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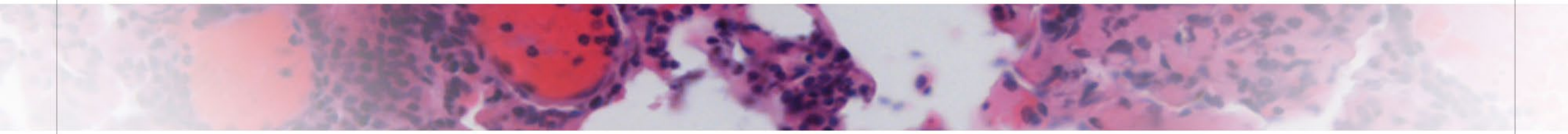

Interim Results of Loncastuximab Tesirine Combined With Ibrutinib in Diffuse Large B-Cell Lymphoma or Mantle Cell Lymphoma (LOTIS-3)

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Introduction

- This two-part, open-label, single-arm Phase 1/2 study (NCT03684694) is evaluating Lonca and ibrutinib in patients with R/R DLBCL and patients with R/R MCL

- Patients with R/R DLBCL and patients with R/R MCL have a poor prognosis and the development of an effective and less toxic salvage treatment remains an unmet need[1,2]

Loncastuximab tesirine (Lonca) is an ADC comprising a humanized monoclonal anti-CD19 antibody conjugated to a pyrrolobenzodiazepine (PBD) dimer toxin, through a protease cleavable valine-alanine linker

Ibrutinib is a small-molecule inhibitor of BTK

- Approved for use in MCL, CLL/SLL, WM, MZL, and cGVHD[3]

- We present updated **Phase 1** data for patients receiving the MTD of Lonca 60 µg/kg Q3W and ibrutinib 560 mg/day
  - Initial Phase 1 results identified the MTD[4]

This trial combines an investigational treatment with a licensed drug (ibrutinib) used outside of its label.

1. Levin A, Shah, NN. *Am J Hematol* 2019;94: S18–S23; 2. Maddocks K, *Blood* 2018;132:1647–56; 3. Janssen Biotech, Ibrutinib PI, April 2020; 4. Depaus J, *et al.* EHA 2020. Abstract 1284.

ADC, antibody-drug conjugate; **BTK**, Bruton's tyrosine kinase; **cGVHD**, chronic graft-versus-host disease; **CLL**, chronic lymphocytic leukemia; **DLBCL**, diffuse large B-cell lymphoma; **Lonca**, loncastuximab tesirine; **MCL**, mantle cell lymphoma;
MTD, maximum tolerated dose; **MZL**, marginal zone lymphoma; **PBD**, pyrrolobenzodiazepine; **Q3W**, every 3 weeks; **R/R**, relapsed/refractory; **SLL**, small lymphocytic lymphoma; **WM**, Waldenström's macroglobulinemia.

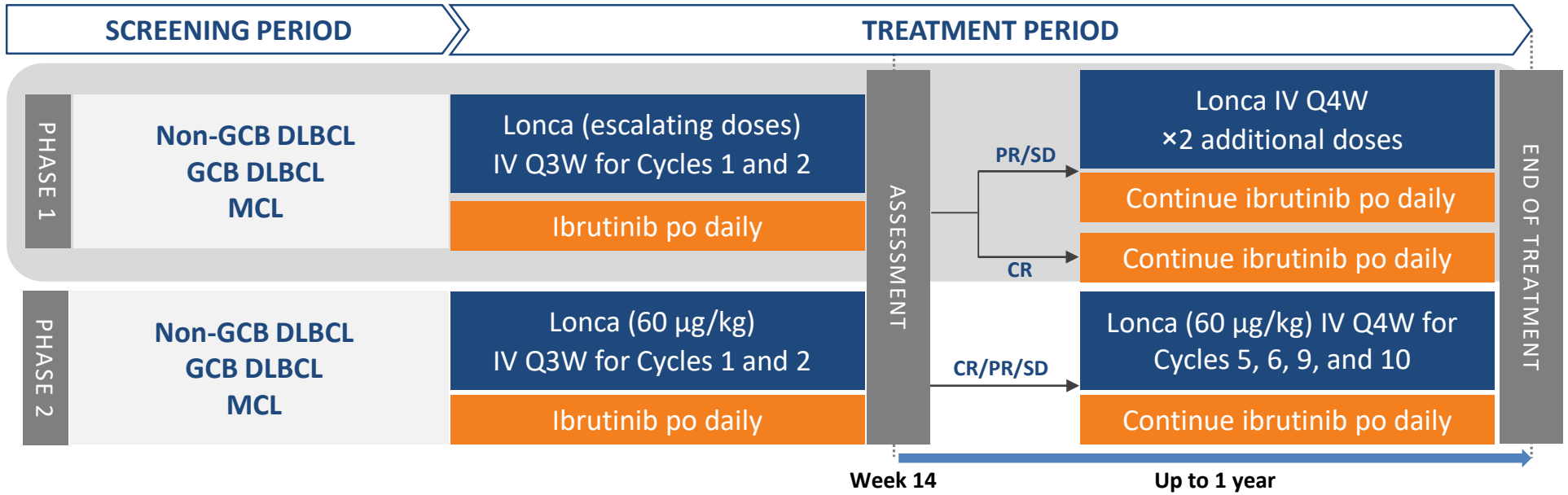
Objectives and Study Design

Primary objective for Phase 1:

- Characterize safety/tolerability and identify the RP2D and schedule for use in Phase 2

Secondary objectives for Phase 1:

- Evaluate antitumor effect
- Characterize pharmacokinetics
- Evaluate immunogenicity



CR, complete response; **DLBCL**, diffuse large B-cell lymphoma; **GCB**, germinal center B-cell; **IV**, intravenous; **Lonca**, loncastuximab tesirine; **MCL**, mantle cell lymphoma; **po**, taken orally; **PR**, partial response; **RP2D**, recommended Phase 2 dose; **SD**, stable disease; **Q3W**, every 3 weeks; **Q4W**, every 4 weeks.

Baseline Characteristics

Median Lonca cycles: **2** (range 1–4)

Median ibrutinib cycles: **4** (range 1–14)

As of August 20, 2020, **37 patients** had received Lonca 60 µg/kg plus ibrutinib 560 mg

Characteristic	DLBCL (n=30)	MCL (n=7)	All patients (n=37)
Sex, n (%)			
Male	21 (70.0)	6 (85.7)	27 (73.0)
Age, years, median (range)	72 (40–91)	69 (54–89)	72 (40–91)
ECOG status, n (%)			
0	16 (53.3)	4 (57.1)	20 (54.1)
1	11 (36.7)	3 (42.9)	14 (37.8)
2	3 (10.0)	0	3 (8.1)
NHL subtype, n (%)			
Non-GCB DLBCL	24 (80.0)	-	24 (64.9)
GCB DLBCL	6 (20.0)	-	6 (16.2)
MCL	-	7 (100)	7 (18.9)
Disease stage[a], n (%)			
Stage II	3 (10.0)	0	3 (8.1)
Stage III	5 (16.7)	1 (14.3)	6 (16.2)
Stage IV	22 (73.3)	6 (85.7)	28 (75.7)

Characteristic	DLBCL (n=30)	MCL (n=7)	All patients (n=37)
Number of prior systemic therapies[b]			
Median (range)	2 (1–6)	2 (1–4)	2 (1–6)
First-line prior therapy response, n (%)[c]			
Relapsed	20 (66.7)	4 (57.1)	24 (64.9)
Refractory	7 (23.3)	1 (14.3)	8 (21.6)
Other	3 (10.0)	2 (28.6)	5 (13.5)
Last-line prior therapy response, n (%)[c,d]			
Relapsed	13 (43.3)	4 (57.1)	17 (45.9)
Refractory	17 (56.7)	1 (14.3)	18 (48.6)
Other	0	2 (28.6)	2 (5.4)
Prior SCT, n (%)			
Autologous	2 (6.7)	1 (14.3)	3 (8.1)
Allogeneic	0	1 (14.3)	1 (2.7)

Data cut: August 20, 2020. [a]Ann Arbor Criteria; [b]Prior SCT is included. For patients who received an autologous transplant, the mobilization regimen was considered a line of therapy if it was chemotherapy based and distinct from the other previous lines of treatment. [c]Systemic therapy; Relapsed: complete or partial response, followed by relapse; Refractory: stable disease or progressive disease; Other: missing data or not evaluable. [d]If SCT is most recent line, the variable is defined as response to the therapy immediately preceding SCT.

DLBCL, diffuse large B-cell lymphoma; **ECOG**, Eastern Cooperative Oncology Group; **GCB**, germinal center B-cell; **Lonca**, loncastuximab tesirine; **MCL**, mantle cell lymphoma; **NHL**, non-Hodgkin lymphoma; **SCT**, stem cell transplant.

Safety Results

TEAE (all grades) by preferred term in ≥20% of patients	n (%)
Any TEAE	37 (100)
Thrombocytopenia	11 (29.7)
Anemia	8 (21.6)
Fatigue	8 (21.6)
Diarrhea	8 (21.6)

TEAE (Grade ≥3) by preferred term in ≥5% of patients	n (%)
Any TEAE	23 (62.2)
Anemia	4 (10.8)
Neutropenia	4 (10.8)
Thrombocytopenia	2 (5.4)
Fatigue	2 (5.4)

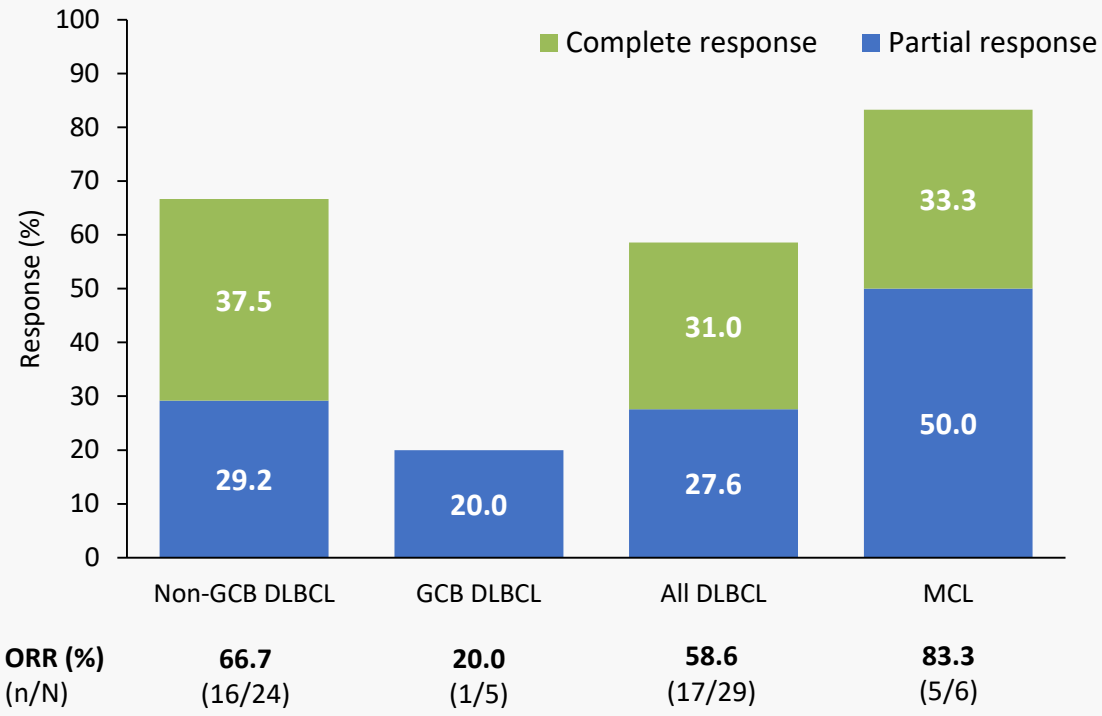
Combination of Lonca plus ibrutinib had manageable toxicity

Data cut: August 20, 2020.

Lonca, loncastuximab tesirine; **TEAE**, treatment-emergent adverse event.

Efficacy Results

Total population: ORR: 62.9% CRR: 31.4%

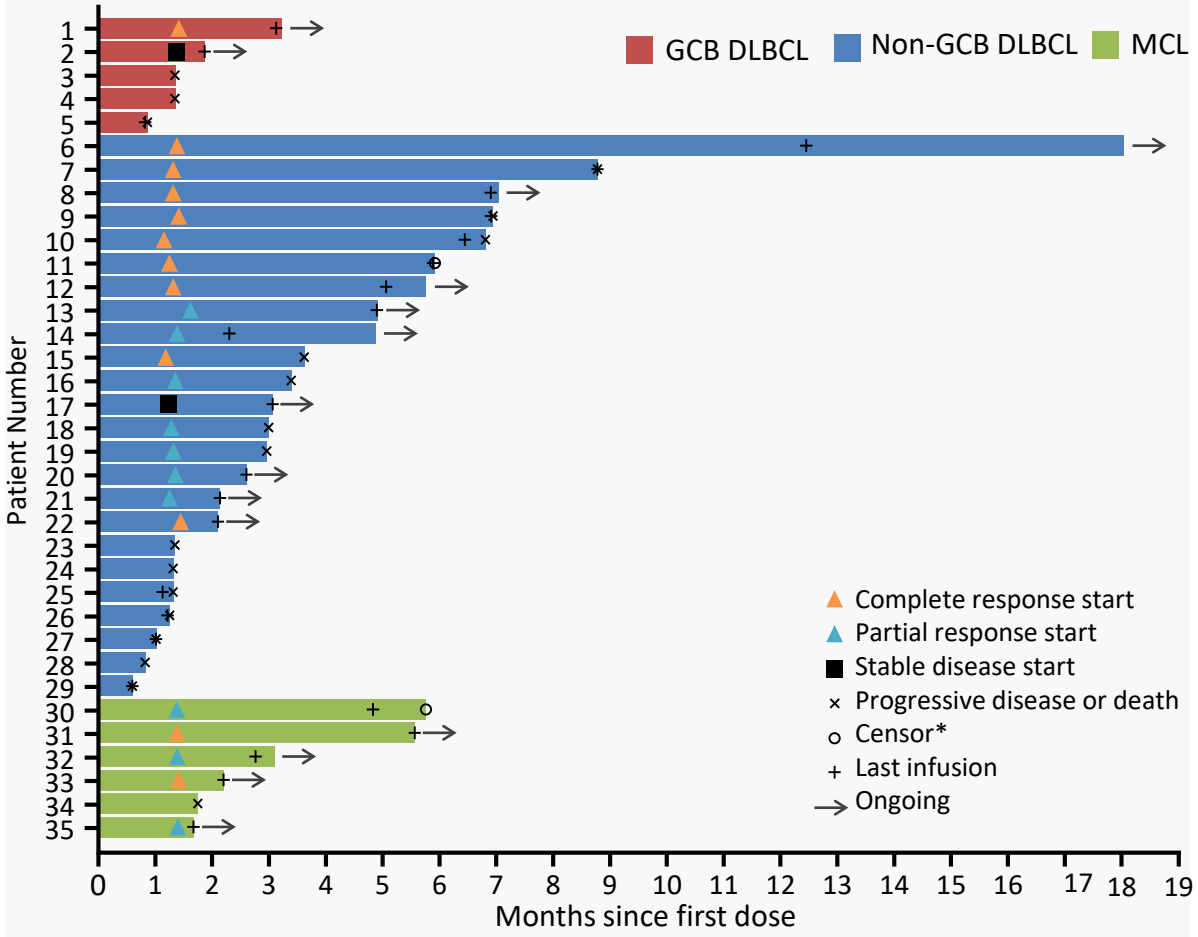


	Non-GCB DLBCL	GCB DLBCL	All DLBCL	MCL
ORR (%) (n/N)	**66.7** (16/24)	**20.0** (1/5)	**58.6** (17/29)	**83.3** (5/6)

Data cut: August 20, 2020; 35/37 patients were evaluable for efficacy; 1 with GCB DLBCL and 1 with MCL were non-evaluable. *Only for censored patients who discontinue trial due to reasons other than progression or who go onto a different anticancer treatment.

CRR, complete response rate; **DLBCL**, diffuse large B-cell lymphoma; **GCB**, germinal center B-cell; **MCL**, mantle cell lymphoma; **ORR**, overall response rate.

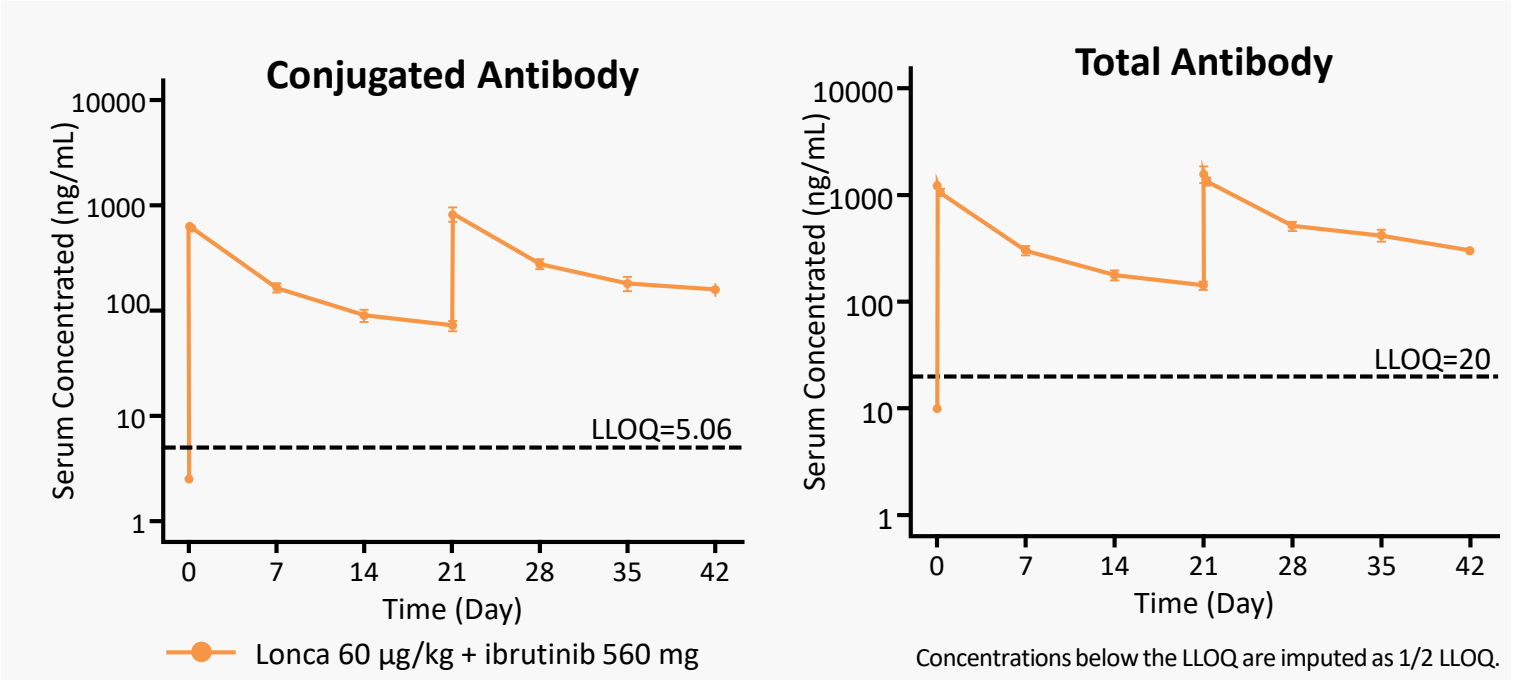
Median treatment duration: 70 days (range 18–379 days)



Pharmacokinetics Results

PK parameters	Conjugated Ab	Total Ab
Cycle 1: Lonca 60 µg/kg and ibrutinib 560 mg		
C_{max} (ng/mL)	659 (45.3) [26]	1280 (41.4) [26]
AUC_{inf} (ng·day/mL)	4364 (61.9) [8]	7449 (54.8) [9]
T_{half} (day)	6.31 (46.7) [8]	5.65 (38.2) [9]
CL (L/day)	0.893 (60.4) [8]	0.590 (50.1) [9]
V_{ss} (L)	5.52 (47.2) [8]	3.43 (43.6) [9]
Cycle 2: Lonca 60 µg/kg and ibrutinib 560 mg		
C_{max} (ng/mL)	761 (91.7) [21]	1461 (80.8) [21]
AUC_{tau} (ng·day/mL)	5582 (65.0) [15]	10,423 (60.1) [13]
T_{half} (day)	7.57 (43.0) [11]	7.79 (33.0) [6]
CL (L/day)	0.705 (63.3) [15]	0.451 (58.8) [13]
V_{ss} (L)	7.85 (64.0) [11]	6.01 (50.0) [6]
AI	1.21 (15.9) [11]	1.20 (10.4) [6]

Blood samples for PK analysis were drawn on Day 1 (pre-dose), Day 8 and Day 15 of treatment Cycles 1 and 2.
Data shown as geometric mean (geometric % coefficient of variation) [n].



- Good exposure coverage seen throughout dosing interval
- Cycle-related increases in PK parameters apparent
- Exposure variability among patients appears moderate

Data cut: August 20, 2020.

Ab, antibody; **AI**, accumulation index; **AUC_{inf}**, area under the curve vs time curve from 0 to infinity; **AUC_{tau}**, area under the curve from 0–21 days; **CL**, apparent clearance; **C_{max}**, maximum observed concentration; **LLOQ**, lower limit of quantification; **Lonca**, loncastuximab tesirine; **PK**, pharmacokinetic; **SE**, standard error; **T_{half}**, apparent terminal half-life; **V_{ss}**, apparent steady-state volume of distribution

Conclusions

Study conclusions

Lonca 60 µg/kg plus ibrutinib 560 mg continues to have encouraging antitumor activity and manageable toxicity in patients with R/R DLBCL and with R/R MCL

ORR for all patients was 62.9%

- Non-GCB DLBCL **66.7%**
- GCB DLBCL **20.0%**
- MCL **83.3%**

CRR for all patients was 31.4%

- Non-GCB DLBCL **37.5%**
- GCB DLBCL **0%**
- MCL **33.3%**

Safety data were consistent with those reported previously[1]

Good Lonca exposure coverage obtained over the Q3W dosing interval

1. Depaus J, et al. EHA 2020. Abstract 1284.

CRR, complete response rate; **DLBCL**, diffuse large B-cell lymphoma; **GCB**, germinal center B-cell; **Lonca**, loncastuximab tesirine; **MCL**, mantle cell lymphoma; **ORR**, overall response rate; **Q3W**, every three weeks; **R/R**, relapsed/refractory.

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