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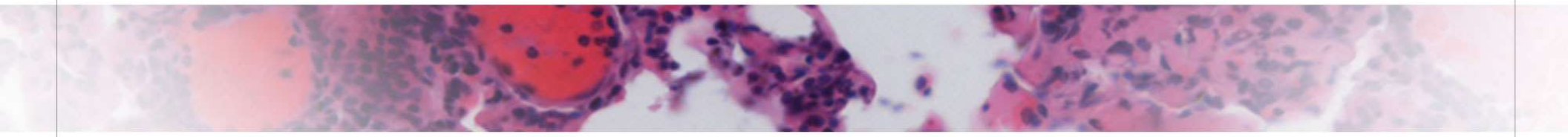


Loncastuximab Tesirine Demonstrated Substantial Single-agent Efficacy and Manageable Safety Profile in Heavily Pretreated Chinese Patients with Relapsed or Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL)

Disclosures

- **Ningjing Lin, Xiuhua Sun, Hui Zhou, Liqun Zou, Keshu Zhou, Lihong Liu, Haiyan Yang, Kai Hu, Qingqing Cai, Yao Liu, Jie Jin, Liling Zhang, Wenyu Li, Ye Guo, Wei Yang, Yuqin Song, Jun Zhu:** no disclosures
- **Feng Luo, Yanyan Li, Mengqi Zhang, Feinan Lu:** employee of Overland Pharmaceuticals.

Introduction

- Patients with R/R DLBCL who failed multi-agent chemoimmunotherapies usually have a poor prognosis, leaving a significant unmet medical need [1].
- Loncastuximab tesirine (Lonca) is an antibody-drug conjugate, composed of a humanized anti-CD19 antibody conjugated to a pyrrolobenzodiazepine dimer toxin that had demonstrated clinical efficacy and manageable safety profiles in heavily pretreated DLBCL patients in a global phase 2 study of Lonca monotherapy (NCT03589469) [2].
- The phase 2 study in China (ChiCTR2300072058) is the first study to evaluate Lonca monotherapy in Chinese patients with R/R DLBCL.

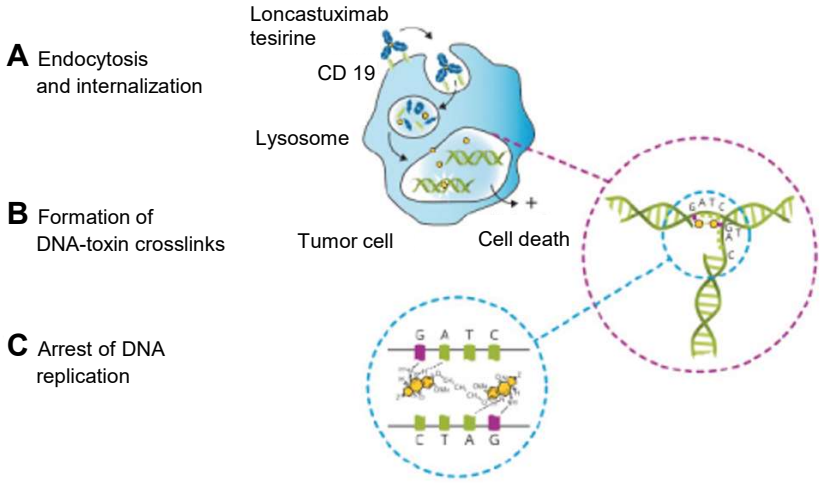


Figure 1. Mechanism of action of loncastuximab tesirine[3]

1. Crump, M, et al. Blood. 2017;130:1800-1808.
2. Caimi, PF, et al. Lancet Oncol. 2021;22:790-800
3. Kingsley, Grosicki et al. 2022 Clinical Lymphoma Myeloma and Leukemia 22: S372.

Study Design

- ✓ This is an open-label, single-arm, phase 2 study of Lonca monotherapy in Chinese patients with R/R DLBCL who had failed ≥ 2 lines of systemic therapies.
- ✓ The primary endpoint was overall response rate (ORR) as assessed by IRC according to the Lugano 2014 criteria.
- ✓ Secondary efficacy endpoints included complete response rate (CRR), DOR, RFS, PFS, and OS. Treatment-emergent adverse events (TEAEs) were reported by CTCAE v4.0.

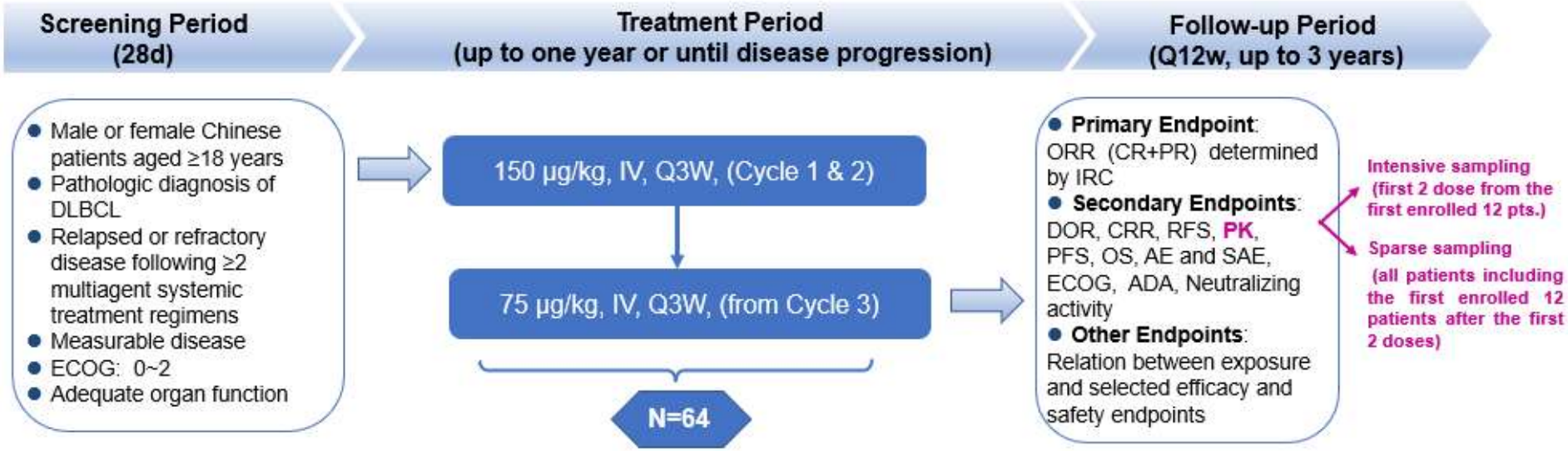


Figure 2. Study Design

Key Eligibility Criteria

Table 1. Key inclusion and exclusion criteria

Key inclusion criteria	Key exclusion criteria
● Male or female patients aged 18 years or older who are current residents of mainland China with Chinese ancestry ● Pathologic diagnosis of DLBCL, as defined by the 2016 WHO classification, to include: DLBCL not otherwise specified, DLBCL transformed from indolent lymphoma, and high-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements ● Relapsed or refractory disease following two or more multiagent systemic treatment regimens ● Patients who have received previous CD19-directed therapies must have a biopsy that shows CD19 protein expression after completion of the CD19-directed therapy ● Measurable disease as defined by the 2014 Lugano Classification ● Eastern Cooperative Oncology Group (ECOG) performance status 0-2 ● Adequate organ function	● Previous treatment with Lonca ● Bulky disease, defined as any tumor ≥ 10 cm in longest dimension ● Autologous stem cell transplant within 30 days prior to start of study drug (Cycle 1 Day 1[C1D1]) ● Allogeneic stem cell transplant within 60 days prior to start of study drug (C1D1) ● Lymphoma with active CNS involvement at the time of screening, including leptomeningeal disease ● Clinically significant third space fluid accumulation (i.e., ascites requiring drainage or pleural effusion that is either requiring drainage or associated with shortness of breath) ● Significant medical comorbidities, including but not limited to uncontrolled hypertension (blood pressure ≥ 160/100 mmHg repeatedly), unstable angina, congestive heart failure (greater than New York Heart Association class II), electrocardiographic evidence of acute ischemia, coronary angioplasty or myocardial infarction within 6 months prior to screening, uncontrolled atrial or ventricular cardiac arrhythmia, poorly controlled diabetes, severe chronic pulmonary disease, or active infections (including but not limited to tuberculosis)

Patient population

As of 11-Jan-2023, data cutoff date :

- 64 Chinese patients with DLBCL were enrolled and received at least one dose of Lonca (median: 4.0 cycles [range: 1-17]).
- The median number of prior lines of therapies was 3.0 (range: 2-12), with 67.2% of patients having ≥ 3 lines of prior therapies.
  - Four patients (6.3%) had received prior CD19 CAR-T therapy. Forty-three patients (67.2%) were refractory to the first-line therapy (primary refractory), 56 patients (87.5%) were refractory to the most recent line of therapy and 40 patients (62.5%) were refractory to all prior lines of therapies.

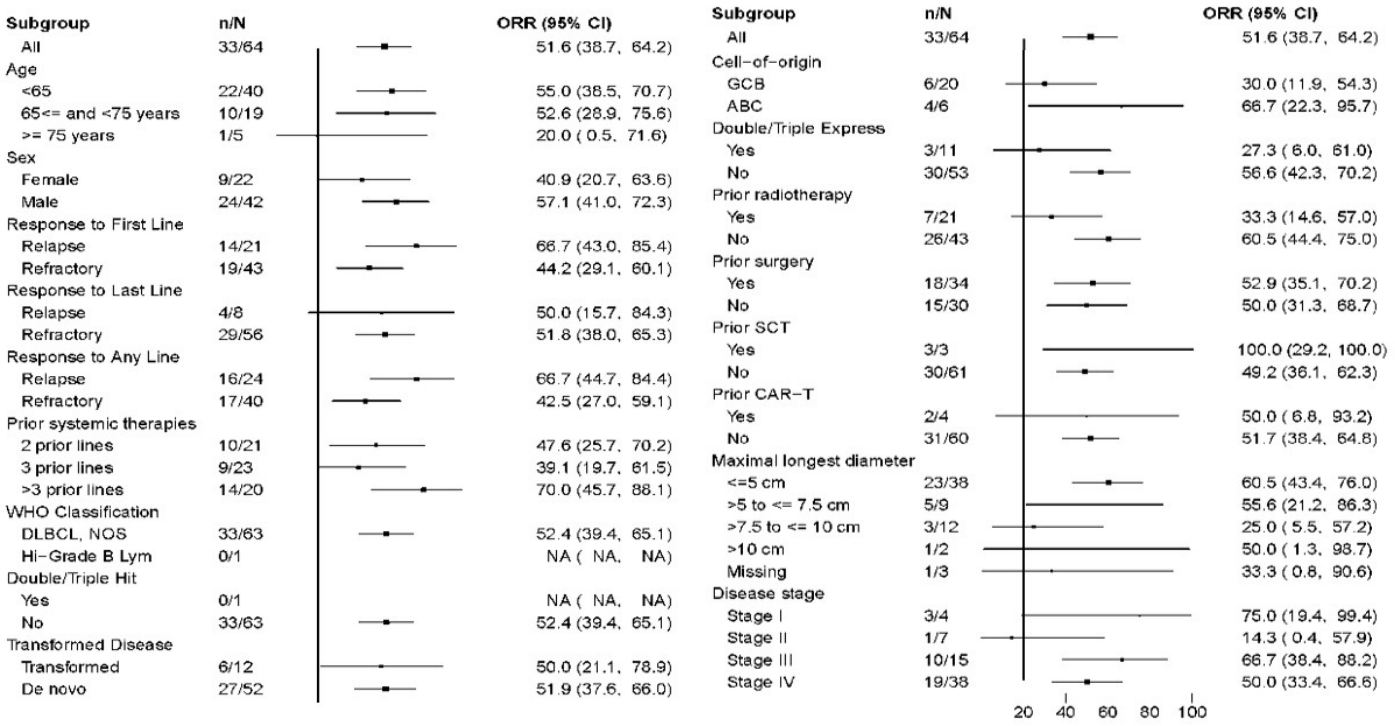
Patient Characteristics		All-Treated Population (N=64)
Gender, n (%)	Female	22 (34.4)
	Male	42 (65.6)
Age, median (range)		60.0 (26-81)
Disease Category, n (%)	DLBCL, NOS	63 (98.4)
	HGBCL	1 (1.6)
Stage (Ann Arbor criteria), n (%)	I–II	11 (17.2)
	III–IV	53 (82.8)
Number of prior systemic therapy,* Median (range)		3.0 (2-12)
First line response, n (%)	Relapse†	21 (32.8)
	Refractory‡	43 (67.2)
Last line response, n (%)	Relapse†	8 (12.5)
	Refractory‡	56 (87.5)
Any line response, n (%)	Relapse†	24 (37.5)
	Refractory‡	40 (62.5)
Prior Radiotherapy, n (%)		21 (32.8)
Prior Surgery, n (%)		34 (53.1)
Prior SCT, n (%)	Autologous	3 (4.7)
	Allogeneic	0
	Both	0
Prior CAR-T, n (%)	Autologous	3 (4.7)
	Allogeneic	1 (1.6)

*Including prior SCT (stem cell transplant) †Relapsed disease defined as progression of disease (PD) at least 6 months after having achieved CR or PR with adequate prior anti-DLBCL therapy. ‡Refractory disease defined as failure to achieve CR or PR or experienced PD within 6 months after having achieved CR or PR, after adequate prior anti-DLBCL therapy.

Table 2. Baseline Characteristics

Efficacy

- The median follow-up time was 8.5 months.
- The ORR by IRC was 51.6% (95% CI: 38.7% to 64.2%), and CRR was 23.4%. The median DOR (mDOR) was 6.37 months as assessed either by IRC or by investigator.
- For patients with a CR, the mDOR was 10.22 months (6.08 months for patients with PR). The median time to first response was 41.0 days.
- The median PFS and median OS were 4.96 months and 9.33 months, respectively.
- Responses, including CRs, were also observed in several high-risk subgroups (Fig. 3)



GCB: Germinal Center B Cell ABC: Activated B cell

Figure 3. Forest Plot of ORR by Subgroup

Safety

- All patients had at least one TEAE and 61 (95.3%) patients had at least one TEAE ≥ Grade 3.
- The most common (≥30%) all-grade TEAEs were GGT increased (71.9%), followed by anaemia (70.3%), platelet count decreased (65.6%), AST increased (64.1%), WBC count decreased (64.1%), neutrophil count decreased (60.9%), ALT increased (51.6%), hypokalaemia (37.5%), and blood ALP increased (32.8%). The rate of febrile neutropenia was low (3.1%).
- The most common (≥15%) Grade ≥3 TEAEs, regardless of the relationship to the study drug, were platelet count decreased (34.4%), neutrophil count decreased (28.1%), WBC count decreased (28.1%), GGT increased (25.0%), anaemia (18.8%), hypokalaemia (18.8%), neutropenia (17.2%), and lymphocyte count decreased (15.6%) (Table 3).
- The majority of Grade ≥ 3 TEAEs were clinical laboratory abnormalities, rather than clinical symptoms, and were generally reversible.
- Treatment-related TEAEs leading to treatment discontinuation occurred in 10 patients (15.6%), with GGT increased being the most common TEAE leading to treatment discontinuation (3 patients; 4.7%).
- No increase in toxicity was seen in patients aged ≥65 years compared with younger patients.

Safety: Grade≥3 TEAEs

Preferred Term	Grade 3	Grade 4	Grade 5	Grade 3-5
Hematologic TEAEs				
Platelet count decreased	16 (25.0)	6 (9.4)	0	22 (34.4)
Neutrophil count decreased	11 (17.2)	7 (10.9)	0	18 (28.1)
White blood cell count decreased	16 (25.0)	2 (3.1)	0	18 (28.1)
Anaemia	12 (18.8)	0	0	12 (18.8)
Neutropenia	4 (6.3)	7 (10.9)	0	11 (17.2)
Lymphocyte count decreased	9 (14.1)	1 (1.6)	0	10 (15.6)
Non-hematologic TEAEs				
Gamma-glutamyltransferase increased	16 (25.0)	0	0	16 (25.0)
Hypokalaemia	11 (17.2)	1 (1.6)	0	12 (18.8)

Table 3. Most Common Grade≥3 TEAEs

CONCLUSION

- Lonca has consistent efficacy and safety profile in Chinese patients as compared with LOTIS-2 study.
- Lonca demonstrated substantial and clinically meaningful single-agent efficacy and was well-tolerated in heavily pretreated Chinese patients with R/R DLBCL.
- Toxicities were generally manageable and reversible in most patients in routine clinical practice , with neither unexpected safety concerns nor different toxicity profile in patients aged ≥65 years.
- Encouraging and durable responses were also observed in high-risk patient groups, including patients with advanced stage, transformed or refractory DLBCL.

Acknowledgement

This study is funded by ADC Therapeutics SA and Overland Pharmaceuticals. The authors would like to thank all participating patients and their families, all study coinvestigators, and the research coordinators.