Health-Related Quality of Life, Symptoms, and Tolerability of Loncastuximab Tesirine in Older Versus Younger 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, is indicated 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 improvement in health-related quality of life (HRQOL),[1,2] based on a multicenter, open-label, single-arm, phase II clinical trial.
- Patients who are 75 years or older often face treatment challenges including inability to tolerate standard therapy. Previous analysis suggested antitumor activity of Lonca in older patients. The knowledge of the impact of Lonca on HRQOL among older patients is needed.

OBJECTIVE

- This analysis evaluates the impact of Lonca on HRQOL, symptoms, and tolerability stratified by age group.

METHODS

- The LOTIS-2 study (NCT03589469) is a single-arm, open-label, phase 2 study in patients aged 18 years or older with relapsed or refractory DLBCL after two or more systemic treatments, who had measurable disease and Eastern Cooperative Oncology Group performance status 0-2.
- Eligible patients received Lonca intravenously on day 1 of each 21-day cycle, at 150 µg/kg for two cycles, then 75 µg/kg thereafter, for up to 1 year or until disease relapse or progression, unacceptable toxicity, death, major protocol deviation, pregnancy, or patient, investigator, or sponsor decision (Figure 1).

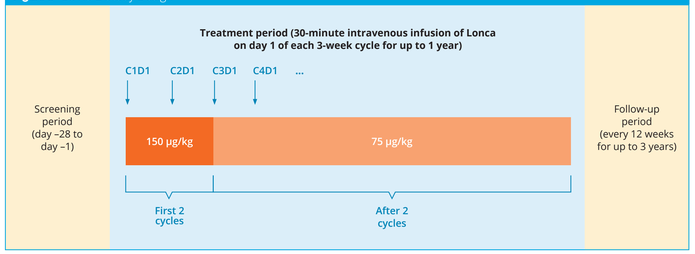
Patient-Reported Outcome Assessments

- The 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.
  - Overall health (current health state) was measured by the EQ visual analog scale (VAS), with a score of 100 indicating "the best health you can imagine" and a score of 0 indicating "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), Functional Well-Being (range, 0-28), and the Lymphoma Subscale (LymS) (range, 0-60).
  - The LymS score is a summary score of 9 items of symptoms (pain, lumps or swelling, fever, night sweat, weight loss, itching, trouble sleeping, loss of appetite, and fatigue) and 6 additional items of patients' concerns. Items were measured on a 5-point Likert scale.
  - Patient-reported tolerability was assessed using the FACT-Lym Item GP5 ("I am bothered by side effects of treatment"). This single item provides a measure of overall side effect impact on patients.[3,4]

Analysis Method

- HRQOL change from baseline scores were summarized descriptively for EQ VAS and FACT-Lym total by visit and age group (< 65 years, 65 to < 75 years, and ≥ 75 years).
- Percentages of patients with improved (by at least 1 point), stable (no change), or worsened (by at least 1 point) symptoms compared with baseline were calculated.
- Percentages of responses to GP5 (tolerability) were summarized by visits and age group.
- Analysis was conducted using data collected from study initiation (August 2018) through March 2021 in the ongoing LOTIS-2 study.
- Data were analyzed as observed without imputation on missing data.

Figure 1. LOTIS-2 Study Design

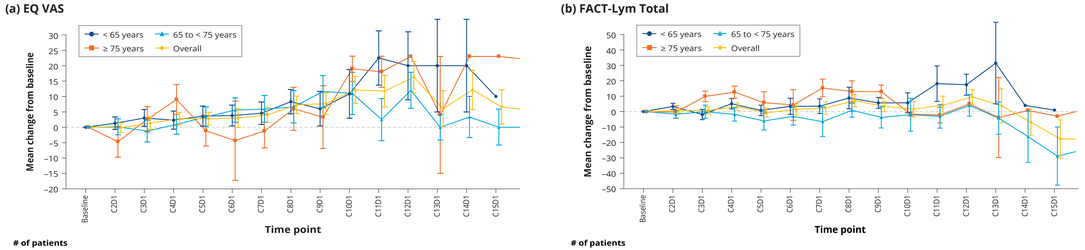


Notes: Patients could continue treatment for up to 1 year or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurred first. Patients benefiting clinically at 1 year could have continued treatment after a case-by-case review.

RESULTS

- A total of 130 treated patients with a baseline HRQOL score and at least 1 postbaseline score were included in analysis (58% male, 88% White).
  - Of those 130 patients, 57 patients were age < 65 years, 53 patients were aged 65 to < 75 years, and 20 patients were aged ≥ 75 years.
  - At baseline, the mean EQ VAS score was 71.4 (SD = 19.1), and the mean FACT-Lym total score was 118.4 (SD = 23.8).
- The median number of Lonca cycles administered was 4 (range, 1-26).
- HRQOL completion rate among patients treated at each cycle was greater than 77% through cycle 13.
- Change from baseline in the EQ VAS and FACT-Lym total was stable or improved over the treatment period across all age groups, including aged ≥ 75 years (Figure 2).
- In the age group ≥ 75 years, more patients reported improvement than worsening in symptoms of pain, lumps/swelling, weight loss, and fatigue compared with baseline for a majority of visits (Figure 3). In the two younger age groups, the percentage of patients reporting improved symptoms was smaller but still the majority reported no change or improved symptoms (Figure 4).
- For all symptoms included in LymS, a majority of patients had stable or improved symptom scores at nearly all visits regardless of age group (see Figure 4 showing cycle 3 day 1 as an example).
- A majority of patients reported "a little bit" or "not at all" when being asked how much they were bothered by side effects of treatment and a higher percentage of patients in age group ≥ 75 years reported "not at all" than in younger age groups (Figure 5).

Figure 2. Mean Change From Baseline in EQ VAS and FACT-Lym Total by Visit and Age Group

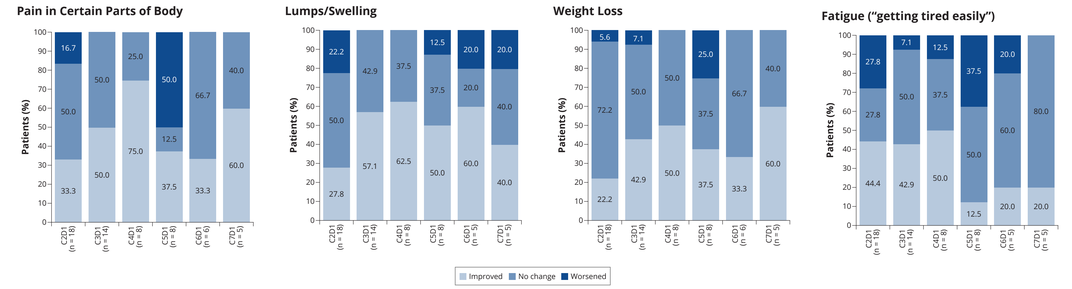


# of patients	Baseline	C2D1	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13D1	C14D1	C15D1
< 65 years	56	47	34	25	21	15	13	10	8	6	4	4	2	2	1
65 to < 75 years	51	44	29	24	16	12	10	8	8	5	6	5	4	3	3
≥ 75 years	20	17	13	9	7	6	5	4	4	2	2	1	2	1	1
Overall	127	108	76	58	44	33	28	22	20	13	12	10	8	6	5

# of patients	Baseline	C2D1	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13D1	C14D1	C15D1
< 65 years	55	45	33	26	20	16	14	11	8	6	4	4	2	1	1
65 to < 75 years	51	44	28	25	15	11	9	7	8	5	6	5	4	2	3
≥ 75 years	19	17	13	8	8	6	5	4	4	2	2	1	3	1	1
Overall	125	106	74	59	43	33	28	22	20	13	12	10	9	4	5

Notes: Error bars indicate ± standard error. Note that sample sizes are small (< 5) in all age groups at C13D1, C14D1, and C15D1. Visits with fewer than 5 assessments in total are not displayed. A change of 7 points for the EQ VAS or FACT-Lym total is considered a minimally important difference. A positive change indicates improvement.

Figure 3. Symptom Improvement During the Course of Treatment in Patients ≥ 75 Years



Note: Visits with fewer than 5 assessments are not displayed. Data on the two younger age groups are not shown due to space limit.

CONCLUSIONS

- The overall health state and HRQOL were stable or improved in all age groups of patients treated with Lonca.
- The older age group (≥ 75 years) reported greater improvement in pain, lumps/swelling, weight loss, and fatigue and better tolerability to treatment side effects.
- The findings further support that Lonca could be a valuable treatment option in elderly patients with relapsed or refractory DLBCL.

Figure 4. Symptom Improvement and Worsening at Cycle 3 Day 1 by Age Group

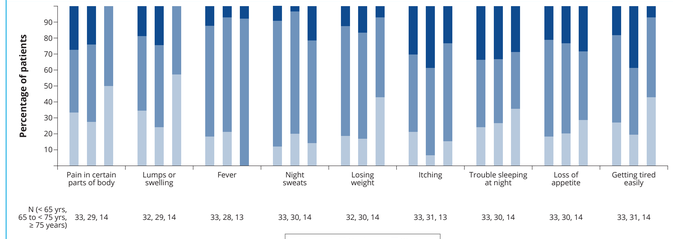
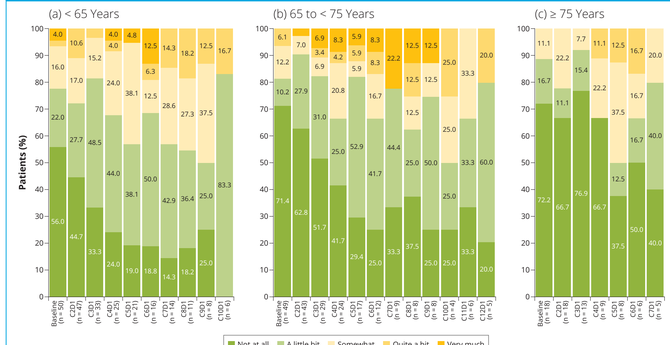


Figure 5. Percentages of Responses to Item GP5 ("I am bothered by side effects of treatment") by Visit and Age Group



Note: Visits with fewer than 5 assessments are not displayed.

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