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POSTER ABSTRACTS

626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

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)

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Introduction: Patients with R/R DLBCL who failed multi-agent chemoimmunotherapies usually have a poor prognosis, leaving a significant unmet medical need. Loncastuximab tesirine (Lonca) is an antibody-drug conjugate, composed of a humanized anti-CD19 antibody conjugated to a pyrrolobenzodiazepine dimer toxin that showed clinical efficacy and manageable safety in heavily pretreated DLBCL patients in a global phase 2 study of Lonca monotherapy (NCT03075696). Here we present results from a phase 2 study (ChiCTR2300072058) of Lonca monotherapy in Chinese patients with R/R DLBCL for the first time, including analyses of responses in high-risk DLBCL subgroups.

Methods: This open-label, single-arm, phase 2 study was designed to confirm the safety, efficacy and PK profiles 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 include complete response rate (CRR), DOR, RFS, PFS, and OS. Treatment-emergent adverse events (TEAEs) were reported by CTCAE v4.0.

Results: As of data cutoff (11-Jan-2023), 64 Chinese patients with DLBCL were enrolled and received at least one dose of Lonca (median: 4.0 cycles [range: 1-17]) and were evaluable for safety and efficacy analyses. 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. At data cutoff, the median follow-up 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 and 9.33 months, respectively.

Responses, including CRs, were observed in several high-risk subgroups (Fig. 1): ORR was 54.7% in patients with advanced stage disease (Stage III/IV) and 50.0% in patients with transformed disease. Patients who were refractory to first-line therapy, to the most recent therapy, or to all prior therapies had ORRs of 44.2%, 51.8% and 42.5%, respectively. Three patients who had received a prior SCT had an ORR of 100%. Lonca was also effective in elderly patients ≥ 65 years (ORR of 45.8%, mDOR of 6.37 months) and in patients who had received prior CD19 CAR-T therapy (ORR of 50%).

Overall, 64 (100%) 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 most common (≥15%) TEAEs of Grade ≥3 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%). The rate of febrile neutropenia was low (3.1%). The majority of Grade ≥ 3 TEAEs were abnormalities of clinical laboratory values as opposed to clinical symptoms and were generally reversible. Treatment-related TEAEs leading to treatment discontinuation occurred in 10 patients (15.6%), most commonly GGT increased (3 patients; 4.7%). No increase in toxicity was seen in patients aged ≥65 years compared with younger patients.

Conclusions: 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 by routine clinical practice and/or with dose modifications, 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.

Disclosures No relevant conflicts of interest to declare.

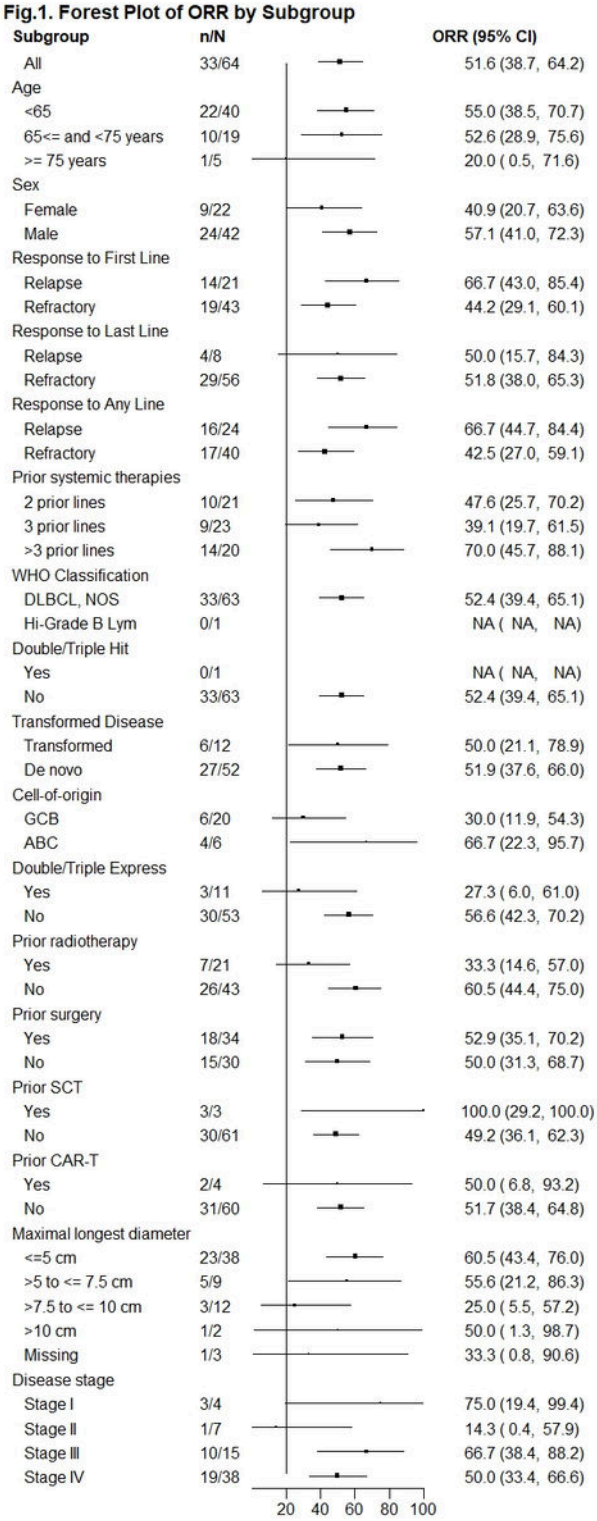

Figure 1

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