

Loncastuximab on R/R DLBCL

Applying the evidence to our daily practice

Alvaro Alencar, MD

Division of Hematology – Lymphoma Section

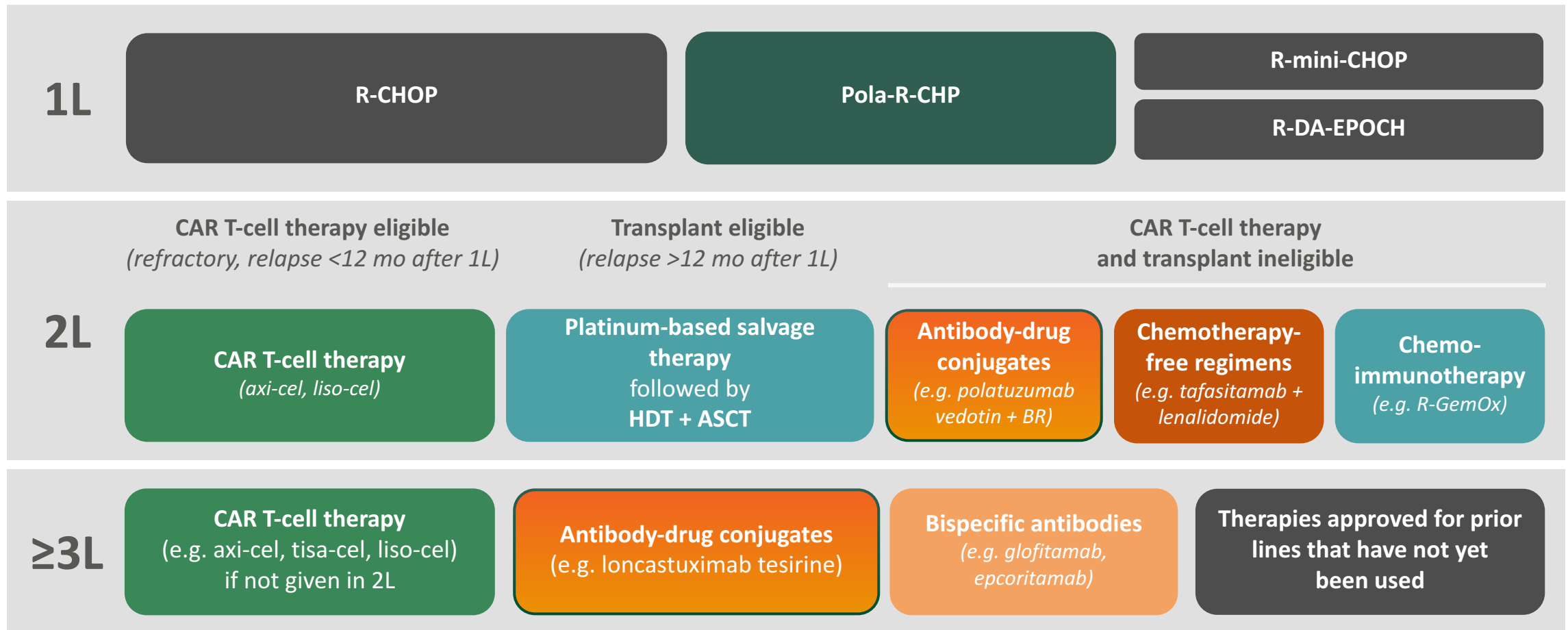
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Disclosures

- *AdBoard: Amgen, Kite, SeaGen, Epizyme, Janssen, BeiGene, Abbvie, Incyte, TG Therapeutics, ADC Therapeutics, Lilly, Genentech*
- *Research Funding: Loxo, BeiGene, Incyte*

Numerous treatment options are now available for DLBCL in each line¹⁻⁸



Many factors impact how we sequence treatments in R/R DLBCL¹

Disease factors

Biomarkers Clinical presentation
Refractoriness Antigen expression

Healthcare facility factors

Processing Logistics

Treatment factors

Efficacy Tolerability
Sequencing Cumulative toxicity
Schedule of administration

Patient factors

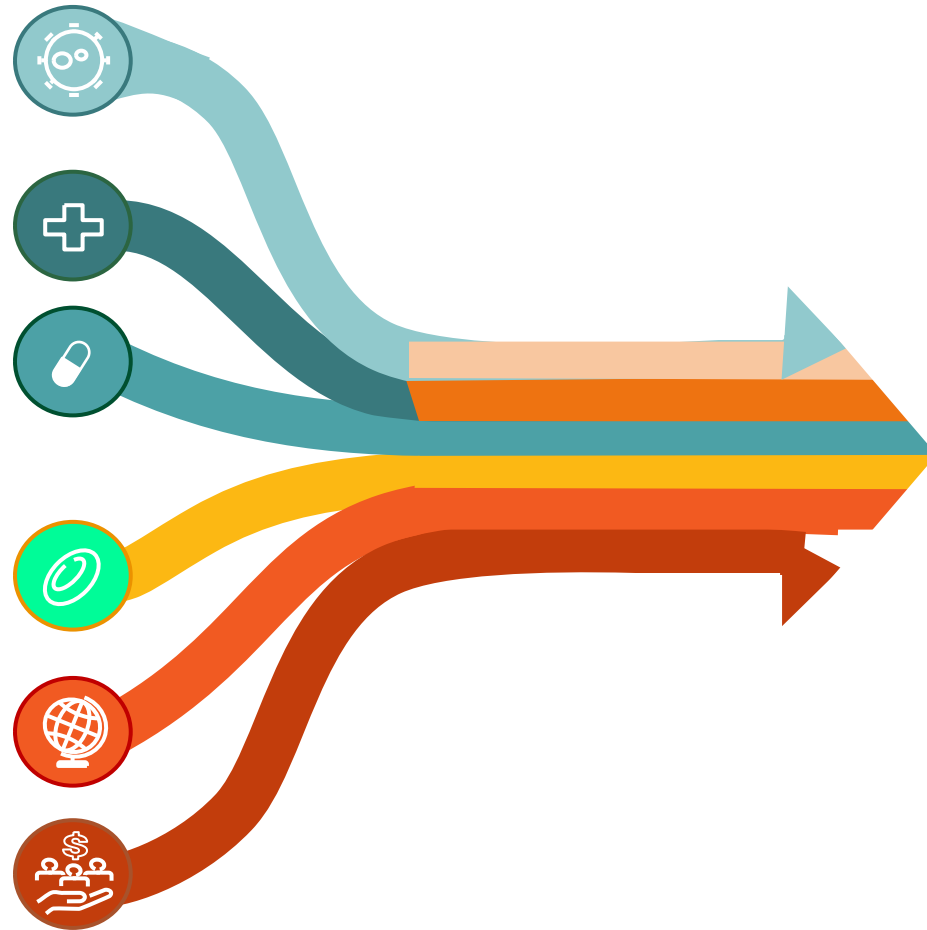
Age Fitness
Comorbidities Patient preference

Geographic factors

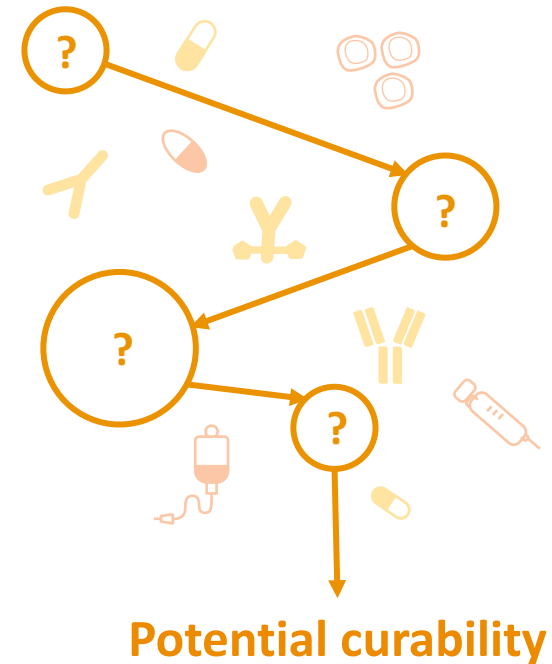
Access to care Drug availability

Socioeconomic factors

Family/social support



Optimal sequence of agents for an individual patient with R/R DLBCL



Reference

1. Brooks TR & Caimi PF. A paradox of choice: Sequencing therapy in relapsed/refractory diffuse large B-cell lymphoma. *Blood Rev* 2023; 101140. Online ahead of print; doi: 10.1016/j.blre.2023.101140.

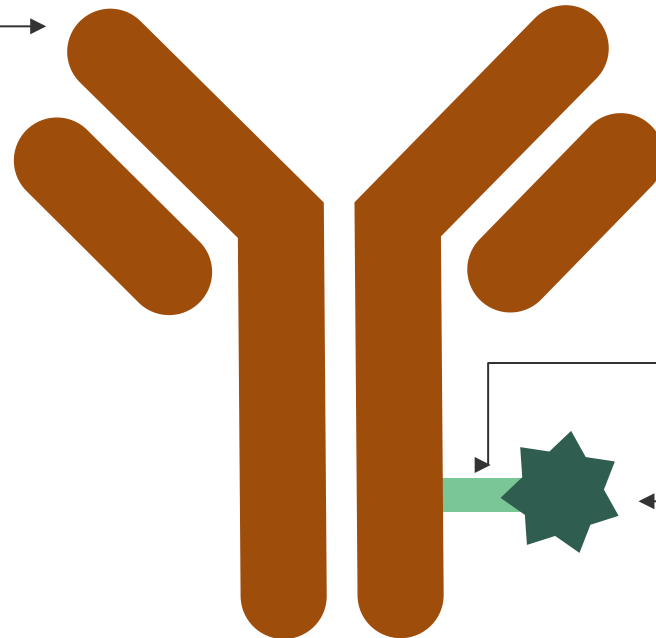
Antibody-drug conjugates have multiple properties that can be varied for clinical efficacy¹⁻³

Antibody

- Strong antigen recognition, low immunogenicity, long half-life, and high molecular weight

Target antigen

- High tumour expression, low healthy tissue expression, strong antibody recognition



Linker

- Stable in circulation, efficient payload release at target site, prevents premature release at non-target tissue, efficient linker technology, and site of conjugation.

Cytotoxic payload

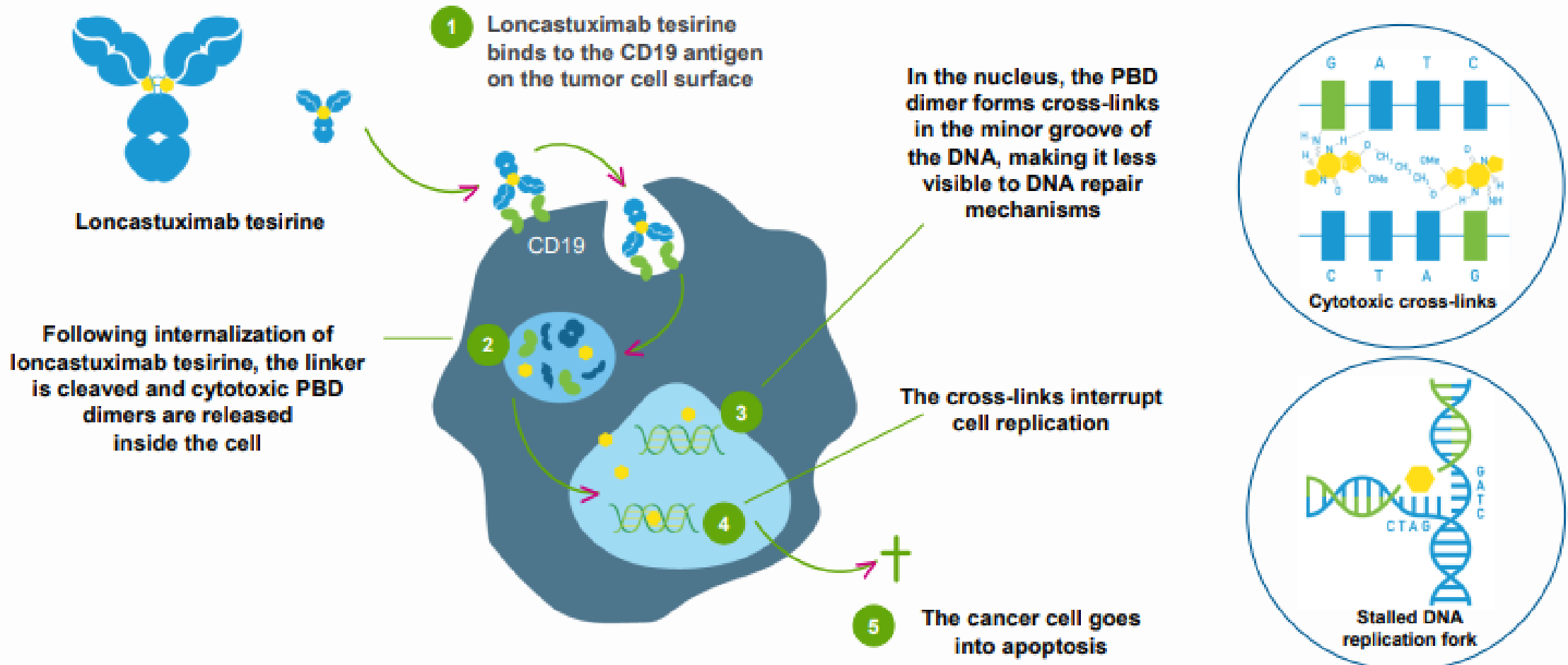
- Pyrrolobenzodiazepines (PBDs)
- Highly potent
- Optimal DAR, which affects drug distribution and PK

=DAR, drug-antibody ratio; PK, pharmacokinetics.

1. Nathwani and Chen. *Clin Investig* 2014 2. Chau et al. *Lancet* 2019 3. Barreca et al. *Explor Target Antitumor Ther* 2022.

Mechanism Of Action:

Loncastuximab Tesirine: CD19 ADC





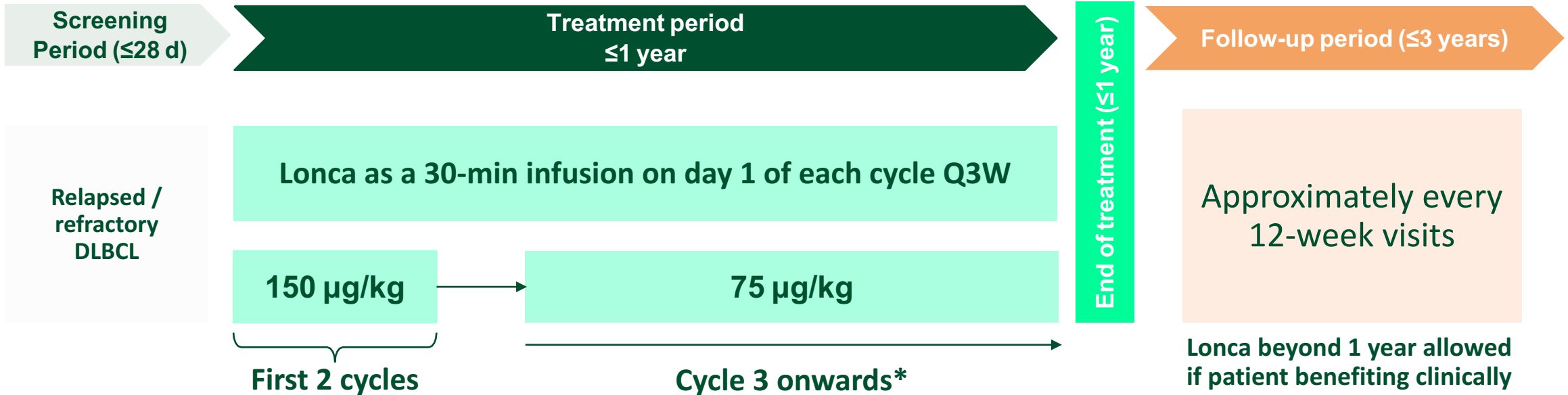
Part 1

Loncastuximab tesirine

Pivotal clinical trial data

LOTIS-2: Study design

145 patients were enrolled
Multicentre study: US, UK, Italy, Switzerland
Study period: August 2018 – August 2022



- Patients with R/R DLBCL for whom salvage chemotherapy/SCT is unsuccessful and who have a poor prognosis and limited treatment options^{1,2}
- Loncastuximab tesirine comprises a humanized anti-CD19 antibody conjugated to a potent PBD dimer toxin³
- LOTIS-2 is a multicenter, open-label, single-arm, phase II study in patients aged ≥18 years with pathologically defined R/R DLBCL and ≥2 prior systemic treatments⁴⁻⁶
 - Included patients with high-risk characteristics such as double-hit, triple-hit, transformed, or primary refractory DLBCL⁴

Primary objective:
Evaluate efficacy, using ORR (central review), and safety of the full phase 2 study population

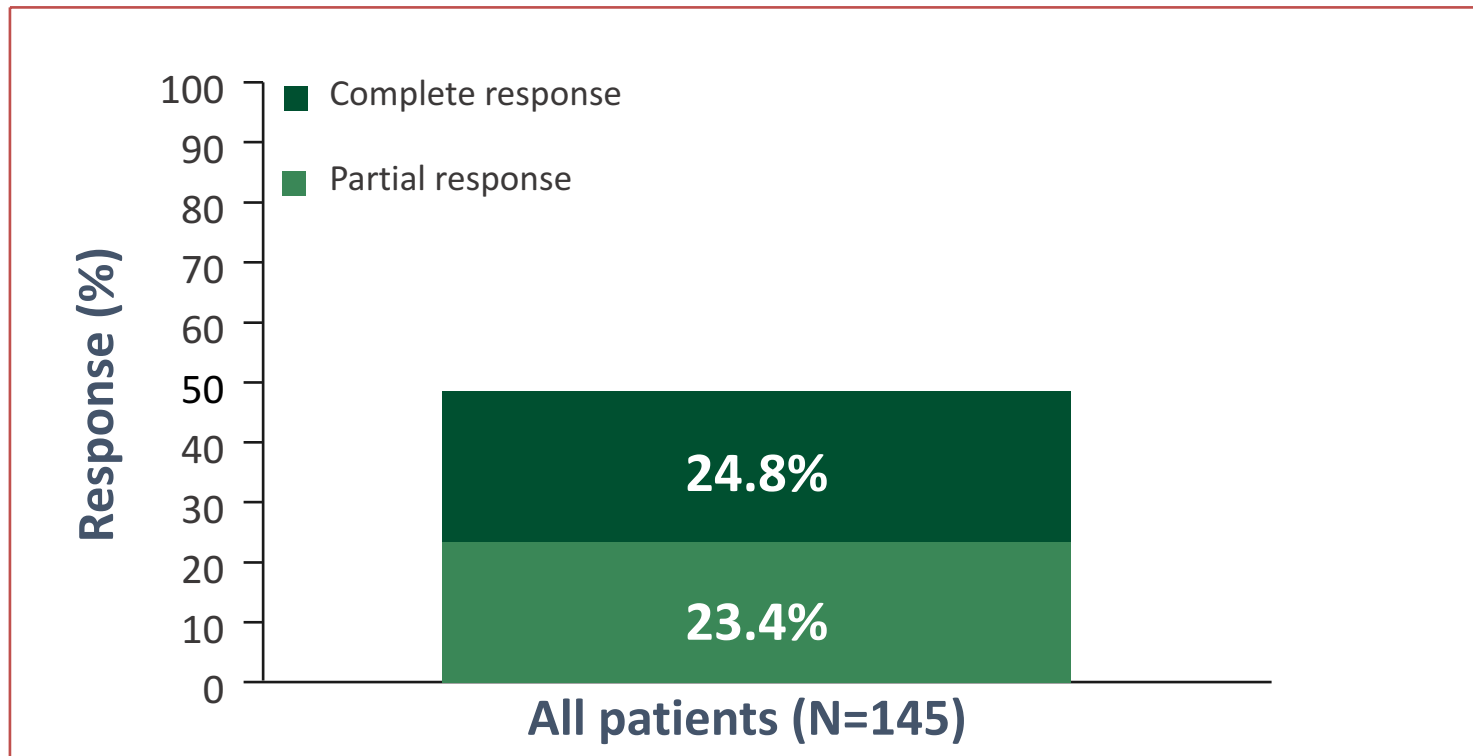
Patients continued on treatment up to one year or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurs first.
DLBCL, diffuse large B-cell lymphoma; Q3W, every 3 weeks.
Caimi et al. *Lancet Oncol* 2021.

LOTIS-2: Baseline Characteristics

Patient characteristics [§]		Total (N=145)	Patient treatment history		Total (N=145)	
Sex, n (%)	Female	60 (41)	No. of previous systemic therapies, * median (interquartile range)		3 (2–4)	
	Male	85 (59)				
Age, years, median (min, max)		66 (23, 94)	First-line systemic therapy response, n (%)		Relapse	99 (68)
Histology, n (%)		DLBCL, NOS			127 (88)	Refractory [†]
		HGBCL	11 (8)	Other [‡]	17 (12)	
		PMBCL	7 (5)	Last-line systemic therapy response, [¶] n (%)		Relapse
Double hit DLBCL ^{§§} , n (%)	15 (10)	Refractory [†]	84 (58)			
Double expressor DLBCL, n (%)	20 (14)	Refractory to all prior therapies, [†] n (%)		Other [‡]	18 (12)	
Transformed DLBCL, n (%)	29 (20)			Yes	25 (17)	
Disease Stage ^{††} , n (%)		I–II	33 (23)	No	115 (79)	
		III–IV	112 (77)	Other [‡]	5 (3)	
		Prior stem cell transplant, n (%)		Allogeneic		2 (1)
Autologous						21 (14)
		Prior CAR T-cell therapy, n (%)		Both		1 (1)
Yes						13 (9)
		No		132 (91)		

[§]Data cut-off: 06 April 2020. ^{§§}Some patients had a diagnosis of double-hit or triple-hit lymphoma based on institutional pathology before the WHO classification of HGBCL with MYC and BCL2 or BCL6 rearrangements, or with MYC and BCL2 and BCL6 rearrangements. [†]Disease stage at study entry. ^{**}Prior SCT is included. For patients who received an autologous transplant, the mobilisation regimen was considered a line of therapy if it was chemotherapy based and distinct from the other previous lines of treatment. ^{††}Refractory disease defined as no response to therapy. [‡]Other defined as unknown, not evaluable or missing. [¶]If SCT is most recent line, the variable is defined as response to the therapy immediately preceding SCT. ^{**}Data cut-off: 01 March 2021. CAR-T, 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; PMBCL, primary mediastinal B-cell lymphoma; SCT, stem cell transplant; SD, standard deviation. Caimi PF, et al. *Lancet Oncol.* 2021

LOTIS-2: Efficacy Results – ORR



ORR:
48.3%
(70 of 145 patients)

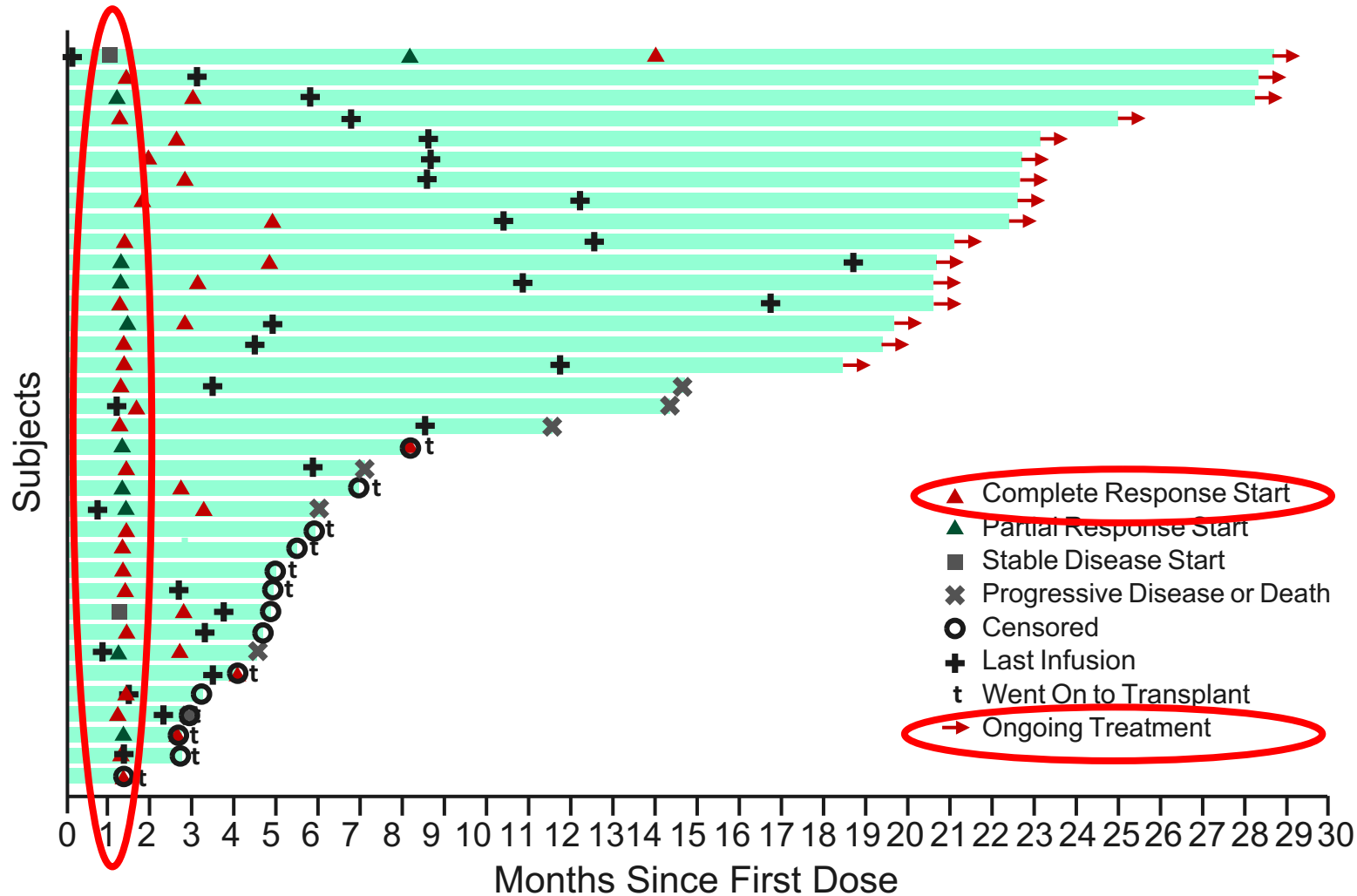
Mean No. of Cycles (SD) for the 70 responders:
6.8 (5.0)

Median No. of Cycles (range) for the 70 responders:
5.0 (1.0–26.0)

24 (34.3%) of the 70 responders received ≥ 7 cycles

Patients received a mean (SD) of 4.6 cycles (4.3) and median (range) of 3.0 cycles (1.0-26.0) of Loncastuximab.
Median (range) of follow-up for all patients: 7.8 months (0.3-31.0)
37 patients remain in follow up**

LOTIS-2: Median Time to Response



Median Time to First Response
in All Responders (n=70):

1.3 months (range: 1.1 to 8.1)

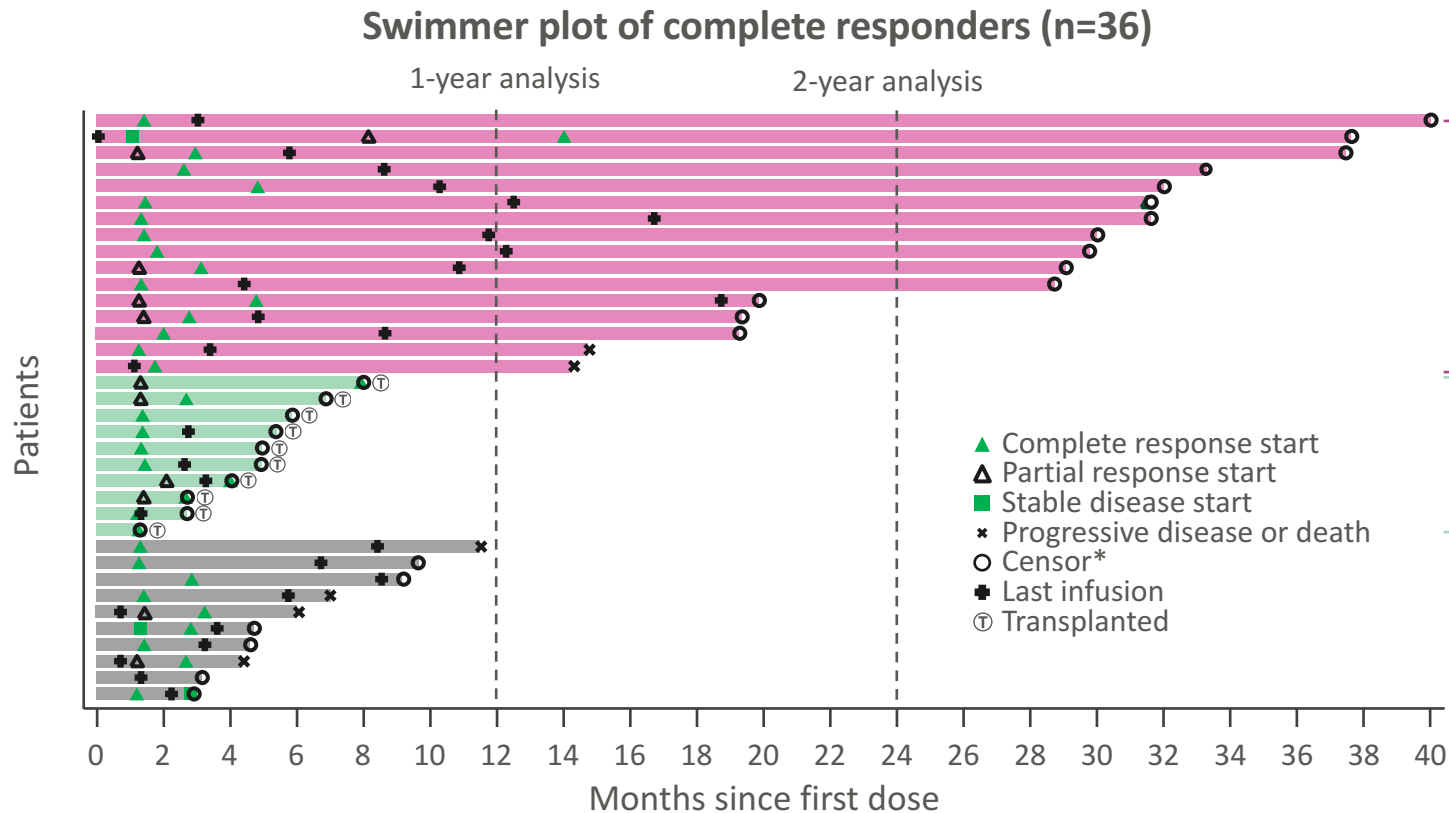
Patients in CR

(36 of 145 patients)

- **44.4% (16/36)** of patients remained in CR with no further treatment
- **36.1% (13/36)** had disease progression or death

Lotis-2: Follow-up of complete responders¹

Final analysis: 2-year update



44% (n=16) and **31%** (n=11) of patients in CR were **event free** for **≥1 year** and **≥2 years**, respectively

10 patients censored while in CR went on to **transplant**

The median duration of time patients with CR remained treatment-free post-Loncastuximab was 6.1 months (range: 1.0–37.5)

Data cut-off: September 15, 2022 (final analysis).

Each bar represents one patient in the study. Response was determined by an independent review.

* Reasons for censoring included study discontinuation† (15 patients; 41.7%), transplant (10 patients; 27.8%), new anticancer therapy (5 patients; 13.9%); progressive disease (3 patients; 8.3%) and death (3 patients; 8.3%).

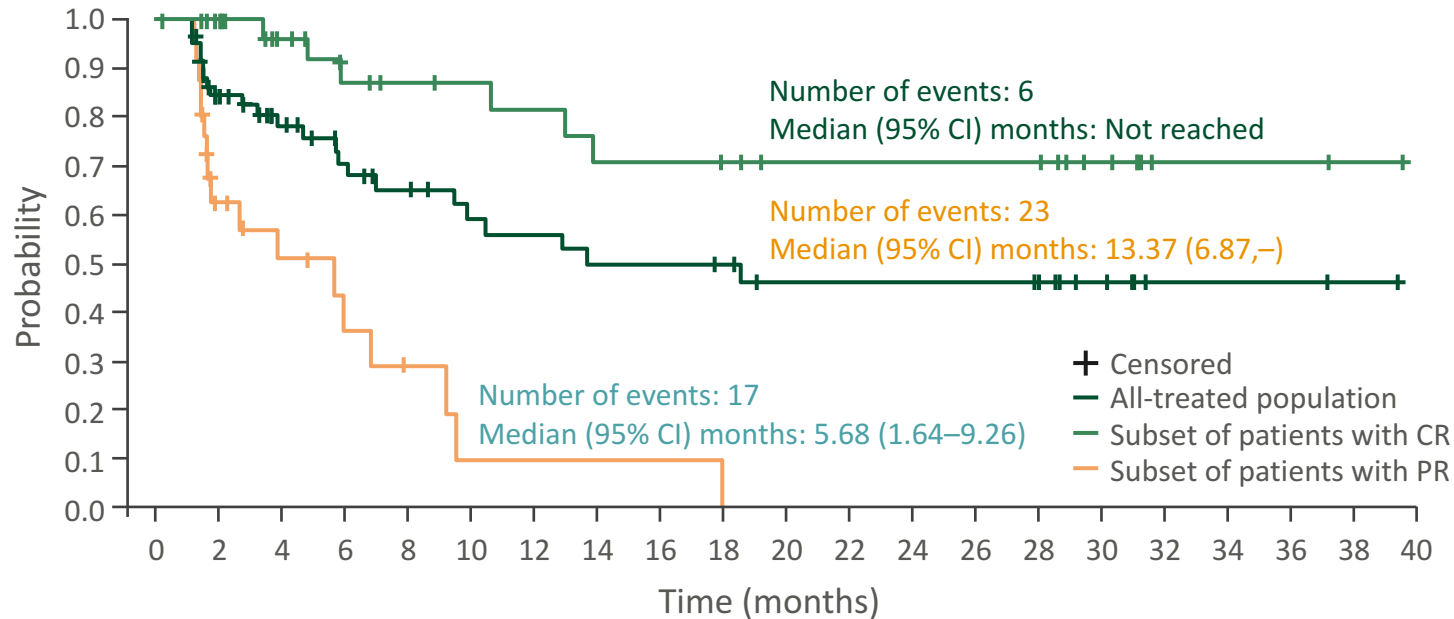
† Reasons for study discontinuation in patients with a CR included unacceptable toxicity (8 patients), withdrawal by subject (4 patients) and physician decision (3 patients).²

CR, complete response; PD, progressive disease.

1. Caimi et al. *Haematologica* 2023 2. Data on file.

Lotis-2: Duration of response by best overall response¹

Final analysis: 2-year update



Patients at risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40																			
All-treated population	70	63	42	38	33	29	25	22	21	20	18	17	17	16	15	15	15	15	13	11	11	11	11	11	11	11	11	7	6	5	2	2	2	2	2	2	1	1	0	
Subset of patients with CR	36	35	30	29	25	22	20	18	18	17	17	16	16	15	14	14	14	14	14	12	11	11	11	11	11	11	11	11	7	6	5	2	2	2	2	2	2	1	1	0
Subset of patients with PR	34	28	12	9	8	7	5	4	3	3	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

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

mDOR for patients with a CR (n=36)
Not reached

mDOR for patients with a PR (n=34)
5.7 months
 (95% CI: 1.6-9.3)

Data cut-off: September 15, 2022 (final analysis).
 CI, confidence interval; CR, complete response; mDOR, median duration of response; NE, not estimable; PR, partial response.
 1. Caimi et al. *Haematologica* 2023.

Lotis 2: Exploratory analyses of overall response rate¹

Response in select patient subgroups (primary analysis)

Subgroup	Patients achieving ORR (n/N)	ORR, % (95% CI)
All ²	70/145	48.3 (39.9–56.7)
Age		
<65 years	32/65	49.2 (36.6–61.9)
≥65 to < 75 years	27/59	45.8 (32.7–59.2)
≥75 years	11/21	52.4 (29.8–74.3)
WHO classification		
DLBCL NOS	64/127	50.4 (41.4–59.4)
PMBCL	1/7	14.3 (0.4–57.9)
HGBL*	5/11	45.5 (16.7–76.6)
Double hit[†]		
No	65/130	50.0 (41.1–58.9)
Yes	5/15	33.3 (11.8–61.6)
Double expressor		
No	60/125	48.0 (39.0–57.1)
Yes	10/20	50.0 (27.2–72.8)
Transformed disease		
Transformed	13/29	44.8 (26.4–64.3)
De novo	57/116	49.1 (39.7–58.6)
Cell-of-origin[‡]		
GCB	26/48	54.2 (39.2–68.6)
ABC	11/23	47.8 (26.8–69.4)

Subgroup	Patients achieving ORR (n/N)	ORR, % (95% CI)
All ²	70/145	48.3 (39.9–56.7)
First-line response		
Relapse	53/99	53.5 (43.2–63.6)
Refractory	11/29	37.9 (20.7–57.7)
Prior HSCT		
Yes	14/24	58.3 (36.6–77.9)
No	56/121	46.3 (37.2–55.6)
Prior CAR T cell-therapy		
Yes	6/13	46.2 (19.2–74.9)
No	64/132	48.5 (39.7–57.3)
Prior systemic therapies		
2 prior lines	30/63	47.6 (34.9–60.6)
3 prior lines	17/35	48.6 (31.4–66.0)
>3 prior lines	23/47	48.9 (34.1–63.9)

Data cut-off: April 6, 2020 (primary analysis). Subgroup analyses were limited in statistical comparison due to small sample size. * HGBL with *MYC* and *BCL2* and/or *BCL6* rearrangements defined by the 2016 revision of the WHO classification of lymphoid neoplasms. [†] Some patients had a diagnosis of double-/triple-hit lymphoma based on institutional pathology prior to the WHO classification of HGBL with *MYC* and *BCL2* and/or *BCL6* rearrangements. [‡] ABC and GCB were investigator-reported with no independent testing. ABC, activated B-cell-like; CAR, chimeric antigen receptor; CI, confidence interval; DLBCL, diffuse large B-cell lymphoma; GCB, germinal centre B-cell-like; HGBL, high-grade B-cell lymphoma; HSCT, haematopoietic stem cell transplantation; NOS, otherwise specified; ORR, overall response rate; PMBCL, primary mediastinal large B-cell lymphoma; WHO, World Health Organization.

1. Caimi et al. *Lancet Oncol* 2021 (suppl.) 2. Caimi et al. *Lancet Oncol* 2021.

Lotis 2: Exploratory analyses of complete response rate¹

Response in select patient subgroups (primary analysis)

Subgroup	Patients achieving CR (n/N)	CRR, % (95% CI)
All ²	35/145	24.1 (17.4–31.9)
Age		
<65 years	12/65	18.5 (9.9–30.0)
≥65 to < 75 years	15/59	25.4 (15.0–38.4)
≥75 years	8/21	38.1 (18.1–61.6)
WHO classification		
DLBCL NOS	30/127	23.6 (16.5–32.0)
PMBCL	0/7	0.0 (NE)
HGBL*	5/11	45.5 (16.7–76.6)
Double hit[†]		
No	30/130	23.1 (16.1–31.3)
Yes	5/15	33.3 (11.8–61.6)
Double expressor		
No	31/125	24.8 (17.5–33.3)
Yes	4/20	20.0 (5.7–43.7)
Transformed disease		
Transformed	7/29	24.1 (10.3–43.5)
De novo	28/116	24.1 (16.7–33.0)
Cell-of-origin[‡]		
GCB	12/48	25.0 (13.6–39.6)
ABC	5/23	21.7 (7.5–43.7)

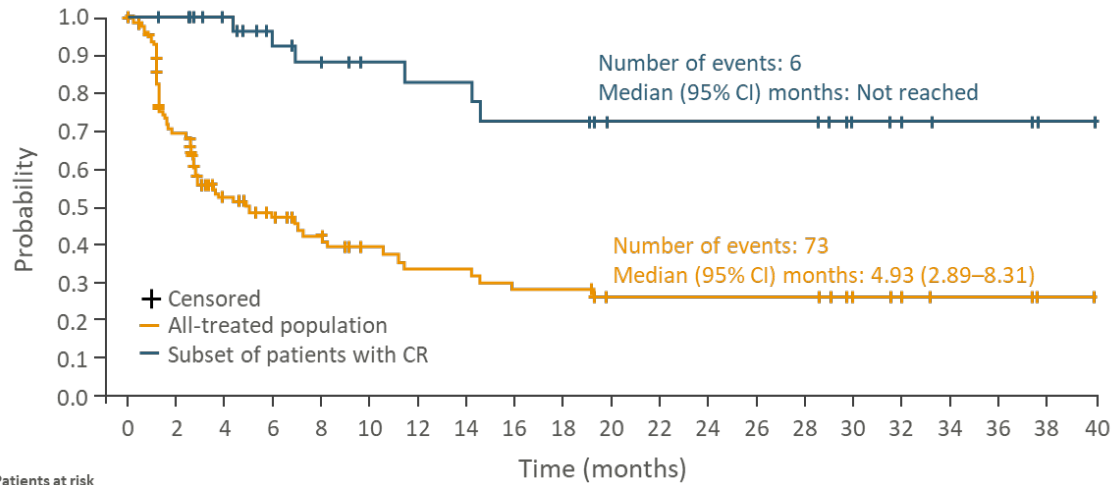
Subgroup	Patients achieving CR (n/N)	CRR, % (95% CI)
All ²	35/145	24.1 (17.4–31.9)
First-line response		
Relapse	26/99	26.3 (17.9–36.1)
Refractory	5/29	17.2 (5.8–35.8)
Prior HSCT		
Yes	7/24	29.2 (12.6–51.1)
No	28/121	23.1 (16.0–31.7)
Prior CAR T cell-therapy		
Yes	2/13	15.4 (1.9–45.4)
No	33/132	25.0 (17.9–33.3)
Prior systemic therapies		
2 prior lines	15/63	23.8 (14.0–36.2)
3 prior lines	5/35	14.3 (4.8–30.3)
>3 prior lines	15/47	31.9 (19.1–47.1)

Data cut-off: April 6, 2020 (primary analysis). Subgroup analyses were limited in statistical comparison due to small sample size. * HGBL with *MYC* and *BCL2* and/or *BCL6* rearrangements defined by the 2016 revision of the WHO classification of lymphoid neoplasms. † Some patients had a diagnosis of double-/triple-hit lymphoma based on institutional pathology prior to the WHO classification of HGBL with *MYC* and *BCL2* and/or *BCL6* rearrangements. ‡ ABC and GCB were investigator-reported with no independent testing. ABC, activated B-cell-like; CAR, chimeric antigen receptor; CI, confidence interval; CR(R), complete response (rate); DLBCL, diffuse large B-cell lymphoma; GCB, germinal centre B-cell-like; HGBL, high-grade B-cell lymphoma; HSCT, haematopoietic stem cell transplantation; NE, not estimable; NOS, otherwise specified; ORR, overall response rate; PMBCL, primary mediastinal large B-cell lymphoma; WHO, World Health Organization.

1. Caimi et al. *Lancet Oncol* 2021 (suppl.) 2. Caimi et al. *Lancet Oncol* 2021.

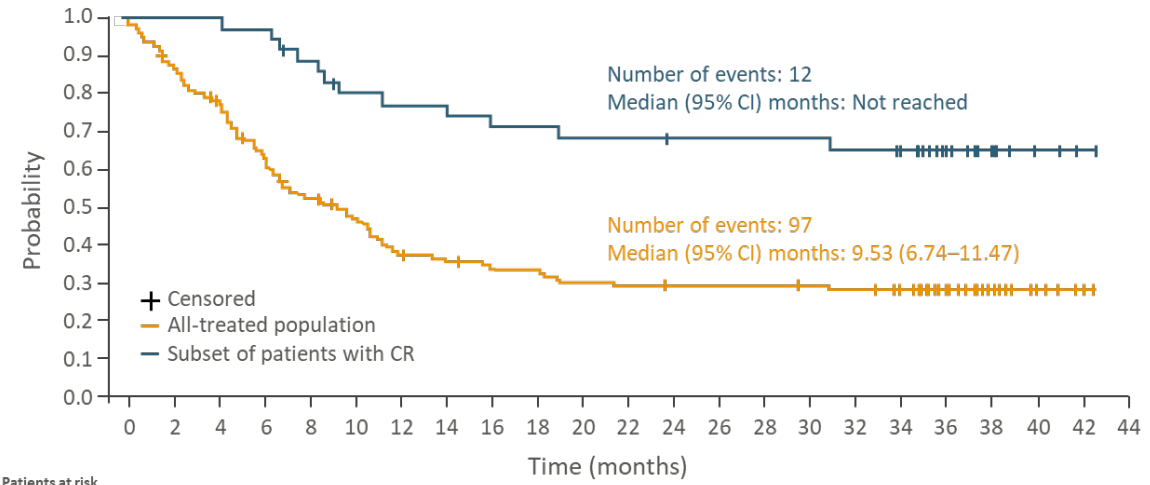
LOTIS-2 PFS and OS¹

Final analysis: 2-year update



Patients at risk

All-treated population	145	124	85	56	46	37	34	29	27	24	21	20	18	18	16	15	15	15	15	11	11	11	11	11	11	11	11	11	10	7	7	4	4	3	3	3	3	1	1	0
Subset of patients with CR	36	36	35	32	31	25	23	20	20	19	17	16	16	16	14	14	14	14	14	14	11	11	11	11	11	11	11	11	10	7	7	4	4	3	3	3	3	1	1	0



Patients at risk

All-treated population	145	136	126	115	110	98	89	78	72	68	63	56	51	48	47	45	44	42	42	40	38	38	37	37	36	36	36	36	36	36	36	35	35	34	34	32	29	24	20	14	9	7	5	3	0
Subset of patients with CR	36	36	36	36	36	35	35	33	31	29	27	26	26	25	25	25	24	24	24	23	23	23	23	23	22	22	22	22	22	22	22	22	22	21	21	20	18	14	12	8	4	3	3	1	0

mPFS for all-treated population (N=145)
4.9 months
 (95% CI: 2.9–8.3)

mPFS for patients with CR (n=36)
Not reached

mOS for all-treated population (N=145)
9.5 months
 (95% CI: 6.7–11.5)

mOS for patients with CR (n=36)
Not reached

Data cut-off: March 1, 2021.

Patients with events after start of subsequent anticancer therapy or procedure, or progression free and alive at data cut-off, or who had unknown status were censored at last valid tumour assessment on or before start of subsequent anticancer therapy or procedure or data cut-off.²

CI, confidence interval; m, median; OS, overall survival; PFS, progression-free survival.

1. Caimi et al. *Haematologica* 2023.

LOTIS-2 Safety results: Overall TEAEs

Overall TEAEs (all-treated population)

TEAE	Patients, n (%) (N=145)
Patients with any TEAE	143 (98.6)
Grade ≥3 TEAE	107 (73.8)
TEAE related to lonca*	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)

No new safety concerns reported

Treatment-related TEAEs leading to discontinuation (27 patients; 18.6%)

- Most common reason was increased GGT (17 patients; 11.7%)
- **Dose delays** (62 patients, 42.8%) were mostly short (<1 week) and enabled patients to continue treatment
 - Dose delays were used to liver enzyme elevation and haematological events
- Few patients had **dose reductions** due to adverse events
 - Increased GGT was the leading cause

LOTIS 2: TEAEs occurring in $\geq 10\%$ of patients

Haematological TEAE	All Grades, %	Grades 3 or 4, %
Neutropenia	40	26
Thrombocytopenia	33	18
Anaemia	26	10
Febrile neutropenia	3	3

Laboratory TEAE	All Grades, %	Grades 3 or 4, %
GGT increase	40	16
ALP increase	20	1
AST increase	16	1
ALT increase	16	3

- Hematological parameters generally decreased with treatment but tended to partially recover between cycles
- Increased gamma-glutamyl transferase increase was not associated with synthetic dysfunction or severe hepatic events.

LOTIS 2: TEAEs occurring in $\geq 10\%$ of patients

Non-haematological TEAE	All Grades, %	Grades 3 or 4, %
Fatigue	27	1
Nausea	23	0
Cough	22	1
Peripheral oedema	20	1
Pyrexia	19	1
Diarrhoea	17	2
Decreased appetite	15	0
Vomiting	13	0
Rash	13	1
Pruritus	12	0
Constipation	12	0
Insomnia	11	0
Abdominal pain	11	3
Dyspnoea	11	1
Headache	11	1
Erythema	11	1
Pleural effusion	10	2
Photosensitivity reaction	10	2

- Treatment-emergent adverse events considered likely to be related to the pyrrolobenzodiazepine (PBD) payload include **edema or effusion, skin toxicity (rash, erythema) or photosensitivity, and liver enzyme elevation**
- After introduction of dexamethasone premedication, standard spironolactone diuretics, and more stringent recommendations on sun exposure, **PBD-related adverse events were generally mild-to-moderate in severity and were generally reversible and manageable** with dose delays as required

LOTIS-2: Response to lonca related to CAR T-cell therapy

1- LONCA AFTER CAR-T = ORR 46.2%

13 (9.0%) patients from LOTIS-2 had received prior CAR T-cell therapy
No prior CAR-T patients were screened failed due to a lack of CD19
ORR to lonca was **46.2%** (6/13 patients), with two CRs (15.4%)

2- LONCA BEFORE CAR-T = ORR 46.7%

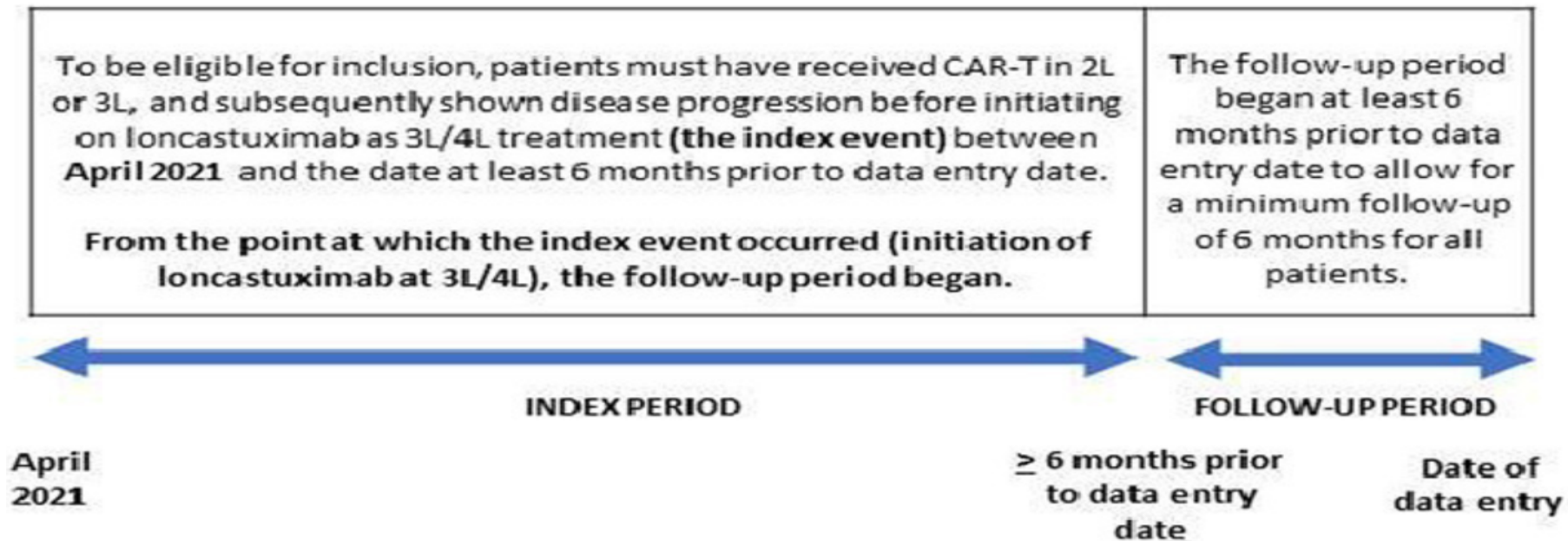
Response to CAR T-cell therapy in patients who previously received lonca (LOTIS-2)^{1,2}
15 (10.3%) patients received subsequent CD19-directed CAR T therapy*
Investigator-assessed ORR to CAR-T after lonca was **46.7%** (7/15 patients; 95% CI: 21.3, 73.4)

Real-World Clinical Effectiveness of Loncastuximab Tesirine Monotherapy for the Treatment of Relapsed/Refractory Diffuse Large B-Cell Lymphoma Following CAR-T (Chimeric Antigen T Cell) Therapy in the US

Study design

This was a **retrospective chart review** conducted by oncologists and hematologists, including adult patients who initiated **loncastuximab tesirine** as the next treatment after receiving **commercial CAR-T therapy** in the **second (2L) or third line (3L)** setting.

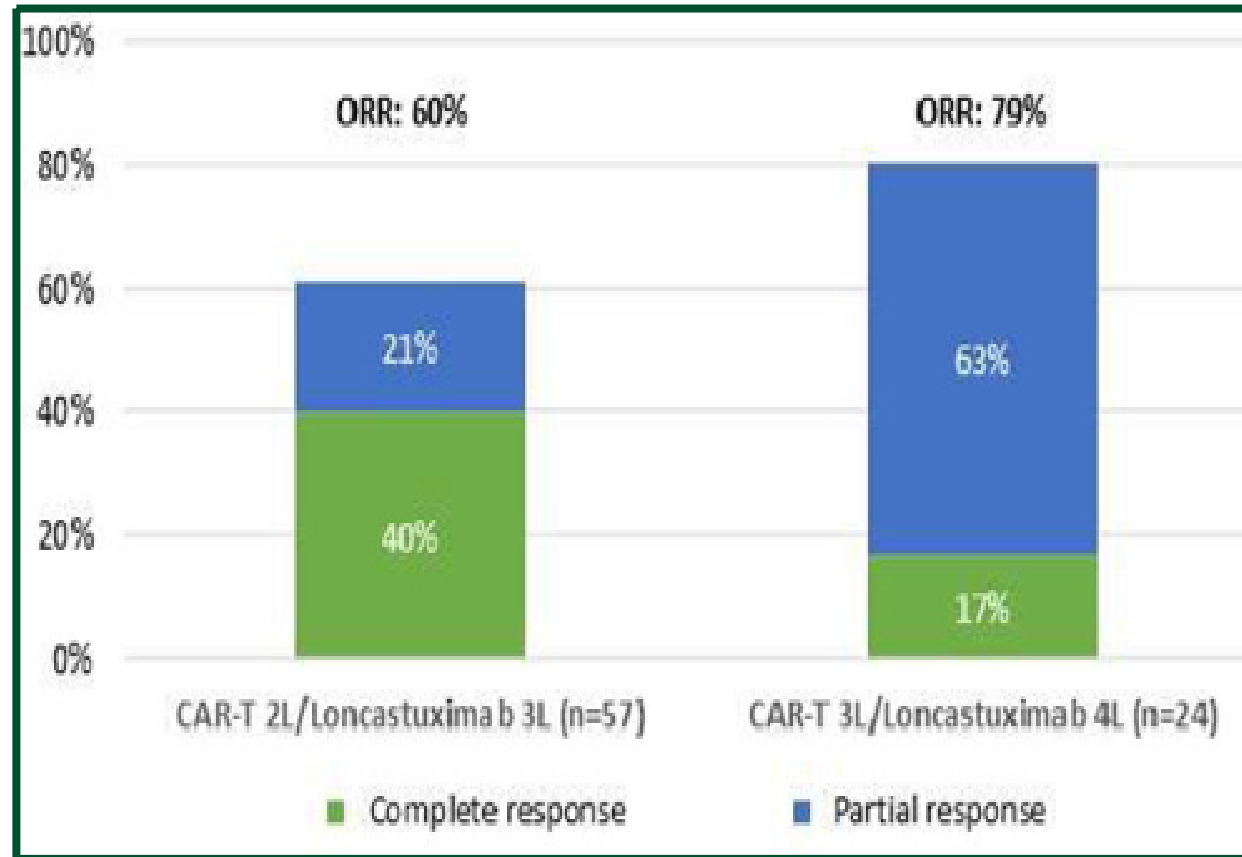
* ORR, DOR, PFS, OS,



Real-World Clinical Effectiveness of Loncastuximab Tesirine Monotherapy for the Treatment of Relapsed/Refractory Diffuse Large B-Cell Lymphoma Following CAR-T (Chimeric Antigen T Cell) Therapy in the US

Results

Best response for **loncastuximab** treatment received at 3L and 4L post CAR-T



This is the first study to examine lonca at 3L following CAR-T at 2L and suggests that lonca can be a reasonable and effective treatment option for pts who are resistant/progressed after CAR-T.



Part 2

Combinations

The next frontier — combination strategies with loncastuximab

Loncastuximab tesirine

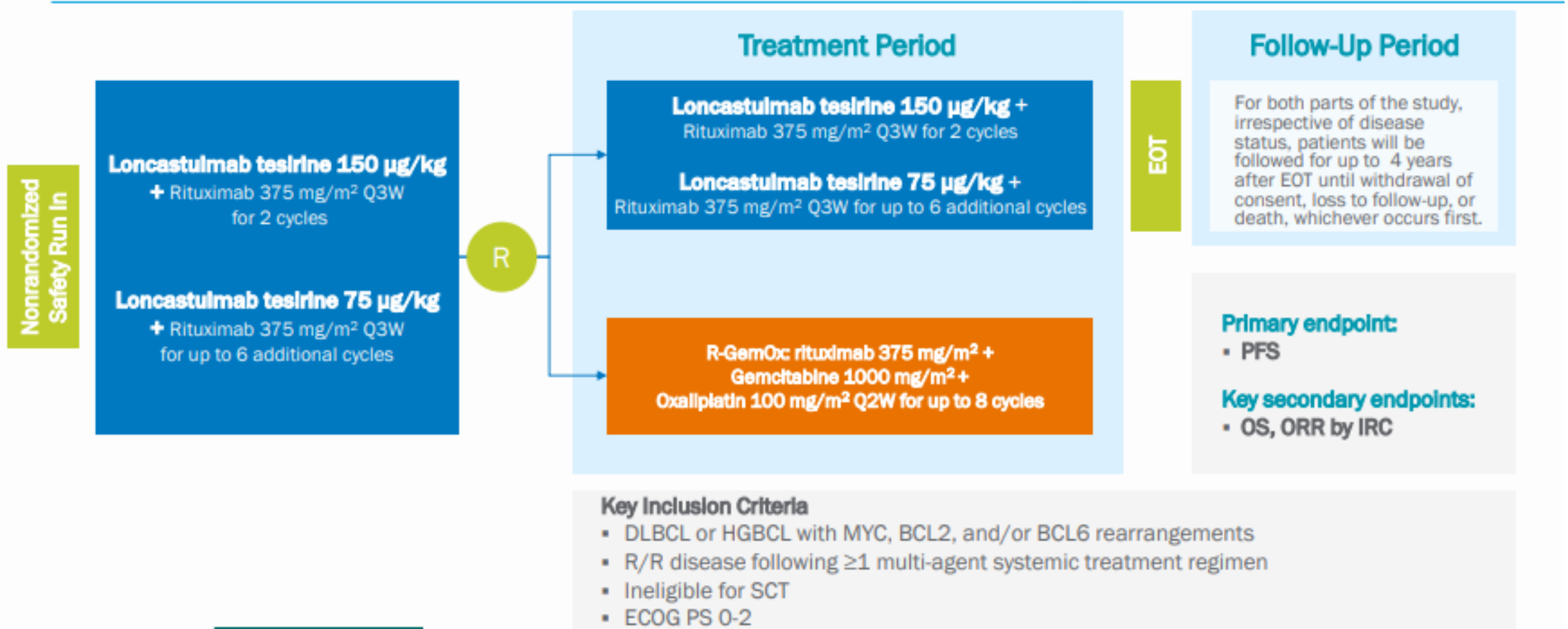


LOTIS - 5

A Phase 3 Randomized Study of
Loncastuximab Tesirine Combined With
Rituximab Versus Immunochemotherapy in
Patients With Relapsed or Refractory
Diffuse Large B-Cell Lymphoma (DLBCL)

Study Design

LOTIS 5: A Phase 3, Randomized trial of Loncastuximab Tesirine With Rituximab (Lonca-R) vs Immunochemotherapy in R/R DLBCL/HGBL



Updated Safety Run-In results from LOTIS-5: A Phase 3, Randomized trial of Loncastuximab Tesirine With Rituximab (Lonca-R) Versus Immunochemotherapy in Patients With R/R DLBCL/HGBL (Poster EHA-2025)

OBJECTIVE

To characterize the safety, efficacy, and PK profile of loncastuximab tesirine + rituximab (Lonca-R) and explore the correlation of clinical activity and tumor/blood biomarkers in the safety run-in population of the LOTIS-5 trial

PHASE 3 LOTIS-5 TRIAL

Eligibility criteria

- ✓ R/R DLBCL/HGBL
- ✓ ≥1 prior systemic therapy
- ✓ Not a candidate for SCT

Part 1: Safety run-in (N=20)

Lonca-R

Part 2: Lonca-R vs R-GemOx (N≈420)

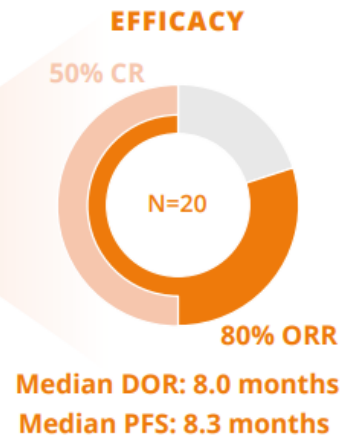
Lonca-R

R-GemOx

Up to 8 cycles of treatment

UPDATED SAFETY RUN-IN RESULTS

Median duration of follow-up:
37.2 (range, 34.1-41.5) months



SAFETY

- There were no new safety signals
- The most common grade ≥3 TEAEs were increased GGT (n=5) and neutropenia (n=4)

BIOMARKERS

- CD19 IHC staining was not predictive of efficacy
- Response to therapy was associated with early ctDNA decrease
- All 3 CR patients with ctDNA results were MRD negative at C3D1

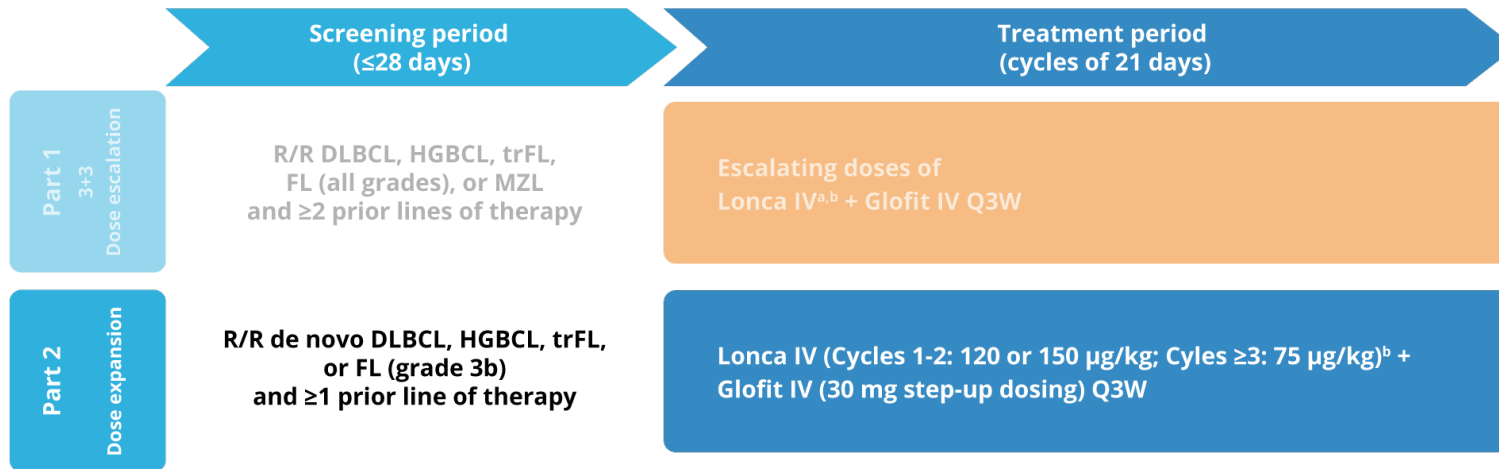
Results

Efficacy

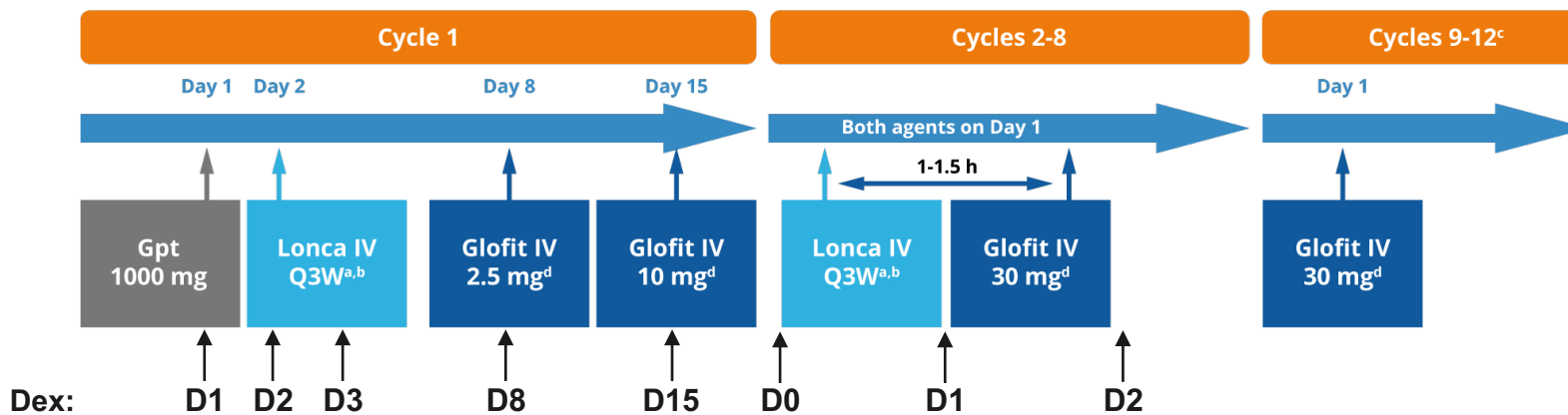
- **ORR[†] 80%**
- **CR 50%**
- **PR 30%**

Fixed treatment duration of Lonca-R showed no new safety signals and demonstrated encouraging antitumor activity, with early signs of durable response in patients with R/R DLBCL/HGBL maintained for >28 months after EOT

Phase Ib LOTIS-7



Lonca + Glofit treatment sequence



Study population

- Patients with 3L+ R/R B-NHL (part 1) and 2L+ R/R LBCL (part 2)
- ECOG PS score of 0-2
- Prior autologous SCT (>100 days) or CAR-T therapy (>100 days) is allowed
- Measurable disease (per 2014 Lugano Classification)
- Excludes patients with clinically significant third-space fluid accumulation

Endpoints

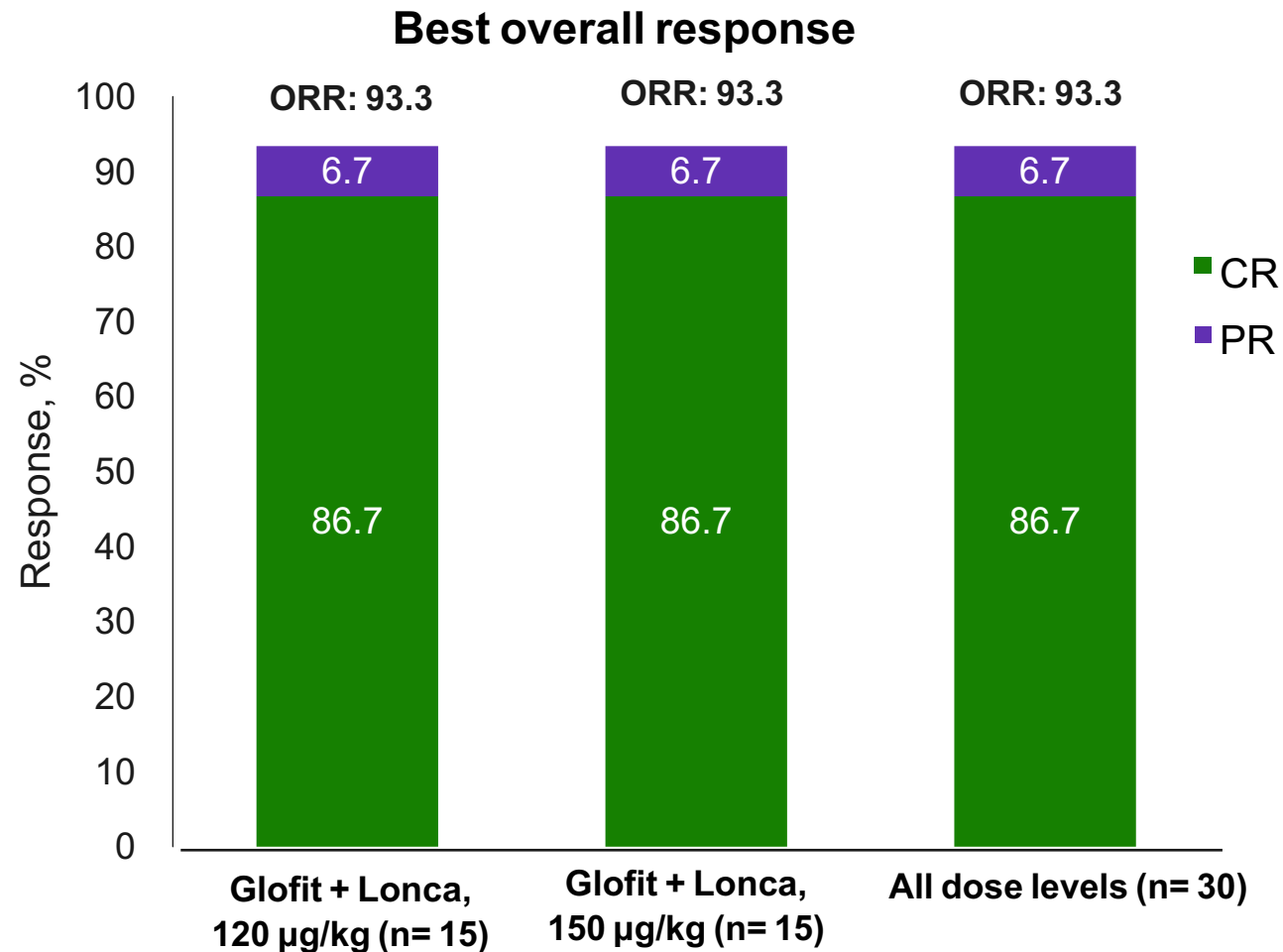
- **Primary:** safety and tolerability; MTD and/or RDE
- **Secondary:** ORR, DOR, CR rate, PFS, RFS, and OS; PK and immunogenicity
- **Exploratory:** Glofit concentration in circulation; biomarker and PK correlations with clinical outcomes

Baseline Characteristics

	Glofit + Lonca, 120 µg/kg ^a (n=20)	Glofit + Lonca, 150 µg/kg ^a (n=21)	All dose levels (N=41)
Age, median (range), y	70 (50-82)	74 (26-85)	71 (26-85)
Male sex, n (%)	11 (55.0)	12 (57.1)	23 (56.1)
ECOG PS score, n (%)			
0	9 (45.0)	14 (66.7)	23 (56.1)
1	10 (50.0)	7 (33.3)	17 (41.5)
2	1 (5.0)	0	1 (2.4)
Ann Arbor disease stage, n (%)			
Stage I/II	3 (15.0)	3 (14.3)	6 (14.6)
Stage III/IV	17 (85.0)	18 (85.7)	35 (85.4)
IPI score, n (%)			
0-2	9 (45.0)	10 (46.7)	19 (46.3)
3-5	11 (55.0)	11 (52.4)	22 (53.7)
Bulky disease, n (%)	2 (10.0)	2 (9.5)	4 (9.8)
LDH levels high, n (%)	11 (55.0)	10 (47.6)	21 (51.2)
LBCL histology, n (%)			
de novo DLBCL	13 (65.0)	17 (81.0)	30 (73.2)
HGBCL	4 (20.0)	2 (9.5)	6 (14.6)
trFL	2 (10.0)	2 (9.5)	4 (9.8)
FL grade 3b	1 (5.0)	0	1 (2.4)

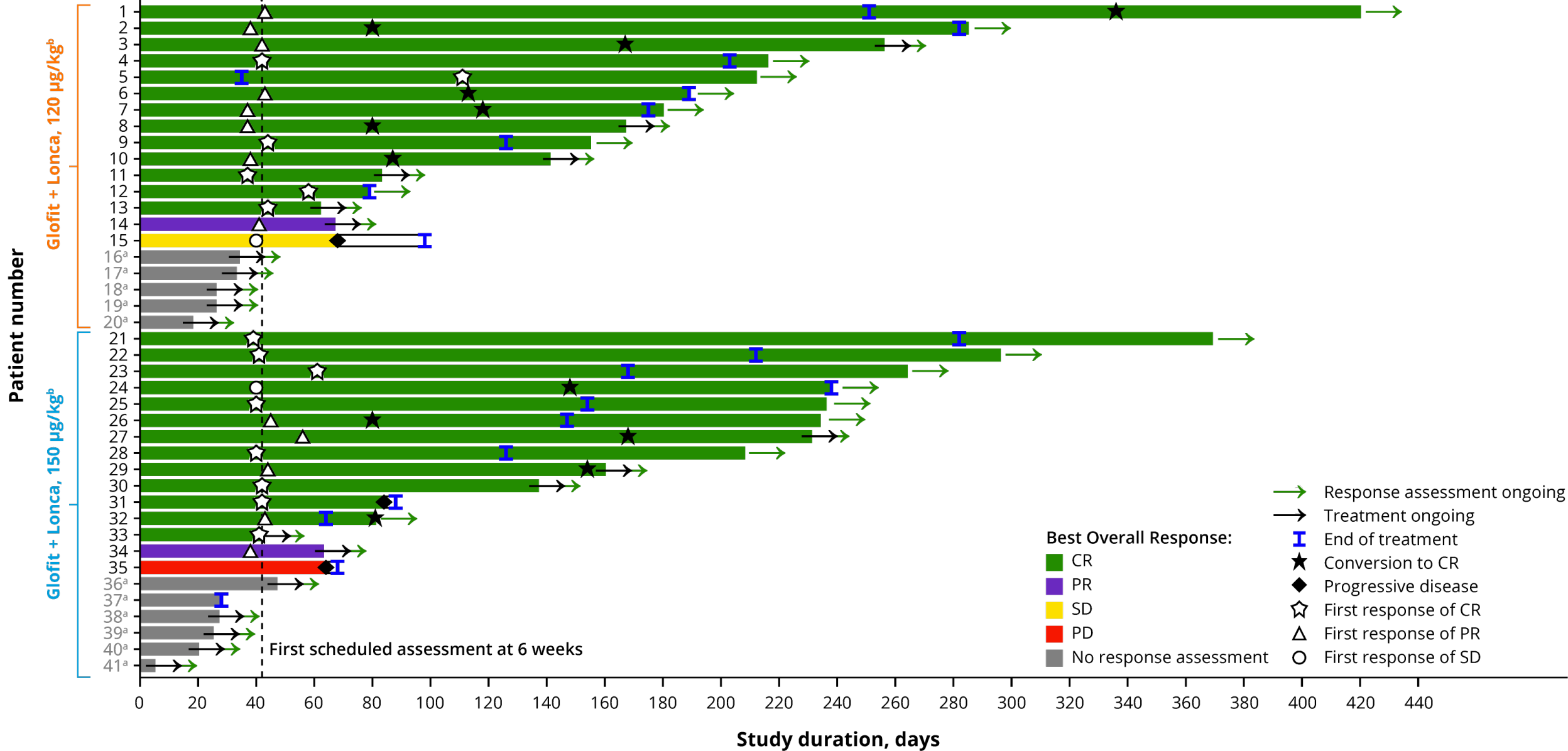
	Glofit + Lonca, 120 µg/kg ^a (n=20)	Glofit + Lonca, 150 µg/kg ^a (n=21)	All dose levels (N=41)
DLBCL subtype, n (%)			
GCB	10 (50.0)	11 (52.4)	21 (51.2)
non-GCB	5 (25.0)	8 (38.1)	13 (31.7)
Double hit, n (%)	3 (15.0)	5 (23.8)	8 (19.5)
Number of prior LOT			
Median (range)	2 (1-4)	2 (1-5)	2 (1-5)
1, n (%)	10 (50.0)	10 (47.6)	20 (48.8)
≥2, n (%)	10 (50.0)	11 (52.4)	21 (51.2)
Refractory status, n (%)			
Refractory to primary therapy	8 (40.0)	13 (61.9)	21 (51.2)
Refractory to last prior therapy	7 (35.0)	13 (61.9)	20 (48.8)
Prior stem cell transplant, n (%)	3 (15.0)	1 (4.8)	4 (9.8)
Prior CAR-T therapy, n (%)	4 (20.0)	4 (19.0)	8 (19.5)

Efficacy Assessment (n= 30)



Duration of response

Characteristic, n (%)	Glofit + Lonca, 120 µg/kg (n=15)	Glofit + Lonca, 150 µg/kg (n=15)	All dose levels (N=30)
DOR ^d Median	(n=14) NE	(n=14) NE	(n=28) NE
Time to first response (CR or PR) Median, days	(n=14) 42.0	(n=14) 42.0	(n=28) 42.0
Time to first CR Median, days	(n=13) 80.0	(n=13) 42.0	(n=26) 70.5



Safety Results

	120 µg/kg ^b n = 20	150 µg/kg ^b n = 21	All n = 41
Grade 3/4 TEAEs (> 5% of patients)^a	11 (55%)	12 (57.1%)	23 (56.1%)
Neutropenia	4 (20%)	6 (28.6%)	10 (24.4%)
Anemia	1 (5%)	3 (14.3%)	4 (9.8%)
AST increased	2 (10%)	1 (4.8%)	3 (7.3%)
GGT increase	1 (5%)	2 (9.5%)	3 (7.3%)
Thrombocytopenia	2 (10%)	1 (4.8%)	3 (7.3%)
Grade 3/4 AESI (all patients)^a			
Febrile neutropenia	0	1 (4.8%)	1 (2.4%)
Thrombocytopenia	2 (10%)	1 (4.8%)	3 (7.3%)
GGT increase	1 (5%)	2 (9.5%)	3 (7.3%)
Generalized oedema	1 (5%)	1 (4.8%)	2 (4.9%)
Rash	1 (5%)	0	1 (2.4%)
Photosensitivity reaction	0	1 (4.8%)	1 (2.4%)
Sepsis	1 (5%)	0	1 (2.4%)
Upper respiratory infection	1 (5%)	0	1 (2.4%)
Pneumonia	1 (5%)	0	1 (2.4%)
Serious TEAE	11 (55%)	9 (42.9%)	20 (48.8%)

No Grade 5 TEAEs occurred

Safety Results

120 µg/kg
n = 20

150 µg/kg
n = 21

All
n = 41

Cytokine Release Syndrome

Any grade	11 (55%)	5 (23.8%)	16 (39.0%)
Grade 1	7 (35%)	5 (23.8%)	12 (29.3%)
Grade 2	3 (15%)	0	3 (7.3%)
Grade 3	1 (5%)	0	1 (2.4%)
Grade 4/5	0	0	0

ICANS

Any grade	2 (10%)	1 (4.8%)	3 (7.3%)
Grade 1	1 (5%)	0	1 (2.4%)
Grade 2	1 (5%)	1 (4.8%)	2 (4.9%)
Grade <u>≥</u> 3	0	0	0

Take Away Messages

- The DLBCL landscape is expected to extensively change in the next years
- Many clinical studies are ongoing, and some have shown very promising results
- The future approach is led by combinations as in LOTIS 7 (Lonca & Glofitamab)
- Lonca efficacy, safety, and convenience as outpatient monotherapy is an extremely valuable alternative in 3rd line

THANK YOU

Alvaro Alencar, MD
aalencar@med.miami.edu

