# Health-Related Quality of Life and Tolerability of Loncastuximab Tesirine in High-Risk Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma Treated in a Phase 2 Clinical Trial (LOTIS-2)

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## INTRODUCTION

- Loncastuximab tesirine (loncastuximab tesirine-lpyl; Lonca), a CD19-directed antibody-drug, was granted approval by the US Food and Drug Administration for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low-grade lymphoma, and high-grade B-cell lymphoma.
- Lonca has shown antitumor activity with an acceptable toxicity profile and provides stable or improved health-related quality of life (HRQOL) in adult patients with relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) after ≥ 2 prior therapies.[1,2]
- Lonca has also shown promising results for patients who are at high risk of a poor prognosis (i.e., with double-/triple-hit, primary refractory, or transformed disease).

## OBJECTIVE

- This analysis evaluates the impact of Lonca on HRQOL and treatment tolerability stratified by high-risk group.

## METHODS

- The LOTIS-2 study (NCT03589469) in a single-arm, open-label, phase 2 study of adult patients with R/R DLBCL after ≥ 2 prior treatments who had measurable disease and Eastern Cooperative Oncology Group performance status 0-2.
- Eligible patients received Lonca as an intravenous infusion on day 1 of each 3-week treatment cycle at 150 µg/kg for two cycles then at 75 µg/kg thereafter for up to 1 year or until disease relapse or progression; unacceptable toxicity; death; or patient or investigator decision (Figure 1).
- The high-risk group included patients with double-/triple-hit, primary refractory, or transformed disease at baseline. Primary refractory disease was defined as no response to first-line therapy.

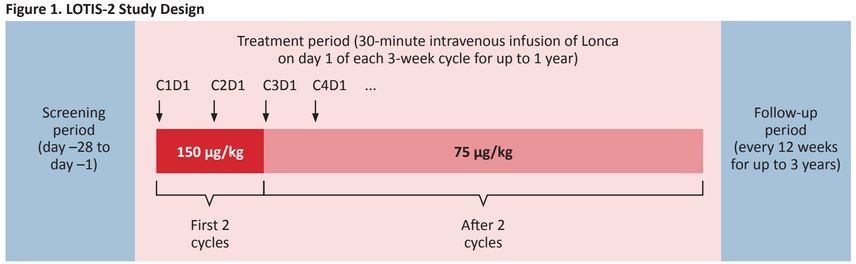
### Patient-Reported Outcome Assessments

- The EuroQol EQ-5D-5L and Functional Assessment of Cancer Treatment–Lymphoma (FACT-Lym) were assessed at baseline (cycle 1, day 1 predose) and day 1 of each subsequent treatment cycle until end of treatment.
  - The EQ-5D visual analog scale (VAS) measures overall health (current health state). A score of 100 indicates "the best health you can imagine," and a score of 0 indicates "the worst health you can imagine."
  - The FACT-Lym total score (range, 0-168) is the sum of Physical Well-Being (range, 0-28), Social/Family Well-Being (range, 0-28), Emotional Well-Being (range, 0-24), and Functional Well-Being (range, 0-28) subscales plus the Lymphoma Subscale for lymphoma-specific symptoms and concerns (range, 0-60).
  - Treatment tolerability was measured by FACT-Lym item GP5 ("I am bothered by side effects of treatment"). This single item has been used to measure overall side effect impact on patients.[3,4]

### Analysis Method

- Changes in HRQOL from baseline were summarized descriptively for EQ-5D VAS and FACT-Lym total by visit and risk group.
- Analysis of covariance models were conducted for EQ-5D VAS and FACT-Lym total to estimate the least squares mean changes from baseline in high-risk and non-high-risk groups, as well as the differences between risk groups, after adjusting for age, sex, race, and baseline score.
- Percentages of responses to GP5 (tolerability) were summarized by visits and risk group.
- Analysis was conducted using data collected from study initiation (August 2018) through March 2021 in the LOTIS-2 study.
- Data were analyzed as observed without imputation on missing data.

**Figure 1. LOTIS-2 Study Design**




Notes: Patients could continue treatment for up to 1 year or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurred first. Patients benefiting clinically at 1 year could have continued treatment after a case-by-case review.

## RESULTS

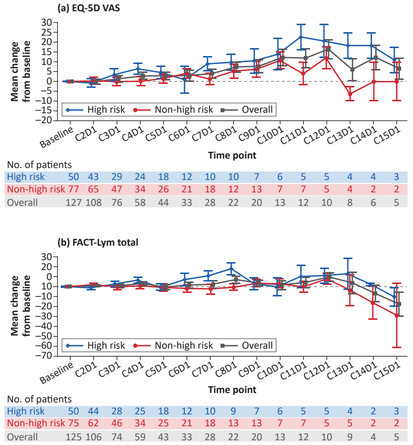
- The study enrolled 145 patients. Through cycle 9, the completion rate among patients treated at each cycle was ≥ 92% for EQ-5D and ≥ 88% for FACT-Lym. At cycle 9, 20 patients were still on treatment with Lonca, and only 5 were still on treatment at cycle 15.
- Patients with a baseline score and at least one postbaseline score were included in the analysis (Table 1).
  - Of the 130 patients included, the median age was 66.0 years, 59% were male, and 88% were White.
  - Among the 51 patients in the high-risk group, 27% were double/triple hit, 43% were primary refractory, and 47% had transformed DLBCL.
  - At baseline, the mean EQ-5D VAS score was 71.4 (standard deviation [SD] = 19.1), and the mean FACT-Lym total score was 118.4 (SD = 23.8), similar in both groups.
  - The median number of Lonca cycles administered was 4 (range, 1-26) in the high-risk group and 3 (range, 1-22) in the non–high-risk group.
- In the high-risk group, the mean changes from baseline in VAS overall health score improved at almost all visits from cycle 3 day 1 to cycle 15 day 1 (Figure 2); the mean changes from baseline in FACT-Lym total score also improved across most visits, especially between cycle 6 day 1 and cycle 8 day 1.
- In the non–high-risk group, the mean changes from baseline in VAS and FACT-Lym total remained stable or improved except for later cycles with small sample sizes (n ≤ 5).
- In the analysis adjusting for age, sex, race, and baseline score (Table 2), the least squares mean differences between high risk and non-high risk were positive for all visits (for FACT-Lym) or nearly all visits (for EQ-5D VAS) between cycle 3 day 1 and cycle 9 day 1. The *P* value is < 0.10 for FACT-Lym total at cycle 7 day 1 and cycle 8 day 1, suggesting better improvement in the high-risk group. The least squares means were not estimated after cycle 9 because of the small sample sizes (n < 20).
- When asked how much they were bothered by treatment side effects, a majority of patients reported "a little bit" or "not at all" at most cycles (71%-89% in the high-risk group and 46%-86% in the non–high-risk group) (Figure 3).

**Table 1. Baseline Characteristics**

| | High-Risk Group (N = 51) | Non–High-Risk Group (N = 79) | Overall (N = 130) |
|---|---|---|---|
| Age, years, median (range) | 65.0 (25-85) | 67.0 (24-94) | 66.0 (24-94) |
| Sex, male, n (%) | 27 (53) | 50 (63) | 77 (59) |
| Race, White, n (%) | 46 (90) | 69 (87) | 115 (88) |
| ECOG score, n (%) | | | |
| 0 | 23 (45) | 31 (39) | 54 (42) |
| 1 | 24 (47) | 44 (56) | 68 (52) |
| 2 | 4 (8) | 4 (5) | 8 (6) |
| Prior systemic therapies, n (%) | | | |
| 2 prior lines | 26 (51) | 33 (42) | 59 (45) |
| 3 prior lines | 12 (24) | 20 (25) | 32 (25) |
| > 3 prior lines | 13 (25) | 26 (33) | 39 (30) |
| Disease stage (Ann Arbor criteria),[a] n (%) | | | |
| Stage I | 5 (10) | 5 (6) | 10 (8) |
| Stage II | 6 (12) | 15 (19) | 21 (16) |
| Stage III | 5 (10) | 12 (15) | 17 (13) |
| Stage IV | 35 (69) | 47 (60) | 82 (63) |
| EQ-5D VAS, mean (SD) (score range, 0-100) | 72.6 (20.0) | 70.5 (18.5) | 71.4 (19.1) |
| FACT-Lym total, mean (SD) (score range, 0-168) | 119.0 (23.7) | 118.0 (24.1) | 118.4 (23.8) |

[a] The sum of the percentages may not be 100 due to rounding.

**Figure 2. Mean Change From Baseline in EQ-5D VAS and FACT-Lym Total by Visit and Risk Group**




Notes: Error bars indicate ± standard error. Note that sample sizes are very small in subgroups at later visits. Visits with fewer than 5 assessments in total are not displayed. A change of 7 points for the EQ-5D VAS or FACT-Lym total is considered a minimally important difference. A positive change indicates improvement.

**Figure 3. Percentages of Responses to Item GP5 ("I am bothered by side effects of treatment") by Visit and Risk Group**

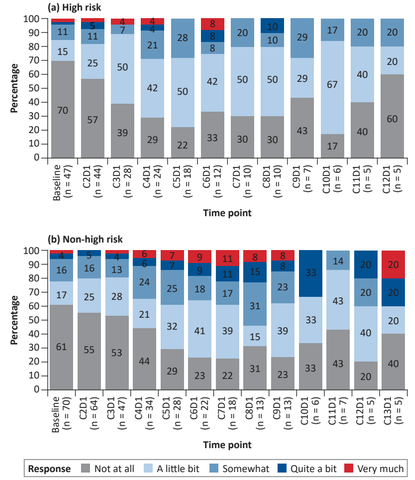



**Table 2. Adjusted Mean Change From Baseline Scores of EQ-5D VAS and FACT-Lym Total**

| | | Least Squares Mean by Visit | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | C2D1 | C3D1 | C4D1 | C5D1 | C6D1 | C7D1 | C8D1 | C9D1 |
| EQ-5D VAS | High risk | −0.6 | 6.8* | 7.5** | 5.8 | 0.3 | 8.7 | 13.0* | 9.9 |
| | Non-high risk | 0.1 | 2.1 | 3.3 | 1.5 | 2.5 | 1.6 | 7.7 | 8.5 |
| | **Difference** | **−0.7** | **4.7** | **4.2** | **4.4** | **−2.2** | **7.1** | **5.3** | **1.4** |
| FACT-Lym total | High risk | −0.7 | 6.7 | 6.8 | 2.5 | 14.1** | 24.5** | 29.1** | 20.6** |
| | Non-high risk | 2.6 | 4.7 | 3.9 | 2.0 | 4.2 | 9.9 | 8.8 | 17.9** |
| | **Difference** | **−3.3** | **2.0** | **2.9** | **0.6** | **9.9** | **14.6*** | **20.3**** | **2.7** |

* 0.05 < *P* < 0.10; ** *P* < 0.05.

Note: Age, sex, race, and baseline score were adjusted in the analysis of covariance model. Visits after C9D1 are not displayed due to small sample sizes. A change of 7 points for the EQ-5D VAS or FACT-Lym total is considered a minimally important difference. A positive change indicates improvement.

## CONCLUSIONS

- The overall health state and HRQOL were stable or improved in high-risk patients during the Lonca treatment period.
- Patients in the high-risk group tolerated the treatment just as well as, if not better than, other patients.
- The findings further support the clinical use of Lonca for the treatment of patients with high-risk R/R DLBCL.

## REFERENCES

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