Loncastuximab in high-risk and heavily pretreated relapsed/refractory diffuse large B-cell lymphoma: a real-world analysis from 21 US centers

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Abstract

Outcomes in patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) are poor. Loncastuximab-teserine (Lonca) is an antibody-drug conjugate which was approved by the Food and Drug Administration for the treatment of patients with R/R DLBCL who have received at least two prior lines of therapy, based on the results of the LOTIS-2 trial. However, there are limited data regarding its efficacy in the real-world setting. This retrospective study included 21 US centers and evaluated outcomes of patients with R/R DLBCL treated with Lonca. Our analysis comprises 187 patients with notably higher-risk baseline features compared to those of the LOTIS-2 population, including a higher proportion of patients with bulky disease (17% *vs*. 0%), high-grade B-cell histology (22% *vs*. 8%), and increased number of prior lines of therapy (median 4 *vs*. 3). The complete response rate was 14% and overall response rate was 32%. The median event-free survival and overall survival were 2.1 and 4.6 months, respectively. Those with bulky disease and high-grade B-cell histology had significantly worse outcomes, and those with non-germinal center cell of origin and a complete response to the most recent line of therapy demonstrated superior outcomes. In summary, in this largest retrospective cohort study of Lonca in the real-world setting, the response rates, event-free survival and overall survival were lower than those reported in LOTIS-2, which is likely reflective of its use in higher risk and more heavily pre-treated patients in the real world compared to the patients enrolled on a clinical study.

Introduction

Patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) have a poor prognosis, with particularly dismal outcomes seen in those who progress following autologous stem cell transplantation and/or chimeric antigen receptor (CAR) T-cell therapy.[1-3] In recent years, there have been several advances in novel therapies, including antibody-drug conjugates and bispecific antibodies, which offer promising results for these patients.[4-11]

Loncastuximab-teserine (Lonca) is one such therapy. Lonca is an antibody-drug conjugate targeting CD19 paired to a pyrrolobenzodiazepine payload that crosslinks DNA upon internalization within the tumor cell.[12,13] Lonca received approval from the Food and Drug Administration in 2021 following the LOTIS-2 trial, a multicenter, single-arm, phase II study of 145 patients with R/R DLBCL who had received two or more prior systemic therapies.[4,14] The LOTIS-2 study reported an overall response rate (ORR) of 48% and a complete response rate (CRR) of 25% with a median progression-free survival and median overall survival (OS) of 4.9 months and 9.5 months, respectively.

An efficacy-effectiveness gap, routinely seen following the commercial approval of new therapies, is a well-document-

Table 1. Baseline demographic and clinicopathological characteristics.

Factor	This analysis N (%)	LOTIS-2 N (%)
Age group	N=177	
<65 years	72 (39)	65 (45)
65-75 years	66 (33)	59 (41)
>75 years	39 (21)	21 (14)
Sex	N=187	
Female	68 (36)	60 (41)
Male	119 (64)	85 (59)
Race	N=169	
African-American	14 (8)	-
Asian	11 (7)	-
White	144 (85)	-
Disease stage	N=184	
I-II	23 (14)	33 (23)
III-IV	161 (86)	112 (77)
IPI	N=111	
<3	39 (35)	-
3-5	72 (65)	-
ECOG performance status	N=150	
0-2	111 (74)	145 (100)
3-5	39 (26)	0 (0)
Bulky disease	N=186	
<10 cm	154 (83)	137 (94)
≥10 cm	32 (17)	8 (6)
CNS involvement	N=169	
Yes	12 (7)	0 (0)
No	157 (93)	145 (100)
Histology	N=160	
HGBL	36 (22)	11 (8)
DH/TH	32 (20)	15 (10)*
De novo DLBCL	85 (53)	-
Transformed DLBCL	28 (18)	29 (20)
Cell of origin – Hans	N=157	
GCB	96 (61)	48 (33)
Non-GCB	61 (38)	23 (16)
Double expressor	N=155	
Yes	61 (39)	20 (14)
No	94 (61)	-
CD19 status	N=128	
Positive	109 (85)	145 (100)
Negative	19 (15)	0 (0)
Post-CAR T-cell therapy	N=90	
Positive	70 (78)	-
Negative	20 (22)	-
Lonca line of therapy	N=187	
2-3rd	36 (19)	98 (68)
4th and beyond	151 (81)	47 (32)
Primary refractory disease	N=187	
Yes	47 (25)	29 (20)
No	140 (75)	
Prior ASCT	N=187	
Yes	31 (16)	21 (14)
No	156 (84)	-
Median time from ASCT in months	26	-
Prior CAR T-cell therapy	N=187	
Yes	112 (60)	13 (9)
No	75 (40)	132 (91)
CAR T cells as second line	11 (10)	-
Median time from CAR T-cell therapy in months	7.7	-
Last best response prior to Lonca	N=187	
Complete response	16 (9)	-
Partial response	15 (8)	-
Stable disease	12 (6)	-
Progressive disease	144 (77)	-

*Includes former *BCL6/MYC* definition of double-hit lymphoma. IPI: International Prognostic Index; ECOG: Eastern Cooperative Oncology Group; CNS: central nervous system; HGBL: high-grade B-cell lymphoma; DH/TH: double-hit/triple-hit; DLBCL: diffuse large B-cell lymphoma; GCB: germinal center B-cell lymphoma; CAR: chimeric antigen receptor; Lonca: loncastuximab-teserine; ASCT: autologous stem cell transplantation.

ed phenomenon wherein real-world outcomes fall short of those reported in prospective clinical trials.[15,16] While retrospective studies are often subject to many widely recognized limitations, these data are still meaningful to inform treating clinicians across a broader base and to generate hypotheses which further advance prospective research. Here, we present the first large-scale analysis of outcomes among patients receiving Lonca in a real-world setting.

Methods

Study design and patients

Patients' data from 21 US centers were collected retrospectively and transferred to the University of Virginia in a de-identified manner. Patient consent was not indicated for this study as all data were collected for standard-of-care clinical purposes and accessed retrospectively.

Patients were 18 years of age or older, diagnosed with R/R DLBCL and treated with Lonca from April 2021 to December of 2022 as standard of care. Patients with incomplete data and those using Lonca as a bridge to consolidative treatment with transplantation or CAR T-cell therapy were excluded from the primary analysis. The study protocol was approved by the University of Virginia Institutional Review Board as well as each contributing institute's review boards. All pathological analyses and treatment decisions were determined according to each institute's standard of care.

Table 2. Response rates by baseline characteristics.

Factor	ORR, %	*P*	CR, %	*P*
Overall	32	-	14	-
HGBL Yes No	 8 34	0.003	 3 15	0.05
Cell of origin Non-GCB GCB	 43 24	0.02	 25 6	0.001
Bulky disease Yes No	 16 35	0.04	 0 16	0.009
Elevated LDH Yes No	 25 51	0.001	 8 30	0.0001
Response prior to Lonca CR <CR	 75 28	<0.001	 63 9	<0.001
CD19 status Positive Negative	 32 26	0.62	 14 21	0.48
Prior CAR T-cell therapy Yes No	 30 35	0.54	 15 12	0.54
Prior tafasitamab Yes No	 27 33	0.65	 6 16	0.24
N of prior therapies >3 ≤3	 33 30	0.74	 14 13	0.83
Age >75 years Yes No	 32 26	0.08	 14 21	0.89

Bulky disease defined as <10 cm. ORR: overall response rate; CR: complete response; HBGL: high-grade B-cell lymphoma; GCB: germinal center B-cell; LDH: lactate dehydrogenase; Lonca: loncastuximab-teserine; CAR: chimeric antigen receptor.

Outcomes

The primary endpoint for this analysis was CRR according to the Lugano criteria.[17] Secondary endpoints included ORR, event-free survival (EFS), defined as the time from start of Lonca therapy to disease progression or change in therapy (censored at death or last follow-up), and OS, defined by time from start of Lonca therapy to death from any cause.

Statistical methods

Baseline characteristics were summarized using descriptive statistics. The impact of categorical variables on CRR and ORR were analyzed using the Fisher exact test. EFS and OS curves were constructed using Kaplan-Meier estimates and compared via the log-rank test. A Cox proportional-hazard model was used to analyze the impact of the same clinicopathological characteristics on EFS and OS. Statistical significance was defined as a *P* value of ≤0.05 for all analyses. R version 1.4.1106 (Boston, MA, USA) was used for the analyses.

Results

Patients

A total of 187 patients from 21 US centers were deemed eligible and included in the final analysis. Eighty-seven patients (47%) would have been ineligible for LOTIS-2 on the basis of renal function, bulky disease, central nervous system involvement, CD19 status, or performance status. As the age distribution listed in Table 1 shows, 39% of the patients were ≤65 years of age and 21% ≥75 years; 64% were male. Eighty-six percent had advanced stage disease (stage III or IV) and 65% had an International Prognostic Index score ≥3. Seven percent of patients had an Eastern Cooperative Oncology Group performance status >2, 19% had an estimated glomerular filtration rate <60 mL/min/1.73 m², and 17% had bulky disease, as defined by a tumor ≥10 cm in longest dimension at the time of starting Lonca treatment.

With regards to prior treatments, the majority of patients (81%) had received more than three prior lines of therapy

for LBCL, with a median of four (interquartile range, 1-7). One-quarter had primary refractory disease as defined by stable or progressive disease after first-line therapy. Sixteen percent had previously undergone autologous stem cell transplantation and 60% had previously received CAR T-cell therapy. The median time from CAR T-cell therapy to Lonca treatment was 7.7 months. Seventy-seven percent of patients experienced progressive disease as the best response to the most recent line of therapy prior to Lonca. A total of 160 patients had full histopathological data available for analysis. Twenty-two percent of patients had high-grade B-cell lymphoma (HGBL) as defined by the 5th Edition of the World Health Organization classification, with the majority (89%) of the HGBL patients having double-hit lymphoma with *MYC* and *BCL2* rearrangements or triple-hit with *BCL6, BCL2*, and *MYC*.[18] Thirty-eight percent of patients were classified as having non-germinal center B-cell (non-GCB) subtype by the Hans algorithm.[19]

CD19 status was available for 128 patients. The majority (85%) were CD19-positive prior to Lonca. Eighty percent of patients who had received prior CAR T-cell therapy had a known CD19 status and 78% were positive. Of the 98 patients who had been given CAR T-cell therapy as their only anti-CD19 therapy, 81 (83%) had known CD19 status, and 67 (83%) were CD19-positive. Among the 19 patients who had received tafasitamab/lenalidomide as their only anti-CD19 therapy, four (21%) had known CD19 status, and all were CD19-positive. Fourteen patients had received both tafasitamab/lenalidomide and CAR T-cell therapy prior to Lonca, nine of whom had known CD19 status, and four (45%) were CD19-positive.

Outcomes

The median follow-up time was 12.5 months (range, 0.1-24.1 months). The CRR was 14% (95% confidence interval: 10-20%) and the ORR was 32% (95% confidence interval: 26-39%) with a median duration of treatment of 42 days. Among evaluated clinicopathological characteristics, HGBL and bulky disease were significantly associated with inferior response rates. Those with HGBL demonstrated a CRR and ORR of 3% and 8%, respectively, compared to 15% and 34% in patients without HGBL (Table 2). There was no statistically significant difference in CRR or ORR between patients with *BCL2/MYC or BCL6/MYC* alterations. Similarly, patients with bulky disease had a CRR and ORR of 0% and 16% compared to 16% and 35% in those patients without bulky disease. An elevated lactate dehydrogenase concentration at the time of starting Lonca treatment was also associated with statistically significant inferior responses with CRR and ORR of 8% and 25%, respectively, compared to 30% and 51%, respectively, in patients with normal lactate dehydrogenase levels. A complete response to the last therapy prior to Lonca treatment (CRR 63% *vs*. 9% and ORR 75% *vs*. 28%) and a non-GCB subtype (CR 25% *vs*. 6% and ORR 43% *vs*. 24%) were associated with significantly superior response to Lon-

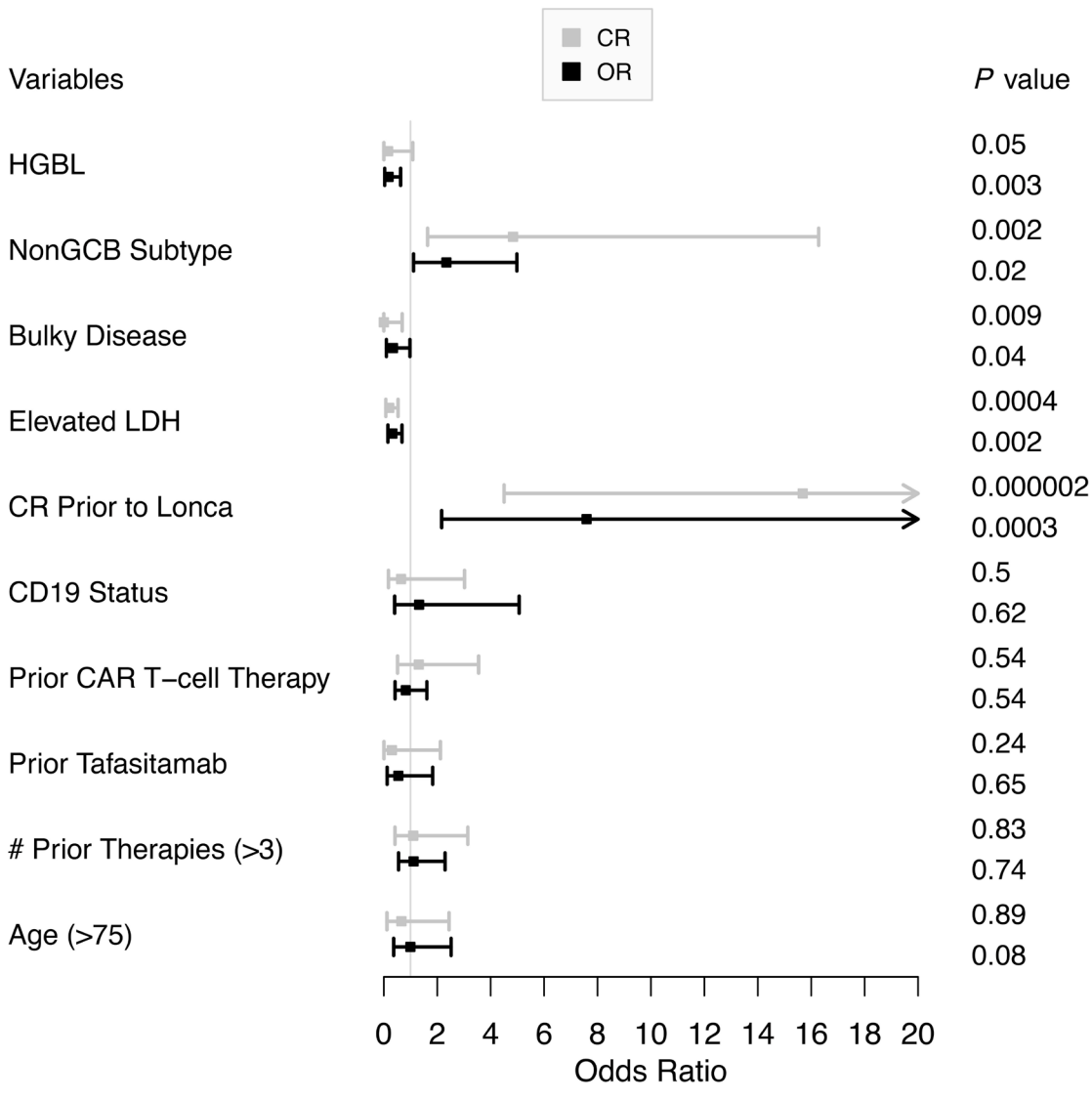

Figure 1. Forest plot for complete response and overall response by clinicopathological features at the start of treatment with loncastuximab-teserine. CR: complete response; OR: overall response; HBGL: high-grade B-cell lymphoma; GCB: germinal center B-cell; LDH: lactate dehydrogenase; CAR: chimeric antigen receptor.

ca. When accounting for patients with double-hit lymphoma, non-GCB subtype remained significant with CRR and ORR of 23% and 40%, respectively, compared to 7% and 26% in the GCB cohort (*P*=0.04 for complete response). These findings are visually summarized in Figure 1. Aside from the higher proportion of HGBL among patients with the GCB subtype, there were no statistically significant differences in baseline characteristics according to GCB or non-GCB subtype. However, a higher proportion of non-GCB patients had a compete response as best response to therapy prior to administration of Lonca (15% *vs*. 5%, *P*=0.04). Multivariate logistic regression corroborated these findings (Table 3).

Notably, in our cohort, CD19 status as assessed by institutional standards, prior CAR T-cell therapy, number of prior lines of therapy, and age (< or ≥ 75 years) were not significantly associated with response rates. Patients with CD19-negative disease had an ORR and CRR of 26% and 21%, respectively. However, with respect to time from CAR T-cell therapy to Lonca treatment, those who received Lonca within 100 days had significantly lower CRR (0% *vs*. 13%, *P*=0.04) and ORR (15% vs. 35%). Of note, patients requiring Lonca within 100 days were almost uniformly refractory to CAR T-cell therapy (18/20, 90%).

The median EFS and OS were 2.1 and 4.6 months, respectively (Figure 2). Similar high-risk features including HGBL, bulky disease, and elevated lactate dehydrogenase concentration were associated with significantly inferior survival (Table 4). Both a complete response prior to Lonca (median not reached *vs*. 1.9 months, *P*<0.01) and non-GCB subtype (median 2.8 *vs*. 1.8 months, *P*=0.04) were associated with significantly superior EFS. However, when accounting for enrichment of the GCB subgroup with double-hit patients, the difference was no longer statistically significant with median EFS of 2.7 *vs*. 2.1 months (*P*=0.2) in patients with non-GCB and GCB subtypes, respectively. Multivariate Cox regression analysis for EFS and OS is displayed in *Online Supplementary Table S1*.

Again, CD19 status and prior CAR T-cell therapy were not associated with a statistically significant difference in EFS or OS. Stratified by response to Lonca, patients achieving a complete response to Lonca demonstrated significantly superior survival compared to those patients who failed to achieve a complete response (median EFS not reached *vs*. 1.8 months, *P*<0.001 and median OS 12.6 *vs*. 3.9 months, *P*<0.001) (Figure 3).

Data were collected regarding five pre-specified adverse events: pleural and pericardial effusion, edema, rash, and cytopenia of any kind (Table 5). Thirty-five percent of patients were reported to experience at least one adverse event with 14% discontinuing treatment due to an adverse event. Cytopenias were both most commonly reported (17%) and the most cited cause of discontinuation (7%). Peripheral edema was reported in 11% of patients.

Data were obtained for 53 (28%) patients who received additional therapies after Lonca. The most common subsequent therapy was immunochemotherapy (31%). Six (10%) patients received CAR T-cell therapy, of whom three had a complete

Table 3. Multivariate logistic regression of response rates.

Factor	Adjusted odds ratio for CR	*P*	Adjusted odds ratio for ORR	*P*
Non-GCB	4.2	0.05	1.7	0.22
Elevated LDH	0.3	0.08	0.5	0.11
HGBL	0.3	0.14	0.4	0.04
Bulky disease	NA (no patients with CR)	-	0.3	0.10
CR prior to Lonca	4.0	0.002	15.2	0.01

Bulky disease defined as <10 cm. CR: complete response; ORR: overall response rate; GCB: germinal center B-cell; LDH: lactate dehydrogenase; HBGL: high-grade B-cell lymphoma; NA: not applicable; Lonca: Lonca: loncastuximab-teserine.

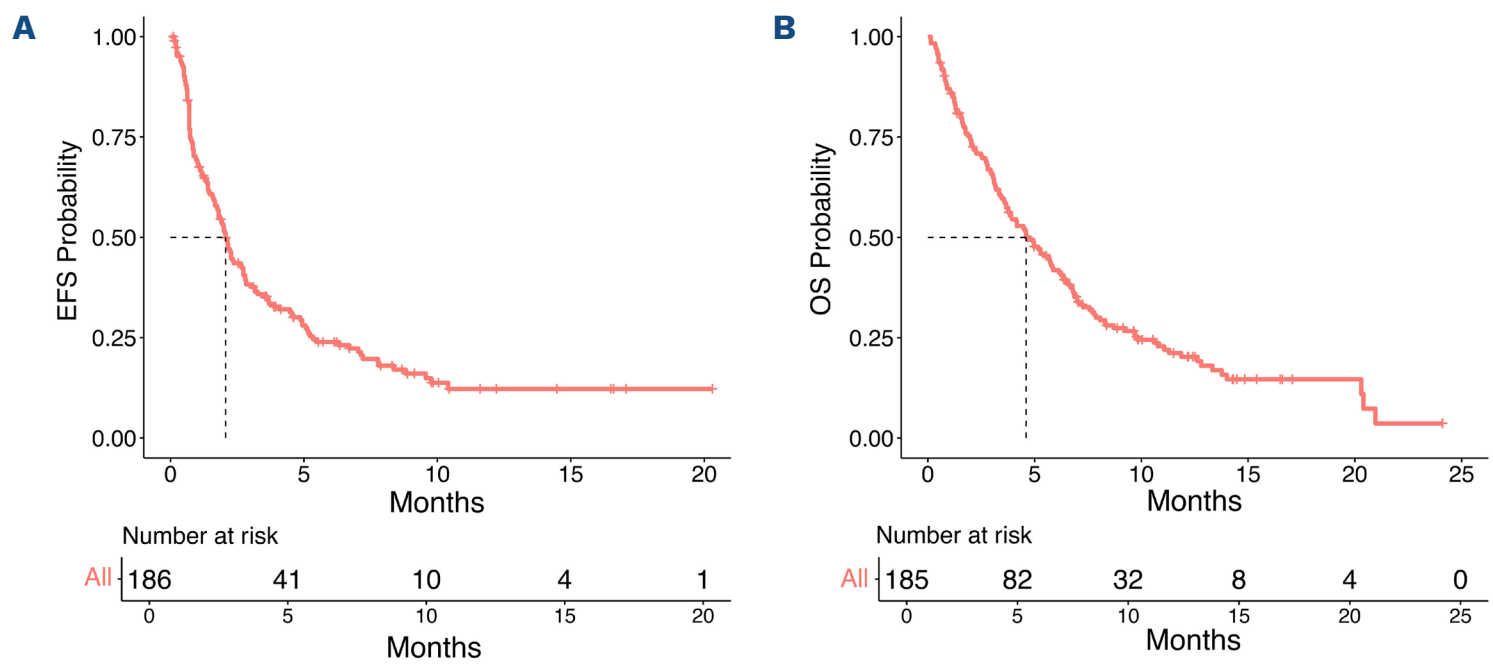

Figure 2. Outcome analysis of patients treated with loncastuximab-teserine. (A) Event-free survival for all patients. (B) Overall survival for all patients. EFS: event-free survival; OS: overall survival.

response (CRR 50%), and ten (17%) received tafasitamab/lenalidomide with a CRR of 10%. Additionally, four patients received Lonca as a bridge to CAR T-cell therapy and were excluded from all other analyses. In these four patients, the ORR to Lonca was 25% and the CRR to subsequent CAR T-cell therapy was 50% with a median OS of 6.0 months.

Discussion

In our study, we found outcomes of Lonca treatment were inferior to those reported in the pivotal LOTIS-2 study. Our cohort was enriched with higher risk and more heavily pretreated patients including those with HGBL, bulky disease, and more than three lines of prior therapy which likely contributed to the inferior outcomes reported here. Although small in numbers, our analysis also included patients who would have been excluded from the prospective clinical trial according to Eastern Cooperative Oncology Group performance status, renal function, bulky disease and CD19-negative status, accounting for 47% of our cohort. A retrospective analysis which included 40 patients treated with Lonca in the real-world setting has demonstrated comparable outcomes, with a median EFS and median OS of 3.0 and 4.7 months, respectively (Nastoupil *et al.*, ASH 2023).

We performed a subset analysis of those patients who would have been potentially egible for the LOTIS-2 trial. This analysis included 100 (53%) patients with ORR and

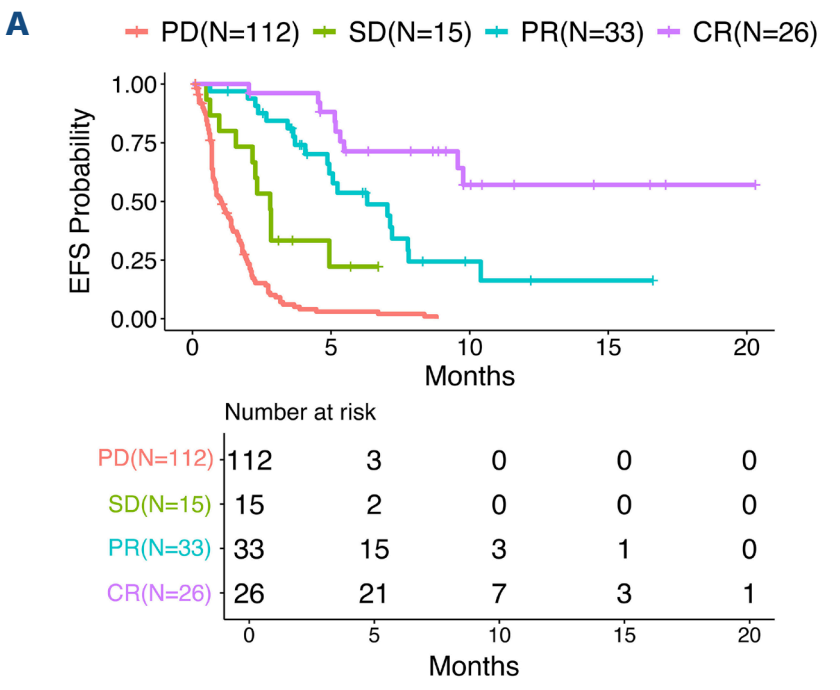

Figure 3. Outcomes stratified by response to loncastuximab-teserine. (A) Event-free survival. The median event-free survival for patients who had a complete response, partial response, stable disease and progressive disease was not reached (NR) (9.6-NR), 6.3 (4.9-10.4), 2.8 (2.2-NR), and 0.9 (0.7-1.4) months, respectively. (B) Overall survival. The median overall survival for patients who had a complete response, partial response, stable disease and progressive disease was 12.6 (10.6-NR), 7.6 (6.2-NR), 5.3 (3.6-NR), and 2.8 (2.0-3.3) months, respectively. EFS: event-free survival; PD: progression of disease; SD: stable disease; PR: partial response; CR: complete response; OS: overall survival.

Table 4. Survival by baseline characteristics.

Factor	Median EFS in months	*P*	Median OS in months	*P*
HGBL				
Yes	0.7	<0.001	1.9	0.002
No	2.2		4.8	
Cell of origin				
Non-GCB	2.8	0.04	5.7	NS
GCB	1.8		3.7	
Bulky disease				
Yes	1.1	0.004	3.1	0.004
No	2.2		5.4	
Elevated LDH				
Yes	1.8	<0.001	3.7	<0.001
No	5.5		9.8	
Response prior to Lonca				
CR	NR	<0.001	10.8	0.008
<CR	1.9		4.5	

Bulky disease defined as <10 cm. EFS: event-free survival; OS: overall survival; HBGL: high-grade B-cell lymphoma; GCB: germinal center B-cell; NS: not statistically significant; LDH: lactate dehydrogenase; Lonca: loncastuximab-teserine; CR: complete response; NR: not reached.

Table 5. Adverse events of interest.

Adverse event	Incidence N (%)	Main reason for discontinuation N (%)
Pleural effusion	6 (3)	1 (<1)
Peripheral edema	21 (11)	7 (4)
Pericardial effusion	1 (<1)	0 (0)
Rash	18 (10)	7 (4)
Cytopenia	31 (17)	13 (7)

CRR of 34% and 16% and a median EFS and median OS of 2.1 and 4.9 months, respectively, similar to the overall cohort described above. While these subjects were "eligible" according to available data in the electronic health records collected for this analysis, the similarly poor outcomes here likely reflect the high-risk features often prevalent in patients treated in the standard-of-care setting who do not make it onto prospective clinical trials, such as rapidly progressive disease and need for urgent therapy, which are not easily captured objectively within the medical records. We found consistent clinicopathological factors which were predictive of both poor response and inferior survival. Specifically, HGBL, bulky disease, and elevated lactate dehydrogenase level were predictive of poor response and inferior EFS and OS compared to patients without these characteristics. A prior subset analysis of the LOTIS-2 study did report a higher CRR of 33% in patients with double/triple-hit HGBL, although there were only 15 patients in this category included on the prospective study, making this finding hard to interpret.[20] Notably, no patient with bulky disease in our study obtained a complete response. This is in line with initial findings in the LOTIS-1/2 study in which patients with bulky disease of ≥10cm were excluded due to lack of benefit with Lonca. While these well-accepted high-risk features should not warrant dismissal of Lonca as a potential therapy on their own, this finding should be taken into consideration when choosing the optimal candidate for Lonca treatment.

In contrast, there were also consistent factors which predicted improved response and survival with Lonca. As one might expect, those patients who achieved a complete response to the last therapy prior to Lonca demonstrated persistently favorable outcomes. Of particular interest here seems to be the improved outcomes among those with non-GCB subtype even after accounting for the enrichment of the GCB subgroup of patients with double-hit lymphoma. This finding is of unclear significance at this time, without any clear biological rationale, but it certainly merits further thought. Interestingly, similar observations have been noted with various polatuzumab-based regimens also for reasons that remain not fully elucidated.[21,22]

Our current analysis is of particular importance due to the high proportion of patients receiving multiple CD19-directed therapies, with prior CAR T-cell exposure in 60% of patients compared to only 9% of those in the LOTIS-2 study. Although prior CAR T-cell therapy was associated with higher rates of CD19-negative disease (22% *vs*. 0%, *P*=0.005), the majority of patients still maintained CD19 positivity following CAR T-cell failure, as has been documented previously.[23] Similarly, a higher proportion of CD19 negativity was seen in tafasitamab-exposed patients and this was even more marked among patients who had received both CAR T-cell therapy and tafasitamab. However, there was no significant difference in outcomes according to CD19 status prior to Lonca treatment, consistent with other published data.[24] Regardless of CD19 status, neither prior CAR T-cell therapy nor tafasitamab/lenalidomide exposure was associated statistically significant differences in outcomes. While patients should still be biopsied following progression on any CD19-directed therapy, the importance of the results remains unclear.

It should be emphasized that, while overall prior CAR T-cell exposure did not portend inferior outcomes, time from CAR T-cell treatment to administration of Lonca is important. Patients receiving Lonca within 100 days of CAR T-cell therapy experience poor outcomes, likely reflective of the highly aggressive nature of large B-cell lymphoma that is refractory to CAR T-cell therapy. This finding should inform practice in treating clinicians trying to choose therapies in this clinical setting. Alternatively, outcomes among patients >100 days from CAR T-cell therapy mirrored those of the general cohort.

Our study is limited by the often-cited and well-recognized limitations of retrospective studies including, but not limited to, unmeasured confounders and selection bias. Lonca treatment was determined according to the treating physician and was variable between both institutions and clinicians. Furthermore, treatment response was determined according to institutional protocols with either positron emission tomography and computed tomography scan or computed tomography scan alone. Details regarding adverse events were imperfectly collected as these were extracted from clinic notes and electronic documentation and were not regulated in a prospective manner. As such, the likely rate of adverse events is potentially higher than reported here.

In addition, CD19 status was not uniformly collected or standardized. Our data reflect CD19 status determined by both flow cytometry and immunohistochemistry and, at this time, it remains unclear whether the method of detection matters.[24] Prior data demonstrate that CD19 status determined by immunohistochemistry is not predictive of response to Lonca, but the importance of CD19 status assessed by flow cytometry is unknown.

There continue to be gaps in clinical data regarding the proper sequencing of therapies in relapsed DLBCL as we have no prospective, direct comparisons between many of the newly approved novel agents. As is seen with other agents, real-world outcomes here fall short of those reported on the clinical trial examining Lonca in R/R DLBCL. However, this study offers insight into the appropriate patients who may derive durable remissions with this overall well-tolerated therapy. It is possible that with better patient selection and with combination therapies currently under investigation with Lonca, we will see better outcomes in the future.

Disclosures

ECA is a member of a Board of Directors or advisory committee for ADC Therapeutics and Genentech. YS has received

research funding from Beigene, TG Therapeutics, and Celgene/BMS. ND has received research funding from EUSA Pharma, a Recordati Group company, and Gilead Sciences. JB has received research funding from Kite Pharma-Gilead, Genentech-Roche, Regeneron Pharmaceuticals, and Cellular Biomedicine Group; and has participated in speakers' bureau for Kite Pharma-Gilead. SFH has provided consultancy services for Janssen Pharmaceuticals, Epizyme, Seagen Inc, Pharmacyclics LLC, AbbVie, Genentech, Merck, TG Therapeutics, Arvinas, Novartis, AstraZeneca, Bayer Healthcare, BeiGene, Servier Pharmaceuticals LLC, Tyme Inc, and ADC Therapeutics. MN has received honoraria and research funding from Genentech-Roche, Kite, and ADC Therapeutics; has received honoraria from AbbVie; and has received research funding from Gilead, TG Therapeutics, BeiGene, EUSA, and Adaptive. ZF is a member of the Board of Directors or an advisory committee for Seagen; and has received research funding from Roche, Sanofi, Antegene, AstraZenica, Genmab, AbbVie, Acerta, BeiGene, and Merck. SDS is a member of the Board of Directors or an advisory committee for BeiGene; has received research funding from ADC Therapeutics, AstraZeneca, Bayer, BeiGene, De Novo Biopharma, Enterome, Epizyme, Genentech, Inc., Incyte Corporation, Kymera Therapeutics, Merck Sharp and Dohme Corp., MorphoSys, and Nanjing Pharmaceu; has sat on advisory boards for ADC Therapeutics, AstraZeneca, BeiGene, Epizyme, Karyopharm, Kite Pharmacutical, Incyte, Numab Therapeutics AG, AbbVie and Coherus Biosciences; and has provided consultancy services for Genentech Inc; his spouse has received research funding from Ayala, Bristol Myers Squibb, and Ignyta. AW has provided consultancy services for BeiGene, AstraZeneca, Seattle Genetics, Janssen, and ADC Therapeutics. DL is a member of the Board of Directors or an advisory committee for Epizyme; Novartis, Calithera, ADC Therapeutics, Karyopharm, and Morphosys; and has received research funding from Curis. MH has received research support or funding from ADC Therapeutics, Spectrum Pharmaceuticals, and Astellas Pharma; has provided consultancy services for ADC Therapeutics, Omeros, BMS, Kite, AbbVie, Genmab, Allovir, CRISPR, Caribou, Autolus, Forte Biosciences; and participated in speakers' bureau for ADC Therapeutics, AstraZeneca, Kite, and Beigene. JR has provided consultancy services for Kite, Astra Zeneca, and ADC Therapeutics. RA is a member of the Board of Directors or an advisory committee for Epizyme, Genentech, Beigene, Incyte, ADC Therapeutics, and Roche; and has received research funding from Regeneron, ADC Therapeutics, Cyteir, Merck, Gilead, and Seagen. PCJ has received research funding from Medically Home; and provided consultancy services for and received research funding from ADC Therapeutics, AstraZeneca, AbbVie, Seagen, BMS, and Incyte. NSG has provided consultancy services for and received honoraria from ADC Therapeutics; is a current holder of stock options of Sangam; has received honoraria from Novartis, Caribou Biosciences, Seagen, Genentech, and Kite; has received research funding from Tessa Therapeutics; and has provided consultancy services for Seattle Genetics. JLC has provided consultancy services for ADC Therapeutics, Genmab, Karyopharm, Incyte, Kite, and Seagen; and has received research funding from Roche, Merck, Abbvie, and Bayer. LJN has received honoraria from ADC Therapeutics, DeNovo, AbbVie, Regeneron, and AstraZeneca; and has received honoraria and research funding from Caribou Biosciences, Daiichi Sankyo, Genentech Inc., Genmab, Gilead/Kite, Janssen, Merck, Novartis, Takeda, Bristol Myers Squibb/Celgene. NE has received research funding from Beigene, Lilly, and Incyte; participated in speakers' bureau for Biegene and Genentech; has been a member of an advisory board for ADC Therapeutics and has received an honorarium from Novartis. The other authors have no conflicts of interest to disclose.

Contributions

VZ and ECA collected and analyzed data and wrote the manuscript. AG, YA, KA, AS, ND, DQ, BA, BK, JB, PC, SFH, JS, SB, MN, SL, ZF, CH, SDS, AW, DL, FF, MH, KB, JR, HA, JL, LB, RA, BU, PCJ, NSG, MM, JLC, NS, CS, LJN, and NE collected data and helped to edit and/or revise the manuscript.

Data-sharing statement

Data will not be shared openly to protect patients' privacy but may be accessed on a case-by-case basis upon request.

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