical testing; instead, numerical trends were noted across age groups.

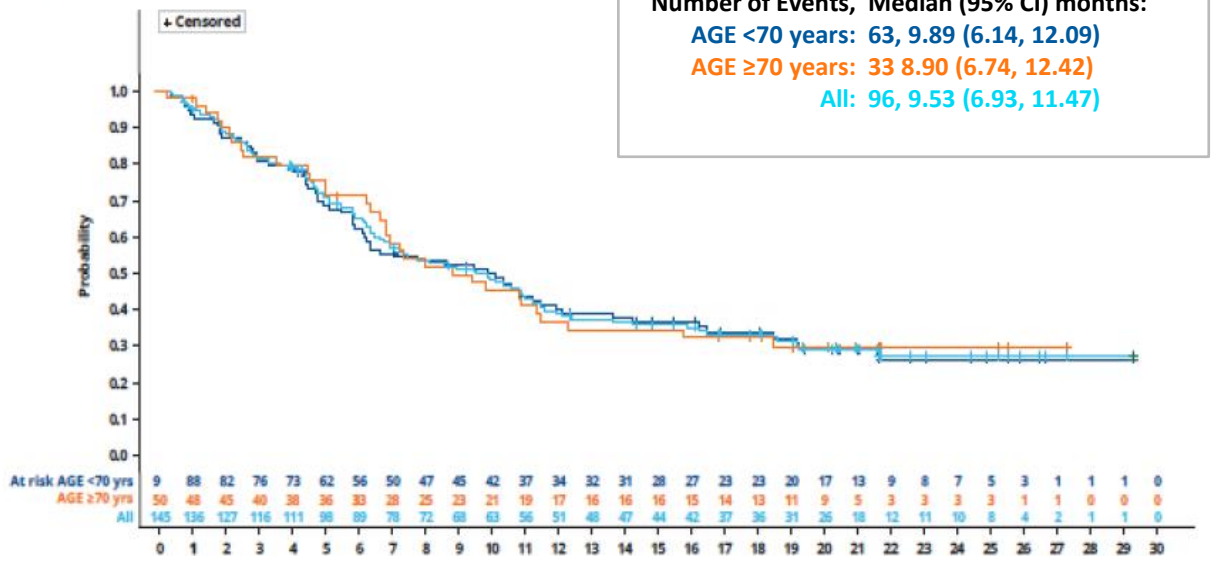
LOTIS-2 Subgroup: Progression-Free Survival and Overall Survival by Age

Progression-free survival



Number of Events, Median (95% CI) months:
AGE <70 years: 49, 3.81 (2.69, 8.08)
AGE ≥70 years: 24, 7.36 (2.99, NA)
All: 73, 4.93 (2.89, 8.31)

Overall survival



Number of Events, Median (95% CI) months:
AGE <70 years: 63, 9.89 (6.14, 12.09)
AGE ≥70 years: 33 8.90 (6.74, 12.42)
All: 96, 9.53 (6.93, 11.47)

Time (Months)

Age Groups: <70 yrs ≥70 yrs All

- Median PFS was numerically longer in the older group, 7.36 months (95% CI, 2.99 – NA), compared with the younger group, 3.81 months (95% CI, 2.69-8.08).[a]
- Median OS was similar across groups, younger group: 9.89 months (95% CI, 6.14-12.09), and the older group: 8.90 months (95% CI, 6.74-12.42).[a]

REFERENCES

Data cutoff: March 1, 2021.

[a]Comparative analyses between age groups were not performed with statistical testing; instead, numerical trends were noted across age groups.

LOTIS-2 Subgroup: Safety by Age

Safety	<70 years (n = 95)	≥70 years (n = 50)	Total (N = 145)
Number of cycles, median (range)	3 (1 – 17)	4 (1 – 26)	3 (1–26)
Grade ≥3 AEs[a], n (%)	73 (76.8)	34 (68.0)	107 (73.8)
Neutropenia	28 (29.5)	10 (20.0)	38 (26.2)
Thrombocytopenia	21 (22.1)	5 (10.0)	26 (17.9)
GGT increased	22 (23.2)	3 (6.0)	25 (17.2)
Anemia	11 (11.6)	4 (8.0)	15 (10.3)
Leukopenia	8 (8.4)	5 (10.0)	13 (9.0)
Patients with any TEAE, n (%)	94 (98.9)	49 (98.0)	143 (98.6)
Leading to a dose delay or reduction	49 (51.6)	26 (52.0)	75 (51.7)
Leading to a withdrawal	23 (24.2)	13 (26.0)	36 (24.8)

Safety Summary[b]

Overall, TEAEs were similar across age groups.

Percentages of patients with any TEAE leading to dose delay or reduction or any TEAE leading to withdrawal were similar across age groups.

Grade ≥3 AEs occurring in ≥10% of patients also revealed similar rates of hematologic TEAEs.

There was a lower percentage of increased GGT in older patients.

Consistent with overall results from the LOTIS-2 study, Lonca had an acceptable safety and tolerability profile and produced quick and durable responses in both younger and older patients with R/R DLBCL in this subgroup analysis.

REFERENCES

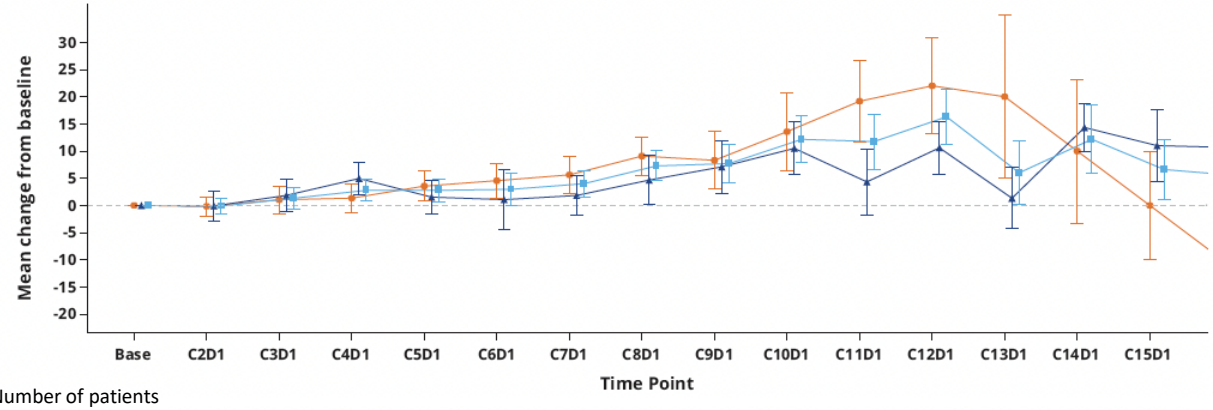
Data cutoff: March 1, 2021.

[a]Grade ≥3 AEs reported in ≥10% of patients.

[b]Comparative analyses between age groups were not performed with statistical testing; instead, numerical trends were noted across age groups.

LOTIS-2 Subgroup: Change From Baseline by Age

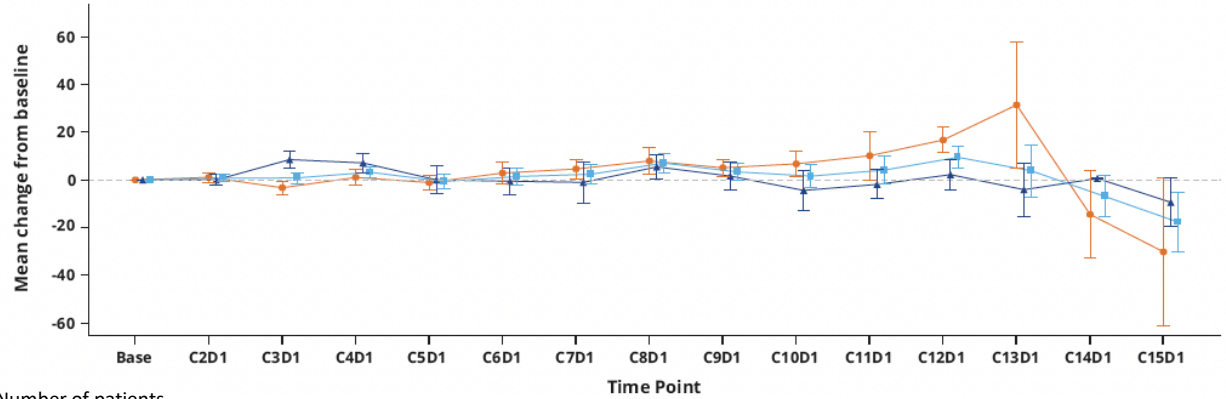
EQ-VAS



Number of patients

	Base	C2D1	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13D1	C14D1	C15D1
<70 yrs	79	66	49	35	27	18	16	13	10	7	6	5	2	3	2
≥70 yrs	48	42	27	23	17	15	12	9	10	6	6	5	6	3	3
Overall	127	108	76	58	44	33	28	22	20	13	12	10	8	6	5

FACT-Lym



Number of patients

	Base	C2D1	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13D1	C14D1	C15D1
<70 yrs	79	65	48	38	26	19	17	14	10	7	6	5	2	2	2
≥70 yrs	46	41	26	21	17	14	11	8	10	6	6	5	7	2	3
Overall	125	106	74	59	43	33	28	22	20	13	12	10	9	4	5

- Change from baseline in EQ-VAS and FACT-Lym total scores were stable or improved over the treatment period in both age groups.

REFERENCES

Data cutoff: March 1, 2021.

LOTIS-2 Subgroup: Change From Baseline by Age

FACT-Lym[1]

- Consists of a generic core questionnaire, the FACT-G (27 items), and the LymS (15 items) specifically for evaluating the response to treatment in patients with non-Hodgkin lymphoma.
  - A higher score (0-168) indicates better HRQoL.
  - The recall period consists of the past 7 days.
- Patient-reported tolerability was assessed with the FACT-Lym item GP5 ("I am bothered by side effects of treatment").

EQ-VAS[2]

- EQ-VAS (0-100, a higher score indicates better overall health):
  - A score of 100 = "the best health you can imagine"
  - A score of 0 = "the worst health you can imagine"
- Recall period: Day of visit

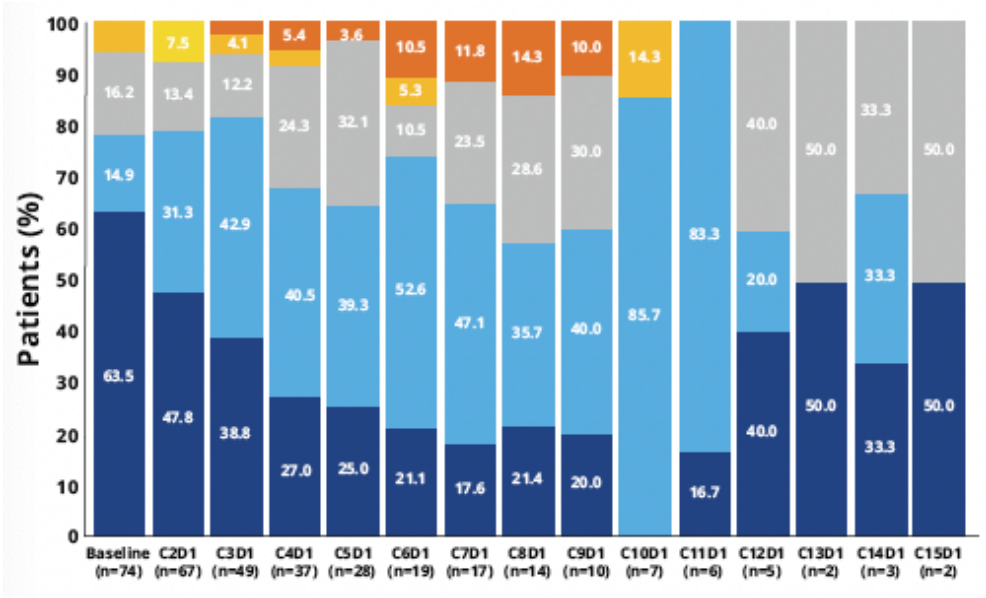
REFERENCES

Data cutoff: March 1, 2021.

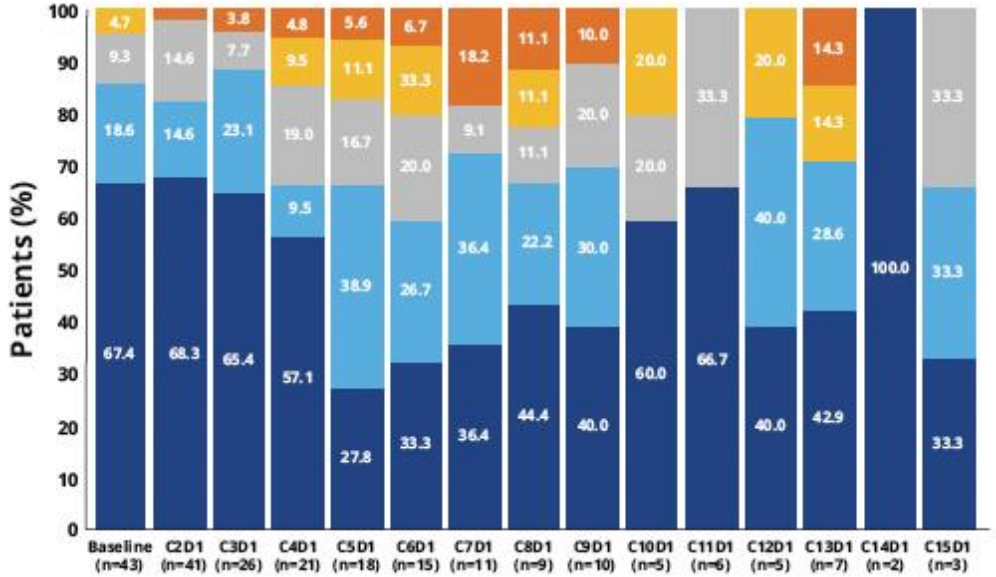
LOTIS-2 Subgroup: Percentages of responses to GP5 by Age

"I am bothered by side effects of treatment[a]"

Age <70 years



Age ≥70 years



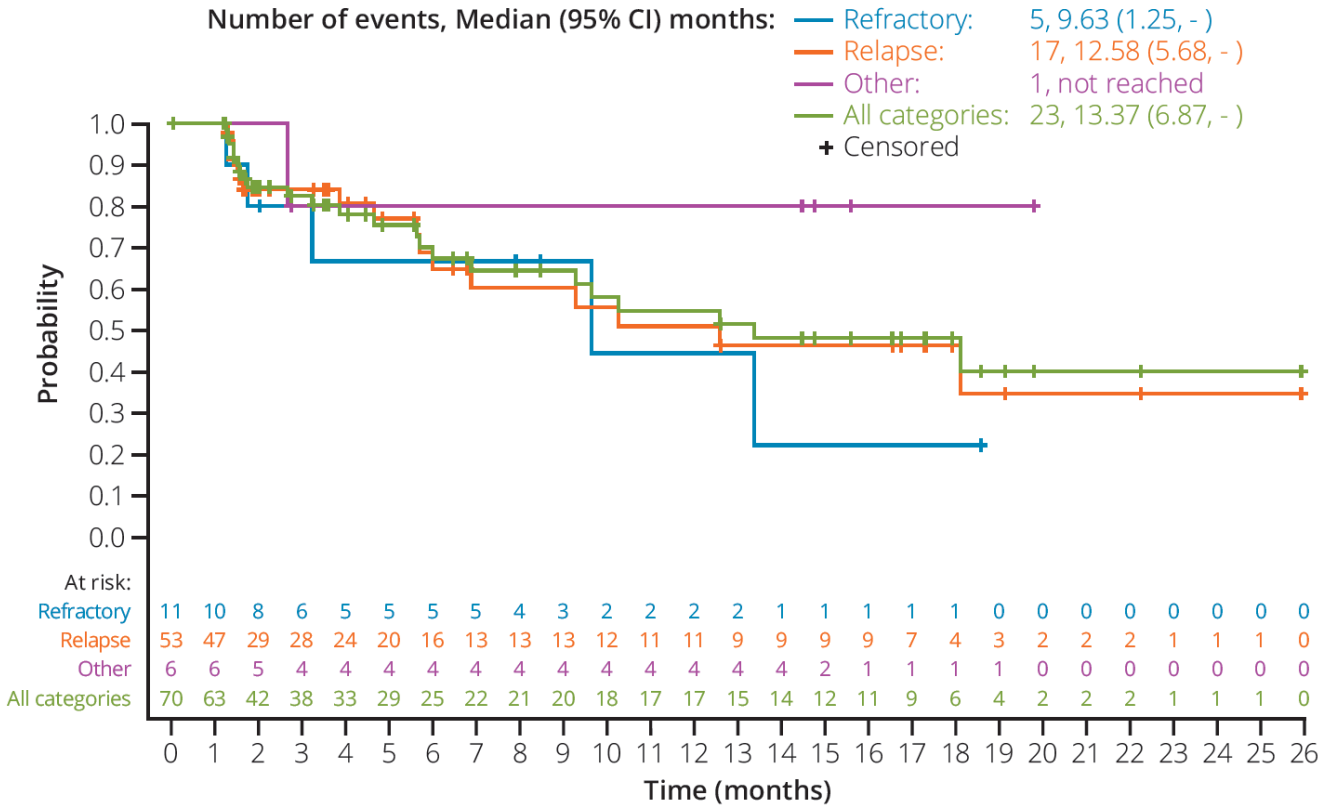
- A majority of patients in both groups responded, "A little bit" or "Not at all," to the GP5 (FACT-Lym) question on tolerability; however, a higher percentage of patients in the older age group responded, "Not at all," than in the younger age group.

REFERENCES

Data cutoff: March 1, 2021.

[a]Visits with <5 assessments in total are not displayed.

LOTIS-2 Subgroup: Duration of Response to Lonca by Response to First-Line Systemic Therapy



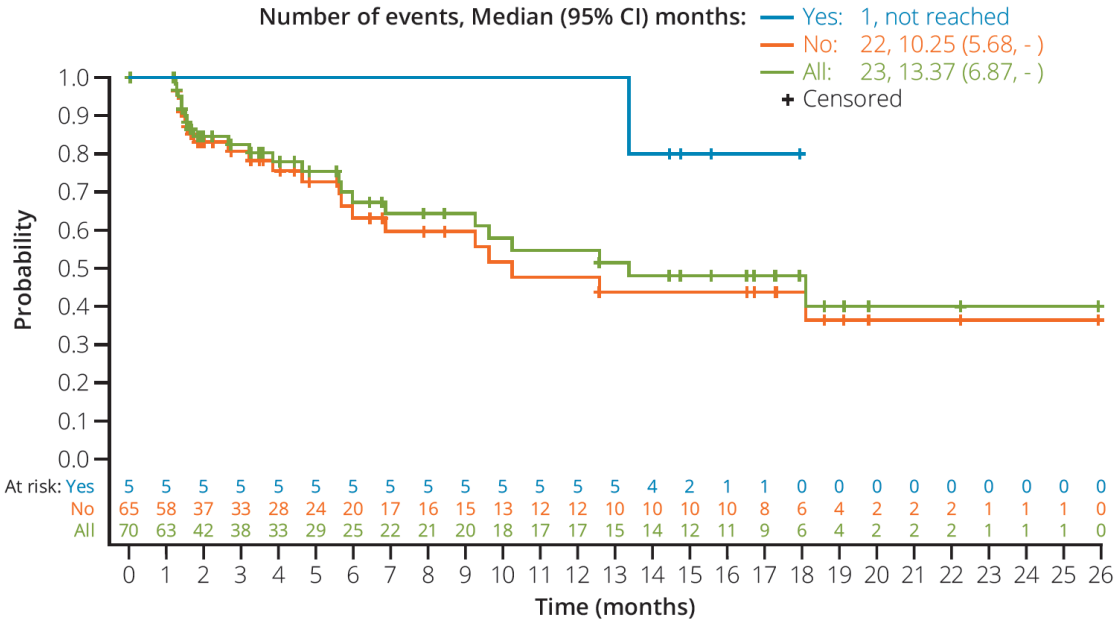
- Patients with DLBCL refractory to first-line systemic therapy had a median DOR of 9.6 months compared with 12.6 months for patients who relapsed after responding to initial therapy

REFERENCES

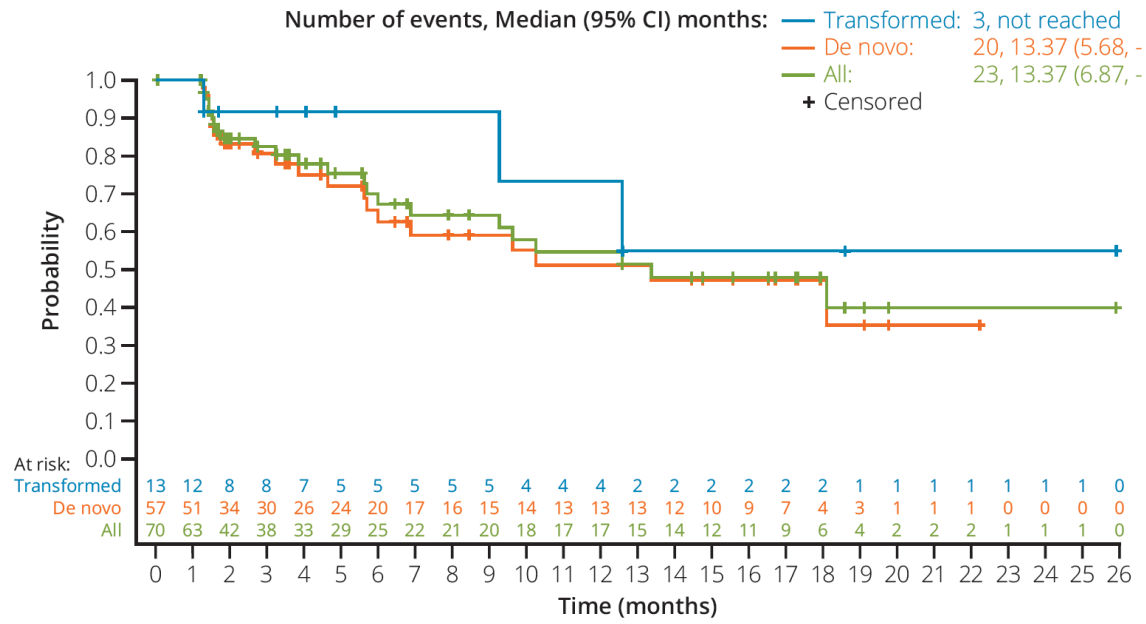
Data cutoff: March 1, 2021.
Other defined as unknown, not evaluable or missing.

LOTIS-2 Subgroup: Duration of Response to Lonca by Double-/Triple-Hit Disease and Transformed Disease

DOR by Double-/Triple-Hit Disease (Yes/No)



DOR by Transformed and De Novo Disease



- Patients with double-/triple-hit or transformed DLBCL each had a median DOR of not reached
- Patients with advanced stage disease (Stage III–IV) had a median DOR of 12.6 months

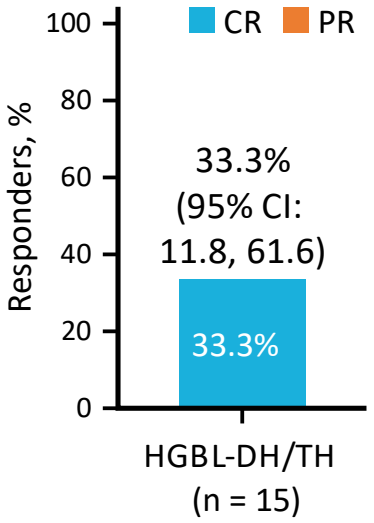
REFERENCES

Data cutoff: March 1, 2021.

LOTIS-2 Subgroup: Characteristics and Responses in Patients With HGBCL[a]

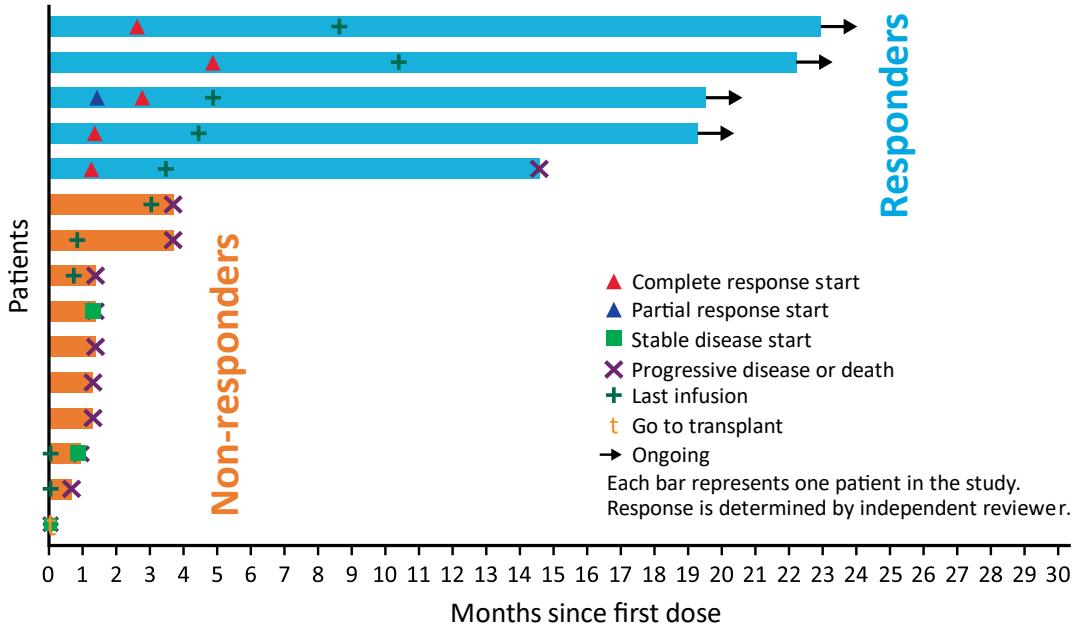
Baseline Characteristics	Responders (n=5)	Non responders (n = 10)
Age, median (min, max), years	75 (53, 84)	74 (27, 85)
Age group, n (%)		
<65 years	2 (40.0)	3 (30.0)
≥65 to <75 years	0 (0.0)	4 (40.0)
≥75 years	3 (60.0)	3 (30.0)
Time from diagnosis to first dose, median (min, max), months	50.0 (23.6, 86.6)	11.0 (5.4, 73.2)
Prior systemic therapies[b], n (%)		
2 prior lines	1 (20.0)	3 (30.0)
3 prior lines	1 (20.0)	5 (50.0)
>3 prior lines	3 (60.0)	2 (20.0)
Prior stem-cell transplant, n (%)	1 (20.0)	3 (30.0)
Response to most recent line of systemic therapy, n (%)		
Relapse	2 (40.0)	2 (20.0)
Refractory[c]	0 (0.0)	8 (80.0)
Other[d]	3 (60.0)	0 (0.0)

Overall Response Rate



ORR in DLBCL-NOS (n = 127): **50.4%**

Duration of Response in Patients With HGBCL



Data cutoff: March 1, 2021.

[a]High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements, this analysis also includes patients who received a diagnosis of DLBCL-DH/TH before the current WHO classification. Among patients with HGBCL, 4/15 patients had prior CAR T-cell therapy, and 3/15 patients had triple-hit lymphoma. [b]Prior stem cell transplant is included. [c]Defined as no response to therapy. [d]Defined as unknown, not evaluable, or missing.

REFERENCES

LOTIS-2 Subgroup: Characteristics and Reponses in Patients Who Received Prior CAR-T

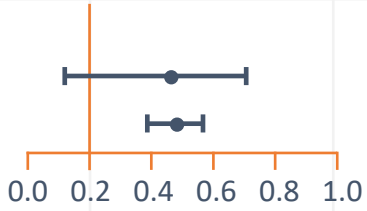
- 14 (9.7%) patients from LOTIS-2 had received prior CAR-T cell therapy[1]
- Patients were required to have a biopsy demonstrating persistence of CD19 expression

CAR–T-Cell Therapy Characteristics (n = 13)[2,a]	
Time between diagnosis and CAR-T, median (range), mo	10 (2–79)
# of LOT prior to CAR-T, median (range)[c]	3 (1–6)
Time from CAR-T to Lonca, median (range)[c]	7 mo (45–400 d)
Type of CAR-T, n (%)	
Axicabtagene ciloleucel	7 (54)
Lisocabtagene maraleucel	2 (15)
Investigational CD19	2 (15)
Investigational CD19/CD20	1 (8)
Investigational CD19/CD22	1 (8)

- Patients received a median of 2 cycles of Lonca (range 1–9)[2,a]
- Median follow up: 8 months; median DoR to Lonca: 8 months[2,a]

Response to Lonca (n = 14)[1,b]

Subgroup	Patients (n/N)	ORR	ORR (95% CI)
Prior CAR-T therapy			
Yes	6/14		42.9 (17.7, 71.1)
No	64/131		48.9 (40.0, 57.7)



- 3 patients (21%) achieved a CR, 3 patients (21%) achieved PR to Lonca[1,b]

[a]Data cut-off: April 6, 2020. [b]Data cutoff: September 15, 2022.

[c]**Lonca was the first treatment after CAR-T in 10 patients.**

3 patients received other treatments prior to Lonca, including chemoimmunotherapy (n=1, R-GemOx) and allogeneic SCT (n=1), and one patient received chemoimmunotherapy (R-GemOx) followed by a clinical trial with venetoclax and a bromodomain inhibitor.

REFERENCES

Retrospective Analysis: Characteristics and Reponses to Subsequent CAR-T in Patient who Previously Received Lonca

- 14 patients with disease relapsing or progressing after treatment with Lonca and subsequently received CD19-directed CAR-T cell therapy were identified from the 2 multicenter, open-label phase 1 and phase 2 (LOTIS-2) trials
- 10/14 patients were screened for CD19, and all had positive CD19 expression by IHC prior to CAR-T
  - 4 patients were not assessed for CD19 expression

Patient & Disease Baseline Characteristics	N = 14
Sex, male, n (%)	11 (79)
Race, n (%)	
White	13 (93)
African American/Black	1 (7)
Lymphoma subtype, n (%)	
DLBCL[a]	10 (71)
Transformed DLBCL	4 (29)
c-MYC rearrangement, n (%)	3 (21)
Stage at diagnosis, n (%)	
Stage III – IV	4 (29)
Best response to Lonca, n (%)	
Complete response	1 (7)
Partial response	5 (36)

CAR T-Cell Therapy Characteristics	N = 14
Time between Lonca and CAR-T, median (range), day[b]	120 (22 - 600)
Type of CAR-T, n (%)	
Axicabtagene ciloleucel	5 (36)
Tisagenlecleucel	2 (14)
Investigational CD19	4 29)
JCAR017	3 (21)
Best response to CAR-T, n (%)	
Complete response	6 (43)
Partial response	1 (7)
Refractory disease	7 (50)

[a]One patient had mediastinal large B-cell lymphoma.
[b]Six patients received additional lines of therapy between Lonca and CAR T-cell therapy. Additional therapy included radiation alone (n = 3), radiation, ifosfamide/vinblastine/etoposide (n = 1), radiation; rituximab/methotrexate (n = 1), lenalidomide, anti-CD47 antibody, ibrutinib (n = 1).

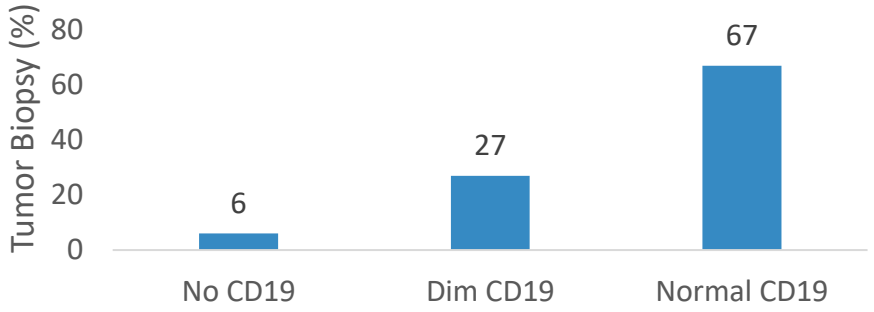
REFERENCES

CD19 Expression Level Alone Is Not a Predictor of Response

Retrospective analysis of first therapy after CD19-directed CAR-T treatment failure[1]

- A retrospective analysis of patients with R/R LBCL treated with CD19-directed CAR-T cell therapy described patient outcomes following CAR-T treatment failure
- CD19 expression was assessed by flow cytometry in 52 available tumor biopsies

CD19 Expression



- Patients with CAR-T resistance had similar CD19 expression at disease progression to those with relapsed disease

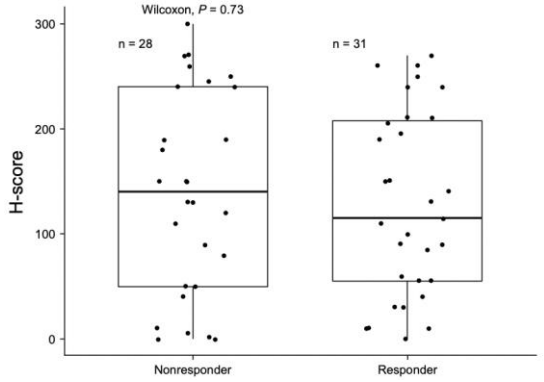
Loss of CD19 was infrequent (6%) and CD19 expression at CAR-T treatment failure showed no correlation with CAR-T refractoriness versus later relapse; persistence of CD19 may render tumor susceptible to further CD19-directed therapies[1]

Results from the LOTIS-2 Clinical Trial[2]

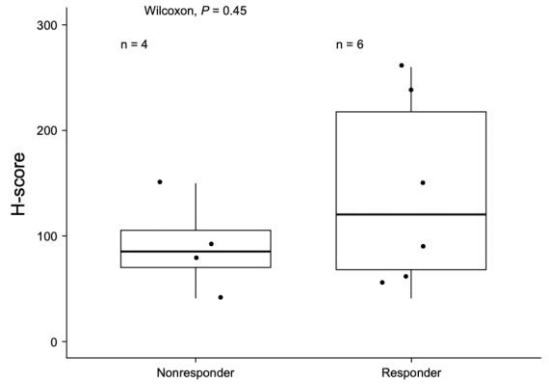
- CD19 expression was assessed by IHC and H-Score[a] in a subgroup of LOTIS-2 patients that had a biopsy taken after the last systemic anticancer treatment, prior to receiving Lonca[2]
- Response to Lonca was observed in patients with R/R DLBCL with very low CD19 expression as measured by IHC[2]

Baseline tumor CD19 H-score by response (independent assessment)[2a,b]

Subgroup with biopsies after last prior therapy (n=59)



Subgroup with prior CAR-T (n=10)



Findings indicate that Lonca is an effective treatment option for patients with R/R DLBCL following ≥ 2 lines of treatment, even in patients expected to have a low level of CD19 expression[2]

REFERENCES

[a] No statistically significant differences are apparent among the response categories; data to be interpreted with caution.
[b] H-score is a semiquantitative assessment of percentage of CD19 positive cells and staining intensity.

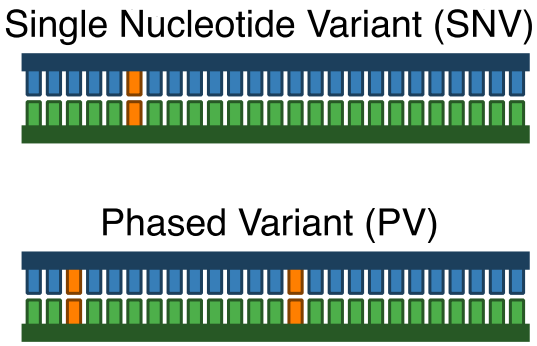
Early and Sustained Circulating Tumor DNA Response Dynamics After Lonca Treatment

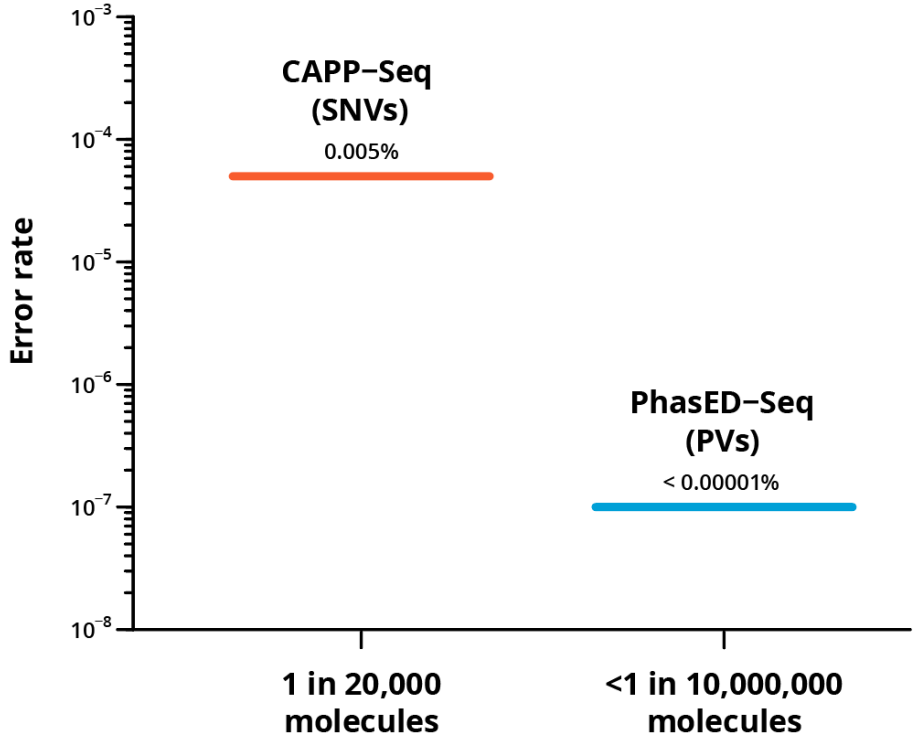
Analysis of LOTIS-2 Subgroup

ctDNA Analysis: Overview of Genotyping

Overview

- ctDNA has emerged as a tool to characterize tumors and track MRD in many malignancies, including DLBCL
- Genotyping PVs on a single cfDNA molecule improves the limit detection of ctDNA-MRD





- PhasED-Seq improves the detection limit for ctDNA-MRD
- Background error rate is reduced and sensitivity is increased by approximately 100 times when genotyping PVs versus SNVs

REFERENCES

ctDNA Analysis: Study Design and Patient Population

Study Design

- This study is the first to evaluate ctDNA in the setting of treatment with Lonca
- Baseline plasma + PBMC were used to identify tumor-specific PVs
- ctDNA-MRD levels and mutational genotypes were identified before treatment, after 1 cycle of treatment (C2D1), and at EOT

OBJECTIVE: To apply the ultrasensitive ctDNA-MRD detection method, phased variant enrichment and detection sequencing (PhasED-Seq), to evaluate mutational profiles and ctDNA-MRD response dynamics with Lonca

Response to Lonca

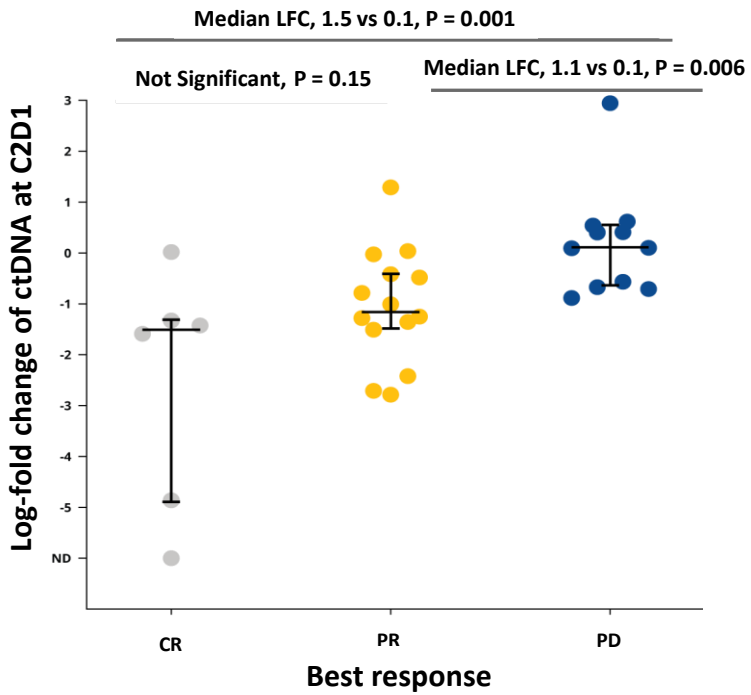
- Samples from patients in the LOTIS-2 study were profiled by PhasED-Seq to represent a range of best responses to therapy; PVs were successfully genotyped on 31/33 (94%) of patients
  - 6 (19%) of patients experienced a CR
  - 14 (45%) of patients experienced a PR
  - 11 (35%) of patients experienced PD

Patient Characteristics		N = 31
Age, median (range)		65 (25-83)
Stage, n (%)	I-II	10 (32)
	III-IV	21 (68)
Prior LOT, median (range)		3 (2-7)
IPI, n (%)	0 - 1	9 (29)
	2	6 (19)
	3	13 (42)
	4 - 5	3 (10)
Diagnosis, n (%)	DLBCL, NOS	26 (84)
	PMBCL	2 (6)
	HGBCL with *MYC* and *BCL2*/*BCL6*	3 (10)
Cell of origin, n (%)	GCB	9 (29)
	ABC	6 (19)
	Not evaluable	16 (52)

REFERENCES

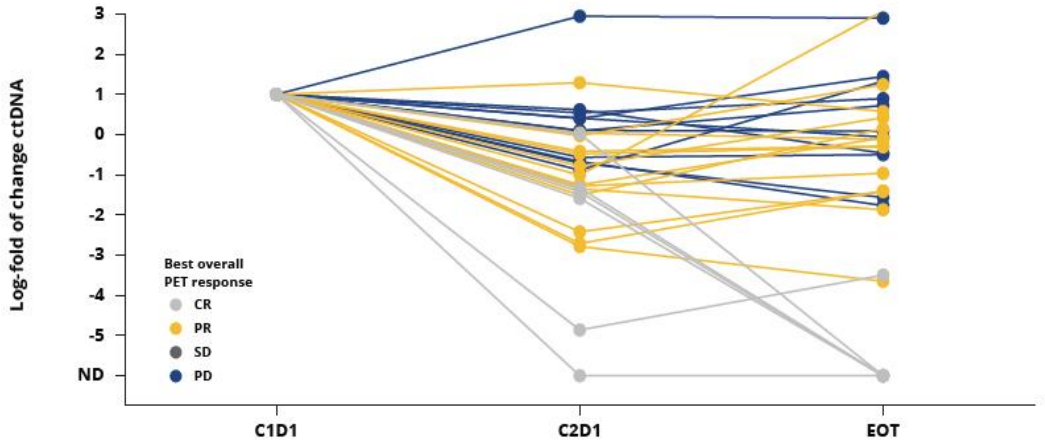
ctDNA Analysis: ctDNA Levels During Lonca Treatment

ctDNA levels at C2D1



- Patients achieving either a CR or a PR had a significantly greater reduction in their ctDNA levels than those failing to respond
- Patients achieving a CR or a PR did not have significantly different changes in ctDNA at C2D1 (P = 0.15)

ctDNA dynamics throughout therapy



- For patients with CR as best response, 5 of 6 patients cleared their ctDNA-MRD to undetectable levels by EOT, as compared with only 1 of 6 patients at C2D1, suggesting a deepening response beyond C2D1
  - In contrast, 0 of 10 patients with PR and 0 of 15 patients with PD cleared their ctDNA-MRD
  - The patient with a CR who did not show a deepening of molecular response was the only patient with a CR who ended treatment for radiographic disease progression
  - All other patients with a CR ended treatment for other reasons (eg, toxicity, transplant, or persistent complete remission)

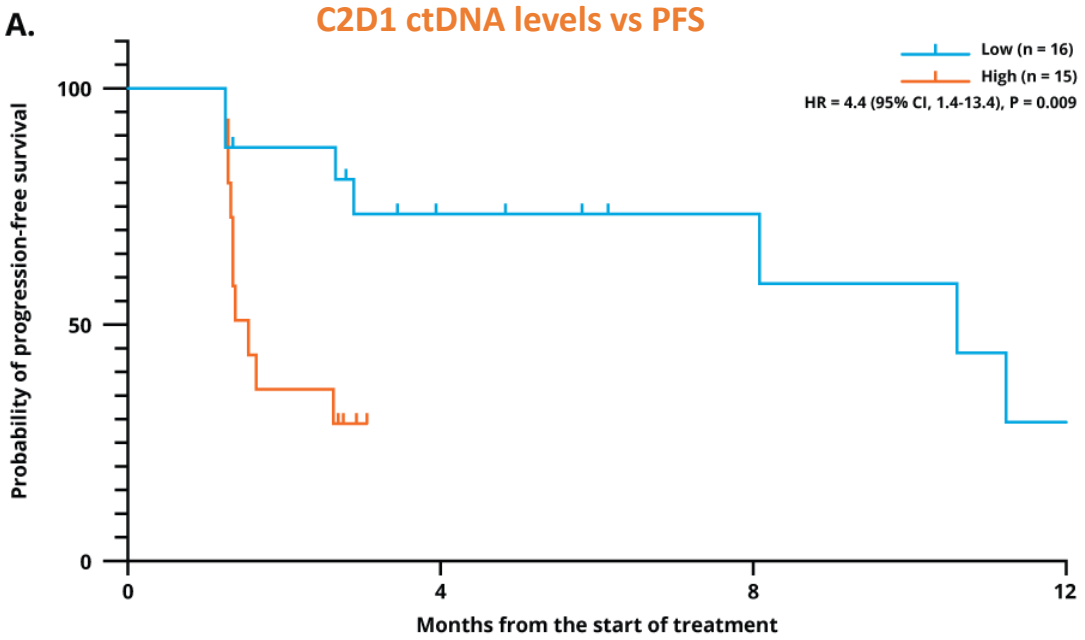
- Both the absolute levels and the change in ctDNA at C2D1 were prognostic for a response to treatment with Lonca
- Molecular response to Lonca continues to deepen beyond C2D1 in patients achieving a CR

REFERENCES

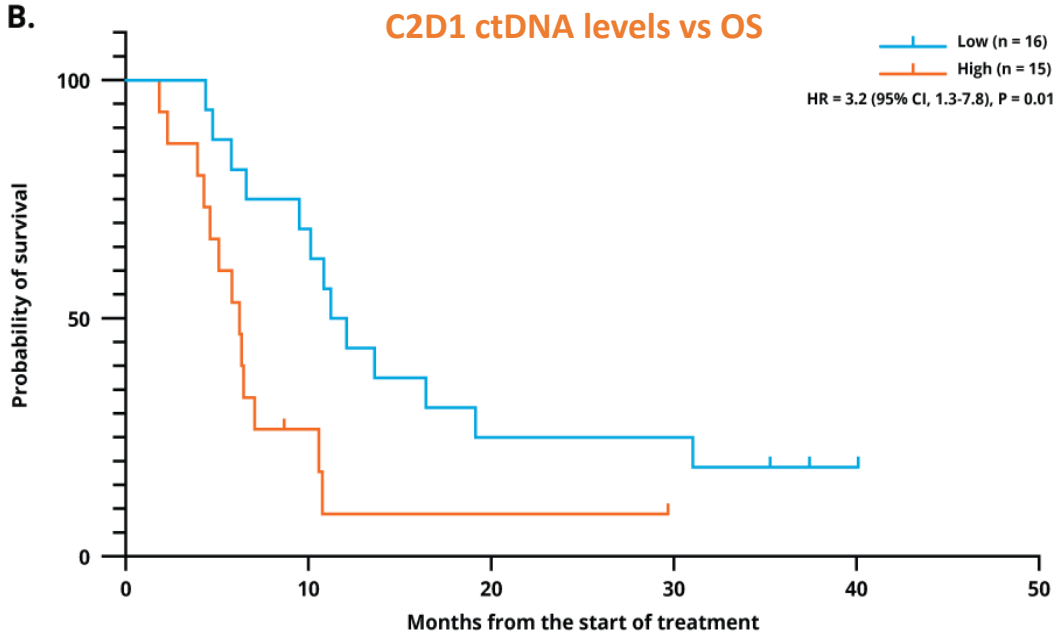
ctDNA Analysis: Prognostic for Survival

- The median concentration of pretreatment ctDNA in patients was 141 hGE/mL (range, 0.4-3608 hGE/mL)
- When dividing patients into those with high vs low pretreatment ctDNA levels, based on the median value, the pretreatment levels were not prognostic of PFS
  - HR = 1.2 (95% CI, 0.4–3.5), P = 0.73
- At C2D1, lower levels of ctDNA were significantly associated with PFS (Figure A) and OS (Figure B)

A.



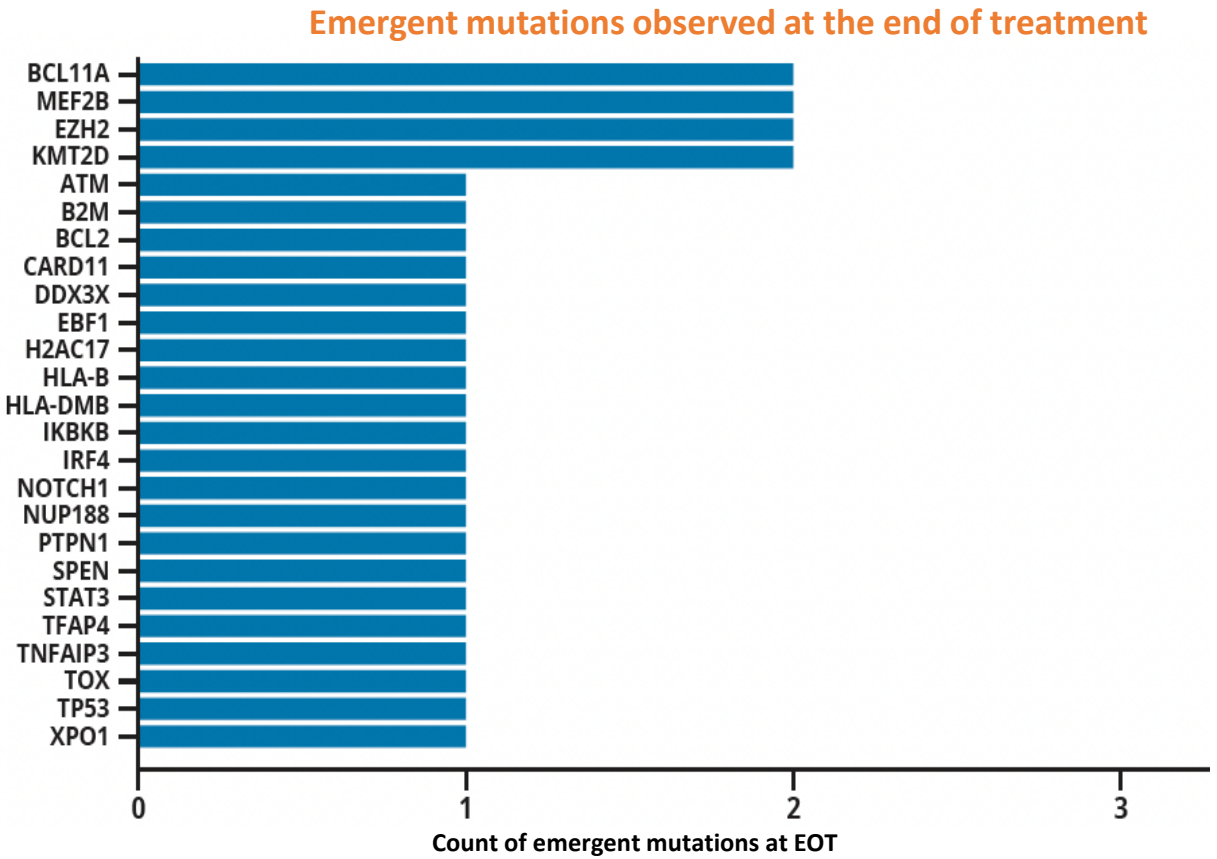
B.



- Levels of ctDNA at C2D1, after treatment with Lonca, are prognostic for PFS and OS

REFERENCES

ctDNA Analysis: Observed Mutations at EOT



- ctDNA assessments included *CD19* and were performed prior to treatment with Lonca and at progression in all patients
- Only one mutation in CD19 (R363C) was observed in a pretreatment sample; this patient achieved a PR followed by PD after 3 cycles of treatment with persistence of the mutation in CD19
- No emergent mutations in *CD19* were observed at the EOT (0/31)
- Mutations in several other genes were observed at the EOT but not in the ctDNA collected prior to therapy; these mutations were present at high relative VAF in the relapse sample, suggesting clonal selection during treatment
  - Few genes demonstrated recurrent emergent mutations at EOT, indicating the absence of specific patterns emerging at relapse

- Clonal selection after Lonca does not select for CD19 mutations

REFERENCES

Other Lonca Studies

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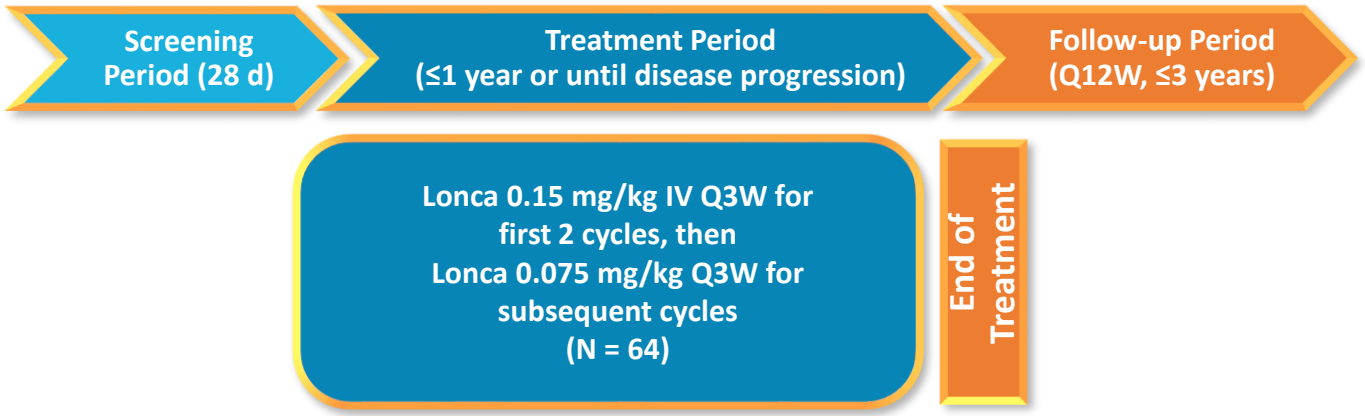
OL-ADCT-402-001 Trial Design

Pivotal phase 2 trial to evaluate Lonca monotherapy in Chinese patients with R/R DLBCL



PRIMARY ENDPOINTS

- ORR (CR + PR) determined by IRC

SECONDARY ENDPOINTS

- DOR, CRR, RFS, PK[a], PFS, and OS
- AEs and SAEs, ECOG PS, ADAs, and neutralizing activity

Select Patient and Disease Characteristics (N = 64)

Age, median years (range)	60 (26–81)
Histology, n (%)	
DLBCL NOS	63 (98.4)
HGBCL	1 (1.6)
Stage III-IV (Ann Arbor), n (%)	53 (82.8)
Number of prior systemic therapies[b], median (range)	3.0 (2-12)
Primary refractory[c], n (%)	43 (67.2)
Refractory to all prior lines of therapy[c], n (%)	40 (62.5)
Prior SCT, n (%)	
Autologous	3 (4.7)
Prior CAR-T, n (%)	
Autologous	3 (4.7)
Allogeneic	1 (1.6)

KEY INCLUSION/EXCLUSION CRITERIA

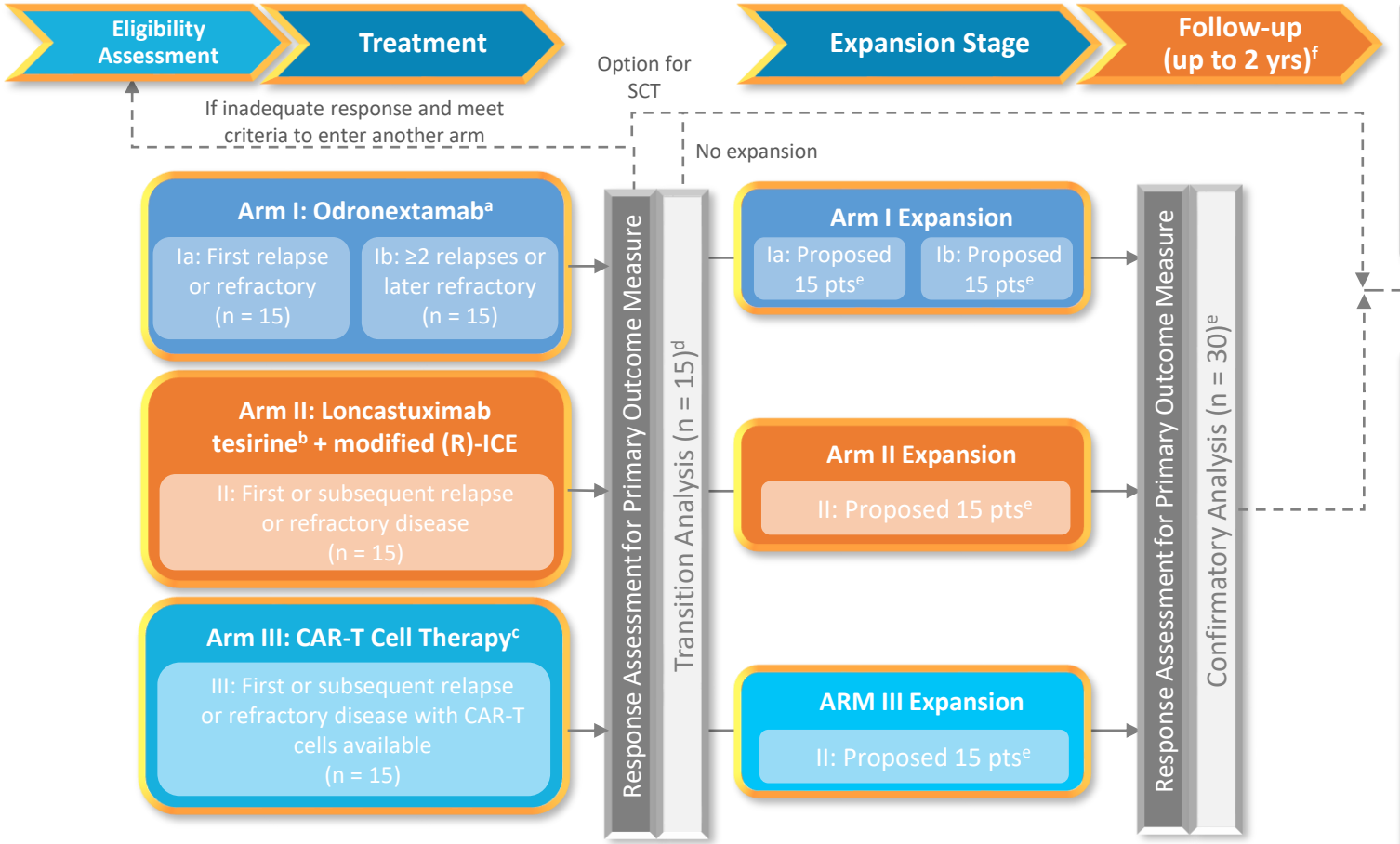
- Male/female Chinese patients aged ≥18 years
- Pathological diagnosis of DLBCL, 2016 WHO classification (including DLBCL NOS, DLBCL transformed from indolent lymphoma, and HGBCL with *MYC* and *BCL2* and/or *BCL6* rearrangements)
- Relapsed/refractory disease following ≥2 multiagent systemic treatment regimens
- Measurable disease (2014 Lugano Classification)
- ECOG 0-2
- Adequate organ function
- Excludes bulky disease (any tumor ≥ 10 cm in longest dimension)
- Excludes autologous SCT within 30 days prior to start of study drug or allogeneic SCT within 60 days prior to start of study drug
- Excludes lymphoma with active CNS involvement at time of screening
- Excludes clinically significant third space fluid accumulation

OL-ADCT-402-001 is a joint venture between Overland Pharmaceuticals and ADC Therapeutics.
[a]Intensive sampling for the first 2 doses of the first enrolled 12 patients. Sparse sampling for all patients after the first 2 doses.
[b]Including prior SCT. [c]Refractory disease defined as failure to achieve CR or PR or experienced PD within 6 months after having achieved CR or PR, after adequate prior anti-DLBCL therapy.

REFERENCES

Glo-BNHL Trial Design

Prospective global study to evaluate novel agents in pediatric/adolescent patients with R/R B-NHL



PRIMARY ENDPOINTS

Arm I: OR after 12 weeks of Tx
Arm II: CR within 3 cycles of Tx
Arm III: OR following CAR-T infusion

SECONDARY ENDPOINTS[g]

- Efficacy: EFS, PFS, OS, ORR, BOR, DOR
- Safety: AESI, TEAEs
- PK profile and PD markers

KEY INCLUSION AND EXCLUSION CRITERIA

- Pts will be enrolled from ≥45 sites in 18 countries, spanning Europe, Asia, North America, and Australasia
- Pts are aged ≤25 years
- Radiological or histological evidence of relapsed or refractory B-NHL with evaluable disease
- Adequate organ function
- Negative pregnancy test and agreement to use contraception
- Excludes recent SCT, craniospinal radiation, or investigational treatment
- Excludes pts with on-going moderate or severe acute toxicities, uncontrolled infection, or primary immunodeficiency

Glo-BNHL is an independent, prospective global study led by the University of Birmingham, UK.
[a]IV infusion weekly for 12 weeks, then at decreasing frequency for up to 2 years or disease progression. [b]IV infusion given with each cycle of R-ICE for up to 3 cycles. [c]Product negotiations are on-going. [d]Agents demonstrating sufficient promise will be further evaluated in an expansion stage. [e]Or as agreed upon with regulators. [f]Subject to regulatory requirements; follow-up for CAR-T may be up to 15 years. [g]Follow-up period was ≤2 years for secondary outcome measures.

REFERENCES

Summary

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Summary

- Lonca is indicated for the treatment of patients with relapsed or refractory large B-cell lymphoma after ≥2 lines of systemic therapy [1]
- Efficacy and safety of Lonca were established based on the primary analysis[2]
  - In the final analysis, the ORR was 48.3%, the same as the primary analysis[1,3]
    - 24.8% of patients achieved a CR and 23.4% of patients achieved a PR[3]
    - 11 of 36 patients with a CR were event-free for ≥2 years with no evidence of disease and no new anticancer therapy post-Lonca[3]
    - Patients with a CR maintained a median treatment-free period of 6.1 months from the last Lonca dose[3]
- Responses were seen across difficult-to-treat subgroups including patients aged ≥70 years, HGBCL, and post-CAR-T cell therapy[4]
  - Lonca had an acceptable safety and tolerability profile across age groups and produced quick and durable responses[4]
    - ORR was 48.4% for patients <70 years and 48.0% for patients ≥70 years[4]
    - Median DOR was 9.26 months in the younger group and not reached in the older group[4]
- The most common grade 3/4 adverse events (>5%) were platelets decreased (17%), neutrophils decreased (30%), hemoglobin decreased (10%), GGT increased (21%), and glucose increased (8%)[1]
  - No new safety concerns were reported in the final analysis[3,4]
- CD19 expression alone may not be predictive of a response to Lonca, but levels of ctDNA may be prognostic for outcomes in patients receiving Lonca monotherapy[5,6]
  - ctDNA levels as early as C2D1 can predict outcomes and are indicative of a fast response to Lonca[6]
  - Lower levels of ctDNA at C2D1 after Lonca treatment were significantly associated with PFS and OS[6]

Appendix

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