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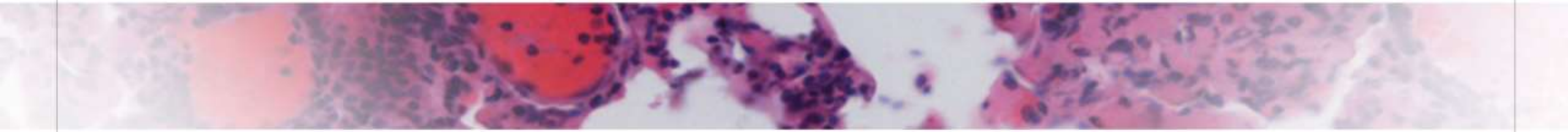

Efficacy and Safety of Loncastuximab Tesirine (ADCT-402) in Relapsed/Refractory Diffuse Large B-Cell Lymphoma

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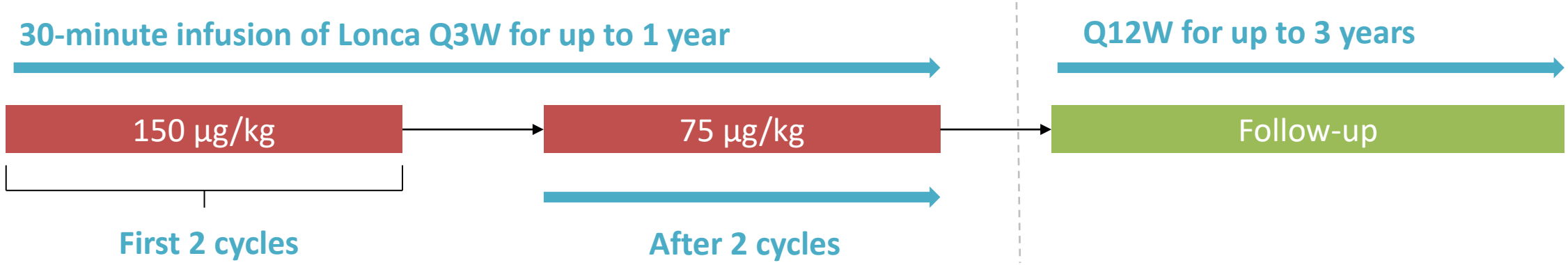
Poster slides, 62nd ASH Annual Meeting and Exposition Virtual Meeting, December 5–8, 2020

Poster session I, Saturday, December 5, 2020: 7:00 am – 3:30 pm (Pacific Time)

Introduction and Methods

- Patients with R/R DLBCL have a poor prognosis and unmet need for new treatment options[1,2]
- Lonca comprises a humanized anti-CD19 antibody conjugated to a potent PBD dimer toxin[3]

Lonca had substantial antitumor activity and an acceptable safety profile in this single-arm open-label Phase 2 study (NCT03589469) in adult patients with R/R DLBCL, who had failed ≥2 established therapies[4]



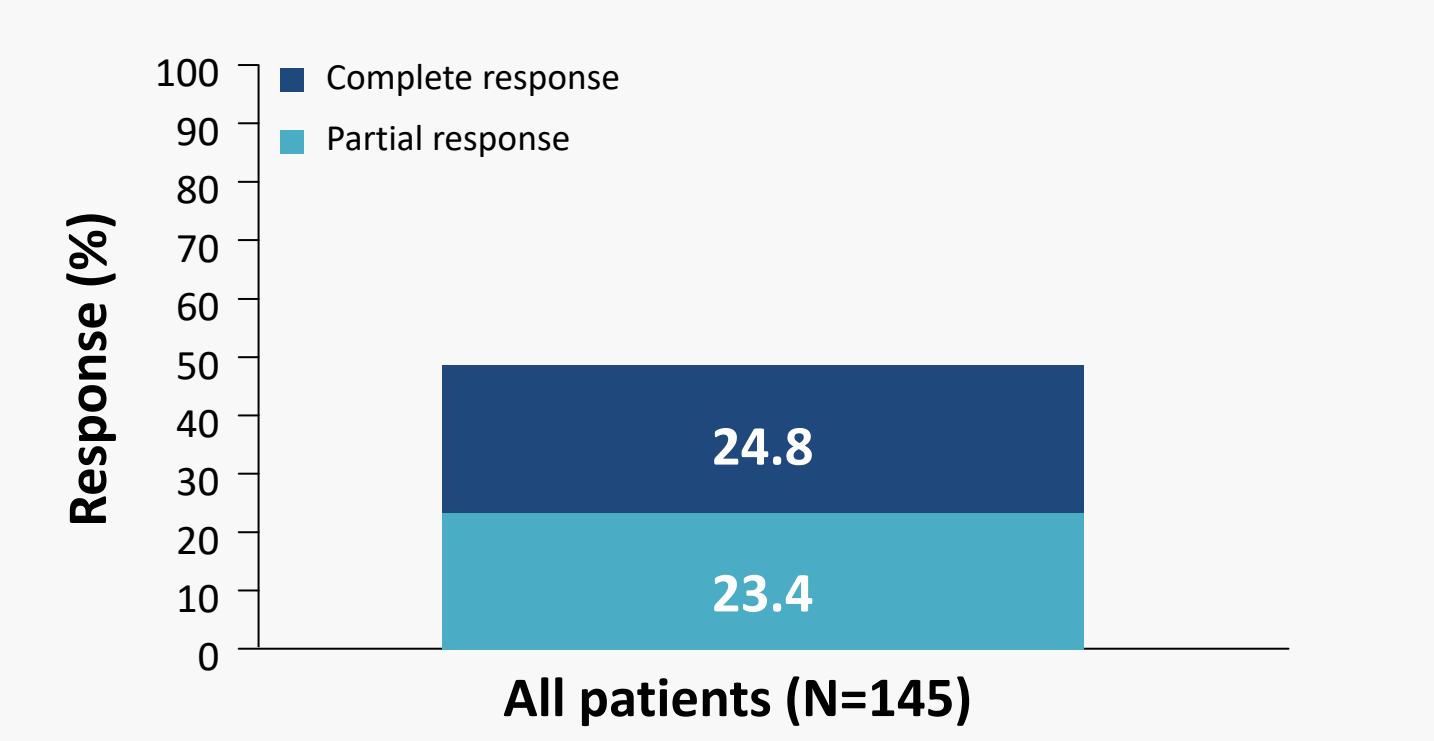
Here, we present updated results including analysis of response in subgroups with high risk for poor prognosis

- Pre-specified analyses of ORR and DoR by demographic and clinical characteristics were performed

1. Levin A, Shah NN. *Am J Hematol* 2019;94:S18–S23; 2. Nagle SJ, et al. *Am J Hematol* 2013;88(10):890–4; 3. Zammarchi F, et al. *Blood* 2018;131(10):1094–105;
4. Carlo-Stella C, et al. EHA Congress 2020. Abstract S233.

DLBCL, diffuse large B-cell lymphoma; **DoR**, duration of response; **Lonca**, loncastuximab tesirine; **ORR**, overall response rate; **PBD**, pyrrolobenzodiazepine; **Q3W**, every 3 weeks; **Q12W**, every 12 weeks; **R/R**, relapsed/refractory.

Efficacy Results – ORR



Lonca ORR:

48.3%

(95% CI: 39.9, 56.7)

Lonca CRR:

24.8%

(95% CI: 18.0, 32.7)

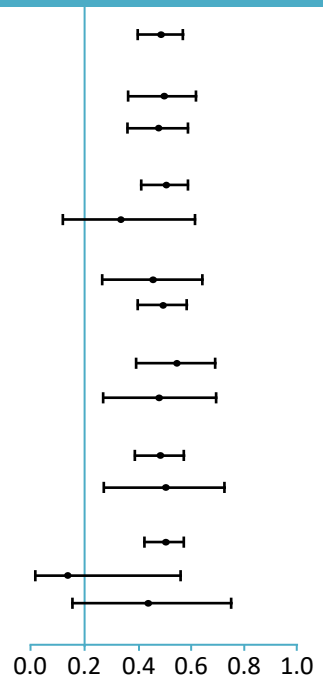
Most responders had a response after 2 cycles; median time to first response was 41.0 days (range: 35–247)
Mean Lonca cycles: 4.5 (Std: ± 3.89) (Min, max: 1, 18)*

ORR was assessed by independent reviewer. Data cut-off: 06 August, 2020. *4 patients had treatment ongoing at data cut-off.
CI, confidence interval; **CRR**, complete response rate; **Lonca**, loncastuximab tesirine; **max,** maximum; **min**, minimum; **ORR**, overall response rate; **Std**, standard deviation.

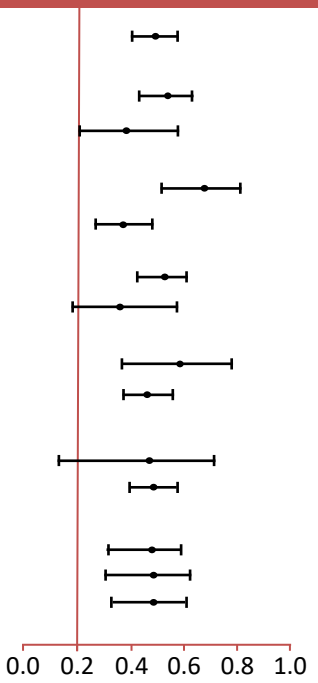
Efficacy Results – ORR

High-risk subgroup analysis of ORR

Subgroup	Patients (n/N)	ORR	ORR (95% CI)
All	70/145		48.3 (39.9, 56.7)
Age			
<65 years	32/65		49.2 (36.6, 61.9)
≥65 years	38/80		47.5 (36.2, 59.0)
Double/triple hit			
No	65/130		50.0 (41.1, 58.9)
Yes	5/15		33.3 (11.8, 61.6)
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)
Double/triple expressor			
No	60/125		48.0 (39.0, 57.1)
Yes	10/20		50.0 (27.2, 72.8)
WHO classification			
DLBCL NOS	64/127		50.4 (41.4, 59.4)
PMBCL	1/7		14.3 (0.4, 57.9)
HGBCL	5/11		45.5 (16.7, 76.6)



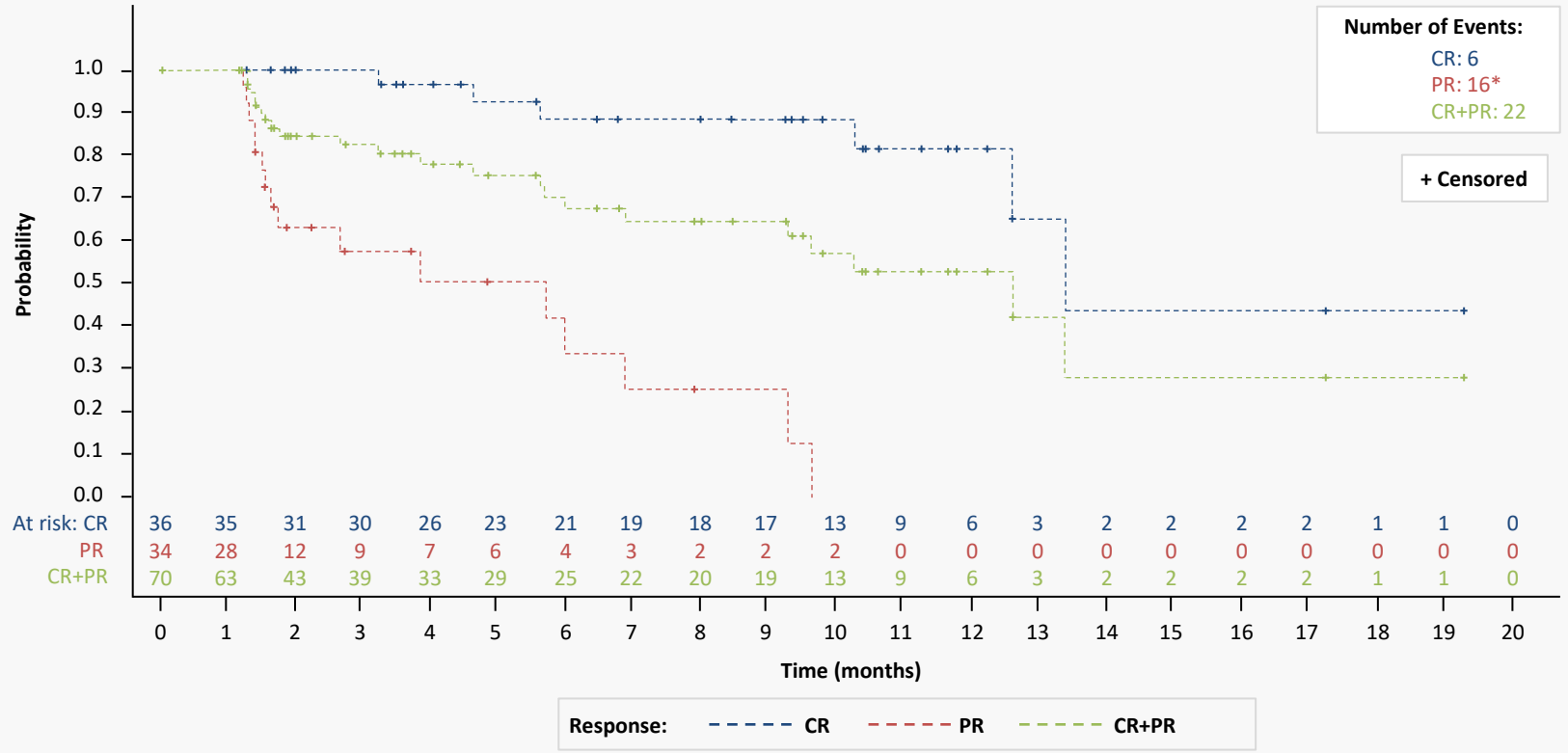
Subgroup	Patients (n/N)	ORR	ORR (95% CI)
All	70/145		48.3 (39.9, 56.7)
First-line response*			
Relapse	53/99		53.5 (43.2, 63.6)
Refractory†	11/29		37.9 (20.7, 57.7)
Last-line response*			
Relapse	29/43		67.4 (51.5, 80.9)
Refractory†	31/84		36.9 (26.6, 48.1)
Response to any prior line*			
Relapse	60/115		52.2 (42.7, 61.6)
Refractory†	9/25		36.0 (18.0, 57.5)
Prior stem cell transplant			
Yes	14/24		58.3 (36.6, 77.9)
No	56/121		46.3 (37.2, 55.6)
Prior CAR-T 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)



Encouraging ORRs were seen in high-risk subgroups

ORR was assessed by independent reviewer. *Prior systemic therapies. †Refractory disease defined as no response to therapy. Data cut-off: 06 August, 2020.
ABC, activated B-cell-like; **CAR-T**, chimeric antigen receptor T-cell; **CI**, confidence interval; **CRR**, complete response rate; **DLBCL**, diffuse large B-cell lymphoma; **GCB**, germinal center B-cell-like; **HGBCL**, high grade B-cell lymphoma; **NOS**, not otherwise specified; **ORR**, overall response rate; **PMBCL**, primary mediastinal B-cell lymphoma; **WHO**, World Health Organization.

Efficacy Results – DoR



mDoR for the 70 responders:
12.58 months
(95% CI: 6.87, -)

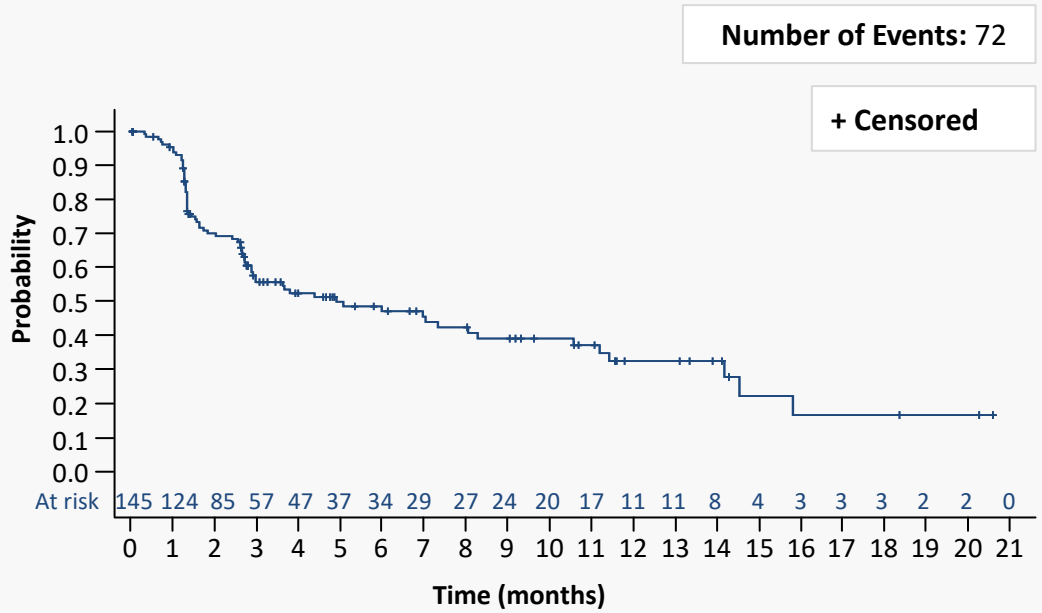
mDoR for patients with a CR:
13.37 months
(95% CI: 12.58, -)

mDoR was comparable to the whole study population in subgroups at high risk of poor prognosis
Patients continue to be followed for DoR

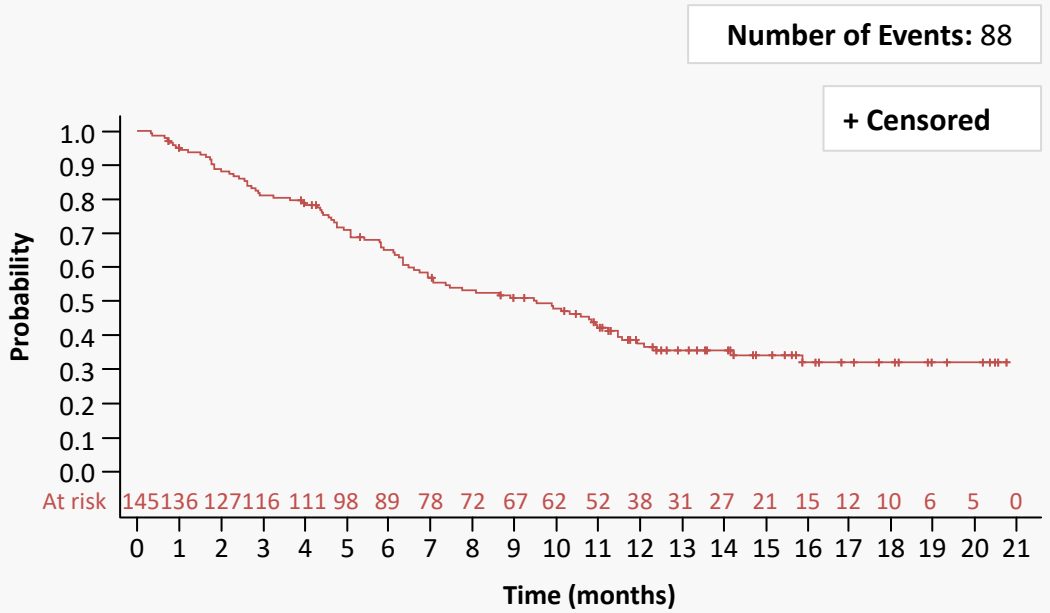
DoR was defined as the time from earliest date of first response until the first date of either disease progression or death due to any cause. *mDoR for patients with a PR: 5.68 months (95% CI: 1.64, 6.87).
Data cut-off: 06 August, 2020
CI, confidence interval; **CR** complete response; **mDOR**, median duration of response; **PR**, partial response.

PFS, OS, and Subsequent Treatment Results

Median PFS: 5.09 months (95% CI: 2.89, 8.31)



Median OS: 9.53 months (95% CI: 6.93, 11.24)



Subsequent Treatment

- **15 patients** received CD19-directed CAR-T therapy with an investigator-assessed ORR of 46.7% (6 CR; 1 PR)
- **9 patients** proceeded to SCT as consolidation after Lonca response

Data cut-off: 06 August, 2020.

CAR-T, chimeric antigen receptor T-cell; **CI**, confidence interval; **CR**, complete response; **Lonca**, loncastuximab tesirine; **ORR**, overall response rate; **OS**, overall survival; **PFS**, progression-free survival; **PR**, partial response; **SCT**, stem cell transplant.

Safety Results

TEAEs in ≥20% of the all-treated population			
	Patients n (%)		
Preferred term	<65 years (N=65)	≥65 (N=80)	Total (N=145)
Patients with any TEAE	65 (100)	78 (97.5)	143 (98.6)
GGT increased	33 (50.8)	27 (33.8)	60 (41.4)
Neutropenia	34 (52.3)	24 (30.0)	58 (40.0)
Thrombocytopenia	28 (43.1)	20 (25.0)	48 (33.1)
Fatigue	21 (32.3)	19 (23.8)	40 (27.6)
Anemia	23 (35.4)	15 (18.8)	38 (26.2)
Nausea	17 (26.2)	17 (21.3)	34 (23.4)
Cough	19 (29.2)	13 (16.3)	32 (22.1)
Alkaline phosphatase increased	18 (27.7)	11 (13.8)	29 (20.0)
Peripheral edema	11 (16.9)	18 (22.5)	29 (20.0)

Most common (≥10%) grade ≥3 TEAEs were:

- Neutropenia (38 patients; 26.2%)
- Thrombocytopenia (26 patients; 17.9%)
- GGT increased (25 patients; 17.2%)
- Anemia (15 patients; 10.3%)

Treatment-related TEAEs leading to treatment discontinuation occurred in 26 (17.9%) patients, most commonly (≥2%):

- GGT increased (16 patients; 11.0%)
- Peripheral edema (4 patients; 2.8%)
- Localized edema (3 patients; 2.1%)

No increase in toxicity was seen in patients aged ≥65 years compared with younger patients

TEAEs were reported for the all-treated population. Data cut-off: 06 August, 2020.
GGT, gamma-glutamyltransferase; **TEAE**, treatment-emergent adverse event.

Conclusions

Lonca had substantial single-agent antitumor activity in patients with R/R DLBCL; ORR was 48.3% and CRR was 24.8%

Durable responses were reported (mDoR 12.58 months), particularly in patients achieving a CR (mDoR 13.37 months)

Encouraging and durable responses were observed in high-risk patient groups, including double- or triple-hit, transformed or refractory DLBCL, and notably in those who had progression after prior CAR-T therapy

No new safety concerns were identified and no increase in toxicity was observed in patients aged ≥65 years

CAR-T, chimeric antigen receptor T-cell; **CR**, complete response; **CRR**, complete response rate; **DLBCL**, diffuse large B-cell lymphoma; **Lonca**, loncastuximab tesirine; **mDoR**, median duration of response; **ORR**, overall response rate; **R/R**, relapsed or refractory.

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