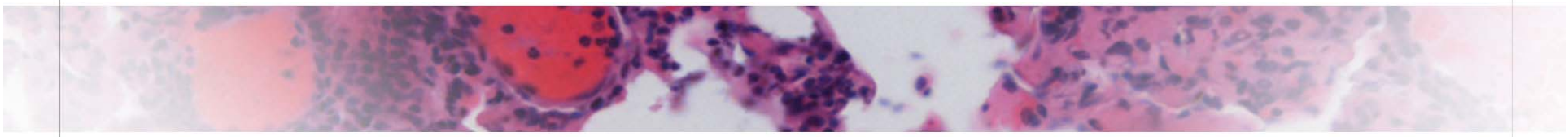

The Anti-CD19 Antibody-Drug Conjugate Loncastuximab Tesirine Achieved Responses in Patients With Diffuse Large B-Cell Lymphoma Who Relapsed After Anti-CD19 CAR T-Cell Therapy

Poster slides, 63rd ASH Annual Meeting and Exposition Meeting, December 11-14, 2021

Prospective Therapeutic Trials: Poster session II, Sunday, December 12, 2021, 6:00-8:00 PM (EST), GWCG, Hall B5

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Background

- Patients with R/R DLBCL have limited options for long-term disease control[1]
  - CD19-targeted CAR T-cell therapy can achieve high response rates, but durable CR rates are approximately 40% in the clinical trial setting[2-4]
  - Patients with DLBCL that is resistant to CAR T-cell therapy have poor outcomes[5]
- The majority of patients with DLBCL who relapse after CAR T-cell therapy have disease that continues to express surface CD19[6]
- It is unknown whether treatment with CD19-targeted agents is an effective strategy for patients with prior failure of anti-CD19 CAR-T therapy

Loncastuximab tesirine (loncastuximab tesirine-lpyl; Lonca) is an FDA-approved CD19-directed antibody-drug conjugate (ADC) with single-agent activity and acceptable safety in non-Hodgkin lymphoma, including DLBCL[7-9]

CAR, chimeric antigen receptor; DLBCL, diffuse large B-cell lymphoma; R/R, relapsed or refractory.

1. Crump M, et al. *Blood*. 2017;130:1800-8; 2. Neelapu SS, et al. *NEJM*. 2017;377:2531-44; 3. Schuster SJ, et al. *NEJM*. 2019;380:45-56; 4. Abramson JS, et al. *Lancet*. 2020;396:839-52; 5. Chow VA, et al. *Am J Hematol*. 2019;94:E209-E13; 6. Shah NN, Fry TJ. *Nat Rev Clin Oncol*. 2019;16:372-85; 7. Hamadani M, et al. *Blood*. 2021;137:2634-45; 8. Caimi PF, et al. *Lancet Oncol*. 2021;22(6):790-800; 9. ZYNLOTA [package insert]. Murray Hill, New Jersey: ADC Therapeutics, SA; 2021.

LOTIS-2 Clinical Trial: Study Design and Methods

- Efficacy and safety of single-agent Lonca was evaluated in the pivotal phase 2 LOTIS-2 trial (NCT03589469); methods for LOTIS-2 have been published[1]
- Patients with previous anti-CD19 CAR-T therapy were required to have persistent CD19 expression, evaluated by local review of the immunohistochemistry of a post–CAR-T biopsy
- Kaplan Meier survival analysis was performed from the initiation of Lonca treatment

LOTIS-2 Trial Design

Population: Patients with R/R DLBCL after ≥2 lines of systemic therapy

Dosing regimen: Patients received Lonca at doses of 0.15 mg/kg for 2 cycles then 0.075 mg/kg for subsequent cycles as a single 30-min infusion, Q3W for up to 1 year or until progressive disease or unacceptable toxicity.
Follow-up was approximately every 12 weeks for up to 3 years after treatment discontinuation.

Primary outcome:
Overall response rate*

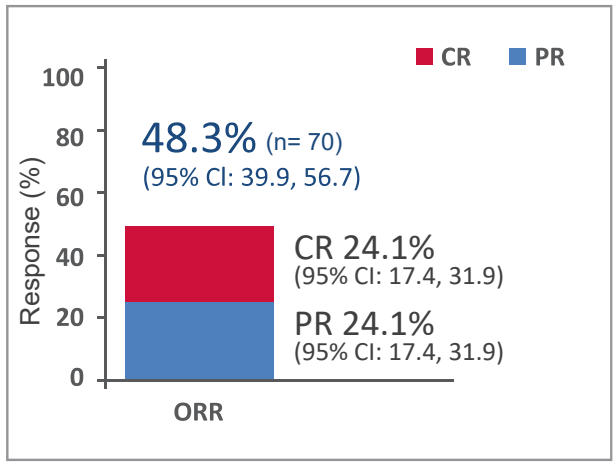
Secondary outcomes included:

CR	PFS
DoR	OS

*Defined as the proportion of patients with best overall response of complete response (CR) or partial response (PR) determined by independent review.
DoR, duration of response; Lonca, loncastuximab tesirine; NE, not estimable; OS, overall survival; PFS, progression free survival; Q3W, every 3 weeks; R/R, relapsing/refractory.
1. Caimi PF, et al. *Lancet Oncol*. 2021;22:790-800.

LOTIS-2 Clinical Trial: Overall Results

Overall Results of the LOTIS-2 Clinical Trial



LOTIS-2 Secondary Outcomes (N=145)

DoR
10.3 mo
(6.9-NE)

OS
9.9 mo
(6.7-11.5)

PFS
4.9 mo
(2.9-8.3)

Here, we present results of a post hoc analysis evaluating the outcomes of patients with DLBCL who had refractory disease or relapsed after anti-CD19 CAR T-cell therapy and were subsequently treated with Lonca within the LOTIS-2 clinical trial

Data cutoff: April 6, 2020.
CR, complete response; DoR, duration of response; OS, overall survival; ORR, overall response rate; PFS, progression-free survival; PR, partial response.
Caimi PF, et al. *Lancet Oncol*. 2021;22:790-800.

Patient and Disease Baseline Characteristics

- Thirteen (9.0%) patients from LOTIS-2 had received prior CAR T-cell therapy
- The median number of systemic therapies prior to Lonca was 4 (range 3-7)

Baseline Characteristics of Patients Treated with Lonca Post–CAR T-Cell Therapy

Variable	Patients (n=13)
Age, median (range), years	63 (23-79)
Sex, male, n (%)	9 (69)
Race, white, n (%)	12 (92)
Lymphoma subtype, n (%)	
• DLBCL, NOS	5 (38)
• Transformed follicular	4 (31)
• Richter transformation	1 (8)
• HGBCL	3 (23)
Double hit/triple hit, n (%)	5 (38)
Stage at diagnosis, n (%)	
• Stage I-II	2 (15)
• Stage III-IV	11 (85)
Primary refractory, n (%)	10 (77)
Prior stem cell transplant, n (%)	
• Autologous	2 (15)
• Allogeneic	1 (8)

Data cut-off: April 6, 2020.
DLBCL, diffuse large B-cell lymphoma; DLBCL-NOS, DLBCL not otherwise specified; HGBCL, high grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* rearrangements.

CAR T-Cell Therapy Characteristics

Variable	
Type of CAR-T (n, %) • Axicabtagene ciloleucel • Lisocabtagene maraleucel • Investigational targeting CD19 • Investigational targeting CD19/CD20 • Investigational targeting CD19/CD22	 7 (54) 2 (15) 2 (15) 1 (8) 1 (8)
Best response to CAR-T (n, %) • Complete response • Partial response • No response	 7 (54) 2 (15) 4 (31)
Interval between diagnosis and CAR-T infusion, months, median (range)	10 (2-79)
Survival from CAR-T infusion, months (95% CI), median (range)	18 (347 days-NR)
PFS from CAR-T infusion, months (95% CI), median (range)	3.2 (64 days-NR)
Number of lines of therapy prior to CAR-T, median (range)[a]	3 (1-6)

Data cut-off: April 6, 2020.

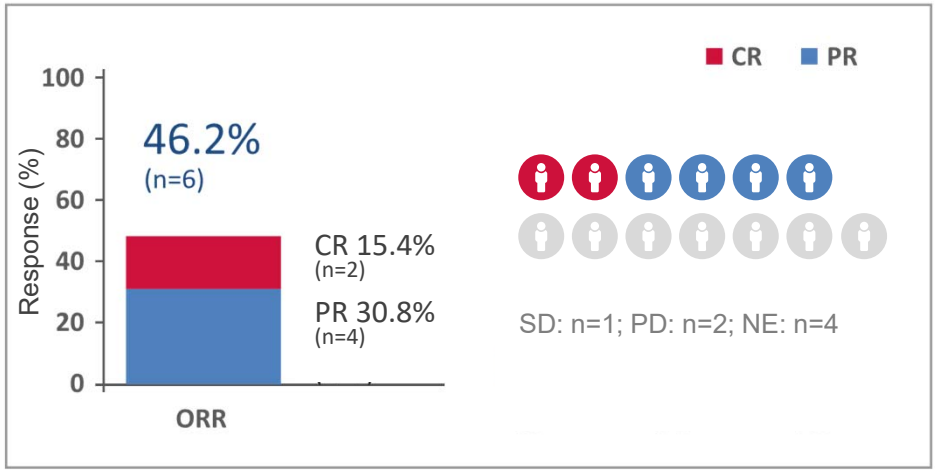
[a]Lonca was the first treatment after CAR-T in 10 patients. Three patients received other treatments prior to Lonca, including chemoimmunotherapy (n=1, R-GemOx) and allogeneic SCT (n=1), and one patient received chemoimmunotherapy (R-GemOx) followed by a clinical trial with venetoclax and a bromodomain inhibitor.

CAR-T, chimeric antigen receptor T-cell; NR, not reached; PFS, progression-free survival; SCT, stem-cell transplant; TH, triple-hit.

Efficacy Results: ORR and Duration of Response

Best Response to Lonca Post–CAR-T

Responses after a median of 2 cycles of Lonca (range 1-9)



Of the 6 patients who responded to Lonca,

- 5 had a previous response to CAR-T
- 1 had prolonged stable disease for >1 year after CAR-T

Responders to Lonca included patients with double-hit/triple-hit lymphoma, transformed lymphoma, and high-grade lymphoma

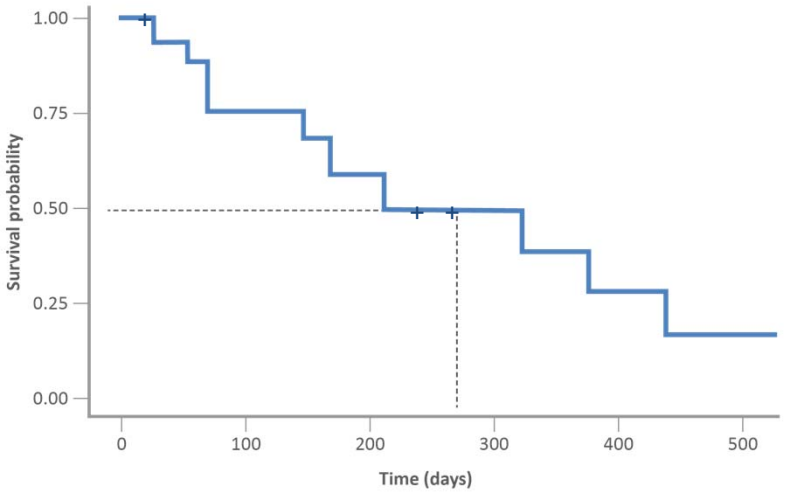
Data cut-off: April 6, 2020. Median follow-up: 8 months.

CAR-T, chimeric antigen receptor T-cell; CR, complete response; NE, not evaluable; ORR, overall response rate; PR, partial response; SD, stable disease.

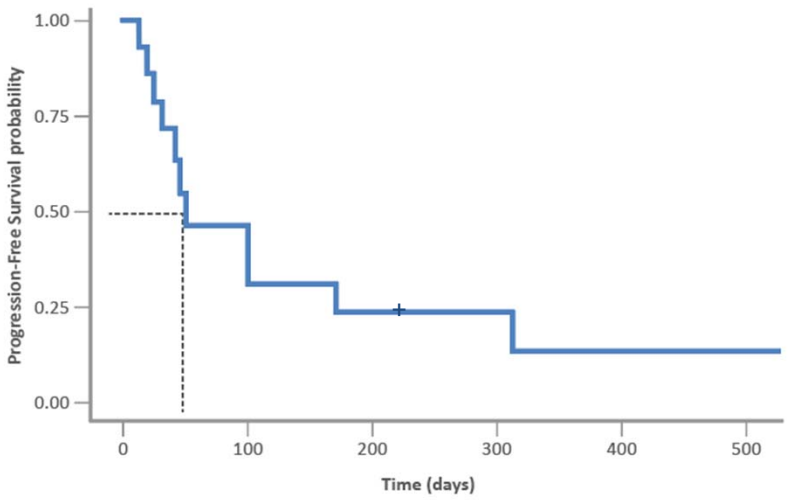
Efficacy Results: Overall and Progression-Free Survival

Overall and Progression-Free Survival of Patients Treated with Lonca Post–CAR-T (n=13)

Median OS: 8.2 months (95% CI: 144 days – NR)[a]



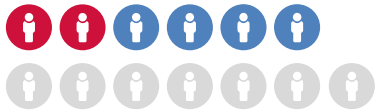
Median PFS: 1.4 months (95% CI: 21 days – NR)



Data cut-off: April 6, 2020. Median follow-up: 8 months.
[a]1-year OS estimate: 33.3% (95% CI: 15%-74.2%).
NR, not reached; OS, overall survival; PFS, progression free survival.

Conclusions

Lonca achieved a response in six out of 13 patients who had failed prior CAR-T therapy



- Five out of six responding patients had a previous response to CAR-T therapy

Prior response to anti-CD19 therapy may be associated with subsequent response to a second anti-CD19 treatment

These data suggest that in patients without CD19 antigen loss, repeat therapy with another agent targeting this antigen can result in disease control

Further studies are needed to confirm the feasibility and value of repeated anti-CD19 treatments in patients with R/R DLBCL

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

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